PATHOLOGY OF THE PROSTATE GLAND IN DOGS

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DECLARATION

I hereby declare that this thesis entitled **"PATHOLOGY OF THE PROSTATE GLAND IN DOGS"** is a bonafide record of research work done by me during the course of research and that this thesis has not previously formed the basis for the award to me of any degree, diploma, associateship, fellowship or other similar title, of any other University or Society.

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Certified that the thesis entitled "**PATHOLOGY OF THE PROSTATE GLAND IN DOGS**" is a record of research work done independently by **Dr. Dhanya Menon** under my guidance and supervision and that it has not previously formed the basis for the award of any degree, diploma, fellowship or associateship to her.

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Dhanya Menon

CONTENTS

LIST OF TABLES

LIST OF FIGURES

10.	Glandular hyperplasia of the prostate: Papillary proliferation of acinar cells. Cells appear tall columnar with basally placed nucleus. H&E x 400
11.	Cystic hyperplasia of the prostate: Cystic dilatation of the acini, lined by flattened cells, accumulation of pink staining secretion in the acini. H&E x 400
12.	Cystic hyperplasia of the prostate: Large cystic acini with accumulated secretion and infiltration of mononuclear cells in the interstitial stroma H&E x 400
13.	Complex hyperplasia of the prostate: Papillary proliferation of the acinar epithelium and cystic acini with accumulated secretion. H&E x 400
14.	Squamous metaplasia of the prostate: Metaplasia of the columnar type of acinar cells in to a squamous type. H&E x 1000
15.	Acute prostatitis and prostatic hyperplasia: Intense infiltration of neutrophils in the interstitial tissue together with proliferation of acinar cells. H&E x 250
16.	Suppurative prostatitis: Complete destruction of the prostatic parenchyma with formation of cystic spaces containing accumulated secretion and inflammatory cells. H&E x 100
17.	Suppurative prostatitis: Dilated prostatic acini lacking an epithelial lining, pink staining secretion together with neutrophils and desquamated cells within the acini. H&E x 400
18.	Chronic prostatitis: Accumulation of mononuclear cells within the interstitial stroma and congestion of blood vessels. H&E x 400
19.	Prostatic atrophy: Shrunken and collapsed acini seen as irregular slits, proliferation of fibrous tissue and smooth muscle. H&E x 100

20.	Prostatic atrophy: Interstitial fibrous tissue proliferation .H&Ex400
21.	Prostatic adenocarcinoma: Hyperchromatic, anisokaryocytic sheets of cells filling the lumen of the acini. H&E x 400
22.	Prostatic adenocarcinoma: Loss of architecture of prostatic parenchyma with proliferating sheets of cells. H&E x 400
23.	Oval or elongated disorderly arranged prostatic epithelial cells showing aberrant nuclear patterns like karyomegaly and anisokaryosis. H&E x 1000
24.	Acid phosphatase activity appearing as blackish deposits in cryostat section of the neoplastic prostate. Gomori's staining method x 1000
25.	Hyperplastic prostate- acid phosphatase activity appearing as blackish deposits. Gomori's staining method x1000
26.	Impression smear of the normal prostate: Prostatic epithelial cells with minimal to moderate enzyme activity seen as black dots. Gomori's staining method x 400
27.	Impression smear of the hyperplastic prostate: Hyperplastic prostatic epithelial cells with more enzyme activity, seen as intense black granular deposits. Gomori's staining method x 400

Introduction

1. INTRODUCTION

Prostate, the only accessory sex gland of the male dog, is a musculo glandular organ encircling the neck of the urinary bladder. It plays an important role in the reproductive performance of the male dog. The prostate starts to develop before the dog reaches puberty and attains its maximum size by the time the dog is two years old. The prostatic fluid forming the major portion of the canine ejaculate contains a variety of constituents like citric acid, calcium, zinc, acid phosphatase and fibrinolysin, which aids in sperm motility and nourishment.

The growth and functional status of the prostate is androgen dependent. Hormonal imbalances can lead to development of pathological changes in the gland. Prostate disorders are very common in aged dogs. The prevalence of prostate disorders is more than actually reported as many cases of hyperplasia, prostatitis and neoplasia are asymptomatic and remain undiagnosed.

The canine prostate is considered to be a suitable animal model for the study of prostate disorders in human beings as it is morphologically similar to the human prostate (Bashi *et al.* 2003) .Of hundreds of species of mammals, only dogs and humans are known to develop prostate diseases like benign prostate hyperplasia and prostate cancer. Prostate hyperplasia is very common in ageing men and has been estimated to be present in 100 per cent of intact old dogs. Prostate cancer is astoundingly heterogenous in its biological behaviour and ranks as one of the most significant challenges faced by researchers in the field of oncology. With exception of skin tumours it represents the most common malignant transformation occurring in humans (Eschenbach, 1999). Prostate cancer appears to be rare in dogs and occurs with relatively high frequency in castrated animals. Comparative studies in the canine prostate may reveal new elements to a better understanding of the pathology of prostate carcinoma in humans.

Autopsy studies focussing on the pathology of the canine prostate are scanty. Prostate diseases are no less a killer in dogs than it is in men. Considering its significance, an in depth study on the various pathological disorders commonly affecting the canine prostate gland was undertaken with the following objectives.

1. Correlate the morphometry of the prostate with the pathological conditions affecting the prostate gland.
2. Study the gross and histopathological features of affections of the prostate
3. Correlate the presence of acid phosphatase activity of the glandular tissue with the pathological conditions.
4. Study the role of bacterial infections in prostate pathology.

Review of Literature

2. REVIEW OF LITERATURE.

2.1 PROSTATIC ANATOMY AND HISTOLOGY

Dyce *et al.* (1996) stated that the prostate comprises of a compact mass that encircles the bladder neck, and a small disseminate part spread within the urethral mucosa. A dorsal groove and internal septum divide it into right and left lobes, which are subdivided into lobules by finer septa that radiate outwards to the capsule.

Kustritz and Klausner (2000) stated that the prostate is the only accessory sex gland of the male dog. It is surrounded by a fibro muscular capsule and is divided into two lobes by the median raphe. Histologically the gland is divided into different lobules by the smooth muscle and the glandular lining cells differed from low cuboidal to high columnar type.

2.2. EFFECTS OF AGE AND BODYWEIGHT ON PROSTATE

Bloom (1954) opined that weight and size of the prostate gland was variable depending on the age and breed. The normal ratio recorded varied from 0.1 to 0.7 g with an average of 0.4 g of prostate to 1 kg of body weight.

Gordon (1961) observed that weight of the prostate increased with the bodyweight of the animal. He stated that all dogs over five years of age showed enlargement of the prostate gland.

O'shea (1963) stated that Scottish terriers had a prostate gland that was larger than the prostate glands of other dogs of similar weight and age.

Howard (1969) noticed that most of the prostate disorders occurred in dogs over five years of age.

James and Heywood (1979) examined the prostate glands of 198 Beagle dogs between the age of 37 weeks and eight years and stated that less than five per cent of glands weighed less than 10 g where as over 50 per cent exceeded 20 g.

Berry *et al.* (1986 a) reported that testosterone secretion and ageing were paramount factors in predicting prostate weight and that the weight of the organ increased up to four years and then reached a plateau.

Lowseith *et al.* (1990) stated that the weight and volume of the prostate increased with age. They recorded a ratio of 1.08± 0.22g/kg body weight at three years of age, which increased to 2.64±0.37g/kg at 14 years of age.

Kraweic and Heflin (1992) reported that prevalence of prostate disorders increased with age. Dobermann dogs were reported to have a high prevalence of prostate diseases.

Waters *et al.* (1996) compared the age at detection of prostate cancer in humans and dogs and concluded that the development of prostate cancer in dogs and humans were similarly influenced by age.

Atalan *et al.* (1999) demonstrated that prostate weight and volume were related to body weight and age in entire dogs and indicated that prostate width and length were the best predictors of prostate volume and weight.

The normal size of the prostate varied with age, breed and body size. (Kustritz and Klausner, 2000; Davidson, 2003)

2.3. PATHOLOGY

Kraweic and Heflin (1992) studied prostate diseases in 177 dogs. The most common prostate disease identified was prostatitis, followed by prostatic cyst,

prostatic adenocarcinoma and benign hyperplasia. The most common disease identified in neutered dogs was prostatic adenocarcinoma.

2.3.1 Benign Prostatic Hyperplasia (BPH)

2.3.1.1 *Factors of etiological significance*

Benign Prostatic Hyperplasia is a spontaneous and age related change of intact male dogs. (Gordon, 1961; James and Heywood, 1979 ; Barsanti and Finco, 1995).

Brendler *et al.* (1983) in their study reported that with age, the prostate developed an increased sensitivity to serum testosterone such that lower testosterone levels in aged dogs maintained larger glands.

Isaacs (1983) stated that the prostate with BPH had an increased ability to metabolise androgen and a high correlation existed between the size of the prostate and the ability to form 5 alpha dihydro testosterone from testosterone.

Zirkin and Strandberg (1984) demonstrated that prostate weight increased steadily in Beagles from two to six years of age, paralleled by a progressive increase in the incidence of BPH.

Berry *et al.* (1986 b) noticed that BPH occurred with high incidence in human beings and dogs. They reported that 50 per cent of dogs had histologic evidence of BPH by four to five years of age.

Bell *et al.* (1991) stated that BPH developed only in intact dogs and not in neutered dogs.

Hyperplasia of prostate was evident at about five years of age with the incidence and degree increasing with advancing age (Ladds, 1993).

Benign prostate hyperplasia was observed initially in intact dogs between one and two years of age, with prevalence increasing linearly so that 60 per cent of intact male dogs were affected by the age of six (Klausner *et al.* 1995).

More than 80 per cent of intact male dogs over five years of age exhibited BPH and their prostate volume increased two to six times than that of normal dogs of similar body weights (Puri *et al.*, 2002).

2.3.1.2 ***Gross pathology***

Runnells (1953) reported that a hyperplastic prostate was enlarged with smooth or nodular surface. The cut surface showed cysts and distinct lobulation with nodules surrounded by heavy connective tissue stroma.

Bloom (1954) noticed that in canine prostate hyperplasia, the gland was severely enlarged with the outer surface smooth or irregularly nodular. The length of the gland showed a greater increase in dimension than width. On sectioning the lobules varied in size and were outlined by wide irregular whitish grey bands of stromal tissue, along with cysts containing clear or cloudy fluid, irregularly distributed through out the parenchyma.

Archibald and Cawley (1956) observed that the capsule of hyperplastic canine prostate was extremely thin, transparent and vascular.

Diffuse glandular hyperplasia of the prostate, which might be accompanied by cyst formation, and stromal hyperplasia, was very common in older dogs, but has not been shown to be a preneoplastic change (O'shea, 1963).

Pearson and Gibbs (1971) stated that hyperplasia, the most common pathological change of the canine prostate, was associated with marked enlargement of the gland.

Gilson *et al.* (1992) observed a pale tan, firm prostate mass well encapsulated by fibrous tissue in a nine year old Labrador Retriever. On sectioning there were many small cystic spaces interspersed with thick, firm, white bands of tissue.

Klausner *et al.* (1995) suggested that canine prostate hyperplasia occurred in two phases, glandular and complex. Glandular hyperplasia was common in dogs less than five years and was characterised by symmetric enlargement of the prostate. Complex hyperplasia common in dogs over five years was characterised by asymmetric enlargement of the prostate.

Jones *et al.* (1997) observed that in prostate hyperplasia the gland was enlarged because of an increase in both, the size and number of glandular acini, augmentation of fibrous tissue and smooth muscle of the septa and supporting structures

Davidson (2003) opined that hyperplastic prostate was symmetrically enlarged, smooth and contained small intra parenchymal cysts with bloody fluid.

2.3.1.3 *Histopathology*

Runnells (1953) noticed cystic dilatations of the acini lined by atrophied epithelium together with proliferation of epithelial cells that resulted in papillary infolding into the acini.

Bloom (1954) observed that glandular hyperplasia was characterised by increase in the glandular tissue and irregularity in the size and shape of the acini. The lining epithelial cells were tall columnar and formed villous and papillary intra luminal projections. Cystic hyperplasia was characterised by cysts lined by flattened cuboidal epithelium. The cystic lumen contained desquamated epithelium and accumulated secretion. The inter lobar stroma frequently increased in connective tissue with accumulation of inflammatory cells.

Berg (1958) suggested that prostate hyperplasia in the dog was due to proliferation of epithelial cells lining the acini of the prostate, along with moderate proliferation of stromal tissue.

Leeds and Leav (1969) reported cases of hyperplasia with and without concurrent inflammation. Hyperplastic prostate without inflammatory changes contained dilated acini, lined by hyperplastic tall columnar cells that had eosinophilic granular cytoplasm and ovoid basal nuclei. Dilated acini were surrounded by smooth muscle and fibrous connective tissue. Hyperplasia with concurrent inflammation was characterised by the presence of inflammatory cells.

Epstein (1976) in his study on the morphologic correlation between aspiration cytology and needle biopsy histology of the prostate, observed that benign prostatic epithelium was aspirated as sheets of cells with a honeycomb pattern, which had round or oval nuclei and a fine granular chromatin pattern.

Brendler *et al.* (1983) observed that complex BPH in canines represented a histological pattern in which cystic, glandular, atrophic and normal elements were intermixed.

Isaacs (1983) suggested that hyperplasia in the canine prostate was diffuse, that occurred throughout the gland and primarily involved the glandular cells, with less stromal involvement. He concluded that not only age, but also a net increase in the dihydro testosterone formation in the prostatic tissue was responsible for the development of BPH.

Zirkin and Strandberg (1984) concluded that proliferation of glandular and stromal components, and increase in epithelial size resulted in prostate enlargement during ageing.

Coffey and Walsh (1990) observed that BPH was a complex pathologic process that varied with age and produced a gland that was composed of a mixture of glandular, cystic and stromal hyperplasia juxta positioned with foci of atrophy.

Gilson *et al.* (1992) reported that nodular hyperplasia of prostate was characterised by simple tall columnar epithelial cell lined ducts and acini, separated by large amount of smooth muscle stroma. Epithelial cells were monomorphic with basal nuclei and bright eosinophilic granular cytoplasm.

Klausner *et al.* (1995) stated that in glandular hyperplasia proliferation was primarily epithelial with increase in number and size of secretory cells and with minimal stromal involvement. He suggested that in complex hyperplasia there was prominence of stromal component together with dilated cystic alveoli filled with eosinophilic material.

Jones et al. (1997) noticed that in prostate hyperplasia, there was an increase in number and height of the epithelial cells lining the prostate acini. The augmented cellular population was accommodated by formation of tortuous folds in the acinar lining. In cystic hyperplasia there was formation of cysts lined by flattened and stretched epithelium.

Shah *et al.* (2001) identified post atrophic hyperplasia of the prostate in 40 men who underwent radical prostatectomy. The features included dilated ducts or acini with adjacent foci of small crowded glands with an atrophic appearance. Nuclear enlargement with prominent nucleoli was also observed.

2.3.2 Squamous metaplasia

Leeds and Leav (1969) stated that the identifying characteristic of squamous metaplasia of prostate was the presence of concentrically arranged squamous cells

that were flattened towards the acini, which contained eosinophilic material with pyknotic nuclei.

Brendler *et al.*(1983) concluded that squamous metaplasia was induced by increased estrogen concentration either by exogenous administration or from relative increase in serum estrogen concentration that occurred in normal aged dogs as androgen secretion declined.

Kraweic and Heflin (1992) noticed that squamous metaplasia was a morphologic change from normal cuboidal or columnar epithelium to squamous epithelium within the prostate.

Metzger and Hattel (1993) reported a case of squamous metaplasia consistent with prostatitis in a bilaterally cryptorchid dog with sertoli cell tumor. The cytologic examination of prostatic fluid revealed numerous red blood cells, degenerated neutrophils containing variable numbers of bacteria, and numerous squamous epithelial cells.

2.3.3 Prostatic and Paraprostatic cysts

2.3.3.1 *Gross pathology*

Brodey and Prier (1962) observed a case of prostatic cyst studded with stony cauliflower like masses, which also had strands of fibrinous material adherent to it.

Pearson and Gibbs (1971) observed an orange sized cyst in a six year old Boxer, attached to the prostate gland, that contained 800 ml of viscid, slightly turbid white secretion.

Weaver (1978) described prostate cysts in 12 dogs. The content of the cysts varied from colourless pink or red serous material through a grey or cloudy

appearance to a dark brown viscid material with fibro necrotic debris. The smallest cyst had a volume of 90 ml and the largest approximately a volume of 800 ml. The degree of attachment to the prostate varied from relatively limited pedicle to extensive adhesions.

Weaver (1981) observed prostate cysts of variable size, colour and position, thin walled and thick walled which had a capacity of approximately 300 ml.

White *et al.* (1987) stated that prostate cysts in dog included cystic change associated with androgen dependent BPH, as well as retention and paraprostate cysts which were observed as cavitating lesions with a distinct wall containing straw or brown coloured fluid.

Bell *et al.* (1991) noticed intra prostatic cysts or cavities in cases of canine prostate carcinomas.

Kraweic and Heflin (1992) stated that paraprostatic cysts were most commonly seen in the craniolateral or caudal aspect of the bladder and prostate in older large breed dogs.

Balasubramanian (1993) reported a case of intraabdominal paraprostatic cyst that weighed 900g and contained 1.2 litres of serosanguinous fluid.

Giard and Despots (1995) observed that paraprostatic cysts were thin walled structures outside the prostatic parenchyma that often contained malodorous fluid with fibro necrotic debris.

Black *et al* (1998) reported that the prevalence of prostatic cysts in adult intact male dogs was 14 per cent and that approximately 42 per cent were infected with bacteria.

Ramani *et al.* (2001) reported a paraprostatic cyst in a four year old Doberman, which contained approximately 500 ml of yellow coloured fluid.

Davidson (2003) suggested that prostatic cysts were produced as a result of ductal occlusion from squamous metaplasia and were present as multiple cavitating areas or large fluid filled structures extending into the abdomen or pelvic canal.

2.3.3.2 *Histopathology*

Bloom (1954) noticed that prostatic cysts were enveloped by a thin fibrous capsule and lined by flattened endothelial cells. The lumen contained pale eosinophilic homogenous or granular material.

The outer portion of prostatic cyst wall consisted primarily of dense collagenous tissue infiltrated with foci of inflammatory cells predominantly of mononuclear type. The inner portion of the cyst wall consisted of a zone of granulation tissue in which were imbedded many spicules and masses of osteoid. (Brodey and Prier, 1962).

Schuhrke and Kalpan (1978) observed that cuboidal, low columnar, transitional or stratified squamous epithelial cells lined the prostatic utricle cysts. Cyst wall was composed of smooth muscle and fibrous connective tissue, and were noticed to have areas of squamous metaplasia.

Weaver (1978) observed that the prostatic cyst wall was lined by transitional epithelium and contained fibrous tissue, together with severe inflammatory reaction predominantly of neutrophilic type.

Jeyaraja *et al.* (2003) reported a case of paraprostatic cyst in a Dobermann aged six years in which the microscopical examination of the cystic fluid showed numerous erythrocytes and leukocytes.

2.3.4. Prostatitis

2.3.4.1. *Gross pathology*

Bloom (1954) reported that in acute prostatitis, the gland was symmetrically or irregularly enlarged with a part of or the entire organ converted into an abscess. In chronic prostatitis the gland was of small or normal size, firmer, nodular with adhesions to neighbouring structures.

Tomilson and Farrow (1981) observed a thick walled prostatic abscess in a four year old dog with an interstitial cell tumor of testis.

Mapes (1987) reported a case of prostatic abscess that caudally displaced the urinary bladder and resulted in perineal herniation.

Davidson (2003) noticed that in acute prostatitis the prostate was enlarged and asymmetrical with fluctuant areas of abscesses, along with firm areas and adhesions.

2.3.4.2 *Histopathology*

Bloom (1954) observed that in suppurative prostatitis the lumen of the ducts and acini, as well as the stroma contained infiltrations of polymorphonuclear leukocytes, occasional lymphocytes and histiocytes. In chronic prostatitis there was focal or diffuse proliferation of fibrous tissue, which contained varying numbers of lymphocytes and plasma cells.

Morton (1977) reported a case of allergic prostatosis in a 25 year old man, where the prostate was markedly enlarged, and revealed eosinophilic infiltration, edema, vascular dilation and fibro muscular hyperplasia on histopathology.

O'dea *et al.* (1977) observed non-specific granulomatous prostatitis, in which the stromal infiltrate contained epitheloid cells, lymphocytes, plasma cells, a few eosinophils, and scattered multinucleated giant cells.

Barsanti *et al.* (1983) stated that cytologic evidence of inflammation in the ejaculate correlated better with histologic evidence of prostatic inflammation than with results of bacterial culture of prostatic tissue.

Ladds (1993) observed that in acute prostatitis, there was focal or diffuse suppurative inflammation with accumulation of neutrophils in the acini and stroma. In chronic prostatitis lymphocytes were the predominating type of inflammatory cell that invaded the stroma.

Klausner *et al.* (1995) suggested that suppurative and chronic prostatitis were the most common types. They revealed the presence of epithelial cells, degenerated neutrophils, lymphocytes, plasma cells and bacteria in exfoliative cytology in cases of canine prostatitis.

2.3.5 Prostatic atrophy

2.3.5.1 *Gross pathology*

The atrophic prostate was shrunken, hard, firm and difficult to cut (Bloom, 1954).

O'shea (1963) examined the prostates of 331 dogs and reported that from about 11 years, there was a steady decline in the weight of the prostate although histological evidence of atrophy was not seen.

Ladds (1993) stated that atrophy of the prostate occurred in senility and following castration and that gland became small and firm in prostatic atrophy.

2.3.5.2 *Histopathology*

Bloom (1954) suggested that the microscopic appearance in prostatic atrophy varied. The epithelium decreased in size shortly after castration and in well advanced atrophy, the persisting acini collapsed and existed as slits with obliteration of lumen and increased fibrous proliferation in the interstitial tissue.

Mc entee (1990) observed that in prostatic atrophy, the epithelium became flattened and basophilic, along with collapse of acini and abundant inter glandular fibro muscular tissue.

Ladds (1993) described that in prostatic atrophy, the acinar epithelium became smaller, basophilic and characterless. The acini collapsed and persisted as irregular slit like spaces and the smooth muscle in the capsule and trabeculae was replaced by dense fibrous tissue that gave the organ it's firmness.

De Marzo *et al.* (1999) proposed the term proliferative inflammatory atrophy of the prostate to designate discrete foci of proliferative glandular epithelium with the morphological appearance of simple atrophy or post atrophic hyperplasia that occurred in association with inflammation. The key feature included the presence of two distinct cell layers lining the acini, mononuclear or polymorphonuclear inflammatory cells in both the epithelial and stromal compartments and stromal atrophy with variable amounts of fibrosis.

Niu *et al.* (2001) stated that prostate gland was an androgen sensitive organ and that the prostatic stromal cells including the smooth muscle cells and fibroblasts diminished and underwent a serial pathological change of atrophy and apoptosis after castration.

Shidaifat and Daradka (2002) studied the effect of androgen ablation in intact and castrated dogs. Histological evaluation of the prostate from castrated dogs

revealed that secretory epithelial cells became atrophied within one week of castration and underwent massive necrosis after two weeks. Other changes included basal cell hyperplasia with no signs of differentiation into secretory epithelial cells; along with mesenchymal cell proliferation and increase in inter acinar fibro muscular tissue.

Niu *et al.* (2003) stated that the glandular epithelial cells changed gradually from the high-columelliform pre castration to the cuboidal form post castration, which finally turned to flatcytes and small dark cells. They observed that the glandular lumen shrank and components of the stroma diminished in size after castration.

2.3.6 Prostatic calculi

Jones et al. (1997) reported that prostatic calculi were usually small, hard, white and spherical which chiefly consisted of phosphates and carbonates of calcium deposited around a nucleus that was practically always an organic material.

Kustritz and Klausner (2000) stated that prostatic calculi were rare in dogs and typically small, often identified as an incidental finding.

2.3.7 Prostatic Intraepithelial Neoplasia (PIN)

Bostwick and Brawer (1987) stated that prostatic intraepithelial neoplasia was considered a precursor of invasive carcinoma, characterised by proliferation and anaplasia of cells lining prostatic ducts and acini. The highest grade of PIN represented carcinoma *in situ*.

McNeal (1988) defined duct acinar dysplasia as a premalignant lesion characterised by cytologic, and especially nuclear abnormalities that resembled those of carcinoma and affected the lining epithelial cells of pre-existing ducts and acini.

Waters and Bostwick (1997) reported that prostatic intraepithelial neoplasia was the most likely precursor of prostate cancer and stated that high grade prostatic intraepithelial neoplasia was frequently present in the prostate of elderly sexually intact male dogs. Canine high grade prostatic intraepithelial neoplasia showed cytological features identical to human counterpart that included cell crowding, loss of polarity, nuclear and nucleolar enlargement.

Acquilina *et al.* (1998) reported that high grade PIN was the most likely precursor of prostate cancer and was present in a small but substantial number (three per cent) of military working dogs.

Berman *et al.* (2000) observed foamy gland high grade prostatic intraepithelial neoplasia with expansive foci of enlarged, pale and crowded glands with complex and somewhat atypical architecture. The cells lining the glands were plump ovoid, arranged haphazardously with abundant foamy cytoplasm and small hyperchromatic nuclei.

2.3.8 Prostatic carcinoma

O'shea (1963) reported seven cases of prostatic neoplasms, all of which occurred in dogs more than nine years of age.

Allen *et al.* (1991) observed that the prostatic carcinoma developed rarely in dogs less than 10 years old.

2.3.8.1 *Effects of castration*

Obradovich *et al.* (1987) reported that castration at any age showed no sparing effect on risk of development of prostate carcinoma in dogs and suggested that etiology of prostate cancer may not be exclusively related to testicular hormones but also to non testicular androgens.

Bell *et al.* (1991) stated that prostatic adenocarcinoma was most frequent in eight to 10 year old dogs, sexually intact dogs and in dogs castrated at a younger age.

Klausner *et al.* (1995) stated that prostatic carcinoma was an uncommon highly malignant disease of intact and castrated male dogs. They suggested non testicular androgens had a role in development of the disease in neutered dogs and the androgen independent basal cells which persisted after neutering provided the cell of origin for development of prostate cancer in both neutered and intact dogs. Neutered dogs were more likely to have poorly differentiated tumours, although well-differentiated tumours with evidence of gland formation also occurred in neutered dogs.

Kustritz and Klausner (2000) stated that identification of an enlarged prostate in a castrated dog should raise the index of suspicion of neoplastic disease.

Teske *et al.* (2002) in their study revealed that dogs with prostate carcinoma were significantly older than dogs with other prostatic diseases and stated that castration favoured tumor progression in the prostate.

Davidson (2003) stated that the risk of prostatic carcinoma was double in case of castrated dogs when compared to intact dogs.

2.3.8.2 *Gross pathology*

Bloom (1954) noticed that the neoplastic prostate was small, normal, or of larger size, hard and nodular with dense capsule and adherence to adjacent structures. The cut surface was greyish or yellowish, granular, dry, opaque, stony, dense and relatively homogenous.

O'shea (1963) observed that the neoplastic prostate was enlarged and irregular, or small and firm which contained fluid filled cysts, abscess and areas of haemorrhage.

Leav and Ling (1968) observed that the neoplastic prostate was usually large, irregular and often cystic.

Weaver (1981) stated that carcinomatous gland was more firm than prostate of a young dog but less firm than cases of chronic prostatitis .He noticed an increased prevalence of prostate cancer in medium to large sized dogs.

Evans *et al.* (1985) reported a case of prostatic adenocarcinoma in a seven year old castrated dog where the prostate was of normal size. The tumor had metastasised to the internal iliac lymph nodes.

Kraweic and Heflin (1992) stated that prostate cancer was not always associated with prostatomegaly. The carcinomatous gland was of normal size, firm, irregular and adhered to the pelvic canal.

Jones et al. (1997) observed that the neoplastic prostate was enlarged, distorted and firm with yellow-tan nodular tumours.

2.3.8.3 *Histopathology*

Bloom (1954) observed that prostatic adenocarcinoma was the commonest among the prostatic neoplasms .The acini was large or small, lined with cuboidal or columnar cells. Multiacinar arrangement that consisted of atypical cells forming secondary acini, tubular and papillary type were also present .The stroma was scanty or abundant and contained irregular cell nests and sparsely scattered small acini. In some lesions, the cells were anaplastic and contained irregular giant sized, hyperchromatic, bizarre nuclei with many mitosis.

O'shea (1963) classified prostatic adenocarcinoma in to anaplastic, small acinar and large acinar types. Anaplastic regions were composed of solid sheets of loosely or densely packed cells, small acinar type showed the presence of small rounded

acini, that lacked papillary infolding where as the large acinar type revealed large acini with epithelial infoldings that subdivided the lumen. Simple, stratified, columnar, or cuboidal epithelium with eosinophilic vacuolated cytoplasm that contained large nuclei with one or more nucleoli, lined the acini.

Leeds and Leav (1969) reported a case of prostatic adenocarcinoma in a 11 year old dog which on histopathology revealed polygonal cells, with large vesicular nuclei and prominent nucleoli, arranged in small nests.

Epstein and Fatti (1976) classified prostatic carcinoma in to medullary- alveolar, tubular scirrhous and mixed types. Medullary- alveolar types grew in nodular pattern with usually little cellular anaplasia. Tubular scirrhous carcinoma infiltrated the stroma as single acini, cords or nests of cells with distinct anaplasia. Mixed type showed features of both.

Zaloudek *et al.* (1976) reported a case of adenocarcinoma with endometrial features in the prostate, which revealed well defined closely, apposed glands lined by a layer of columnar cells together with papillary projections of glandular epithelium and intra glandular bridging. The tumor cells had basally located nuclei, prominent nucleoli and abundant eosinophilic cytoplasm that were occasionally vacuolated.

Schellhammer *et al.* (1977) identified three distinct microscopic patterns of prostatic involvement in cases of transitional cell carcinoma of bladder. Ductal and ducto-acinar, involvements occurred with diffuse involvement of ducts and acini with and without penetration of basement membrane. The third pattern included extensive neoplastic invasion of stroma with no ductal and acinar involvement.

Golimbu *et al.* (1978) studied the differences in the pathological characteristics and classified prostate cancer as well differentiated, moderately differentiated and poorly differentiated. Tumours showing well differentiated small gland pattern with

minimal invasive features were classified as well differentiated. Tumours showing multiple acinar patterns, including small, medium and cribriform types, with cells progressively smaller and more irregular nuclei were grouped as moderately differentiated. Finally, tumours showing solid masses of cells with, little cytoplasm and irregular nuclei, diffusely infiltrating the prostate with complete loss of acinar pattern was classified as poorly differentiated.

Kovi *et al.* (1985) recognized three distinct patterns of ductal penetration for prostatic carcinoma. They concluded that the prostatic carcinoma cells had the ability to penetrate the wall of benign ducts and progressively replace the normal epithelial elements. The general frameworks of the ducts were preserved.

Durham and Dietze (1986) classified prostatic adenocarcinoma into alveolar papillary, acinar and organoid (rosette) types. Alveolar papillary pattern was the most frequently observed histologic type and consisted of papillary ribbons of epithelial cells that projected into various sized alveolar like spaces surrounded by connective tissue. The individual cells had large cytoplasmic vacuoles with proteinacious droplets and mucoid material that displaced the nucleus and resembled a signet ring. The acinar pattern had gland formation with prominent fibro desmoplasia. The organoid pattern had an overall alveolar pattern in which each alveolus was filled with clusters of tumor cells that formed small rosettes, with nuclei located at the periphery.

Bell *et al.* (1991) described intra-alveolar, small acinar and poorly differentiated prostatic adenocarcinoma in dogs. The intra-alveolar prostatic adenocarcinoma revealed large prostatic alveoli with multilayered neoplastic epithelium that formed secondary acini and irregular papillary processes. Small acinar type showed irregular acini and nests of neoplastic epithelial cells embedded in abundant fibro muscular stroma. Poorly differentiated prostatic adenocarcinoma was characterised by

neoplastic cell growth in nests and sheets with moderate amount stroma and no evident gland formation.

Jones et al. (1997) stated that microscopically the prostatic adenocarcinoma revealed acinar formation within a proliferating connective tissue stroma. In some cases the neoplasm was undifferentiated with less or no tendency to form acini

Cornell *et al.* (2000) studied 76 cases of prostatic carcinoma in canines. Prostatic carcinoma was classified based upon the presence of glandular, urothelial, squamous, or sarcomatoid differentiation. Adenocarcinoma was the most frequent type encountered.

Kustritz and Klausner (2000) opined that in addition to neoplastic cells, cancerous prostate might also have inflammatory changes, necrosis, BPH, hemorrhages and fibrous tissue proliferation.

Davidson (2003) observed that adenocarcinoma was the commonest among the prostatic carcinomas followed by locally invasive transitional cell carcinoma, lymphoma, squamous cell carcinoma, adenoma, leiomyosarcoma, leiomyoma, fibroma, and hemangiosarcoma.

2.3.8.4 *Metastasis*

Grant (1957) concluded that carcinoma of the canine prostate was a distinct, highly malignant and widely metastasising neoplasm of low frequency that occurred independent of alterations in the balance of sex hormones and associated changes in the prostate.

Catalona and Scott (1978) suggested that prostatic carcinoma could spread by local invasion, lymphatics and by haematogenous dissemination. They observed that

the earliest evidence of invasion was seen often in the perineural spaces of the intra prostatic nerve.

Bell *et al.* (1991) stated that pulmonary metastasis in dogs with prostatic adenocarcinoma was greater than 40 per cent.

2.4. MICROBIOLOGICAL STUDIES

Reeves (1963) reported a case of prostatic abscess in an eight week old Springer spaniel from which alpha haemolytic streptococci was isolated.

Parker (1975) reported a case of prostatic abscess in a Springer spaniel, from which *Enterobacter sp.* was isolated.

Tomilson and Farrow (1981) isolated *Staphylococcus aureus* from a case of prostatic abscess in a four year old dog.

Barsanti *et al.* (1983) observed that *Escherichia coli* was the most frequently isolated organism from the culture of prostatic fluid in dogs.

Bauer (1986) isolated *Escherichia coli, Pseudomonas sp.*, and *Proteus vulgaris* from three different cases of prostatic abscess in dogs.

Rubin (1990) opined that bacterial prostatitis occurred alone or as complication of other prostatic diseases. *Escherichia coli* was the most common pathogen encountered, but other pathogens like *Pseudomonas sp., Proteus sp., Staphylococcus sp.* and *Streptococcus sp.* were also obtained.

Kraweic and Heflin (1992) isolated *Escherichia coli, Proteus sp., Staphylococcus sp., Klebsiella sp., Enterobacter sp., and Haemophilus sp.* from cases of bacterial prostatitis in dogs.

Klausner *et al.* (1995) stated that *Escherichia coli* was the most common bacterial organism isolated in cases of dogs with bacterial prostatitis.

Johnston *et al.* (2000) reported that fungal prostatitis was rare and associated with systemic fungal infection in the dog.

Kustritz and Klausner (2000) revealed that granulomatous prostatitis could result from fungal infections like blastomycosis and cryptococcosis.

Davidson (2003) stated that prostatitis was concomitant with other prostatic diseases and *Escherichia coli* was the most common pathogen isolated followed by *Staphylococcus sp., Streptococcus sp., Proteus sp., and Pseudomonas sp.*

2.5 HISTOCHEMICAL STUDIES

Bloom (1954) reported that acid phosphatase occurred in small amounts in canine prostate as compared to man and often no positive reaction was obtained.

Pearse (1968) demonstrated acid phosphatase activity in tissue sections by Gomori's method.

Zaloudek *et al.* (1976) stated that it was the enzyme histochemical studies that offered the strongest support for the prostatic origin of tumor. Acid phosphatase was characteristically present in large quantities in the prostatic adenocarcinoma.

Filipe and Lake (1983) reported that the presence of prostatic acid phosphatase could be related to the carcinoma of the prostate.

Bell (1995) stated that the effects of acid phosphatase levels were useful in detection of prostatic carcinoma in canines.

Kaneko et al. (1997) stated that prostatic acid phosphatase was a tumor marker, that allowed the diagnosis of otherwise undifferentiated prostatic carcinoma from carcinomas derived from the urinary bladder and colon.

Rinck *et al.* (1998) opined that an elevated serum acid phosphatase concentration indicated prostatic neoplasms.

Vasudevan and Sreekumari (1999) suggested that prostatic acid phosphatase was an important tumor marker as the levels were highly increased in prostatic cancer. They stated that prostatic acid phosphatase was resistant to the action of formaldehyde.

Materials and Methods

3. MATERIALS AND METHODS

The present study was undertaken at the Centre of Excellence in Pathology (CEP), College of Veterinary and Animal sciences, Mannuthy to investigate the pathological conditions affecting the prostate gland in canines and to classify the lesions encountered.

3.1 MATERIALS

3.1.1 **Data collection**

The history and other details regarding the carcasses brought for autopsy to the CEP during the period of study (January 2003-June 2004) were documented after getting the information from the owners.

Data regarding the symptoms, treatment etc were obtained from the Veterinary Hospital, Mannuthy for those cases referred from the hospital for postmortem examination.

3.1.2 **Sample Collection**

One hundred samples of the prostate gland obtained from the carcasses of dogs brought for autopsy to CEP between (January 2003-June 2004) were used for the study. Prostatic fluid was collected aseptically for bacteriological studies in appropriate cases.

3.2 METHODS

3.2.1 **Analysis of Data**

The details regarding the age, breed, history and clinical signs of carcasses brought for autopsy to CEP during the period of study were obtained and recorded. The weight of the carcasses and individual weights of prostate gland were measured.

3.2.2 **Gross examination**

A detailed systematic postmortem examination of the canine carcasses brought for autopsy was conducted. The prostate gland was dissected out separately and carefully studied for gross lesions like changes in size, nodularity, and presence of cyst, abscess or tumours. The gland was bisected by an incision through the median raphe and the cut surface examined. Prostatic urethra was examined for changes in colour and presence of calculi. Representative samples were collected for histopathological and histochemical evaluation. Gross changes in other organs were recorded.

3.2.3 **Histopathological examination**

Representative samples of the prostate gland obtained from the carcasses were fixed in 10% formalin. The tissues were processed by routine paraffin embedding techniques (Sheehan and Hrapchak, 1980). Sections were cut at four micron thickness and stained with routine Haematoxylin and Eosin stain (Bancroft and Cook, 1984) for histopathological studies. Special staining techniques like Gomori's trichrome and Mallory's PhosphoTungstic Acid-Haematoxylin were done whenever required as per the method described by Luna (1968). The stained sections were examined in detail under light microscope and the lesions were classified.

3.2.4 **Enzyme histochemistry**

Representative samples of the prostate gland were fixed in formol calcium and stored at 4^0 C. Acid phosphatase enzyme was localized in prefixed cryostat sections and imprint smears as per the metal precipitation technique described by Gomori (1941).

Acid phosphatase -Gomori lead method

Fixation

Formol calcium at 4^0C.

Sections - Prefixed cryostat sections, Imprint smears

Preparation of the incubating solution

0.05M acetate buffer pH 5.0	10ml
Sodium -Beta-glycerophosphate	32mg
Lead nitrate	20mg

The lead nitrate was dissolved in the buffer before sodium-beta -glycerophosphate was added. The pH of the incubating solution was approximately 5.0

Method

1. Placed sections or smears in the incubating solution at 37^0C for 1/2 to 2hrs.
2. Washed in distilled water.
3. Immersed in one percent ammonium sulfide (fresh), two minutes.
4. Washed well in distilled water
5. Counterstained in methyl green pyronin.
6. Washed in tap water.
7. Mounted in glycerin jelly.

3.2.5 **Microbiological studies**

Bacterial isolation was attempted from the prostatic fluid in all fresh cases and identification of the organisms was done by the method adopted by Cowan (1974).

Results

4. RESULTS

Pathological investigations were carried out on prostate glands obtained from one hundred cases of canines autopsied at the Centre of Excellence in Pathology, College of Veterinary and Animal Sciences, Mannuthy between January 2003 and June 2004. The carcasses were grouped based on age and breed. Of these, eight dogs were below one year of age, 30 were between one and three years of age, 32 between three and five years of age and 30 were above five years of age. The breeds studied were Non descript (34), German shepherd (25), Doberman (9), Crossbreds (9), Spitz (9), Dachshunds (5), Labrador (5), Boxers (3), and Rottweilers (2).

4.1 INFLUENCE OF AGE AND BODY WEIGHT ON THE PROSTATE

The age wise distribution of the prostatic disorders is shown in the Table 1. The distribution of prostatic disorders were 83.33 percent in dogs above five years of age where as it was only 12.5 percent in dogs below one year of age. The incidence of prostatic lesions in dogs between one and three years of age and in dogs between three and five years of age was 13.3 percent and 59.38 percent respectively. A progressive increase in the number of dogs with prostatic disorders was seen with advancing age. Mean age at detection of various prostatic disorders is shown in Table 2.

The relation of the prostate weight to body weight is shown in the Table 3. The prostate weight in grams per kilogram body weight was higher in the older age group of dogs more than five years of age when compared to the other groups.

The age wise distribution of the prostatic circumference and length is given in the Table 4. The average prostatic circumference and length was highest in the older dogs of more than five years of age. The average prostatic circumference for the age groups below one year, between one and three years, between three and five years

and above five years were 4.43, 8.98, 9.77 and 10.67 centimetres respectively, where as the measurements for the average prostate length were 1.99,3.21, 3.33 and 3.91 centimetres respectively.

4.2 INFLUENCE OF BREED ON THE PROSTATE

The distribution of the prostatic lesions based on the breed of the dog is given in the table 5. German shepherds were most frequently identified to have prostatic disease and accounted for 68 per cent of the cases .The average prostate weights were higher for heavier breeds like Rottweiler, German shepherds and Doberman when compared to the lighter breeds like Dachshunds and Spitz (Table 6).

4.3 GROSS PATHOLOGY

Gross lesions were encountered in 49 dogs. Almost all dogs over five years of age showed varying degrees of prostatomegaly. However, this could be detected only in intact dogs and not in castrated dogs. Prostatic atrophy could be detected in three cases including a castrated dog where the body weight was 19kg but the prostate weighed only 3.21g. In a German shepherd aged 15 years, the gland was very much enlarged, which weighed 94.5 g and exerted pressure on the rectum and caused obstruction to the passage of faecal material. In some other cases of prostatic enlargement, the prostate was found to impinge on the prostatic urethra and resulting in retention of urine in the bladder (Fig.1 and 2). In a 10.5 year old dog the obstruction due to prostatomegaly is suspected to have caused the rupture of the urinary bladder.

Grossly the enlarged gland varied in its appearances from diffuse symmetrical enlargement with a smooth surface to asymmetrical enlargement with an irregular surface. The normal bilobed condition was obscured by nodular formations. The prostatic capsule was thin and transparent. Numerous small cysts that contained

milky fluid were observed beneath the capsule. On sectioning, the prostatic parenchyma had a spongy consistency and on closer examination revealed irregularly distributed small cysts containing milky fluid. Sub capsular haemorrhages and wide whitish bands of stromal tissue were also evident (Fig.3).

The prostatomegaly noticed in a Doberman aged six years revealed abscesses of varying size containing inspissated pus streaked with blood along with gross pathological changes in the kidney and urinary bladder. The kidney revealed numerous small pinpoint greyish white spots scattered in the cortex. The bladder mucosa was thickened and revealed petechial hemorrhages. In another dog aged 12 years along with prostatomegaly, kidney lesions were also seen. The kidney was pale in colour and appeared granular and contracted (Fig.4).

In a cryptorchid dog, the prostate was found to be of normal size, but in two castrated dogs, the prostate was shrunken, small, firm and hard to cut. Among one of the castrated dogs a moderately hard tumor mass measuring about 10 centimetres in diameter was observed subcutaneously on the right side of thoracic wall and was seen extending into the pleura and the lungs.

4.4 HISTOPATHOLOGY

Histologically the prostate lesions were classified into proliferative changes, which included hyperplasia of the epithelium and the stroma, inflammatory changes, atrophic changes, metaplastic changes and neoplastic changes. Based on this the lesions were categorised as benign hyperplasia, squamous metaplasia, prostatitis, prostatic atrophy and prostatic adenocarcinoma (Fig.5).

4.4.1 **Benign Prostatic Hyperplasia**

36 cases (73.47 per cent) out of the 49 affected revealed prostatic hyperplasia of varying degrees. Microscopically there were diverse appearances that consisted of

glandular hyperplasia, stromal hyperplasia, cystic hyperplasia and complex hyperplasia where all these types occurred together. Glandular hyperplasia was seen in 21 cases, cystic hyperplasia in seven cases and complex hyperplasia in eight cases. Stromal hyperplasia was always associated with cystic hyperplasia. (Fig.6). This was due to the proliferation of both the connective tissue and smooth muscle component as revealed by cases by special stains like Gomori's trichrome (Fig.7 and 8) and PTAH (Fig.9). In glandular hyperplasia, the lining epithelium was tall columnar and formed papillary intra luminal projections (Fig.10). In cystic hyperplasia, dilated acini of varying sizes were scattered through out the gland. They were lined by flattened epithelium, and the cystic lumen contained desquamated epithelium along with homogenous pale pink staining secretion (Fig.11). In some of these cases mononuclear infiltration was seen in the interstitial tissue (Fig.12). In complex hyperplasia there were areas of glandular and cystic hyperplasia (Fig.13).

4.4.2 **Squamous metaplasia**

A case of squamous metaplasia of prostate was recorded in a German shepherd aged 10.5 years. Microscopically the acinar epithelium showed metaplastic changes with formation of sheets of stratified squamous epithelium that gradually filled the lumen (Fig.14). There was accumulation of neutrophils, lymphocytes, plasma cells and fibrin in the acini and within the stroma.

4.4.3 **Prostatitis**

20 cases (40.82 per cent) of prostatitis were recorded out of the 49 prostates with gross lesions. It was mostly encountered in middle to old aged dogs and was also seen in a seven month old dog. It was also seen along with other prostatic disorders like benign hyperplasia and squamous metaplasia.

4.4.3.1 *Acute prostatitis*

Four out of the 20 cases revealed acute prostatitis. Microscopically there was focal or diffuse accumulation of neutrophils in the peri acinar regions (Fig.15).

4.4.3.2 *Suppurative prostatitis*

This was observed in one case. Multiple abscesses of varying sizes were frequently scattered through out the glandular tissue producing destruction of the involved acini and stroma. Histopathologically the ducts and acini were devoid of an epithelial lining and contained desquamated epithelial cells along with infiltrations of inflammatory cells predominantly of the neutrophilic type (Fig.16 and 17).

4.4.3.3 *Chronic prostatitis*

Chronic prostatitis was observed in 15 cases. It was mostly seen along with cystic prostatic hyperplasia. The prostatic epithelium showed atrophic changes, with accumulation of lymphocytes and plasma cells within the fibro muscular stroma (Fig.18).

4.4.4 **Prostatic atrophy**

Atrophic changes of the prostate were observed grossly in three cases (6.12 per cent). Microscopical examination revealed the presence of shrunken and collapsed acini with obliteration of the lumen, which was seen as slit like spaces (Fig.19). There was fibrous tissue proliferation in the interstitial tissue and the stroma appeared more conspicuous (Fig.20).

4.4.5 **Prostatic adenocarcinoma**

This was observed in two cases. One was in a nine year old nondescript dog and other in an eight year old castrated Doberman pinscher. In the intact dog, the

carcinomatous gland was moderately enlarged. Histopathological examination of the enlarged prostate revealed aggregations of proliferating cells that were densely packed at some foci and loosely packed in other areas. The neoplastic epithelial cells showed anisokaryosis, vesicular nuclei, and narrow rim of basophilic cytoplasm. At times the proliferating sheets of cells were seen separated and encircled by proliferating fibrous tissue (Fig.21).

In the castrated dog, neoplastic cells were seen embedded in abundant fibro muscular stroma. It was characterised by the presence of disorderly arranged oval or elongated epithelial cells that had prominent hyperchromatic nuclei (Fig.22 and 23). Necrosis of the tumour cells was seen in certain locations. In this case a concomitant neoplasm of osteosarcoma was seen along with the prostatic adenocarcinoma. The moderately hard irregular nodular mass that was noticed on the left intercostal space histopathologically revealed spindle shaped cells with hyperchromatic nuclei and multinucleated osteoclasts confirming it as case of osteosarcoma. Neither of the neoplasms showed metastasis.

4.5 HISTOCHEMICAL STUDIES

Acid phosphatase was localised in cryostat sections (Fig.24 and 25) and impression smears of the prostate (Fig. 26 and 27). The presence of acid phosphatase was observed as blackish granular deposits within the prostatic epithelial cells. The enzyme activity was more intense in the neoplastic and hyperplastic prostatic epithelial cells when compared to the normal prostatic cells, which showed only slight activity.

4.6 MICROBIOLOGICAL STUDIES

A total of 12 bacterial isolates were obtained from 20 animals that showed inflammatory and hyperplastic changes in the prostate. All the isolates were found to

be gram negative rods. Pale pink coloured colonies were obtained on Mc conkey's agar in 11 of the cases, which was further identified as *Escherichia coli* based on the morphological, cultural, and biochemical tests. In one case pale pink mucoid colony was obtained on the Mc conkey's agar and was identified as *Klebsiella sp.*

Age group	Total	Numbers with prostate lesions	Per cent
< 1 year	8	1	12.50
1-3 years	30	4	13.33
3-5 years	32	19	59.38
> 5 years	30	25	83.33
	100	49	

Table 1. Age wise distribution of the lesions in the prostate

Prostatic lesion	Percentage of Occurrence	Mean age at time of Diagnosis
Benign Prostatic Hyperplasia	73.47	6.62
Squamous metaplasia	2.04	10.5
Prostatitis	40.82	6.89
Prostatic atrophy	6.12	8.3
Prostatic adenocarcinoma	4.08	8.5

Table 2. Mean age at detection of prostatic disorders.

Age	Total	Body weight (kg)	Average body weight (kg)	Prostate weight (g)	Average prostate weight (g)	Prostate weight (g) per kg body weight.
< 1 year	8	83.50	10.44	33.12	4.14	0.39
1-3 years	30	518.83	17.29	461.04	15.37	0.89
3-5 years	32	479	14.97	506.27	15.82	1.06
> 5 years	30	460	15.33	785.82	26.19	1.71

Table 3. Relationship of prostate weight to body weight based on age

Age group	Total	Prostate circumference (cm)	Average prostate circumference (cm)	Prostate length(cm)	Average Prostate length (cm)
< 1 year	8	35.44	4.43	15.92	1.99
1-3 years	30	269.32	8.98	96.34	3.21
3-5 years	32	312.53	9.77	106.63	3.33
> 5 years	30	320.14	10.67	117.21	3.91

Table 4. Age wise classification of prostatic circumference and length

Breed	Total	Number of prostate with lesions	Per cent
ND	34	12	35.29
German shepherd	25	17	68.00
*Others	41	20	48.78
Total	100	49	

* Others include 9 Crossbreds, 9 Doberman, 9 Spitz, 5 Dachshunds, 4 Labrador, 3 Boxers, 2 Rottweilers.

Table 5. Breed wise distribution of the lesions in the prostate

Breed	Average body weight (kg)	Average prostate weight (g)
German shepherd	19.46	26.31
Non descripts	11.63	10.61
Crossbreds	15.31	17.11
Doberman	18.52	21.40
Spitz	8.69	17.93
Dachshund	11.22	11.66
Labrador	17.00	12.97
Boxer	19.30	17.19
Rottweiler	50.0	39.70

Table 6. Average prostate weight and body weight based on breed

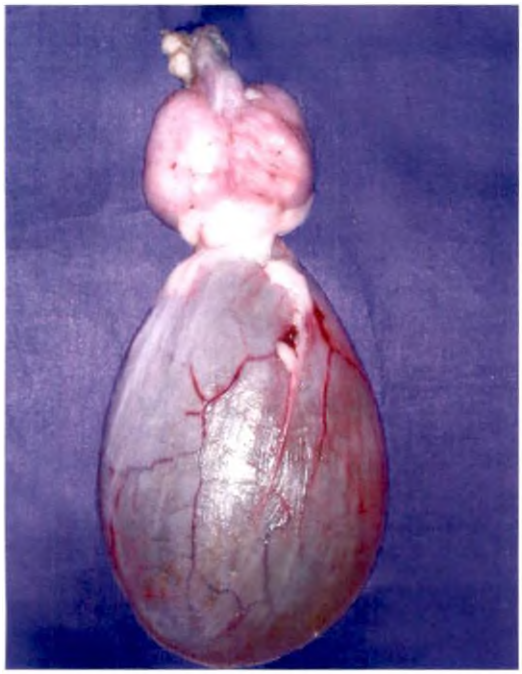


Fig. 1

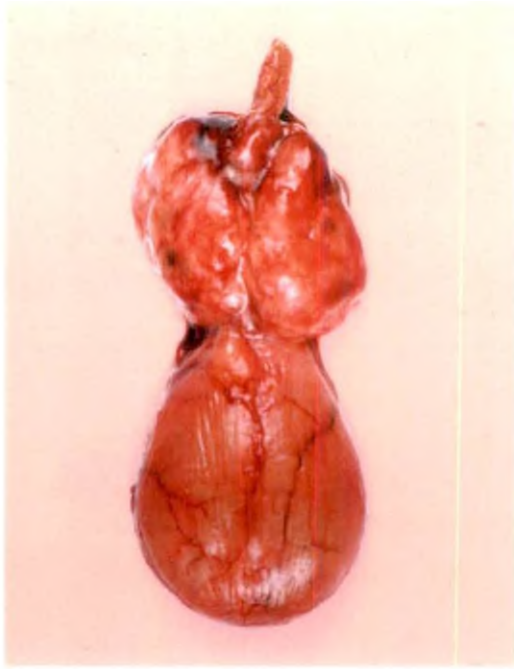


Fig. 2

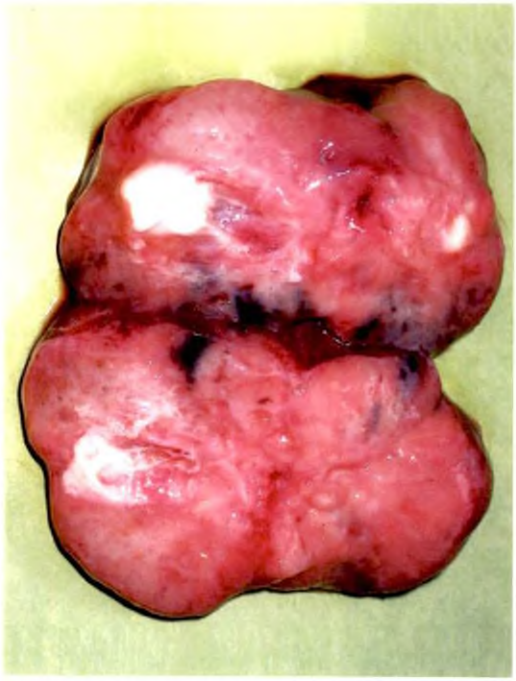


Fig. 3

Fig. 4

Figure – 1.
Prostatomegaly and retention of urine, engorgement of blood vessels of the bladder.

Figure – 2.
Prostatomegaly with asymmetrical enlargement of the lobes and retention of urine in the bladder.

Figure – 3. Prostate cut surface.
Subcapsular haemmorhage, spongy appearance and irregular distribution of small cysts in the parenchyma.

Figure – 4.
Prostatomegaly with irregular nodular appearance and small granular contracted kidney.

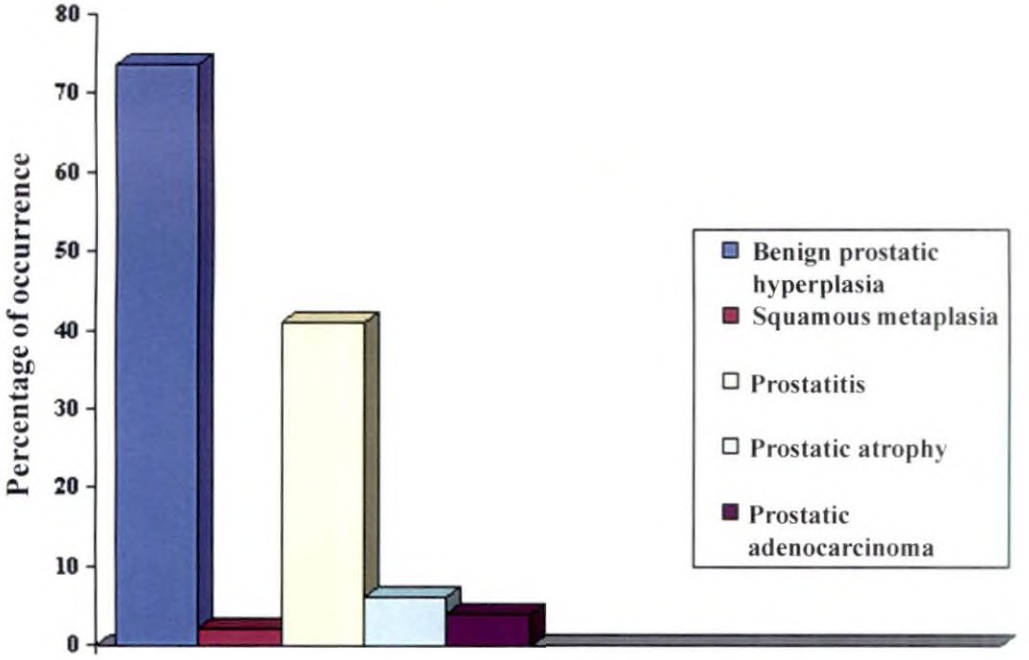


Figure - 5. Classification and incidence of prostatic lesions.

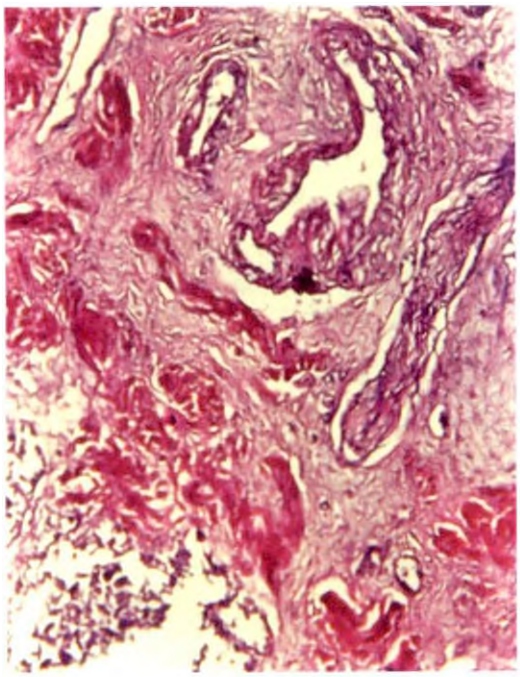


Fig. 6

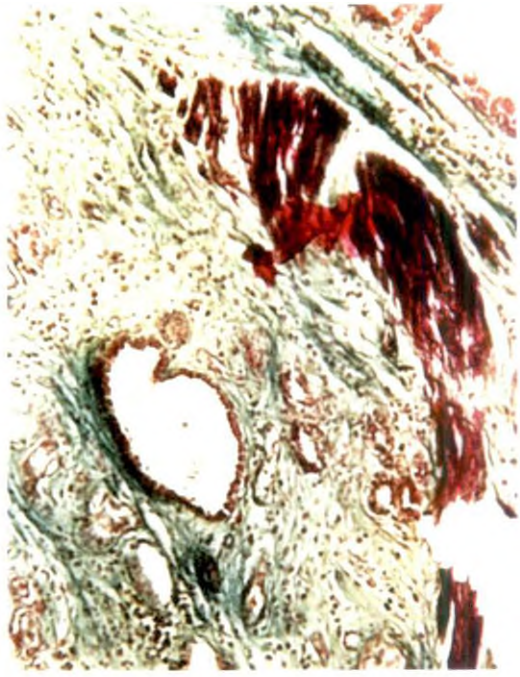


Fig. 7

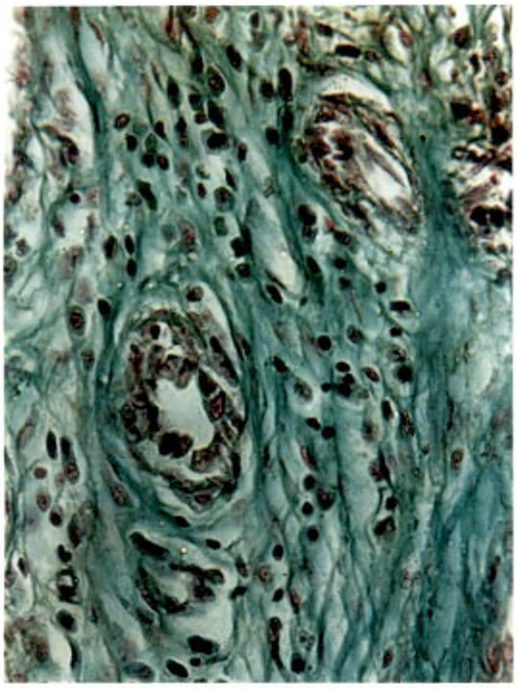


Fig. 8

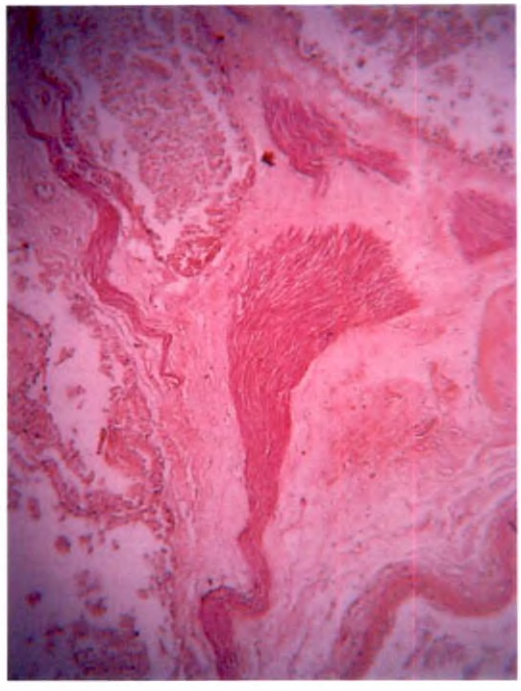


Fig. 9

Figure – 6. Stromal hyperplasia.
Thickening of the stroma with proliferation of the smooth muscle and fibrous tissue, cystic acini and denudation of lining cells – H & E x 100.

Figure – 7. Stromal hyperplasia.
Increase in both fibrous tissue (green) and smooth muscle (red) - Gomori's trichrome x 100.

Figure – 8.
Stromal hyperplasia with increase in fibrous tissue (green) and inflammatory cell infiltration - Gomori's trichrome x 400.

Figure – 9.
Hyperplasia of the smooth muscle (blue) and fibrous tissue (varying shades of brown) – PTAH x 400.

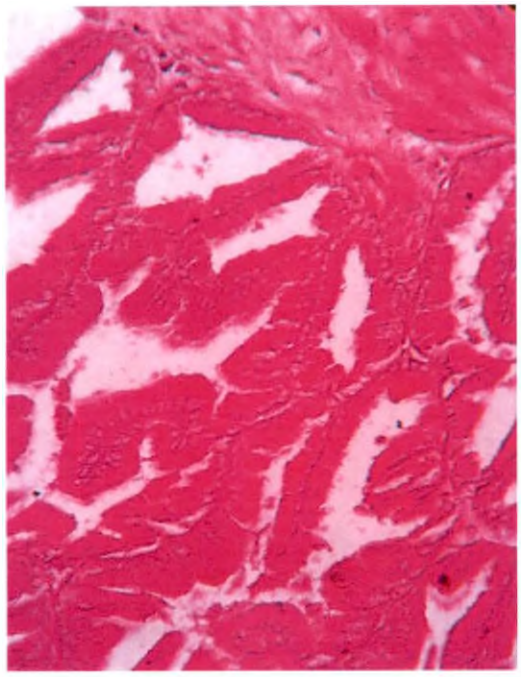


Fig. 10

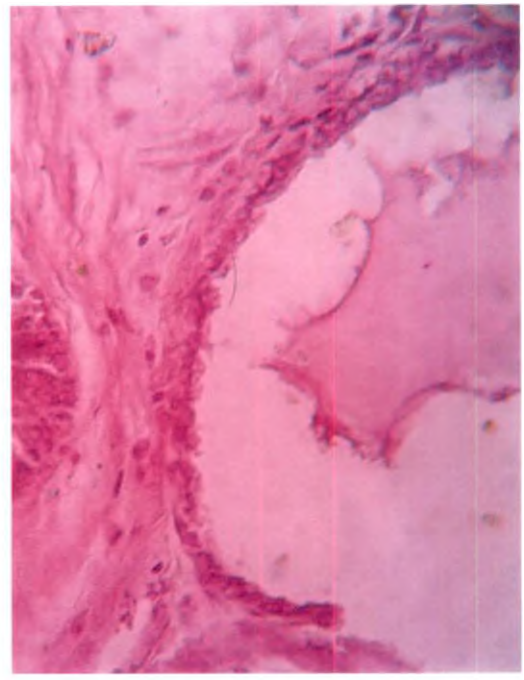


Fig. 11

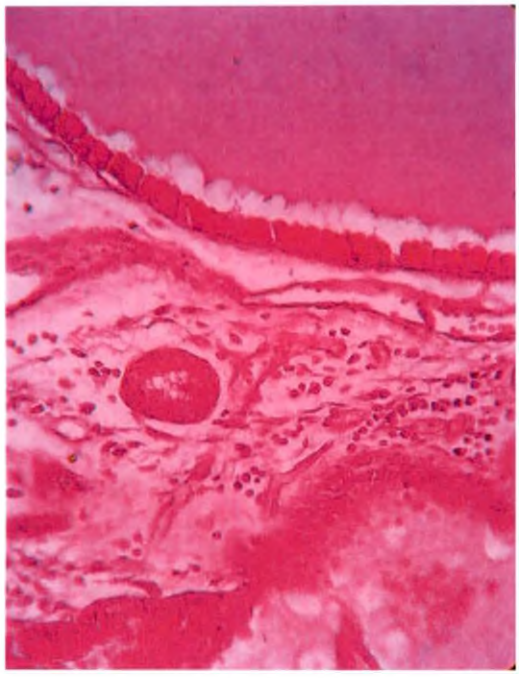


Fig. 12

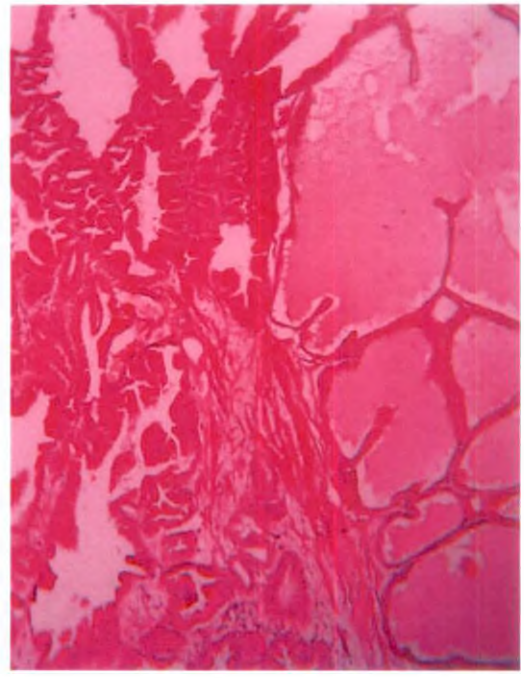


Fig. 13

Figure – 10. Glandular hyperplasia of the prostate.
Papillary proliferation of acinar cells, cells appear tall columnar with basaly located nuclei - H & E x 400.

Figure –11.Cystic hyperplasia of the prostate.
Cystic dilatation of the acini lined by flattened cells, accumulation of pink staining secretion in the acini - H & E x 400.

Figure – 12. Cystic hyperplasia of the prostate.
Large cystic acini with accumulated secretion and infiltration of mononuclear cells in the interstitial stroma - H & E x 400.

Figure – 13. Complex hyperplasia of the prostate.
Papillary proliferation of the acinar epithelium and cystic acini with accumulated secretion - H & E x 400.

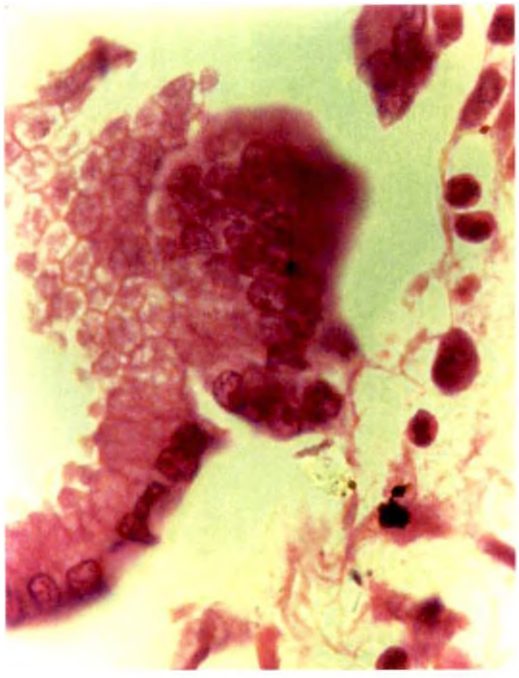


Fig. 14

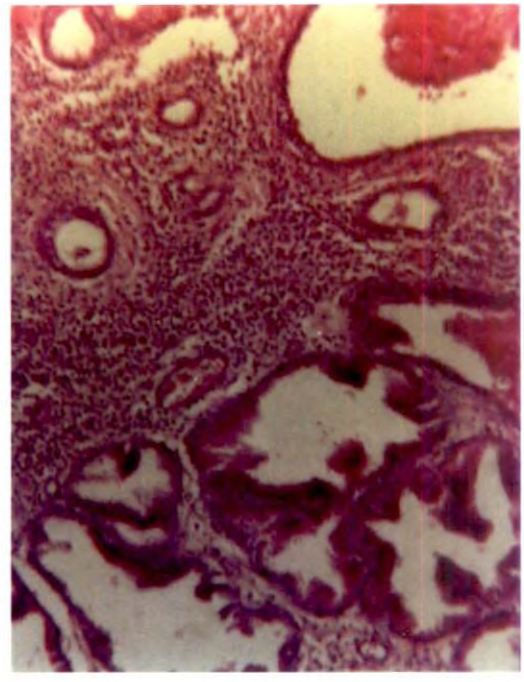


Fig. 15

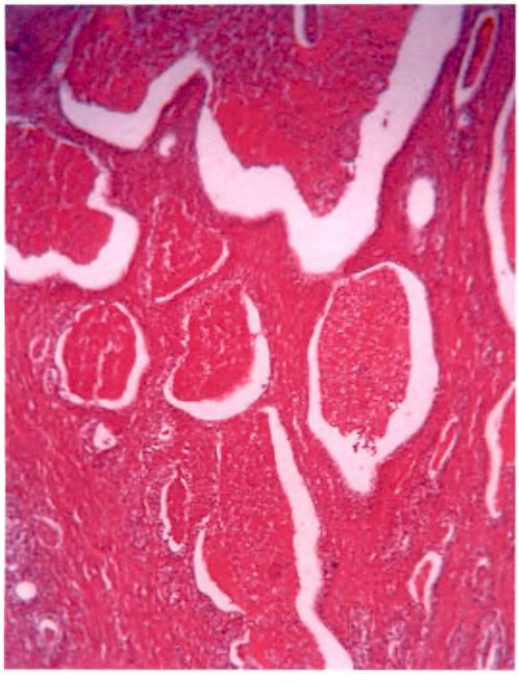


Fig. 16

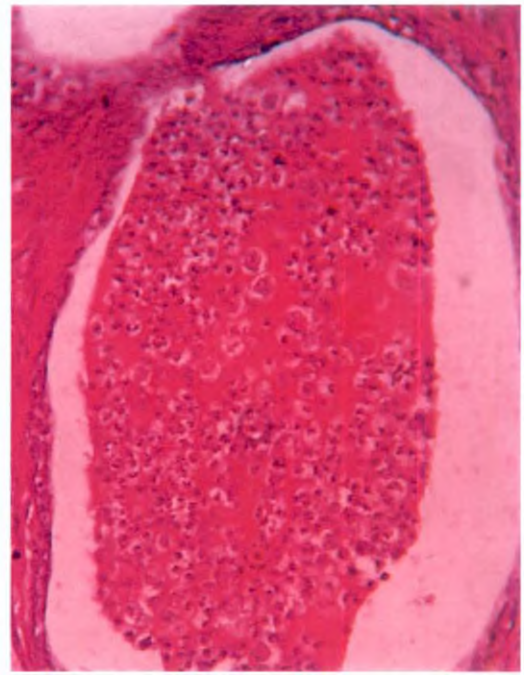


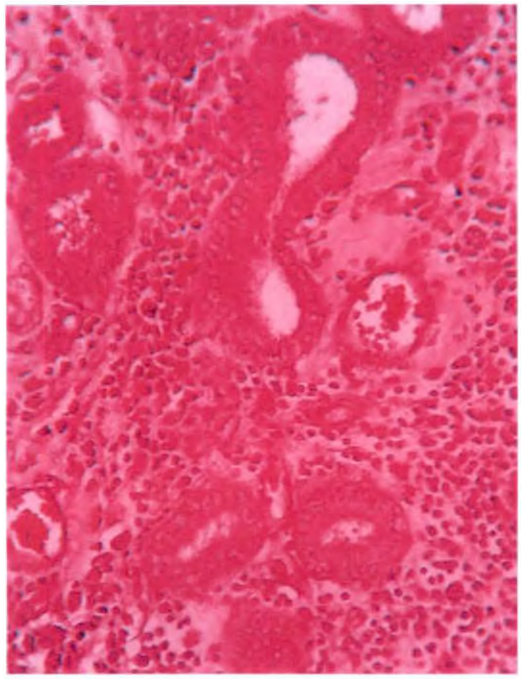
Fig. 17

Figure – 14. Squamous metaplasia of the prostate.
Metaplasia of the columnar type of cells in to a squamous type. H & E x 1000.

Figure -15. Acute prostatitis and prostatic hyperplasia.
Intense infiltration of the neutrophils in the interstitial tissue together with proliferation of the acinar cells-H & E x 250.

Figure -16. Suppurative prostatitis
Complete destruction of the prostatic parenchyma with formation of cystic spaces containing accumulated secretion and inflammatory cells- H & E x 100.

Figure –17. Suppurative prostatitis.
Dilated prostatic acini lacking an epithelial lining, pink staining secretion together with neutrophils and desquamated cells present within the acini - H & E x 400.



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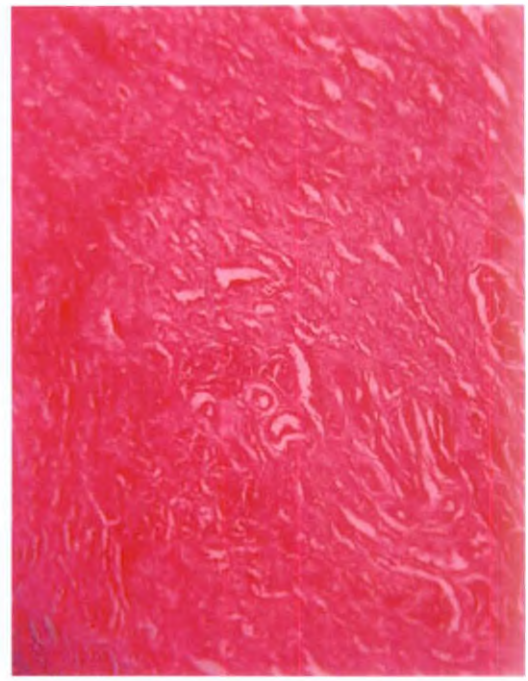

Fig. 19

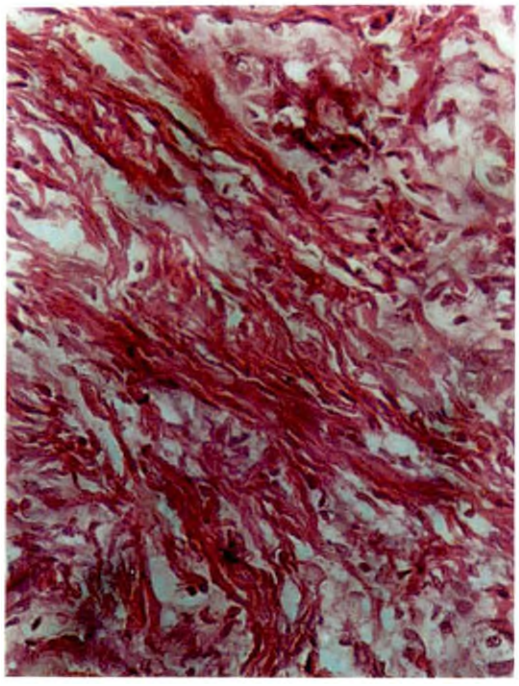

Fig. 20

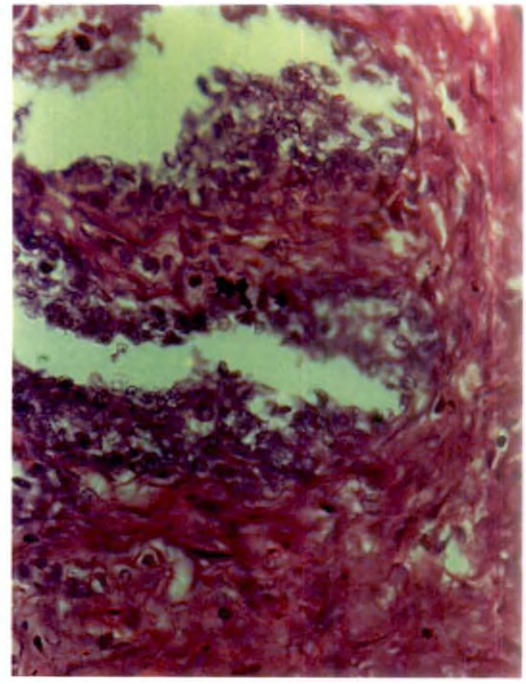

Fig. 21

Figure – 18. Chronic prostatitis.
Accumulation of mononuclear cells within the interstitial stroma and congestion of the blood vessels - H & E x 400.

Figure – 19. Prostatic atrophy.
Shrunken and collapsed acini seen as irregular slits, proliferation of fibrous tissue and smooth muscle - H & E x 100.

Figure – 20. Prostatic atrophy.
Interstitial fibrous tissue proliferation - H & E x 400.

Figure – 21. Prostatic adenocarcinoma.
Hyperchromatic, anisokaryocytic sheets of cells filling the lumen of the acini- H & E x 400.

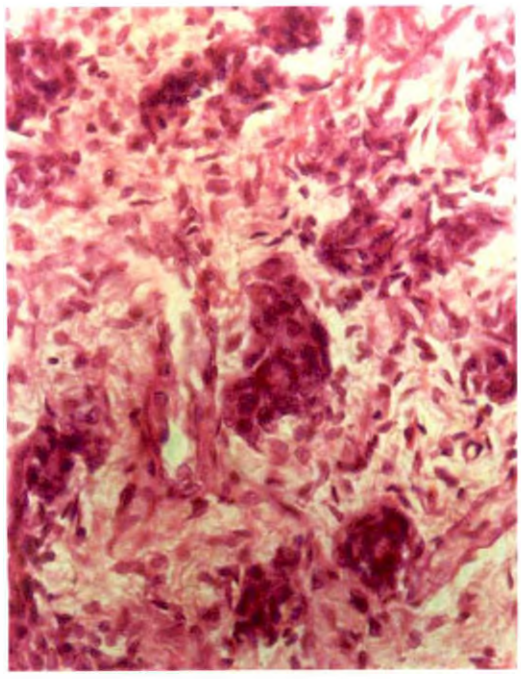

Fig. 22

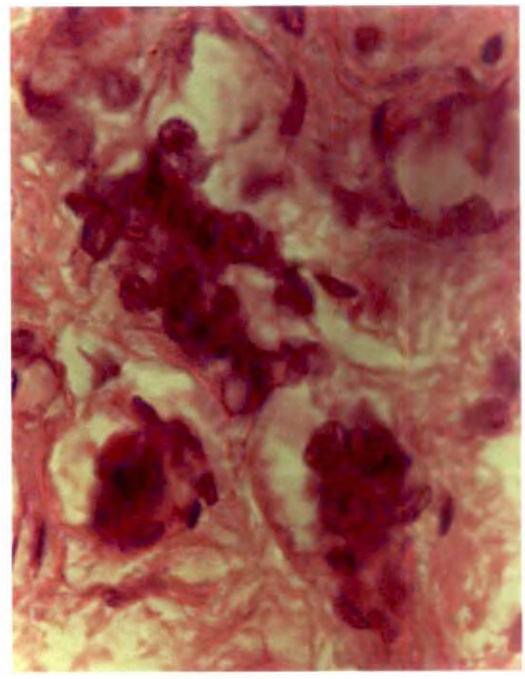

Fig. 23

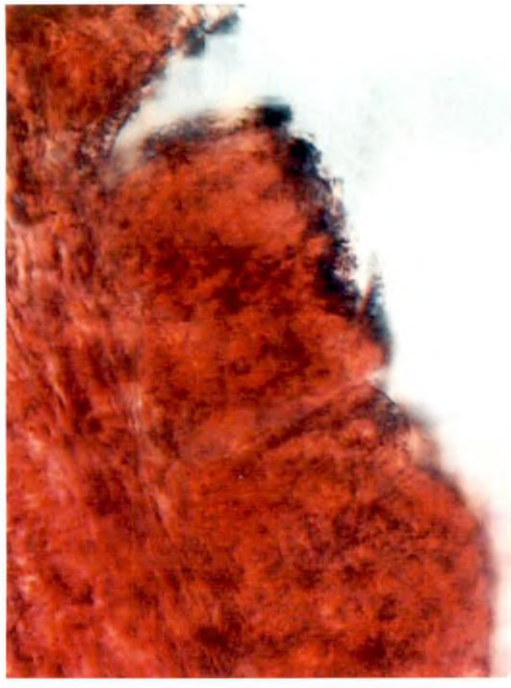

Fig. 24

Fig. 25

Figure – 22. Prostatic adenocarcinoma.
Loss of architecture of the prostate with proliferating sheets of cells - H & E x 400.

Figure – 23. Prostatic adenocarcinoma.
Oval or elongated disorderly arranged prostatic epithelial cells showing aberrant nuclear patterns like karyomegaly and anisokaryosis - H & E x 1000.

Figure– 24. Neoplastic prostate – cryostat section.
Acid phosphatase activity appearing as black deposits - Gomori's staining method x 1000.

Figure – 25. Hyperplastic prostate - cryostat section.
Acid phosphatase activity appearing as black dots- Gomori's staining method x 1000.

Fig. 26

Fig. 27

Figure – 26. Impression smear of the normal prostate.
Prostatic epithelial cells with minimal to moderate enzyme activity seen as black dots - Gomori's staining method x 400.

Figure – 27. Impression smear of the hyperplastic prostate.
Hyperplastic prostatic epithelial cellss with more enzyme activity, seen as intense black granular deposits - Gomori's staining method x 400.

Discussion

5.DISCUSSION

The present investigation was undertaken to evaluate the prevalence and nature of pathological conditions of the canine prostate and to categorise the various prostatic disorders. The information gathered suggested that prostatic diseases in canines are more common than what is generally expected.

The gross pathological observations revealed lesions in 49 cases out of the 100 cases examined. It was found that dogs more than five years and dogs between three to five years were the most affected, followed by dogs between one to three years of age and dogs less than one year of age. Among the different breeds German shepherds were found to be the most susceptible to prostatic diseases. There was an increase in the prostate weight associated with advancing age. The observation of prostatomegaly in aged dogs except in the castrated dogs is in consonance with the findings of Atalan *et al* (1990) that prostate weight and volume are related to the body weight in intact dogs.

Gross pathological changes observed were mainly prostatomegaly. The prostatomegaly observed was either diffuse and smooth or nodular and hard. However, the clinical effects of prostatomegaly depended upon the pressure exerted by the gland on the surrounding tissues as seen in a case where the prostatic enlargement had resulted in impaction of faeces and in another case where the prostatomegaly had resulted in urinary retention and finally the rupture of urinary bladder. Hence the enlargement of the prostate may have differing effects on its clinical manifestation and so a detailed study on the canine prostate is much important.

The histopathological lesions observed were broadly classified into proliferative, inflammatory, metaplastic and neoplastic type. The proliferative types

of lesions were mainly involving the glandular epithelium and the interstitial tissue. Many times the proportion of the glandular and stromal tissues varied. Based on this, the lesions could be classified as benign prostatic hyperplasia, squamous metaplasia, prostatitis, prostatic atrophy and prostatic adenocarcinoma. The most common prostatic disease encountered in this study was benign prostatic hyperplasia followed by prostatitis, prostatic atrophy, prostatic adenocarcinoma and squamous metaplasia. This is in contrary to the reports of Kraweic and Heflin, (1992), where bacterial prostatitis was identified as the most common prostatic disease.

Benign prostatic hyperplasia (BPH) involving mainly the lining epithelium of the prostate was detected mainly as a disorder of aged dogs over five years but could also be seen in three dogs less than three years of age. The BPH observed in younger dogs needs to be investigated further but the hyperplastic changes in the older dogs has to be viewed in the light of reports of Johnston *et al.* (2000) that BPH was a spontaneous age related disorder that occurred in more that 80 percent male dogs over five years of age.

Hyperplasia could not be detected in neutered dogs. This finding is in agreement with that of Ladds (1993). They suggested that an altered androgen to estrogen ratio seemed to underlie prostatic hyperplasia in dogs. Brendler *et al.* (1983) reported that with age there was a moderate decrease in serum androgen levels with no apparent change in serum oestradiol levels. They suggested that growth and functional changes that were associated with development of BPH reflected an altered sensitivity of the prostate to serum androgen or a response to relative decrease in the serum androgen to estrogen ratio. Although the exact cause of BPH was not clear ageing and testicular hormones appeared be the important predisposing factors. In glandular hyperplasia, the acinar epithelium was tall columnar and formed papillary projections into the lumen. Klausner *et al.* (1995) reported that in glandular hyperplasia, the proliferation was primarily epithelial with increase in size and

number of epithelial cells. In the present study, in most of the cases glandular, stromal and cystic hyperplastic changes were coexistent. This correlates with the finding of Ladds (1993) that in BPH, adenomatous, stromal and cystic hyperplasia was seen interspersed. Cystic hyperplasia was characterised by the presence of dilated acini of various sizes, lined by flattened epithelium possibly due to the pressure from the contents in the acini.

Squamous metaplasia of the prostate was seen in a single case, where the gland was severely enlarged and impinged on the prostatic urethra and had resulted in rupture of the bladder. Squamous metaplasia of the prostatic epithelium in canines occurred spontaneously in association with neoplasia of testes, particularly sertoli cell tumor, or following the administration of estrogens (Ladds, 1993). Microscopically the affected epithelium had undergone metaplastic changes to a squamous type and there was accumulation of inflammatory cells in the acini and within the interstitial tissue. Ladds (1993) stated that although squamous metaplasia of the prostate predisposed it to inflammation there was no evidence that it was a preneoplastic change.

20 cases of prostatitis were detected. Middle to old aged intact dogs were the most commonly affected ones but a case of acute prostatitis was observed in a seven month old non descript dog. Ladds (1993) stated that prostatitis though mostly a disease of older dogs with enlarged prostate could also occur in younger dogs with normal prostate.

Bacterial isolations were obtained from 12 out of 20 cases (60 percent) with inflammatory changes in the prostate. This indicated that most of the cases of inflammatory conditions were associated with some infectious cause. *Escherichia coli* and *Klebsiella sp.* were the bacterial pathogens isolated. Same pathogens could be isolated from bacterial prostatitis by Kraweic and Heflin, (1992). Of the male dogs

genital organs, the prostate gland is in close proximity to the micro flora of the distal urethra. This may be the reason for prostatitis being mostly coexistent with nephritis and cystitis as observed in the study. Barsanti (1980) observed that most of the prostatic infections were secondary to the migration of the bacteria up the urethra, although spread through blood, semen and rectal flora was also possible.

Prostatitis was commonly seen along with other prostatic diseases like hyperplasia and metaplasia. This correlates with the findings of Rubin (1990) that bacterial prostatic infection occurred alone or as a complication of other prostatic diseases like benign hyperplasia, cysts or neoplasia. In cases of hyperplasia the prostatic urethra may become elongated and compressed leading to defective emptying and thus accumulation of urine in the bladder. This residual urine may readily get infected and act as a source of infection. In prostatic hyperplasia, the acini may be dilated with accumulated secretion. This may also provide a favourable environment for the growth of pathogens and act as a source of infection.

Acute, suppurative and chronic types of prostatitis were seen with the chronic type being the most common. The predominating types of inflammatory cells were neutrophils in acute prostatitis where as lymphocytes and plasma cells were the predominant type in cases of chronic prostatitis. Similar observations were reported by Ladds (1993). The presence of pink staining secretion within the acinar lumen was a consistent finding in cases of acute inflammatory conditions. In suppurative prostatitis the gland revealed numerous cystic acini devoid of an epithelial lining, and the exudate consisted of degenerating neutrophils and desquamated necrotic epithelial cells.

Prostatic atrophy could be observed in three cases. Two cases were seen in old intact dogs and one case was in a castrated dog. In aged dogs atrophy of the prostate occurs as a senile involutionary change. The cause of atrophy was presumably deficient androgen formation by the testes. Castration was found to

induce atrophic changes in the prostate as reported by Niu *et al.* (2001). Prostatic atrophy always follows bilateral orchidectomy. It did not appear to result from unilateral castration. A cryptorchid dog examined during the study was found to have a normal prostate. Mc entee (1990) reported that atrophy of the prostate could occur in dogs suffering from diabetes mellitus and canine distemper.

Grossly the atrophic gland was shrunken, hard and firm. Microscopically there was flattened lining epithelium, collapsed slit like acini and dense fibrous tissue in the interstitial stroma. Similar lesions were observed by Ladds (1993). The stroma was more conspicuous either because of reactive fibrosis or because the acini was shrunken. The relative large amount of fibro muscular tissue may be the reason for the firm consistency of the atrophic prostate.

Two cases of prostatic adenocarcinoma were encountered in the present investigation, one each in an intact and a castrated dog. The dogs were nine and eight years old respectively. This is in correlation with findings of Bell *et al.* (1991) that prostatic adenocarcinoma is more frequent in eight to 10 year old dogs. Johnston *et al.* (2000) described prostatic adenocarcinoma as an uncommon malignant tumor of intact and castrated male dogs. An increased risk for development of prostatic adenocarcinoma in castrated dogs was suggested by Davidson *et al.* (2003). Bell *et al.* (1991) studied on prostatic adenocarcinoma in dogs and stated that the development of prostatic adenocarcinoma in castrated dogs indicated that testosterone was not an etiologic factor. Alternatively non testicular androgens such as adrenal androgens might contribute to etiopathogenesis of the disease in castrated dogs. Environmental chemicals that have hormonal activity and those which act as endocrine disruptors are theorized to cause preneoplastic or overly neoplastic changes in many tissues, including reproductive tissues. Significance of these chemicals in pathogenesis of spontaneous prostatic adenocarcinoma in the dog is unknown (Johnston *et al.* 2000). The detection of prostatic adenocarcinoma in dogs need special mention that dogs can

be utilized as a very good model for studying the hormonal carcinogenesis. Since one case was in a castrated dog the role of extra gonadal sex hormones in prostate carcinogenesis requires more extensive study.

The concurrent finding of osteosarcoma and prostatic adenocarcinoma indicated that tumours were originating from different tissues of the same animal and growing without collision and was hence diagnosed as a case of concomitant neoplasm. Such concomitant neoplasms are not often seen reported in dogs but a case of oral papilloma and mucinous adenoma of the stomach in an African baboon has been reported by Nair *et al.* (1996).

In the castrated dog with prostatic adenocarcinoma there was tumor metastasis to the lungs. Bell et al. (1991) reported that pulmonary metastases were significantly more common in neutered than in intact dogs with prostatic adenocarcinoma. Reported sites of metastasis from most to least common are lungs, regional lymph nodes, liver, urethra, spleen, colon and rectum, urinary bladder, bone, heart, kidney, distant lymph nodes and adrenal glands.

Grossly the neoplastic prostate was moderately enlarged in the intact dog, where as it was reduced in size, hard and firm in the castrated dog. This is in accordance with findings of Kraweic and Heflin, (1992). Histopathological sections revealed proliferating sheets and nests of neoplastic epithelial cells with marked anisokaryosis and narrow rim of basophilic cytoplasm. Similar observations have been recorded by Bell *et al.* (1991).

Acid phosphatase could be localised in the impression smears and cryostat sections of the prostate. Acid phosphatase is a secretory product frequently utilized as a tumor marker for disseminated late stage prostate cancer in humans (Rubenstein et al., 1988). More enzymatic activity was obtained for hyperplastic and neoplastic prostates when compared to normal prostate. Corazza et al. (1994) reported that

serum concentrations of prostatic acid phosphatase were peculiarly elevated in dogs with benign hyperplasia and prostatic neoplasia. As prostatic acid phosphatase secretion is androgen dependent its increase in serum is probably due to the degeneration of the prostatic epithelial cells induced by increase in the dihydro testosterone concentration in the gland. A negative reaction in medium or low differentiated adenocarcinoma does not rule out the possibility of prostatic carcinoma (Svanholm, 1986). Since prostatic acid phosphatase levels do not become significantly elevated until late stage cancer, better markers such as prostatic specific antigen should be sought which appear earlier and may be more useful for the screening of prostate cancer.

The present study suggests that disorders of the prostate are more than usually expected. This may be due to the fact that many of the lesions may not be manifested clinically till it interferes with the normal functioning of the associated systems. The role of hyperplastic changes in the development of an occult infection in the prostate that may lead to nephritis and cystitis should not be overlooked.

This study further confirms that the prostatic disorders are mainly age - related. The detection of normal prostate in a cryptorchid dog and prostatic adenocarcinoma in a castrated dog points to the need for further studies on the effect of hormones on the prostate. The histochemical localisation of acid phosphatase in both cryostat sections and impression smears can be utilised as a good marker for detection of hyperplastic or neoplastic changes in the prostate. The impression smears can be adopted as a rapid technique to screen the enlarged prostate. As the acid phosphatase level may not be significantly elevated until later stages of neoplasia, a better technique like detection of prostate specific antigen should be considered. The result of this study will create awareness among the clinicians about the various prostatic disorders in canines and aid them in choosing suitable diagnostic, preventive and curative measures.

Summary

6. SUMMARY

An investigation was undertaken to assess the prevalence and nature of pathological conditions of the canine prostate. One hundred samples of the prostate gland obtained from the carcasses of dogs brought for autopsy to Centre of Excellence in Pathology were subjected to a detailed, systematic gross and histopathological examination. Prostatic fluid was collected aseptically for bacteriological studies in appropriate cases. Representative samples of the gland were collected for histochemical evaluation .The influence of age, breed and body weight on the various prostatic disorders were analysed.

It was found that dogs above five years were the most affected. Among the different breeds German shepherds were found to be the most susceptible to prostatic disorders. There was an increase in the prostate weight, prostatic circumference and length associated with advancing age.

Out of the 100 cases examined 49 per cent showed pathological changes in the prostate. Gross pathological changes observed were mainly prostatomegaly. The prostatomegaly observed was either diffuse and smooth or nodular and hard. However the clinical effects of prostatomegaly depended upon the pressure exerted by the gland on the surrounding tissues.

The histopathological lesions observed were classified into benign prostatic hyperplasia, squamous metaplasia, prostatitis, prostatic atrophy and prostatic adenocarcinoma. The most common prostatic disease encountered in this study was benign prostatic hyperplasia followed by prostatitis, prostatic atrophy, prostatic adenocarcinoma and squamous metaplasia. Benign prostatic hyperplasia could be detected in 73.47 per cent of the cases. It was detected mainly as a disorder of aged dogs over five years but could also be noticed in dogs less than three years of age.

Glandular hyperplasia, cystic hyperplasia and complex hyperplasia were seen in 21, seven and eight cases respectively.

Squamous metaplasia of the prostate was seen in one case (2.04 percent). Though neoplasia of the testes particularly sertoli cell tumor has been associated with squamous metaplasia of the prostate, it could not be observed in the present study.

Prostatitis was observed in 40.82 percent of the cases. It was commonly seen along with other prostatic disorders like hyperplasia and was mostly seen concurrent with nephritis and cystitis. In this context the possibility of an ascending or descending infection from the genito urinary tract is to be suspected. Chronic type of prostatitis was found to be the most common. Acute and suppurative prostatitis also could be observed. Specific pathogens could be isolated from 12 cases of prostatitis. The isolates obtained were *Escherichia coli* and *Klebsiella sp.*

Atrophic changes of the prostate were observed in three cases (6.12 per cent), which included two old dogs and a castrated dog. The cause of atrophy was presumably deficient androgen formation by the testes.

Prostatic adenocarcinoma was encountered in 4.08 per cent of the cases. One case noteworthy of mentioning was in a castrated dog. Non testicular androgens such as adrenal androgens might contribute to etiopathogenesis of prostatic neoplasms in castrated dogs. A concomitant neoplasm of prostatic adenocarcinoma and osteosarcoma was observed in one case, which necessitates the need to study the microenvironment at molecular level that favoured oncogenesis.

Acid phosphatase could be localised in the impression smears and cryostat sections of the prostate. More enzymatic activity was obtained for hyperplastic and neoplastic prostates when compared to normal prostate.

The investigation suggests that prostatic diseases in canines are more common than generally expected. The present study helped to demonstrate that the pathological disorders of the canine prostate are more frequent in aged dogs. The occurrence of prostatic adenocarcinoma in a castrated dog suggested the need for further studies to investigate whether castration influenced the incidence of prostatic carcinoma in dogs.

The increased amounts of acid phosphatase in hyperplastic and neoplastic prostates pointed to the fact that prostatic acid phosphatase can be used as a marker for the diagnosis of canine prostate cancer, but the use of better markers like prostate specific antigen which can detect the neoplastic changes at a still earlier stage need to be investigated.

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PATHOLOGY OF THE PROSTATE GLAND IN DOGS

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ABSTRACT

The present investigation was undertaken to evaluate the prevalence and nature of pathological conditions of the canine prostate. A detailed systematic examination of 100 carcasses brought for autopsy during the period of investigation was conducted and the gross and histopathological lesions were studied in detail. The study confirmed prostatic disorders as an age related problem and also warned that involvement of the prostate in concurrent pathological affections of the urogenital system should not be overlooked. Heavy breeds like the German shepherds were found to be the most susceptible to prostatic diseases. An age related increase was also seen in the prostatic weight, circumference and length. Prostatic lesions could be encountered in 49 per cent of the cases. The most common prostatic disease encountered in this study was benign prostatic hyperplasia followed by prostatitis, prostatic atrophy, prostatic adenocarcinoma and squamous metaplasia. Glandular, cystic and complex types of hyperplasia could be observed. The identification of prostatic adenocarcinoma in a castrated dog pointed to the necessity to study the role of extra gonadal sex hormones in prostate carcinogenesis. *Escherichia coli* and *Klebsiella sp.* were isolated from cases of prostatitis. Acid phosphatase activity was more for hyperplastic and neoplastic prostates when compared to the normal prostate. This indicated that prostatic acid phosphatase could be used as a marker for the diagnosis of canine prostate cancer both by impression smears and cryostat sections.