Benign prostatic hypertrophy (BPH) is a natural consequence of ageing. More than 80% of male dogs over 5 years of age are affected. BPH is a modification of the prostatic tissue generally associated to an enlargement of the prostate, and is mainly due to the male hormone testosterone. This might lead to clinical signs such as abdominal pain, difficulties in defaecation and urination, blood in the urine and locomotive disorders which most of the time are not spontaneously associated to the prostate by practitioners. This booklet gathers articles on prostate written by experts with multiple medical competences that are related to prostate: Urology, Reproduction, Cancerology,... Thanks to all of them for their active contribution to this booklet. We hope it will be useful in your day to day practice.
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Chapter I
Physiopathology of benign prostatic hyperplasia (BPH) in the dog

Anatomy, development and roles of the prostate

Anatomically, the prostate is located near the cranial rim of the pelvis and surrounds the terminal portion of the ductus deferens, the proximal part of the urethra, and the bladder’s neck. The prostate is symmetrical and divided into two lobes by a median septum. Its size varies with the weight and breed of the dog (it is physiologically bigger in breeds like Westies and Scottish Terriers for example).

During the dog’s life, the development of the prostate may be divided into three periods. The first one begins at embryogenesis and ends at the age of 2 to 3 years of age. The second phase begins in the young adulthood and ends around 12 to 15 years of age: it is a clear androgen-dependant phase which is characterized by an exponential hypertrophic development. It is commonly accepted that, after 5 years of age, most dogs (> 60%) show a certain degree of prostatic hypertrophy. The prostate is clearly enlarged and hypertrophic in nearly 100% of dogs around the age of 10 to 12 years. The position of the prostate changes slowly as it increases in size. It is located in the pelvis in young dogs, and becomes more abdominal and then fully abdominal after 8-12 years. The third phase is a senile involution which begins when, in very old dogs, the production of androgens slowly begins to decrease (Versteegen).

Fig. 1: Anatomical position of the prostate in the dog
(Fontbonne et al. Reproduction canine. Ed Royal Canin 2006)
The prostate is a glandular tissue made of acini which are collected into ducts, which open inside the urethra. Thirty to fifty ducts open into the prostatic urethra through multiple openings. The acini are lined out with epithelial cells. Mature prostate gland structures from intact dogs are characterised by the presence of differentiated columnar secretory epithelial cells and stem (progenitor) basal cells that are located within the acini and ducts and embedded in a thin fibro-muscular tissue (Shidaifat et al.). The epithelium regenerates itself constantly from stem cells. The glandular part of the prostate is surrounded by stromal cells, which play no endocrine role (Dacheux and Dacheux).

Fig. 2: Schematic structure of the prostatic glandular epithelium within the prostatic tissue in the dog (from Magnol et al. 1998).

Fig. 3: Histology of the prostate gland (from Magnol et al. 1998).

From outside to the inside we can see:

- the external capsule
- conjunctive stroma
- smooth muscle fibers
- glandular tissue
- urethral epithelium
The prostate is the only anatomically significant accessory gland in the dog. During ejaculation, it is responsible for greater than 90% of the volume of the ejaculates (3rd or prostatic fraction) (Hewitt). But, outside ejaculation, a small amount of prostatic fluid is constantly secreted into the prostatic excretory ducts.

Prostatic secretions play several roles. The high concentration of zinc ions plays a bactericidal role - thus preventing ascending bladder infections - and contributes to stabilize DNA nucleoproteins located into the head of the spermatozoa (Dacheux and Dacheux). Surprisingly, in the dog, the prostatic fraction, compared to other species, contains a very few quantity of reducing sugars, which normally help to provide energy suitable for sperm motility.

In the dog, as in other species (man, horse...) it has been found that the prostate secretes also small vesicles (150-200 nm) called prostasomes which contain high quantities of cholesterol, spingomyelin, calcium and proteins that may be transferred to the spermatozoa through a membrane fusion (Dacheux and Dacheux).

What if BPH?

As we have seen, most dogs over a certain age show a clear increase in the size of the prostate. There is no clear breed predisposition of clinical BPH (Johnston et al.).

At the cellular level, BPH is characterised by hyperplasia, which is the increase of the number of cells, and hypertrophy, which is the increase in cells size. In fact, the term “BPH” is used, because it has been shown that the increase of the size of the prostate mainly originates from a cellular proliferation (hyperplasia). (Oliveira et al.). It is mainly the epithelial basal cells found in the acini which create this hyperplasia, as the epithelial duct cells develop much less (Leav et al.). The acinar epithelial cells also become bigger, and the size of cells seems to be related to the amount of androgenic stimulation (Wu et al.).
Role of androgens

Androgens play a clear role in the induction of BPH. However, serum concentration of testosterone are not significantly different between normal dogs and dogs suffering from BPH (Niu et al.). Furthermore, there may be even a slight decrease in the secretory function of testicular androgen-producing cells (Leydig cells) in dogs with BPH. However, the prostate of these dogs may have an increased ability to take up and metabolise testosterone (Johnston et al.).

Within the prostate, testosterone is transformed into its major active metabolite, dihydro-testosterone (DHT), through the action of an enzyme called 5α reductase. DHT is the active androgen at the intracellular level, because it has a twofold greater binding affinity for the intracellular androgen receptor and a five time lower dissociation rate than testosterone itself (Johnston et al.) Using histological immunolabelling, Murakoshi et al. have shown that in dogs suffering from BPH, there is an increased nuclear staining of androgen receptors inside the nuclei of prostatic epithelial cells, while there is also an increased activity of 5α reductase inside the cytoplasm (leading to an increased amount of DHT produced within the prostate). The amount of messenger RNA coding for the androgen-receptors is also clearly increased in case of BPH (Niu et al.), showing that there is an increase in the synthesis of these receptors. In vitro, DHT also provokes a slight increase in the proliferation of smooth muscle cells.

Thus, in vivo, most people think that androgens act in the differentiation of epithelial cells, but also in the proliferation of the fibromuscular prostatic tissue (Shidaifat et al.). All this leads to hypertrophy of the prostate.

However, the role of DHT not fully understood. Dogs treated with androgens alone only show histologic evidence of mild BPH (Johnston et al.). Ewing et al. have shown that there is not always a significant difference in DHT concentration inside the prostatic tissue between normal dogs and dogs suffering from BPH. Thus, DHT may only play a permissive role.

Role of estrogens

Estrogens may play a determining role in the pathogenesis of BPH.

In aged dogs suffering from BPH, there is an increase in the intraprostatic estrogen/androgen ratio. Although for some authors, the serum concentration of estradiol are not significantly different between normal dogs and dogs suffering from BPH (Niu et al.), an increased serum level of estrogens in old dogs has been suspected by most researchers.

Treatments with estrogens alone induce a stromal and glandular hyperplasia, a structural transformation (metaplasia) of the epithelial cells and a decrease of their secretory function.

Experimentally, a chemically-induced reduction of estradiol prostatic concentration and estradiol receptors within the prostate significantly reduces the prostatic volume, which is another fact that suggests that estrogens my play a crucial role in the development of BPH (Yoshinaka et al.)
Role of androgens + estrogens

Experimental induction of BPH requires both androgens and estrogens. Ehrichman et al., have demonstrated that estradiol when combined with DHT induces a three fold increase in prostatic size compared with DHT alone.

In fact, it seems that androgens alone are responsible of the epithelial hyperplasia, while androgens + estrogens may explain a cellular metaplastic transformation. Using an experimental regimen with androgens (3-alpha-androstenediol) and estrogens (17 B estradiol), Tuun et al. have obtained a striking increase in the weight of the prostate, but also a loss of cellular typical structure. The simple glandular epithelium is transformed into a stratified squamous epithelium (metaplasia). The cells become bigger (decrease of DNA content per mg of tissue), the stromal fibro-muscular tissue is stimulated and the amount of zinc in the prostatic fluid decreases to the level of castrated dogs.

A possible pathogenesis of BPH may be an androgen-stimulated growth of prostatic epithelial cells damaged by metabolites of estrogens with free radical activity (Johnston et al.). As already stated, metaplastic changes due to estrogens may be consecutive to a permissive rather than an inductive role of DHT.

Other factors

Role of the blood supply? Recent studies using MRI (magnetic resonance imaging) have shown that during BPH, the prostatic parenchyma is moderately hypo-vascularised, in comparison to the peri-urethral zone, which remains highly vascularised. During treatment for BPH, there is an increase of blood supply within to the prostatic tissues (Heverhagen et al.)

Other mitogens? Some authors have suggested that other androgen independent and synergistic growth promoters may act in the development of BPH. The secretion of these factors may be age-dependant. Especially, there could be factors coming from the testis and/or the epididymis (Grayhack et al.). Experimentally, the ligation of the deferent veins and arteries coming from the testis diminishes BPH (Guo et al.)

It seems also that the epithelium of the hypertrophic prostate and periprostatic tissues secretes an increased amount of relaxin, compared to normal dogs (Niebauer et al.). As relaxin weakens soft tissues, this may explain that perineal hernias are sometimes found as complications of clinical BPH in dogs, as relaxin weakens soft tissues.
References


Key issues:

- Hyperplasia of canine prostatic tissue or benign prostatic hyperplasia (BPH) is a normal phenomenon which starts already when the dog is a young adult (2-3 years) and increases progressively.

- Despite being a normal process in itself, BPH may create the basis for a pathological process which is likely to affect the dog’s welfare and health later in life.

- All dogs should be checked with a prostatic ultrasound at least every 6 months after 4 years of age.

- In the presence of ultrasonographic evidence of prostatic hyperplasia, the possibility of treating the dog with anti-prostatic drugs even in the absence of clinical signs should be discussed with the owner.
Introduction

The prostate gland is the major accessory sex gland in the male dog whose purpose is to produce prostatic fluid as a transport and support media for sperm during ejaculation. Basal prostatic secretion is constantly being produced and entering the prostatic excretory duct and prostatic urethra. From there, prostatic fluid may be moved by urethral pressure backward into the bladder (a mechanism called prostatic fluid reflux), or forward into the penile urethra during ejaculation, micturition or whenever peristaltic urethral contractions are present. Therefore, traces of prostatic fluid can be found in the bladder, in the seminal plasma or may drip outside of the penis even in absence of ejaculation, should an adult male dog be in proximity with bitch/es in heat. This process is responsible for the two major clinical signs which are indicative of benign prostatic hyperplasia (BPH) in the dog, namely presence of blood in the urine sediment and blood dripping outside of the penis. Owners should be taught to look for such simple signs in order to achieve an early diagnosis of BPH, which can greatly help in the management of the disease. This paper will review the various clinical signs which indicate prostatic enlargement in the dog highlighting those which may help to raise owner’s awareness thus allowing an early diagnosis of the condition.

Benign Prostatic Hyperplasia

Benign prostatic hyperplasia (BPH) is the most common canine prostatic disorder, with > 80% of intact dogs developing histologic evidence of BPH with aging. BPH is characterized by an increase in epithelial cell numbers (hyperplasia) as well as an increase in epithelial cell size (hypertrophy), but the increase in cell number is more marked. It begins as glandular hyperplasia in young dogs, with as many as 16% of dogs reported to have histologic evidence of benign hyperplasia of the prostate by 2 years of age. Hyperplasia is probably due to an altered androgen:estrogen ratio, and requires the presence of the testes to start and continue to develop. Dihydrotestosterone (DHT) within the prostate gland probably serves as the main hormonal mediator for hyperplasia. Intraparenchymal fluid cysts often develop in association with hyperplasia. Such cysts are variable in size and contour, contain a thin, clear to amber fluid and may or may not communicate with the urethra. The hyperplastic prostate is highly vascularized and if a small vessel of a hyperplastic prostatic cyst starts bleeding, blood will accumulate within the cyst. If the cyst communicates with the urethra blood will start dripping from the tip of the penis or will appear in the urine. If the cyst does not communicate with the urethral lumen, cystic fluid will accumulate thus causing a rapid (depending on the rate of fluid accumulation) increase in cystic size. Development of prostatic cysts and accumulation of blood within the cyst/s are the two main factors most likely to determine serious health consequences for the dog.

How BPH can affect the dog’s health

The health of a dog with BPH can be seriously affected by a) an increase in prostatic size, especially if cysts are present, and b) the accumulation of blood within the cyst/s.
The increase in prostatic size will affect defecation and urination due to rectal and urethral compression. Such compression may appear rapidly if one or more prostatic cysts are present. When a prostatic cyst communicates with the urethra, cystic fluid will void into the urethra constantly and the size of the cyst may increase very slowly or not increase at all. If not connected to the urethral lumen, prostatic cysts will rapidly increase in diameter due to fluid accumulation. The increase in cyst diameter will cause an increase in prostatic size. As the speed of increase of a cyst is dependant on the rate of testosterone secretion and its conversion to DHT at the prostatic level, the rate of prostatic growth can be very quick in young adult to middle-age dogs, while it generally slows down in older dogs as their androgen production decreases.

Accumulation of blood within a prostatic cyst may lead to the development of prostatitis. The protein-rich prostatic fluid is an excellent source of nutrient for bacteria. Spread of bacteria may occur from the kidneys and bladder via urine, from the testicles and epididymis via semen, or via a hematogenous or lymphatic route, through the vas deferens or through the rectal flora by direct extension. Bacterial prostatic infection can be acute and fulminant or chronic and insidious leading to abscessation.

These two aspects are intimately correlated as the risk of prostatitis increases in the presence of a chronic hyperplastic condition (although theoretically a prostatic inflammatory disease is possible also in dogs without BPH). The increase in prostatic size is the first consequence of BPH but it is often asymptomatic for months or even years as it may progress very slowly, while prostatic inflammatory disease is a serious problem which affects the dog’s health immediately.

Consequence of BPH due to increased prostatic size are difficult defecation, difficult urination and infertility. Apart from the above signs, affected dogs are usually normal and the prostate on palpation
is non-painful, symmetrically enlarged and with variable consistency. Urine may contain blood (gross or microscopic) and a slightly higher than normal count of leukocytes on the urine sediment. No alteration of haematological or biochemical parameters are commonly observed in dogs with BPH. Consequences of BPH due to inflammation of the prostate include all the clinical signs which are typical of prostatitis such as pelvic pain (often causing a difficult gait or reluctance to move), urinary tract disease or a more generalized syndrome characterized by fever, depression and anorexia. Difficult defecation and difficult urination may also be observed during prostatitis. Alterations of haematological or biochemical parameters are commonly observed in dogs with prostatic inflammation.

Increased prostatic size

**Difficulties in defecation** - This is the most common presenting complaint for BPH. Owners typically refer that the dog cannot defecate properly, that defecation is a very long process and sometimes faeces are noticed to have a flat appearance. The prostate is located ventrally to the rectum. An enlarged prostate can push the rectum upward thereby restricting the rectal lumen, causing tenesmus and sometimes making defecation difficult. Depending on faecal consistency and hardness, faeces may appear flat or string-like or the dog may be unable to defecate. Such a condition does not generally persist for a long time as the owner quickly recognizes that the dog has a problem and seeks veterinarian’s help. However, if a dog is not under constant supervision this condition may hexacerbate quickly. The initial approach to this condition must include (apart from antiprostatic drugs) softening faeces through diet or administering enemas with oily solutions.

**Difficulties in urination** - Prostatic enlargement may lead to urethral occlusion. This is a common presenting complaint in men suffering from BPH, but is rather unusual in dogs. However, it has been observed in dogs with chronic prostatic enlargement (Figure n° 1), especially in case of other concomitant micturition problems such as detrusor insufficiency or a neurological condition affecting the voiding process. The contemporary presence of BPH with other urological conditions is not unusual in older dogs, and its treatment is complicated by the relative lack of information on the effect in the dog of human drugs used to treat urethral occlusion problems. Drugs indicate for the treatment of urethral occlusion in men include the alpha-1 adrenergic antagonists tamsulosin, naftopidil, prazosin, silodosin, doxazosin. Very little is known about efficacy and side effects of these compounds in the dog; while most of these
drugs are probably efficacious in relaxing canine urethral musculature and solving urethral occlusion, incidence of side effects such as thoracic pain, liver insufficiency, hypotension, dyspnea, paresthesia, thrombocytopenia, and limb pain (all reported in men) is unknown in the canine.

**Infertility** - The reason for BPH to be a common cause of infertility in the dog is probably due to the alteration of the biochemistry of the prostatic fluid (Table n° 1) which cannot provide a proper media necessary for survival, nutrition and motility of spermatozoa. Such an alteration of prostatic fluid biochemistry may decrease semen quality causing a shorter survival time of semen or an increase in the percentage of secondary abnormalities of spermatozoa. Also, if prostatic cysts communicate with the urethra blood loss in the prostatic urethra can be so intense that the ejaculate may appear completely red (Figure n° 2). Although presence of blood in the semen is typically considered to be a cause for infertility, dogs with various amounts of blood in their ejaculates may sometimes be fertile.

<table>
<thead>
<tr>
<th>Table n° 1</th>
<th>Mean+ SD</th>
<th>Range</th>
<th>Sample size (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>6.2+0.3</td>
<td>5.5-7.1</td>
<td>43</td>
</tr>
<tr>
<td>Specific gravity</td>
<td>1.018+0.005</td>
<td>1.008-1.028</td>
<td>40</td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>27.0+17.0</td>
<td>8.0-73.0</td>
<td>29</td>
</tr>
<tr>
<td>Zinc (mcg/ml)</td>
<td>62.3+35.3</td>
<td>10.3-120.6</td>
<td>20</td>
</tr>
<tr>
<td>Copper (mcg/ml)</td>
<td>7.1+4.8</td>
<td>1.3-19.5</td>
<td>20</td>
</tr>
<tr>
<td>Iron (mcg/ml)</td>
<td>0.7+0.5</td>
<td>0-1.6</td>
<td>20</td>
</tr>
<tr>
<td>Calcium (mcg/ml)</td>
<td>13.3+20.2</td>
<td>0.3-97.0</td>
<td>20</td>
</tr>
<tr>
<td>Magnesium (mcg/ml)</td>
<td>16.4+9.5</td>
<td>3.4-40.0</td>
<td>20</td>
</tr>
</tbody>
</table>

Composition of prostatic fluid from normal dogs. In case of prostatitis, pH and specific gravity are known to become altered. Changes of other parameters may also occur, creating an environment which is unsuitable to sperm survival (from Branam et al., 1984).

**Prostatic inflammation**

**Pelvic pain** - Inflammation is generally characterized by swelling. Prostatic swelling causes increased pressure on the surrounding tissues, with potential compression of some of the prostatic, urethral, pelvic and rear limb nerves and vessels, increased tension on the prostatic capsule and increased stimulation of the sympathetic and parasympathetic innervation of the prostate and bladder. All these conditions create discomfort and sometimes pain at the pelvic or retroperitoneal level, which may cause the dog to be reluctant to walk, jump, stand on his rear limbs or mount. These clinical signs generally reflect an acute prostatic disease which is often characterized also by signs of systemic illness such as anorexia, lethargy and fever. Vomiting is possible, and dripping of fluid from the prepuce can be noted. Caudal abdominal pain can be present which may be localized to the prostate gland by palpation. Prostatitis
may be due to a bacterial prostatic infection originating either primarily from the prostate itself (cysts, squamous metaplasia, neoplasia) or as a secondary diffusion from a urethral disease (urolithiasis, trauma, stricture, neoplasia), a urinary tract infection, an infection of the epididymis or testicle, an infection through the rectal flora by direct extension or, via the hematogenous or lymphatic route. Bacteria involved include E. coli (most common), Staphylococci, Proteus, Klebsiella, Pseudomonas and Streptococcus/Enterococcus. Infections by anaerobic bacteria, fungi or mycoplasma are rare. Granulomatous chronic prostatitis has been rarely reported due to blastomycosis and cryptococcosis. Although bacteria must be identified in order to choose the best antibiotic treatment, they are rarely the primary cause of disease but rather a complicating factor. Under normal conditions, bacterial proliferation does not occur unless there is abundance of nutrients, (such as what happens when prostatic fluid accumulate within a prostatic cyst). Therefore, presence of cyst/s within the prostate is a risk factor for the development of an acute prostatitis. Potential complications of an acute prostatitis include the development of an abscess (generally due to purulent infection of a large prostatic cyst), rupture of the abscess with peritonitis and septicaemia or the dissemination of bacteria to the urinary tract, with cystitis or nephritis. If the abscess ruptures, a localized or generalized peritonitis results in lethargy, fever, pain, vomiting and possibly a shock syndrome. On some surveys, evidence of septic shock (tachycardia, pale mucous membranes, delayed capillary refill and weak pulse) was noted in about 10% of cases, while caudal abdominal pain was noted in >70% of cases.

**Urinary tract disease** - With chronic prostatitis there may be no signs directly referable to the prostate. The dog may be presented for recurrent episodes of cystitis, or for constant and intermittent hemorrhagic or purulent urethral discharge or hematuria, or even chronic infertility. The prostate may not be painful upon palpation, and it may vary in symmetry and consistency with areas of more firm fibrous tissue alternated with areas of normal prostatic tissue. Areas of infection may be focal, multifocal or diffuse. If a large abscess start developing the dog may be initially presented with tenesmus or dysuria. Pressure on the urethra may then lead to partial urethral obstruction causing a chronically distended bladder, detrusor dysfunction and overflow urinary incontinence. Whenever sign/s of prostatic hyperplasia are present, urinalysis should also be performed as it helps to rule out urinary tract diseases as a cause of penile discharge. If present, cystitis should be treated prior to onset of BPH therapy to avoid confounding factors in the interpretation of results.

**Fever, depression, anorexia** - Unspecific signs of disease such as fever, depression and lack of appetite may be due to a variety of conditions affecting almost all the different system. In an intact male dog, differential diagnoses must include also acute and chronic prostatitis. Although acute prostatitis is often accompanied by pelvic pain, this may not always be the case and the disease may only be characterized by generic signs. Chronic prostatitis may be a sequel to an acute infection or may develop insidiously. Although inflammation is present in chronic prostatitis, it may not be severe enough to produce systemic signs. However, the inflamed prostate may serve as a nidus of infection for the urinary tract and the local prostatic infection may gradually turn into an abscess.

**How to prevent BPH**

The normal prostate in the intact male dog increases in weight, due to normal growth and glandular hyperplasia, between 1 and 5 years of age, with a peak at 4 years. The incidence of BPH increases to
over 80% with advancing age. Senile involution of the prostate occurs in dogs from age 11 onwards. The best way to prevent the development of clinical BPH in the dog is to identify its early signs by performing a regular monitoring of prostatic conditions by ultrasound. On ultrasound, the hyperplastic prostate may appear diffusely hyperechoic with parenchymal cavities (which means that intraparenchymal cysts have developed). Conditions such as prostatic cysts can be visualized easily using the sagittal and transverse planes using 5.0 or preferably 7.5 MHz scanners. If signs of BPH (such a presence of prostatic cysts or increased prostatic size) are observed during a routine check while the dog is asymptomatic, owners should be advised to watch for the development of clinical signs in order to start treatment as soon as possible. The most effective treatment is castration, following which prostatic size may decrease as much as 50% in 3 weeks and 70% over 9 weeks. As post-castration involution begins within days of surgery, clinicians should palpate the dog’s prostate 3 weeks post-operatively to make sure the involution rate is normal thus ruling out a more serious prostatic disease such as neoplasia or abscessation. However, recent studies indicate that incidence of prostatic carcinoma could be higher in castrated rather than in intact dogs; reasons for this are not entirely known yet; but it is speculated that once prostatic atrophy starts, neoplastic cells already present will increase their growth rate. Also, castration is often refused by the owner on cultural and/or psychological grounds. When castration cannot be considered, other classes of drugs can be used. There is little information on the value of a preventive treatment for BPH in the dog. In men, preventive treatment is often discourage because of the many side effects which may be caused by alpha-1 adrenergic antagonists. However, incidence of side effects of such drugs in the dog is unknown, and most importantly alpha-1 adrenergic antagonists are not 1st-choice drugs for canine BPH, while steroidal or non-steroidal antiandrogens or GnRH agonists are more indicated for this purpose.

Conclusions

While a low degree of prostatic enlargement should be of little if any concern, one can never foresee how quickly a specific hyperplastic process will progress into a full blown clinically evident BPH. Sexually mature, intact dogs should certainly be considered at risk of developing prostatic disease especially if having ultrasonographic evidence of BPH such as prostatic cyst/s. The risk of an adult, intact dog of developing a prostatic disease has never been fully investigated and is probably underevaluated. The incidence of prostatic infection in the dog is unknown, but chronic prostatitis is believed to be common. Therefore, it should be our responsibility as veterinarians to advice our clients of the seriousness of this condition, of how easy it is to keep it under control and of how dangerous it could be to disregard it. For instance, an untreated prostatic cyst may well develop into a prostatic abscess. Prostatic abscesses are difficult and expensive to treat. Also, failure to control prostatic infection and occurrence of a recurrent urinary tract infections are common, as the prostate may reabscess. Urinalysis and urine culture should be re-evaluated monthly for several months after initial therapy is discontinued, and the prostate gland should be palpated and re-examined by ultrasound at monthly intervals until abscess resolution is confirmed.
Suggested readings


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Chapter III
Diagnostic of BPH
3.1 imaging of the prostate

Ultrasonography is the imaging procedure of choice to determine the size and the parenchymal alterations in the prostate gland.

Ultrasonography

Normal appearance - The prostate is a bilobed gland, traversed in its central-to-dorsal portion by the urethra and delimited by a capsule. The paired ductus deferens penetrate the dorsocranial part of the prostate and join the urethra at the level of the colliculus seminalis. The prostate gland is located ventral to the colon and caudal to the neck of the urinary bladder, in an abdominal or pelvic position. In this latter location, the presence of the pubic bone impairs the ultrasonographic approach. The use of a curved array transducer and scanning the dog in a standing position can facilitate visualization of the gland. A 7.5 or 8 MHz frequency probe is commonly used. The normal prostatic contour is well-delimited by a thin, hyperechoic capsule. The ductus deferens are not easily identified with ultrasound. The urethral tract appears as a linear, hypoechoic image in sagittal sections and as a round, hypoechoic image in transverse sections. This landmark can be used to standardize the measurements of the prostatic gland by allowing the identification of the mid-sagittal, long axis plane (measurement of the prostate height and length) (fig. 1a) and a symmetrical cross-sectional image (measurement of the width) (fig. 1b). The size, position and echogenicity of the prostate vary with age.

Fig. 1a: A mid-sagittal, long axis plane of normal prostate. Homogeneous echoic parenchyma with oval shaped gland. Note the normal hypoechoic urethral tract. Measurement of the height (thick line) and the width (thin line).

Figure 1b: A transverse section of the normal prostate gland. Note the hypoechoic image central-to dorsal portion of the gland corresponding to the urethra. Measurement of the width (line).
In immature dogs, the prostate gland is within the abdominal cavity at birth until 2 months of age and migrates to a pelvic position after rupture of the urachal remnant. The parenchyma is initially hypoechoic and oval-shaped. The prostate gland enlarges at sexual maturity and becomes more abnormally located. The parenchyma has a homogeneous, echoic pattern with medium to fine texture. Significant positive correlations were found in a study between prostatic parameters (length, width, height and estimated volume) and parameters related to body size and age in non-castrated dogs. Conversely, neutered dogs have a small, hypoechoic and oval-shaped prostate in a pelvic location (fig. 2).

**Benign prostatic hyperplasia: BPH** - BPH is a benign enlargement of the prostate gland associated with glandular hyperplasia or squamous metaplasia. BPH has been shown to start in dogs as early as 2 years of age. It is often considered as a common finding related to age but can lead to urologic and digestive disorders. Therefore, identification and characterisation of BPH is important. In one study, 95% of intact beagles over 9 years of age were affected. Prostate enlargement may be symmetrical (fig. 3b) or asymmetrical or associated with loss of the bilobed shape in transverse section (fig. 4).
The prostate gland appears round in sagittal section (fig. 3a). The echogenicity can be variable (fig. 3a, 3b, 4, 5, 6, 7) but usually decreases and the texture becomes coarser (fig. 4). The parenchyma can remain homogeneous (fig. 3a, 3b, 4) but usually anechoic cysts develop (fig. 5, 6, 7). Less commonly hyperechoic foci are observed (fig. 6), which may correspond to scattered tissue or fibrosis. It is important to evaluate the number and size of the cysts for the follow-up. Mineralisations are not frequent with BPH. A study has demonstrated that blood flow is modified in case of BPH with increased systolic and diastolic peak velocity and time averaged maximum velocity of deferential arteries outside and within the gland. BPH can be complicated by infection (fig. 8). Furthermore, in severe cases of BPH with obvious remodelling, it is fairly common to include in the differential diagnosis inflammation, infection (fig. 7, 8) or neoplasia (fig. 9). The assessment of medial iliac lymph-nodes, an ultrasound guided fine-needle aspirate (fig. 7) or biopsy are therefore important.

Figure 5: Transverse section of BPH. Enlarged hypoechoic parenchyma with anechoic small cysts (arrows).

Figure 6: Transverse section of BPH. Enlarged hypoechoic parenchyma with small cysts and hyperechoic foci (arrows).

Figure 7: Sagittal section of BPH. Enlarged hyperechoic prostate with large anechoic and isolated cyst (arrow) within the left lobe. BPH confirmed by fine needle aspiration of prostatic parenchyma and cavity.

Figure 8: Sagittal section of the prostate. Note the presence of two large hypoechoic and irregular cavities corresponding to prostatic abscess.

Figure 9: Sagittal section of prostatic tumor in a neutered dog. Hypoechoic and heterogenous parenchyma with calcifications.
Radiography

**Normal appearance** - The prostate gland has a round to oval shape and a homogeneous soft tissue opacity. On a lateral projection, the colon is identified dorsally, the cranial prostatic surface is underlined by a triangular fat opacity image around the neck of the urinary bladder. On a ventro-dorsal view, assessment of the prostate gland is difficult due to superimposition of the sacrum, the colon and faecal images. The normal prostatic size is evaluated in a lateral survey radiograph. One report states that the prostate gland height should not exceed 70% of the distance between the sacral promontory and the pubis (fig.10). The normal length is approximately 1.5 times the width of the gland.

**Benign hyperplasia: BPH** - The enlarged prostate is evaluated by measuring the width of the gland and assessing the mass effect on the colon dorsally and the bladder position cranially. Enlargement is usually moderate with BPH on lateral radiographs. A width exceeding more than 90% of the distance between sacrum and pubis is mostly in favour of neoplasia or a large abscess or cyst. The preservation of a well defined cranial prostatic border is likely associated with benign or slowly progressive abnormality. Small calcifications or gas pockets can be associated with BPH but are uncommon, so that infection or tumour have to be included in the differential diagnosis. Ultrasonography is a precise imaging procedure which should be used to evaluate the prostate and to diagnose and follow up BPH and its management.

**Figures**

1a, 1b, 3b, 5, 8 Unité fonctionnelle de radiologie École Vétérinaire d’Alfort Maisons-Alfort (France)
ATL 3500 HDI - 2, 3a, 4, 6, 7, 9 Delphine Rault Cagnes-sur-Mer (France) ESAOTE Mylab30 - 10
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**References**

Prostatic disease is frequently seen in the dog. The clinical signs may be diverse and non-specific. Although prostatic enlargement may be easy to diagnose, both by rectal palpation and by ultrasound or radiographs, the nature of the disease is often difficult to assess. Histologic examination for a definitive diagnosis requires either excision biopsies obtained by laparotomy or large-bore needle biopsies, the latter with the risk of sepsis or haemorrhage. Compared to histology, cytology in the diagnosis of prostatic disease may have several advantages. The collection of material for cytologic evaluation is less invasive than with histological biopsies. It entails a significantly lower risk of septic complications and of seeding tumor cells. Another advantage is the speed of the method with results available within one hour after biopsy. Both flush techniques and transrectal or transabdominal biopsies techniques have been used to obtain material for cytological examination. With the transabdominal Fine Needle Aspiration Biopsy (FNAB) technique specimens for cytology can be obtained by ultrasound-guided fine needle aspiration, using e.g. a 10 cm 21 gauge modified Menghini
aspiration biopsy needle (Surecut®) with a 10 cc syringe\(^1,2\). The biopsy site in the parapreputial, prepubic area is first prepared surgically and infiltrated with a local anaesthetic. A small skin incision is then made to facilitate entry of the needle. The needle is directed to areas of lucency in the prostatic tissue, avoiding cysts or calcifications. In the author’s experience there is no need for preFNAB coagulation testing.

In addition, cytologic specimens can be obtained by the catheter biopsy technique as described by Mehlhoff and Osborne\(^3\) under ultrasound guidance, because guidance via the rectum cannot always be achieved. A urinary catheter is introduced into the urethra and the opening of the catheter is positioned in the prostatic area of the urethra after which cells are aspirated. No fluid is flushed during this procedure. Successful results have been reported for this method in the dog\(^4\).

The biopsy specimens are smeared on glass slides, air-dried, and stained by the May-Grünwald Giemsa technique or one of the Wright stain based quick stains. In a study of 77 dogs with prostatic disease, the clinical signs appeared to be diverse and non-specific for the different causes of prostatic disease\(^1\). Both FNAB and catheter biopsy technique had a moderate sensitivity for detecting prostatic carcinoma (67% each). However, both techniques had a very high specificity for detecting prostate cancer (98%). By combining the two techniques the sensitivity can be enlarged. Both methods combined only failed to obtain sufficient material in 3 dogs (3.9%). No side effects were noticed due to the biopsy method in any of the 77 dogs.

**Benign prostatic hyperplasia** is cytologically characterized by large groups of epithelial cells, frequently in monolayers, with a cell morphology comparable to normal prostatic epithelial cells (Fig 1 and 2).
amount of cytoplasm may be enlarged giving the cells the typical columnar or polygonal appearance. The nuclei are uniform of size, round, often with a prominent small nucleolus, and with fine granular chromatin pattern. The nuclear/cytoplasm (N/C) ratio is usually low. In prostatitis very often there is quite a degeneration of the epithelial cells, intermixed with many neutrophils with or without intracellular bacteria (Fig 3). Macrophages and other round nuclear inflammatory cells may also be present. Squamous metaplasia, associated with estrogen production of Sertoli cell tumours or iatrogenic causes, can be present in both benign prostatic hyperplasia and prostatitis. Several large squamous cells with a large amount of basophilic cytoplasm, without a nucleus or with a small condensed nucleus, can be seen (Fig 4). The amount of cells that can be seen in fluid from prostatic cysts can vary enormously. Usually only small numbers of prostatic epithelial cells with some inflammatory cells can be seen against a protein rich background pattern. Several types of neoplasia can be diagnosed in the prostate. However, most of them like the malignant lymphoma and sarcomas occur very infrequently. The most common prostatic neoplasia is the prostatic carcinoma. Especially in FNABs these tumours are easy to differentiate from benign prostatic hyperplasia. The majority of carcinoma are poorly differentiated carcinomas, sometimes transitional call carcinomas and rarely adeocarcinomas can be diagnosed. Small to large clusters of very basophilic epithelial cells, with many malignancy criteria are present like anisocytosis, anisokaryosis, prominent and multiple nucleoli, variable N/C ratio, abnormal mitotic

Fig. 3 Sheets of benign prostate epithelial cells are intermixed with several, often degenerated neutrophils. (Photo: courtesy E. Teske, Utrecht University)
figures, and irregular and clumped chromatin pattern (Fig 5 and 6). Occasionally the cytoplasm of the tumour cells may contain small to large vacuoles, filled with a granular magenta material, presumably of mucoid origin (Fig 6).

When collecting material for cytology one should try to avoid the use of gel, for the ultrasound guidance or for the introduction of the catheter in the urethra, as this may result in excessive amount of granular, often dark red coloured material (Fig 7).

References


Fig. 4 Prostate with squamous metaplasia. Large cells are present with sky-blue partially cornified cytoplasm and pyknotic nuclei. (Photo: courtesy E. Teske, Utrecht University)
Fig. 5 Poorly differentiated prostate carcinoma. Anisocytosis, anisokaryosis, prominent and multiple nucleoli, variable N/C ratio, and irregular and clumped chromatin pattern. (Photo: courtesy E. Teske, Utrecht University)

Fig. 6 Transitional cell carcinoma of the prostate. Cytoplasmic vacuoles are filled with granular, magenta material. (Photo: courtesy E. Teske, Utrecht University)
Fig. 7 Granular, dark red material caused by ultrasound gel is lying between the sheets of epithelial cells and inflammatory cells in this dog with prostatitis. (Photo: courtesy E. Teske, Utrecht University)
Benign prostatic hyperplasia (BPH) is an age related change of the prostate with an increase in both the number of glandular epithelial cells (hyperplasia) and cell size (hypertrophy), along with the development of small intraparenchymal fluid cysts. The underlying pathophysiological mechanism is the accumulation of Dihydrotestosterone (DHT) within the prostate, due to two hormonal changes of the aging male dog. With age the secretion of testosterone is reduced and thus the balance of the sexual steroids changes in favor of the estrogens and 17B-Estradiol induces the expression of DHT-receptors. Additionally, with increasing age the catabolism of DHT in the prostate is reduced. These two age related changes result in the accumulation of DHT, with the prostate becoming a “trap” for DHT. Because DHT has a trophic effect on the prostatic tissue, the whole gland increases in size over time. This age related increase in size affects each human and canine prostate under the influence of gonadal sexual steroids.

There is no difference between human and canine species in regard to the pathophysiology of BPH. However, the clinical manifestation is different due to a different distribution of the DHT-receptors within the prostate. In men DHT-receptors are principally expressed in the stroma which is mainly situated around the urethra. The trophic effect of DHT in this area, which means an increase in cell number and cell size, generally results in a narrowing of the urethra with the classic clinical signs. In contrast, canine DHT-receptors are expressed in the peripheral, glandular part of the prostate. Thus, the age related proliferation in this area is more likely to result in pressure on the surrounding organs without normally having an effect on urination. In male dogs the structural change of the glandular epithelium already starts at the age of 2 years and with time results in multiple, small intraprostatic cysts, filled with a clear to amber fluid, and at an advanced stage these protrude from the surface of the prostate. By the age of 9 years 95% of the prostate is interspersed with cysts of variable size, which rarely cause clinical signs.

Clinical signs are usually present at an advanced stage of BPH, including difficult defecation, flattened, ribbon-like stool, intermittent yellowish or clear to hemorrhagic urethral discharge from the urethra and intermittent or persistent mild hematuria. The general health of the dog is not affected. On digital rectal palpation the prostate is indolent, symmetrically enlarged and may have an irregular surface. On a latero-lateral radiograph the prostate is seen as a soft tissue mass situated caudally to the bladder neck. The prostate is too large if the ventro-dorsal diameter exceeds 2/3 of the distance from
the pelvic symphysis to the iliolesal joint. At an advanced stage the prostate compresses the rectum and displaces the urinary bladder cranially. On ultrasonographic examination the prostate is normal to hyperechoic and hypoechoic cysts of variable size can be seen.

In male dogs the distal part of the urethra is inhabited by bacteria. Any pathological change in the area of the urethra, prostate and/or urinary bladder favors an ascending infection. The presence of fluid filled cysts predisposes the animal to a bacterial infection, resulting in a possible acute or chronic prostatitis or prostatic abscessation. Through the excretory ducts of the prostate fluid is constantly secreted into the urethra and flows retrograde into the bladder between micturitions. The same is true for the seminal fluid which is constantly secreted through the spermatic duct into the urethra. The reverse presumably occurs with some urine entering the prostatic excretory ducts and spermatic ducts during micturition. This explains why it is uncommon for a single organ to be colonized by bacteria. Most often there is a combination of two or more of cystitis, prostatitis, epididymitis and/or orchitis, all caused by the same bacterium. These usually are ubiquitous bacteria, and in decreasing frequency E. coli, Staphylococci, Streptococci Klebsiella etc.

From the anatomical situation it is obvious that when there is a bacterial infection of one organ of the urogenital tract, it is important to examine the other organs. An early diagnose of a urogenital tract infection is decisive for a successful medical therapy. As soon as an abscess forms within the prostate a surgical intervention is unavoidable. Unfortunately, prostatic surgery often results in urinary incontinence, which is difficult to control in male dogs.

From the history, urinary and blood results, as well as clinical and ultrasonographic findings, a presumptive diagnosis of BPH can be made. To confirm the diagnosis a cytological examination of prostatic fluid or histopathology of a prostatic biopsy is needed, but in most cases this is unnecessary. The pars prostatica of the urethra is of particular interest for the urologist as it is mainly responsible for maintaining continence. The distally situated pars membranacea apparently also contributes to continence. However, the recording of urethral pressure profiles of continent male dogs and incontinent dogs due to urethral sphincter incompetence suggests that the pars membranacea has no effect on continence. In incontinent dogs the maximum urethral pressure of the pars membranacea was equal to that of continent male dogs. Thus, for the urethral closure pressure it is crucial that the prostate is under the influenced of testosterone. It is known that in intact male dogs with urethral sphincter incompetence the condition deteriorates after castration.

In contrast to bitches, male dogs with urinary incontinence due to urethral sphincter incompetence do not respond well to alpha-adrenergic substances. For such cases the endoscopic injection of collagen is the treatment of choice. After a caudal laparotomy and cystotomy the collagen is circularly injected into the submucosa of the prostatic urethra, forming cushion-like elevations at the site of injection. It is important to perform the injections in the area of the prostate, the main area responsible for continence. During endoscopy the cumulus seminalis can be used for the orientation, as it bulges into the urethral lumen at the center of the prostate. Intact male dogs, incontinent due to urethral sphincter incompetence, should be castrated 3 weeks before the collagen injection, to minimize the risk of a iatrogenic prostatitis.
Chapter V

Importance of prostatic exploration during the examination of the old dog

First of all, the geriatric consultation is the time to realise a complete overview of the general condition of the animal. Therefore, a complete and systematic examination is necessary at the time of entering in geriatric age (age over 2/3 life expectancy). This exhaustive clinical evaluation has to be performed whatever the purpose of the visit, including a geriatric check-up. At the end of the clinical exam, the practitioner ranks his clinical conclusions by importance in order to optimise the choice of further complementary analysis.

The aim of the geriatric consultation is above all prevention i.e highlighting diseases when their clinical expression is coarse, even nil from the pet-owner’s point of view. In the male dog, disorders of urogenital tract and particularly of the prostate gland are a typical example of an imperceptibly clinical evolution (1 dog among 10 in the geriatric consultation). In the first steps of the disease, its is really difficult for the pet-owner to notice the urinary functional symptoms (microscopic haematuria, pollakiuria associated to territory marking or not observed at all if the animal lives outside). Therefore, a complete clinical check of the animal is necessary during the geriatric consultation as its does not require specific techniques at first intention.

Eventually, history and commemoratives collection can be a good method to suspect urinary infection. Even without evidence of clinical signs, exploration of the urinary tract is imperative

- Evaluation of prepuce and penis: highlighting of blood dripping or ptosis of the prepuce
- Abdominal palpation: complete evaluation including kidneys, bladder, and prostate (if in an abdominal position). Every abnormalities of shape, size or texture, pain shall be noticed.
- Testicular palpation: easy to perform – asymmetry of the testis or abnormal texture provides a strong presumption of tumour. A link with a prostatic problem is possible.
- Rectal exam: the best way to perform a first clinical approach of the prostate. Prostate enlargement or asymmetry, abnormal shape or texture (liquid sack), pain provides indication on the organ and its interaction with the surroundings organs. It is also possible to check ventrally a part of the proximal urethra, and dorsally the caudal part of the lumbar arch over (lymph nodes) and anal margin. Rectal exam is easy to perform and rich in information.
- Urinary analysis: urinary collection and analysis is completely part of the clinical evaluation of the prostate. Simple, non-invasive and cheap, urinary analysis is fundamental. Collection of urine can be done by spontaneous urination or cystocentesis to avoid haematuria due to the passing of the probe.

At the end of collection of history and clinical exam, a disorder of the prostate gland can be suspected (whatever the purpose of the consultation) leading to the decision of further specific analyses necessary for the diagnosis. If prostate troubles were not the motive of the consultation, the rigorous and complete clinical evaluation will permit to discuss the complementary exams. This is not only intellectually satisfying but also makes easier to justify further exams as it is now the rule. Hence, a pet-owner will accept more easily secondary analyses if a clinical abnormality is already noticed. Furthermore, the prostate is well-known in Human Medicine for its clinical consequences. Pet-owners are often receptive for their dog, leading to an easy discussion and highlighted consent. Nevertheless, as incidence of tumours are less frequent in dogs than Humans, a special focus shall be done on benign affections of the prostate.

Decision for the treatment relies on clinical findings and also on imaging examination (prostatic lesions and associated disorders). It is essential to balance clinical and imaging findings before the outset of the treatment. Benign prostate hypertrophy (BPH) is a very frequent affection in the old dog. It can be difficult to initiate a therapy while the dog doesn’t demonstrate any symptoms but as a positive detection of the disease (clinical exam and urinary analysis). Even though, BPH predisposes to further complications such as prostatitis and prostatic cysts. Current therapies of prostatic troubles are generally speaking well tolerated in the old dog.