

CANINE PROSTATE PATHOLOGY

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Summary

The aim of this bibliographic study is to review the main prostatic diseases which affect dogs from different breeds and ages, as follows: benign prostate hyperplasia, squamous metaplasia of the prostate, prostatitis, intra and paraprostatic cysts, prostatic neoplasms and prostate atrophy. For each of the mentioned diseases will be present the most important characteristics.

Key words: prostate pathology, dog, reproduction

Prostate, the most important accessory sex gland is a musculoglandular body that completely encompasses the proximal portion of the urethra in most domestic males. It has a bilobed structure and it is situated in the pelvic cavity, the dorsal surface of the gland being separated from the ventral surface of the rectum by two layers of peritoneum and ventrally being partially separated from the symphysis pelvis by a double layer of peritoneum. In an adult 25 pound dog, the prostate is ovoid in shape, but it may vary from 1.7 cm in length, 2.6 cm in transverse diameter, and 0.8 cm dorsoventral diameter, to an almost perfect spheroid, 2 cm in diameter. The average weight of the prostate ranging from 2 to 5 years of age, is 6.8 g. The normal size and weight of the prostate vary, depending on age, breed, and body weight.[3; 8; 9; 16]

During a dog life, prostate gland has three phases of developing:

- First phase is corresponding to the embryogenesis and first period of post natal developing. This period ends when the dog achieves 2-3 years of age.

- Second phase is corresponding to the hypertrophic exponential development period, and it is clearly androgen – dependent. This developing period ends at 12-15 years of age.

- The last is the senile involution period of the gland. During this phase androgen secretion is significantly decreasing. [14]

Prostate functions are under androgenic control and are correlated with ejaculate volume. This gland is responsible for the ejaculate volume in proportion of over 90-95 %. On the other hand prostatic fluid has also antibacterial properties which protect the sperm, and, in addition, decrease occurrence possibilities of some genital infections in female. [15]

Prostatic diseases are most common in dogs because these breeds have a relatively great prostate gland. [16]

The most frequent canine prostatic diseases are benign prostatic hyperplasia (BPH), squamous metaplasia, cysts, neoplasms, atrophy and bacterial prostatitis. All the affections specified above results in prostate enlargement, a consequence of prostate inflammation and in conclusion, have the same clinical signs.[1]

BENIGN PROSTATE HYPERPLASIA (BPH). Benign prostatic hyperplasia is the most common disease which affects canine prostate. It is present in almost 100% of adult intact dogs over 7 years old. Over 4 years of age it may become cystic but it may begin as early as 2-3 years of age. It arises spontaneously in the gland as a consequence of ageing and endocrine influence in the dog. It is the result of androgenic stimulation, proved by the prostate regression following castration, but it is not already known why some dogs are affected and also why others are not. However, androgen action alone cannot explain BPH, so that also dihydrotestosterone (DHT), resultant from testicular Testosterone, is considered important in promoting this affection, by the action of 5- α reductase in prostatic epithelial cells. DHT interacts with gland receptors to regulate prostate growth. The receptors number is increasing with the age of dog, same as the percent of testosterone secretion is also growing with age. Oestradiol and other various mitogenic growth factors are also implicated in BPH pathophysiology. Chronic inflammation may additionally play a role in disease progression. [6; 10; 11]

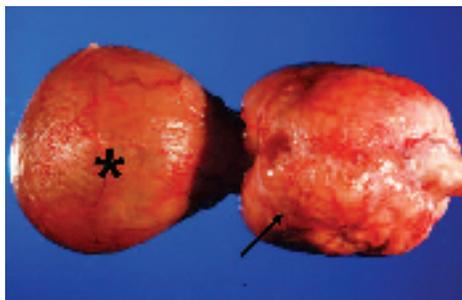


Fig 1. Gross appearance of BPH: urinary bladder (asterisk) and bilaterally symmetrically enlarged prostate gland (arrow). [PERRY, 2007]

Most dogs develop BPH, but many show no clinical signs. When present may include constipation, blood stained urethral discharge and blood in the urine and semen. Prostatomegaly is evident in radiography and ultrasonography demonstrates a normoechoic to slightly hyperechoic symmetrically enlarged gland. Affected dogs are usually painless at this level. Ultrasonography shows a symmetrical hypertrophy of the gland with or without small fluid-filled cysts. For definitive diagnosis a cytological and a histopathological examination are required. Two microscopic forms of BPH occur:

- *Glandular hyperplasia* mostly occurs in dogs below four years of age;

- *Complex hyperplasia* in older dogs, with increased stromal tissue and occasionally cystic change.

Castration is the most effective and recommended treatment for most dogs, with prostatic size decreasing by 50-70% within three weeks of surgery. Definitive decreasing of the gland occurs in some months. In cases where the risk of anesthesia and surgery is unacceptable, if the affected dog is required for breeding, or if owners do not wish their dog to be castrated, conversely, medical treatment is often considered [11].

Finasteride, a 5- α reductase inhibitor, is a compound that has been successfully used in human BPH. It is used to reduce prostate size in affected dogs, although not specifically licensed for veterinary use. It has been shown to have teratogenic potential in humans, and is present in semen of treated patients, so its use may not be advisable for breeding males. KAITKANOKE et al. [7] had shown that Finasteride significantly decreased prostatic diameter - mean percentage decrease, 20%, prostatic volume - mean percentage decrease, 43%, and serum DHT concentration with mean percentage decrease of 58%. Finasteride decreased semen volume but did not adversely affect semen quality or serum testosterone concentration. No adverse effects were reported by owners of dogs in the study [7].

Although estrogenic compounds can effectively treat BPH, they are not valuable long-term treatments and their use cannot be recommended due to severe toxic effects on bone marrow (anemia, thrombocytopaenia and pancytopaenia) as well as causing prostatic squamous metaplasia and decreased spermatogenesis.

Antiandrogens are effective in reducing prostate size but are not recommended for breeding dogs because of their inhibitor effect on spermatogenesis.

In conclusion, castration remains the only effective long-term BPH treatment, the other methods being only temporary solutions [1; 11].

SQUAMOUS METAPLASIA. Squamous metaplasia of prostatic epithelial cells results from excessive estrogenic stimulation. Mucous membrane and submucosal layer of prostatic urethra, stroma of the gland and periurethral ductal epithelium, are all carriers of oestrogen receptors. Squamous metaplasia develops after exposure of these receptors to oestrogen stimulation. Oestrogen sources are divided in two groups:

- exogenous – oestrogenic substance administrations;
- endogenous - Sertoli cell tumors.

After treatment with estradiol-cyclopentylpropionate, squamous metaplasia has been diagnosed in about 67% of exposed patients. Squamous metaplasia can lead to ductal obstruction and cyst or abscess formation. Oestrogens can produce prostate atrophy due to testosterone inhibition, although mild prostatomegaly may result with chronic exposure. Secondary development of cysts and abscesses may further enlarge the gland. With short-term exposure, periurethral tissue metaplasia

occurs, and with a long-term exposure, the metaplasia involves the entire gland. Other signs of hyperoestrogenism include alopecia, hyperpigmentation and gynaecomastia [10; 11].

Radiography and ultrasonography may demonstrate prostatomegaly. Increased numbers of squamous cells will be seen in prostatic fluid, with or without inflammatory cells.

Treatment involves removing oestrogenic source. The lesion is reversible either by castration if Sertoli cell tumor is causative, or cessation of exogenous estrogen therapy.

PROSTATIC CYSTS . Prostatic cysts are relatively rare in dogs; in a study made on 177 dogs with prostatic problems finding prostatic cysts in only 2 of the 177 cases [2]. These are most often observed as a result of BPH [10].

The most frequent incriminated cause of prostatic cysts is hyperestrogenisation, but while some are thought to be of prostatic origin, some are considered to arise as remnants of the uterus masculinus. Cystic prostate may be asymmetrically enlarged on rectal examination. Intraprostatic (*retention*) cysts, arise within the parenchyma, are encapsulated, and centrally cavitated, containing either clear or cloudy fluid. *Paraprostatic* cysts are single or multiple structures often invading the space between prostate body and urinary bladder. They are big, sometimes obstructing pelvic inlet. They can compress descending colon and rectum, as well as other pelvic organs and structures. They can be even factor in developing perineal herniation. Sometimes paraprostatic cysts undergo mineralization, so we can occasionally find segments of cartilaginous or osseous metaplasia within these cystic structures [10; 11].

Cysts are producing the same symptoms as the other diseases wherein prostate is increased in volume, but usually, are only observed when they get at great dimensions and compress the adjacent tissues. Great cysts entail abdominal distension and must be differentiated from urinary bladder and from prostate abscesses.

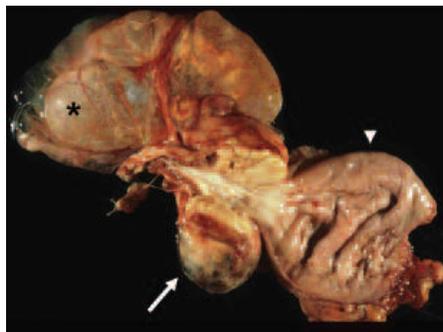


Fig 2. Paraprostatic cysts (asterisk) with slightly enlarged prostate gland (arrow). Urinary bladder indicated by arrowhead . [PERRY, 2007]

Treatment is consisting of surgical resection of the cysts marsupialisation or partial prostatectomy.

PROSTATITIS. Represents the inflammation of prostate gland and it is occurring and is not an uncommon urologic disorder which affects older intact male dogs, being the second most frequent prostatic disease which affects dogs, after BPH. 10% of dogs had these at 6 months but 45% had them at 7 years.

Generally is associated with prostatic infection (bacterial prostatitis), but it can occur also as a result of BPH. Prostate infection can occur on *ascending* way, from the urinary track, or on hematogenous rote (descending). The most important pathogens incriminated for prostatic infections are: *Escherichia coli*, *Staphylococcus*, *Streptococcus spp.*, *Mycoplasma spp*, *Proteus*, *Klebsiella spp.*, *Pseudomonas aeruginosa*, *Enterobacter* and *Pasteurella spp*. Even *Brucella canis* spread into prostate gland, but as a main target, remains in testicles and epididimis.

In healthy dogs, prostatic tissue discharges so called prostatic antibacterial factor (PAF). PAF is a low molecular peptide, containing zinc, responding to bacterial invasion. It is thermo-stable and water-soluble substance. In mycoses, although they are rare, *Blastomyces dermatitidis*, *Cryptococcus neoformans* and *Coccidioides immitis* play a dominant role [1; 5; 10].



Fig 3. Canine prostatitis [BUERGELT; 2008]

Prostatitis evolves with more severe signs than BPH: pain, dysuria, fecal tenesmus, haematuria, pyuria, bacteriuria, fever, abdominal or pelvic discomfort and it can have two evolution forms: acute intraacinar or **glandular phase** and later a chronic, **interstitial phase**.

Acute (catarrhal) severe prostatitis is a painful condition that is usually accompanied by systemic illness. Such cases will have abundant secretion, edema and hemorrhage of the prostatic and periprostatic tissues, which will reduce spermatozoa viability due to increased chlorides level in spermatic medium.

Suppurative form evolves with abscesses formation in prostate parenchyma. Abscesses have abcedation tendency, producing sepsis and peritonitis. In this case, the sperm has greenish aspect, with pus, leukocytes and erythrocytes. [6; 12; 13]

Chronic form occurs in the interstitial phase when body responds to infection with plasmatic cells and lymphocytes, or can evolve without clinical signs.

In this case, stroma is increased, epithelium is atrophied and mononuclear cells are present. Fibrosis will develop as well, with decreasing secretion surface. Atrophy of glands in the areas near inflammation may occur. [5; 13]

Abscesses can be evidenced by radiography and ultrasonography, which, together with sperm fluid examination are the base of a certain diagnosis.

The treatment consists of antibiotics administrations on the base of antibiogram. These will be administrated for 1-4 weeks (for more than 4 weeks in chronic prostatitis). Abscesses of big dimensions are recommended to be surgically drained. After infection is under control, castration is indicated. Within 2-4 weeks of treatment, prostatic fluid or urine (or both) should be examined once again, to certify prostatitis recovery.

NEOPLASMS. Primary prostatic neoplasia occurs most frequently in dogs, of the domestic species. Of all patients suffering from prostatic disorders, only 5% do have malignant tumors. Prostatic adenocarcinoma (PAC) is the most frequent of the prostatic neoplasms and is considered to arise from ductal epithelium. Incidence of PAC in dogs varies from 0.2 to 0.6%. PAC occurs most frequently in older dogs, the mean age of occurrence being of 9-10 years. PAC is given to metastasis to lumbar lymph-nodes, both inner and outer, to the vertebral body and lungs. The other targets for metastasis are the bladder neck, ureters, colon and pelvic muscle.

It was proved that in castrated dogs the risk factor of developing PAC is 2,38 fold higher than in intact ones. On the other hand, malignant prostatic tumor growth in dogs is not involved by decrease of androgen level in serum. In conclusion, castration cannot offer protection and it is not an effective treatment against PAC.

Prostatic adenocarcinoma is followed, regarding the frequency, by the transitional cell carcinoma (from the prostatic ducts) rising from urinary bladder. There were reported also cases of leiomyosarcoma and haemangiosarcoma.

High grade prostatic intraepithelial neoplasia (HGPIN) also occurs in many older dogs with or without adenocarcinoma, and is suggested to be a precursor to adenocarcinoma.



Fig 4. Gross appearance of prostatic adenocarcinoma: the prostate gland has an irregular contour due to effacement by neoplasia. [PERRY, 2007]

Neoplastic prostate glands are often significantly and asymmetrically enlarged and may impinge on abdominal organs causing faecal tenesmus and dysuria. Haematuria, anorexia and weight loss may also occur. Some dogs may present signs of myelopathy or lameness that are manifestations of skeletal metastases. Radiography may demonstrate prostatomegaly with or without mineralization and sublumbar lymphadenomegaly. Ultrasonography will similarly demonstrate prostatomegaly with an irregular contour. Neoplastic epithelial cells may be seen cytologically on evaluation of urine or prostatic fluid. Haemogram and serum biochemistry are usually normal. Biopsy may also be advisable for diagnosis establishment.

The lack of markers for prostatic adenocarcinoma makes early diagnosis difficult, so that surgical prostatectomy is rarely recommended as PAC is not usually diagnosed at an early stage. [1; 5; 10; 11]

PROSTATIC ATROPHY. The prostate is under hormonal control with both estrogens and androgens contributing to size. The prostate undergoes atrophy when there is a reduction in hormone concentration. Castration causes atrophy, especially of the epithelial component. Dogs with Sertoli cell tumours develop atrophy, but there is also a risk of development of squamous metaplasia. The affected prostate gland is reduced in sizes. [5]

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