Treatment of prostatic disease
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Abstract
Prostatic disease is common in dogs, with the majority of intact dogs over the age of five years exhibiting benign prostatic hyperplasia, which then predisposes the dog to prostatitis, prostatic cysts, and prostatic abscessation. Prostatic neoplasia occurs in both neutered and intact male dogs. Clinical signs of prostatic disease can be quite severe and include pain, dysuria, dyschezia, and, in the case of neoplasia, death. Treatment options for prostatic diseases are the subject of much active research, since man is the only other known animal with significant prostatic disease. This review will discuss the current state of medical and surgical treatment for prostatic disease in dogs.

Keywords: Prostate, prostatitis, benign prostatic hyperplasia, prostatic neoplasia, canine

Introduction
Prostatic disease affects a significant proportion of dogs with reportedly over 80% of intact male dogs over five years of age and over 95% of intact male dogs over nine years of age exhibiting benign prostatic hyperplasia (BPH), which then further predisposes them to developing prostatitis, prostatic abscesses, and prostatic cysts. Prostatic neoplasia affects both intact and neutered males, with the latter group showing an increased risk for prostatic neoplasia. Other reviews have covered the pathogenesis and diagnosis of canine prostatic disease. This review will focus on current treatment options.

Prostatic anatomy and physiology
The prostate in the dog is a bilobed, oval to spherical-shaped organ with both a dorsal and ventral sulcus located in the cranial pelvic canal or in the caudal abdomen. The proximal urethra runs through the prostate between the two lobes. Testosterone is converted to dihydrotestosterone (DHT) via the enzyme 5α-reductase and it is this androgen, DHT, which stimulates prostatic development, growth, and secretions. The enzyme 5α-reductase is found in two isoenzymes in the body, type 1 and type 2. Each isoenzyme is encoded by a different chromosome, but common coding sequences indicate a common evolutionary precursor. Isoenzyme type 1 is found throughout the body, including the skin, liver, and prostate. Isoenzyme type 2 is found predominantly in the prostate and other genital tissue. Testosterone and DHT both bind to the same androgen receptors and cause the same effects. The binding of DHT to the androgen receptor, however, is much tighter and of longer duration than that of testosterone. The resultant effect is that lower concentrations of DHT cause an amplified response compared to testosterone.

Benign prostatic hyperplasia
The majority of intact male dogs will develop BPH by the age of five years. The disorder consists of both cellular hyperplasia and hypertrophy. Most dogs with BPH do not show any clinical signs, and therefore require no treatment. Clinical signs may include sanguinous prostatic fluid dripping from the prepuce, hemospermia, hematuria, dysuria, constipation, or tenesmus. The prostate may be palpated per rectum and would feel bisymmetrically enlarged and non-painful. Ultrasound evaluation of the prostate allows accurate measurement of the prostatic lobes and visualization of the parenchyma. Prostatic parenchyma in a dog with BPH should be uniformly echogenic. Evaluation of the third fraction of the ejaculate often reveals a marked number of red blood cells. Treatment should be considered in any dog displaying clinical signs to resolve both discomfort from constipation or dysuria and potential subfertility from hemospermia.
BPH treatment

Resolution of prostatic hyperplasia is achieved by removing the androgen source of prostatic stimulation. In a dog without a breeding career, the treatment of choice is bilateral orchidectomy. Castration removes the source of testosterone and consequently eliminates the production of DHT. In the absence of DHT stimulation the prostate rapidly reduces in size 80% by 12 weeks after castration. In dogs considered valuable breeders, castration is obviously not indicated. In these cases, medical treatments aim at disrupting the androgen stimulation on the prostate. This review will consider treatments including 5α-reductase inhibitors, androgen receptor inhibitors, androgen antagonists, aromatase inhibitors and other antiestrogen therapies, and gonadotropin releasing hormone (GnRH) agonists. Treatments of the past that are no longer in widespread use due to serious adverse effects, such as estrogens, will not be discussed in this review. In men, lower urinary tract symptoms are common sequelae of BPH and an effective treatment is the use of \(\alpha_1\)-adrenergic receptor antagonists to relax smooth muscle in the lower urinary tract. As this is not usually a concern in dogs, this treatment is not used and will not be discussed.

5α-reductase inhibitors. In the United States, the most common medical treatment for BPH is the daily administration of finasteride, an azasteroid which at human clinical doses selectively inhibits the action of 5α-reductase type 2, thus reducing the conversion of testosterone to DHT. Because testosterone itself is not inhibited, its effects on libido and spermatogenesis are preserved. The removal of DHT, the active androgen in the prostate, significantly decreases androgenic stimulation to the prostate, which consequently reduces in size due to apoptosis of prostatic cells.

Dose ranges have not been definitively established for the use of finasteride in the dog, though the safety margin appears to be quite large. Finasteride in its popular commercial forms marketed for men comes in 5 mg tablets (Proscar™, Merck, West Point, PA) and in one mg tablets (Propecia™, Merck, West Point, PA). Perhaps because the former is marketed for treatment of BPH in men and the latter for treatment of male pattern baldness, veterinarians have used the five mg tablet (Proscar™) as a once-daily treatment for dogs with BPH. At a dosages ranging from five mg/dog once daily (0.5 mg/kg in a 10 kg beagle dog) up to 45 mg/kg once daily, a 50-70% reduction in prostatic volume has been noted after 16-53 weeks of treatment. This ends up being a much higher dose, pound for pound, in dogs than men. The dose in men is 5 mg/person once daily, which for a 200 lb man works out to be about 0.05 mg/kg daily. At this dose, prostatic volume in men was reported to decrease by 18% after one year of treatment, after which further reductions in size were insignificant, compared to a 14% increase in volume in the placebo group. A study reducing the dose to 0.1-0.5 mg/kg in dogs achieved a 43% reduction in prostatic volume after 16 weeks of daily treatment with no negative effects on serum testosterone concentrations or semen quality.

In humans, side effects include erectile or ejaculatory dysfunction and teratogenic effects in pregnant women, predictably with regard to sexual differentiation in male fetuses. Problems with libido and fertility have not been reported with dogs, in fact reports indicate normal fertility and libido in dogs on finasteride. Teratogenic effects should not be an issue in dogs since female dogs do not receive finasteride. Some veterinary clinicians have reported concerns about male dogs passing the drug on to females through the semen in mating, but passage of the drug in the semen has not been shown to be a concern in humans (who have sexual relations during pregnancy, whereas dogs do not) and the half-life of finasteride is short enough to not be a teratogenic concern even if it were passed in the semen.

Another concern is the use of finasteride in dogs used in natural mating programs. Semen in natural mating in canines is deposited in the cranial vagina and then it is thought that the continual secretion of large volumes of prostatic fluid during ejaculation of the third fraction pushes the sperm-rich fraction through the cervix into the uterus. Use of finasteride greatly decreases the volume of the third fraction, raising the concern that fertility will be decreased in natural matings using male dogs taking finasteride. This concern has lead to a variety of dosing strategies among clinicians ranging from discontinuing use of finasteride a week or two before an anticipated mating, reducing the dosing schedule...
to once every few days, or only putting the male on finasteride once a year for a few months, as examples. Each of these strategies is untested and purely anecdotal. One study has tested the fertility of dogs on an active finasteride protocol and found no affect on fertility, so it appears that while the concern regarding use of finasteride during natural mating programs makes sense, it may be unwarranted. Certainly more studies on appropriate dosing regimens for finasteride are needed in the dog. The conventional wisdom at this point would be to continue finasteride treatment (somewhat) continuously until the breeding career of the dog is over, and then consider castration.

**Antiandrogen therapy.** Osaterone acetate (Ypozane®, Virbac, Carros, France) is a testosterone analogue with potent antiandrogenic activity attributed to competitive binding to androgen receptors, as well as the overall reduction of androgen receptors, reduction of 5α-reductase, and the inhibition of testosterone transport into prostate cells. In one trial 0.25 mg/kg was administered orally once daily for seven days to 73 dogs with clinical signs of BPH. By 14 days after the start of the trial, nearly half of the dogs had resolution of clinical signs and an average reduction in prostate volume of 38% was noted. By six months after the start of the trial, 84% of dogs had resolution of clinical signs. Using this same dosing regimen, it was determined that peak serum concentrations were reached by day seven, which may explain the initial rapid effect and then slow tapering of effects in the following weeks. Semen quality and fertility do not seem to be negatively affected by osaterone and may, in some cases, improve. Ypozane® is marketed in France and available in some countries in the European Union. It is not licensed in the US.

Progestins exhibit antiandrogen activity and therefore have been used to treat BPH. The antiandrogenic action of progestins is likely due to competitive binding with the androgen receptors and/or suppression of luteinizing hormone (LH) secretion via negative feedback. Dogs in one study were treated for BPH with medroxyprogesterone acetate and, while 84% showed a reduction in clinical signs, only 53% showed a reduction in prostate volume after six weeks of treatment. No effect was noted on semen quality or libido. Concerns regarding the development of diabetes mellitus or mammary nodules has precluded its popular use for BPH treatment.

Delmadinone acetate (Tardak®, Pfizer Animal Health, Sandwich, Kent, UK) is a progestin that is 17 times more potent in antiandrogenic activity than progesterone. Treatment of 69 dogs with clinical signs of BPH using a single intramuscular or subcutaneous injection at 3 mg/kg of delmadinone resulted in complete remission of clinical signs by 14 days after the injection in nearly half of the dogs and in 83% of the dogs by six months after the injection. At 14 days after the injection, a 28% reduction in prostate volume was noted. One of the 69 dogs in the trial developed hypoadrenocorticism, which required treatment to resolve. In another study 1.5 mg/kg delmadinone was administered as a subcutaneous injection at 0, one, and four weeks of the trial and ACTH and cortisol levels were monitored during the trial. Adrenocorticotropic hormone stimulation tests were also conducted. The study noted a significant decrease in basal and two h post-ACTH stimulation concentrations of cortisol in treated dogs compared to control dogs. The authors concluded that treated dogs may be at risk for developing glucocorticoid insufficiency during treatment if subjected to stressful events. Other side effects were of minimal importance, transient, and affected very few of the dogs; these included increases in appetite, behavior changes, vomiting, diarrhea, asthenia, polypus, and polydipsia. In a separate study, male beagle dogs given an single injection of 1 mg/kg of delmadinone showed a temporary change in the maturation of epididymal sperm cells. Tardak® (Pfizer Limited, Sandwich, UK) is marketed in the UK and currently licensed in Austria, Belgium, Finland, France, Luxemburg, Netherlands and the UK. It is not licensed in the US.

**Antiestrogen therapy.** Estrogens have been thought to play either a causative or permissive role in the pathogenesis of BPH. Use of estrogens as a treatment for BPH is no longer in favor due to potentially severe side effects including pancytopenia. Use of antiestrogen therapies, such as estrogen receptor antagonists and aromatase inhibitors have been used to relieve clinical signs of BPH and reduce prostate volume.
Tamoxifen citrate is an antiestrogen drug that has been given at a dose of 2.5 mg/dog once daily for 28 days in male dogs with clinical BPH. Researchers measured testicular parameters, semen parameters, libido, prostatic volume, and serum testosterone. Prostatic volume decreased by 28-50% during the treatment period, but returned rapidly to at or below pretreatment size after treatment ceased. All other parameters measured showed dramatic decreases during treatment, some disappearing altogether, but all gradually returned to pretreatment levels by the end of the monitoring period. Volume of the third fraction of the ejaculate decreased to a few drops or was absent. Maximum scrotal width decreased and the testes softened. Libido decreased and became nonexistent. The volume of the sperm-rich fraction of the ejaculate decreased to nearly nonexistent levels with a corresponding decrease in total sperm numbers. Sperm motility, normal sperm morphology, and serum testosterone concentrations all decreased during the treatment period. After parameters returned to normal limits, three of the male dogs were bred to females which conceived and whelped normal litters. No systemic side effects were noted during the treatment period. Tamoxifen citrate, marketed under various trade names by different pharmaceutical companies, is primarily used as a treatment for breast cancer in women. Tamoxifen may represent a treatment option in very select cases. It offers a rapid prostatic response and an apparently reversible contraceptive effect, at least with limited use.

Anastrazole (Arimidex®, AstraZeneca, London, UK) is a potent, highly selective aromatase inhibitor with no intrinsic hormonal activity that has replaced tamoxifen in many breast cancer treatment protocols for women. Given to dogs at a dose of 0.025 mg/dog once daily for 28 days, a rapid reduction in prostate volume of 21% was noted with no significant changes in libido, testicular consistency and scrotal diameter, or sperm volume, count, motility, and morphological abnormalities. No hematological or other clinical abnormalities were noted. Anastrazole may present veterinary practitioners with a more rapid alternative to protocols using finasteride.

GnRH agonists. Deslorelin acetate (Suprelorin®, Virbac, Carros, France) and azagly-nafarelin (Gonazon®, Intervet, Angers Technopole, France) are potent GnRH agonists that shut down LH release by desensitizing the pituitary gonadotrophs to GnRH and the Leydig cells to LH. Gonadotropin releasing hormone agonists have been used in domestic dogs and in wild carnivores as reversible contraceptives. Spermatogenesis and libido are suspended after an initial stimulatory period and the prostate gland and testes decrease in volume up to 55%. These parameters remain suppressed throughout the duration of the treatment, slowly returning to normal ranges usually two to three months after cessation of the treatment. Male fertility appears to be unaffected after recovery from the treatment. Agonists of GnRH may be very useful in treating dogs for BPH in situations when non-surgical, reversible contraception is also a goal during the treatment period. Gonadotropin releasing hormone implants are not available commercially in the US at the present time.

Prostatitis

Dogs experiencing BPH are predisposed to developing prostatitis. Reports of prostatitis in castrated male dogs are rare and affected dogs often have a history of recent castration prior to presentation. Clinical signs of prostatitis will vary largely depending on the chronicity of the infection, with acute cases showing more serious, painful clinical signs and chronic cases often presenting as subclinical. Clinical signs relate to pain, but may manifest as back pain, abdominal pain, a painful stiff gait or depression. Semen quality and libido may be diminished. Hemospermia, hematuria, pyospermia, and fever may be present. Because prostatic fluid constantly flows both retrograde into the bladder as well as antegrade out the prepuce, these cases can be misdiagnosed as urinary tract infections. Per rectal palpation of the prostate will likely elicit pain in acute cases, but may not in chronic cases. The prostate will feel enlarged in acute cases and may not be bilaterally symmetrical, especially if abscessation is present. Some chronic cases of prostatitis may not have an obvious enlargement as fibrosis may have reduced the size of the prostate. Evaluation of the third fraction of the ejaculate is very helpful, if the dog is not too painful to cooperate with manual collection. Collection of a sample via fine needle aspiration is discouraged because of the concern for seeding the needle track with the infectious agent. The prostatic
fluid will often have a marked number of neutrophils that may show degenerative changes and may have intracellular bacteria. Lack of neutrophils in the third fraction does not entirely rule out prostatitis, as neutrophils may be in a distinct segment of the prostate, not communicating with the secretory ducts. Culture of the third fraction to determine the causative agent should be performed if prostatitis is suspected. While *Escherichia coli* is the most common pathogen in canine prostatitis, any opportunistic bacteria ascending from the urethra may cause the infection. Fungal causes are possible, but much less common and usually part of a systemic fungal infection. A complete blood count will often reveal a regenerative leukocytosis, but some dogs may be leukopenic. Ultrasound evaluation of the prostate is valuable and will usually show a heterogenous echogenic appearance to the prostatic parenchyma, with or without larger hypoechoic regions corresponding to abscessation.

**Prostatitis treatment**

Because BPH predisposes dogs to prostatic infections, treatment aimed at reduction of the hyperplasia is warranted. For dogs without valuable breeding potential and no signs of systemic infection, castration coupled with antibiotic therapy is the preferred treatment. Otherwise, choosing from one of the medical options discussed above in this review for BPH treatment should accompany treatments directed at the infection. Antibiotic therapy should be based on culture and sensitivity results and on consideration of the unique physiology of the prostate. Due to the profound inflammation present in acute prostatitis, the blood-prostate barrier is less functional and allows adequate diffusion of drugs that otherwise would not reach therapeutic concentrations in the prostate. Drugs such as broad-spectrum penicillin derivatives or a third-generation cephalosporin may initially be used to good effect. Once the blood-prostate barrier heals after initial improvement, however, diffusion across the barrier is limited to drugs containing specific pharmacokinetic properties and the antibiotic choice must be switched to an antibiotic with those properties. Drug penetration occurs via passive mechanisms of concentration gradients and diffusion. The blood-prostate barrier permits access only to lipophilic drugs and those not highly bound to proteins. In addition, the pH of the prostate is more acidic than the blood (canine prostatic pH ranges from 6.1 to 6.5). The phenomenon of ion trapping further determines the concentrations of drugs across the membrane. Each drug will have a charged fraction (ionized) and an uncharged fraction. The uncharged fraction of a lipophilic drug, in a stable system, will equilibrate on both sides of the membrane. The charged portion of the drug, however, will concentrate more on one side or the other, depending on the differing pH on each side. The drug will be most concentrated on the side with the greatest ionization (the greatest charge). Weak bases will therefore concentrate in the acidic canine prostatic fluid.

Antibiotic drugs that have proven efficacy in treating prostatic infections are discussed below. Whichever antibiotic is chosen, treatment should continue for between four to six weeks in acute cases and six to eight weeks in chronic cases. The dog should be re-examined after the end of the treatment to confirm resolution of the infection. Treatment for the standard 10-14 days will usually result in recurrence of the condition shortly after cessation of antibiotic treatment and will predispose the dog to resistant infections.

**Trimethoprim.** Trimethoprim has the necessary properties to allow diffusion across the blood-prostate barrier and is a weak base with a $pK_a$ of 7.4, therefore concentrating well in the acidic environment of the canine prostate. Trimethoprim has good broad-spectrum activity, but is not effective against anaerobic infections.

**Fluoroquinolones.** The fluoroquinolones are amphoteric or zwitterionic in that they are neither purely acidic nor basic, but have qualities of both in clinical settings. They essentially have two ionizing groups, one positively charged and one negatively charged. At a pH somewhere in between the two groups, there is a minimal amount of charged drug. This is the isoelectric point. At pH values higher or lower than the isoelectric point, the amount of charged drug increases. So, if an amphoteric drug has an isoelectric point close to the pH of plasma, the drug will tend to concentrate in areas where the pH is higher or lower than that of plasma. This is the case with fluoroquinolones and why their concentrations
are higher in the prostatic environment. The fluoroquinolones have a good broad-spectrum of activity and enrofloxacin is effective against mycoplasma infections. Fluoroquinolones do not act efficiently against anaerobic infections.

**Macrolides.** The macrolides diffuse very well into the prostate, but have poor action against gram-negative bacteria. They should not be used until a sensitivity analysis has been obtained to show that the pathogenic bacteria are gram-positive organisms sensitive to the drug. Examples for veterinary use include erythromycin and tylosin.

**Chloramphenicol.** Chloramphenicol attains good concentrations in the prostate and exhibits good activity against many anaerobes. The toxicity of chloramphenicol in humans is most likely not a concern in adult male dogs. Chloramphenicol, therefore, may be a good choice for an anaerobic prostatic infection.

**Prostatic abscessation**

Dogs with prostatic abscesses should be treated with the same protocols as dogs with prostatitis, using treatment targeted at BPH and appropriate antibiotics for the infection. In addition, active drainage of the abscess is often necessary either via surgical procedures or percutaneous, ultrasound-guided drainage. The latter procedure remains controversial because of the concern for seeding the needle track with infectious bacteria.

Surgical drainage may be accomplished by marsupialization, Penrose drainage, or omentalization. Detailed description of each of these techniques is beyond the scope of this paper, but has been recently reviewed and is covered in veterinary surgical texts. A summary of each technique will follow.

Prostatic abscessation treatment

**Prostatic omentalization.** Omentalization is currently the procedure of choice for surgical drainage of prostatic abscesses. The omentum provides an alternate vascular and lymphatic supply and functions well in the presence of infection. As such, it has been used in multiple small animal surgical procedures. The procedure of placing the omentum through the capsule of 20 dogs with prostatic abscessation (intracapsular omentalization) resulted in complete resolution in 19 dogs, with one dog showing recurrent abscessation and requiring Penrose drain placement. Minimal to no post-operative complications were reported and most dogs were discharged to go home with their owners 48 hours after surgery. If the abscess is in a paraprostatic retention cyst, and not intracapsular, omentalization may still be used to good effect.

**Penrose drainage.** Penrose drain placement was the treatment of choice before the advent of omentalization techniques. Placement of a Penrose drain within the abscess and leading out through the abdominal wall allows continuous drainage of the abscess. Various techniques are described that differ in the exact placement of the Penrose drains. The time during which the drains are left in place varies with the technique from a few days to a few weeks. Active post-operative monitoring and care are necessary until drainage resolves, the drains are removed, and the wounds close. Complications may include recurrent abscessation, urinary incontinence, subcutaneous edema, anemia, sepsis, shock, hypokalemia, and hypoproteinemia.

**Marsupialization.** Marsupialization is not commonly performed due to better post-operative results achieved by omentalization techniques. Marsupialization involves opening the abscess and suturing the edges to prevent the abscess from closing, allowing continual drainage. For treatment of prostatic abscessation, the edges of the opened abscess may be sutured to the external abdominal skin adjacent to the prepuce, or ventral or lateral to the anus. The abscess is thus allowed continual drainage as long as necessary and antibiotic or antiseptic treatments may be placed directly into the abscess. Drainage reportedly usually continues for one to two months, but may continue for many months in
complicated cases. Active post-operative monitoring and care are necessary until drainage resolves, the drains are removed, and the wounds close. Complications potentially are the same as for Penrose drainage, and may also include fistula formation.54-56

Prostatic cysts
Prostatic cysts may be located within the prostatic parenchyma (retention cysts) or in a paraprostatic position. Prostatic cysts may not cause any clinical signs, or may result in urinary or defecation difficulties. Prostatic cysts also predispose the dog to developing abscessation and therefore removal is often recommended, even in the absence of clinical signs. Removal of retention cysts may be done using the techniques described for abscessation, preferably omentalization. Paraprostatic cysts or abscesses do not communicate directly with the prostatic parenchyma, and therefore local resection is often the treatment of choice.53 Omentalization may also a good alternative.52

Prostatic neoplasia
While reported very rarely in a few other species, dogs are the only animal, besides man, with a known, significant occurrence of prostatic neoplasia. Adenocarcinomas or transitional cell carcinomas are the most common canine prostatic neoplastic diseases. While there are apparent similarities in the disease between the dogs and men, important differences also exist. As a result, many screening and treatment modalities used successfully in human medicine fail to be applicable in veterinary medicine. Prostatic neoplasia in men is often diagnosed in the early stages, thanks to heightened awareness and effective diagnostic screening tests (e.g., the prostate specific antigen [PSA] test), and is dependent upon androgens as growth factors. Androgen-deprivation is a foundation therapy for men with prostate cancer and they usually respond rapidly and favorably. Most prostatic neoplasia in men is benign or slow growing. In dogs, however, prostatic neoplasia tends to be highly aggressive and metastatic. Canine prostatic neoplasia is not androgen-dependent and is more commonly diagnosed in castrated males than intact males.5-5 Reasons for the increased incidence of prostatic neoplasia in castrated dogs are unknown, but hypotheses include a loss of protective effects of androgens, a shift in the prostatic stroma from actin-positive smooth muscle cells to vimentin-positive mesenchymal cells, which may favor tumor formation, and increased longevity of castrated animals, predisposing them to age-related neoplastic diseases.7,58 Clinical signs of prostatic neoplasia in dogs resemble those of other prostatic diseases including dysuria, dyschezia, and pain associated with the gait, back, or abdomen. Diagnosis is by history, clinical signs, an irregular, painful prostate on transrectal palpation, heterogenous echogenicity on ultrasound evaluation, neoplastic cells found on cytology, or biopsy results. Usually diagnosis is made at very late stages of the disease and survival times range from days to weeks after diagnosis.7,59,60 Because of these differences, and the fact that no known treatment for canine prostatic neoplasia affects survival time, treatments are palliative and in some cases will result in an increased quality of life for a short time. Many treatment modalities, however, have potential, serious side effects that may result in the death or euthanasia of the dog. This underscores the need to tailor each recommendation to each specific clinical scenario. Clients should be made aware of potential complications, that treatments will not likely extend the life of the dog, but may alleviate clinical signs.

Prostatic neoplasia treatment
Surgery. Prostatic tumors tend to be highly aggressive and metastatic. If, however, there are no signs of metastasis, total prostatectomy may be a suggested therapy. There are some considerations, however, that make total prostatectomy in the dog less likely to produce an acceptable outcome. Even if metastasis has not been documented, there is a highly likelihood that it has happened nonetheless and will manifest itself shortly. Due to the location of the urethra inside the prostate, urinary incontinence and other signs of morbidity are common post-operative complications with total prostatectomy. Surgery has also not been shown to increase survival in many cases.54,55

Sub-total intra-capsular prostatectomy has also been tested, both using traditional surgical instruments and an Nd:YAG laser. In general, survival may be up to five times longer than after total
prostatectomy and with a lower incidence of urinary incontinence.\textsuperscript{61-64} Survival times and post-operative complications are comparable to treatment with piroxicam alone (discussed below).\textsuperscript{60}

Transurethral resection of the prostate has been reported in three dogs. Palliation of clinical signs post-operatively was rapid, but survival times remained short and complications included urinary tract infection, seeding of the tumor, and urethral perforation.\textsuperscript{65}

Surgical therapy may alleviate clinical signs in some cases, but is associated with increased risk for complications and not associated with increased survival times. The decision to use surgery should be based on individual cases and rely on the skill and experience of the surgeon. Post-operative follow-up with systemic therapies to slow the spread of disease will likely aid in a more positive outcome.

\textit{Radiation.} Radiation therapy has been tried in dogs without extending or improving the quality of life and resulting in some cases in severe adverse affects, including chronic colitis, gastrointestinal stricture or perforation, necrotic drainage and ulceration of the skin and subcutaneous tissues, osteopenia, urinary bladder thickening, chronic cystitis, urethral stricture, ileosacral osteosarcoma, pelvic limb edema, and perianal pain.\textsuperscript{7,66,67} Survival time was not affected by the adverse effects, but quality of life decreased and owner expense increased. Radiation may play a role in future treatment regimens, but more work must be done to determine the best protocols.

\textit{Chemotherapy.} The benefits of traditional chemotherapeutic agents have not been well documented with canine prostatic neoplasia. Work has been done to investigate the chemotherapeutic properties of some nonsteroidal anti-inflammatory drugs (NSAIDs). It is thought that cyclooxygenase (COX)-2 inhibition plays a key role through inhibition of angiogenesis, stimulation of apoptosis, and altering immune function.\textsuperscript{68} One study evaluating the use of NSAIDs in the treatment of canine prostatic neoplasia found that a majority of normal and neoplastic prostatic cells expressed COX-1 and that only neoplastic cells expressed COX-2. The study also retrospectively evaluated dogs with prostatic neoplasia that were treated with NSAIDs and those that were not and found that survival time was significantly different between the two groups, with 6.9 months in the former group and 0.7 months in the latter.\textsuperscript{60} The two NSAIDs evaluated were piroxicam and carprofen.

Bisphosphates are osteoclast inhibitors used in human medicine for treatment of skeletal metastasis of prostatic carcinoma. They have been tested in dogs and appear to have similar benefits of increasing bone density and decreasing pain in some patients.\textsuperscript{69} Inhibiting osteoclast activity strengthens bone, which reduces pain and the risk of fracture. It also controls the humoral hypercalcemia of malignancy. Other benefits of bisphosphates in cancer treatment include inhibition of cancer cell proliferation, induction of apoptosis of cancer cells, angiogenesis inhibition, matrix metalloproteinase inhibition, and cytokine expression alteration.\textsuperscript{70}

Samarium-153-ethylenediamine-tetramethylene-phosphonic acid (\textsuperscript{153SM-EDTMP}), an injectable radiopharmaceutical, palliates and may have some curative properties in some restricted cases of canine skeletal metastatic disease (tumors less than two cm in diameter, not invading cortical bone, tumors in the axial skeleton, mineralized tumors, and those with high uptake of \textsuperscript{99m}Tc-MDP during scintigraphy).\textsuperscript{71} The drug is not currently easily accessible.

\textit{Dysuria therapy.} As dysuria is a common effect of prostatic neoplasia, treatment may be focused on relieving this clinical sign. Tube cystotomy may be used, but owners should be aware of complications including urinary tract infection and dissemination of the tumor.\textsuperscript{72} Presence of the tumor may also cause incontinence to persist. Placement of a metallic urinary stent has been reported, which resulted in immediate restoration of urinary function. The treatment is costly and complications may include loss of the stent, reobstruction, and incontinence. Seven of 12 dogs were scored as having an excellent outcome and mean survival time for all dogs was 20 days.\textsuperscript{73}
Prostatic neoplasia treatment summary

No standard protocol for treatment of prostatic neoplasia in dogs exists, nor is it likely that a standard protocol ever will exist as long as most diagnoses are in the late, terminal stages of the disease, as individual patient variation and client wishes will always play an important role in deciding the correct treatment regimen. At the current time, there do not seem to be any treatments that reliably extend both life expectancy and improve quality of life, with the possible exception of COX-2 inhibitors. Some treatments do seem to offer palliative measures to decrease pain and other clinical signs and should be considered as available options on a case-by-case basis, considering owner expectations and concerns, and the current quality of life of the patient.

References


