CHAPTER FOUR

D I S C U S S I O N

DISCUSSION

I. Histopathology:

The present point of discussion concerns with the histopathological alterations occurring due to various prostatic disorders in man.

1) Benign Prostatic Hyperplasia (BPH):

Earlier studies on BPH in different patients and in the artificially induced by administration of hormones in experimental animals show increase in glandular elements, epithelial cell size and number. Proliferation is regular and symmetrical, each acinar structure tends to remain discrete, distinct and it retains the convoluted outline of normal acini. The acini are separated from one another only by delicate strands of fibromuscular structures. The pattern of distribution of acini is more or less similar (Ashley, 1980). Large acini are formed and these may consist of granular or clear cells. Some acini have taller epithelium than others and few acini are composed of clear and eosinophilic cells of varying height. Many acini become tortuous or dilated and others may be partially or completely obliterated by an overgrowth of periacinar tissue (Ashley, 1980). In some cases, vascular obstruction and small areas of infarction are seen. Such areas frequently show formation of squamous metaplasia of the glandular epithelium (Mostofi and Morse, 1951). Ohtsuki et al.

(1982) observed fine structure of nuclear bodies in the human prostatic hyperplasia which varied from 0.3 to 1.8 µm in diameter. Zirkin et al., (1984) studied age-dpendent hyperplasia in dog, in which the proliferation of prostate gland and stromal components increase the epithelial number and epithelial cell size leading to increase in the total weight of prostate. EM study showed that the volume densities of RER and secretion granules are significantly lower in the epithelial cells of immature prostate than in the hyperplastic prostate of mature dog. No significant differences are seen in the volume densities of RER, free ribosomes, secretion granules, SER and mitochondria in prostatic epithelial cells of dog of 1.5 to 9 years of age.

A cursory survey of the various photomicrographs included under observations on BPH in the present investigation indicates that the acini are hyperplastic and are lined with tall columnar epithelium, some of them are dilated and cystic in nature and are lined with flattened epithelium. Some prostatic nodules also show an area of infarction, adjacent to which the acini show the presence of metaplastic squamous epithelium. The stroma of the tissue at certain places is normal but reduced because of dilated acini. The area of infarction also shows the presence of interacinar spaces filled with blood. From the aforementioned discussion it is clear that the histopathological structure in this tissue shows more or less parallel findings as reported by a number of scientists.

2) Chronic Prostatitis:

Histopathological structure in the chronic prostatitis varies in different stages of development. A case of chronic prostatitis reported by Ashley (1980) shows the presence of hyperplastic acini with flat epithelium leading to dilation of the lumen. The hyperplastic process commonly produces intra-acinar papillary elements consisting of one or more rows of tall columnar cells with small core of connective tissue. The luminal borders of papillae are distinct and the oval nuclei are situated basally. Large acini are lined by granular or clear cells. Many acini become dilated and others may partially or completely obliterated by an over-growth of periacinar tissue. The fibromuscular tissue increases in bulk, whereas the acini are more affected. Sometimes infiltration of inflammatory cells occurs (Mostofi and Morse, 1951). Alguacil et al. (1986) studied the histopathology of chronic prostatitis and showed that this tissue shows degenerated lymphocytes and stromal cells with signet ring appearance that can mimic the carcinoma.

In the light of above discussion the second case presented in this present investigation shows more or less similar histopathological alterations. In the present study the tissue shows focal hyperplasia in the acini and the acini are lined with cuboidal epithelium. The acini and ducts are destroyed in places and replaced by an exudate of plasma cells, lymphocytes, few microphages and eosinophils.

Remaining tissue shows proliferation of fibrous stroma with smooth muscle fibres. The cells with hypertrophid nuclei are seen in the hypertrophid acini. The remaining part of the tissue, especially the stromal region, shows the presence of normal blood vessels (arterial supply) but in the neighbouring region these blood vessels show obliteration because of overgrowth of stromal tissue and finally invaded by the stroma. Thus from these findings it is clear that more advanced stage of chronic prostatitis is observed in the present investigation which leads to destruction of the normal and hyperplastic acini, and most of the places are occupied with the overgrowth of fibromuscular tissue.

3) Acute Nonspecific Prostatitis with Abscesses:

Abnormal changes involving structural changes are noted in a number of cases. Among such cases very few but serious enough are the formation of acute microabscesses (Mostofi and Morse, 1951). The microabscesses consist of either collection of lymphocytes and plasma cells or polymorphonuclear leucocytes, either in the stroma or within the lumena of dilated glands. On the basis of references cited above one of the prostatic disorders selected for the present investigation shows more or less identical pattern of histopathological changes. The tissue shows presence of prostatic acini with normal appearance and lined with single columnar epithelial cells (very few), while in the rest of the area the acinar epithelium is distorted.

The acini also show necrosis and hence most of the acini are filled with necrotic substance. Besides this, the prostatic tissue consists of highly increased amount of stroma (as large number of functional acini become necrotic and degenerated. The stroma also shows diffused, dense and acute inflammatory cell-infiltration, predominantly composed of polymorphs forming many groups of such cells. This structure is generally named as microabscesses in pathology. Infarction of tissue is also seen in the degenerated region. The aforementioned characteristic alterations in the prostate from that of the normal prostate tissue represent a case of acute nonspecific prostatitis with abscesses. In the present investigation more differentiating features of histopathology are observed when compared with earlier studies which can help in correct diagnosis of such prostatic disorder.

4) Prostatic Carcinoma:

Among the prostatic disorders reported by a number of research workers, the carcinomas of prostate are of common occurrence. Nearly 3-5% of the deaths occurring in males during old ages are due to cancers of prostate. A detailed histological examination of prostate removed at routine necropsies has shown a significantly high frequency of unsuspected foci of malignancy which structurally are carcinomas (Franks, 1954 b). It is very difficult to identify the prostatic cancer with the help of histological appearance, as microscopic structures of prostatic malignancy are not of regular

consistant occurrence (Ashley, 1980). Similarly varieties of carcinomas represent their individual characteristic form of histological appearance. The major groups of carcinomas occurring in human prostate are adenocarcinomas (Foot, et al., 1950; Edwards et al., 1953). Further, they are classified on the basis of the affected region of prostate. They may be of ductal, tubular, tubuloalveolar or stromal variants. Both early and advanced cancers of prostate consist of well or poorly formed, small, medium or large acini and tubules. The glandular elements may be closely packed together with little intervening stroma and grouped in the nodular or linear arrangement (Ashley, 1980). Other group of adenocarcinomas is more obviously infiltrative in nature. Their branching tubules are dispersed irregularly in the disorderly radial fashion throughout the variable amount of fibromuscular stroma. The convoluted outlines found in normal acini are disturbed. In the better differentiated carcinomas, occasionally the intra-acinar proliferation is seen. Such intra-acinar proliferation results in secondary gland formation within the lumina of the glands. In the more advanced adenocarcinomas infiltration of neoplastic acini leading to the separation or rupture of the strands of muscles is observed. Sometimes the neoplastic acini burrow deeply into the bundles of smooth muscles. Malignant acini usually show the presence of single row of columnar and cuboidal cells and nearly always lack a basal layer of cells which is found in normal and hyperplastic acini. Totten et al. (1953) claimed that the presence of prominent, relatively large, complex and deeply staining nucleoli are most useful in the identification of

malignant cells, the chromatin material of such cells remains concentrated at the nuclear membrane. Melicow (1966) showed nuclear hyperchromatism and nucleolar prominence in the malignant cells. Similarly, this study further showed that when the acinar structures differentiated in the tumor are small, the nuclei are large and hyperchromatic and when the acini are large, and tubuloalveolar, the cytoplasm is abundant then the nuclei are comparatively small and pyknotic. Schubert et al. (1981) studied histological types of prostatic carcinomas and their relations with the hormones and showed that the hormone therapy induces reticularization and vacuolization of the nuclear chromatin. A case of cystosarcoma phyliodus of prostate studied by Manivel et al. (1986) showed sarcomataus appearance of stroma, whereas other tumors show cellular stroma.

In relation to the above mentioned discussion one of the tissues studied in the present investigation represents typical case of prostatic adenocarcinoma. A cursory glance on various photomicrographs of H-E staining shows that the tissue mainly consists of tumor reducing the normal glandular appearance of the prostate. The tumor region is composed of glandular cells arranged in adenoid cysts and streaks. The tumor cells show round vesicular nuclei and clear cytoplasm which is eosinophilic in nature. The stroma in the tumor region is thin and it is thick in the neighbouring region where normal acini are found. The above histopathological characters represent clearly a case of glandular adenocarcinoma. Thus, the

histopathological structures described in the present investigation are very much useful in identification of glandular adenocarcinoma of the prostate.

Another case of prostatic malignancy studied in this dissertation is Anaplastic carcinoma. This tissue shows somewhat different histopathological characters when compared with the prostatic adenocarcinoma. In this tissue strips of transitional epithelium are observed beneath which a tumor is seen. The tumor consists of cells arranged in sheets and clusters. The cytological structure of cells shows hyperchromatic nuclei and vacuolated eosinophilic cytoplasm. Inflammatory cell infiltration is also seen. Proliferation of the tumor cells leads to infiltration of these cells in the muscle fibres. Major part of the tissue is transformed into tumor and hence the normal glandular appearance of the prostate is lost. Similarly, the arterial blood supply is obliterated as the malignant cells grow over the wall of the blood vessels, destroying them. Thus all these characters shows more advanced and well differentiated carcinoma of prostate. When these histopathological characters are compared with the histopathological characters reported earlier by a number of scientists, it gives additional clue for identification of anaplastic carcinoma of prostate. The important and differentiating characters of Anaplastic carcinoma in the present investigation are proliferation of tumor cells leading to formation of sheets and clusters in the stroma, cells showing hyperchromatic nuclei and vacuolated cytoplasm. Most

of the tumor cells show increased amount of nuclear material, occasionally mitotic figures are also observed.

II. Histochemistry:

. The histochemical results in normal prostate and prostate under various pathological disorders studied in the present investigation show that:

1) In the normal prostate the acini show the presence of neutral mucins in high concentration, sialomucins in moderate concentration and sulfomucins in traces. Similar results are noted in the case of acinar secretion, showing the presence of neutral mucins in high concentration, sialomucins in moderate concentration and sulfomucins in traces. The mucopolysaccharide component of the duct is also of similar nature, i.e., neutral mucins are in intense to moderate concentration, carboxymucins in moderate to weak concentration and sulfomucins in weak to moderate concentration. The stroma revealed the presence of neutral mucins, acidic mucins and sulfomucins in weak concentration, whereas smooth muscle fibres show the presence of neutral mucins, acidic mucins and traces of glycogen.

2) In the case of BPH with prostatitis the hyperplastic acini showed more or less similar results when compared with

the normal acini of normal subject. The acini indicate the presence of neutral mucins in moderate to high concentration, acidic mucins (sialomucins) in weak concentration and traces of sulfomucins. The secretion found at various regions of the affected prostate show the presence of neutral mucins in high concentration, sialomucins in less to moderate concentration and sulfomucins in traces. The corpora amylacea, occasionally found in the dilated acinar lumen show presence of neutral mucins in moderate concentration and sialomucins in weak concentration. In some of the regions where hyperplastic acini are lost and they are transformed into metaplastic squamous epithelium show the presence of neutral, acidic, and sulfated mucins but their distribution varies in different cells. According to the staining reactivities the metaplastic cells can be differentiated into three categories:

a) cells elaborating neutral mucins only,
b) cells elaborating mixture of neutral and acidic mucins,
c) cells elaborating only sulfated mucins,

thus indicating cytochemical differentiation at cellular level in metaplastic epithelium developed in the BPH. This is a significant new addition to the present information on the mucopolysaccharides in BPH.

The duct system revealed the presence of neutral mucins in high to moderate concentration, carboxymucins

in weak to moderate concentration and sulfated mucins in traces.

The stromal components also show the presence of high concentration of neutral mucins, less concentration of acidic mucins and traces of sulfomucins, whereas muscle fibres of stroma show the presence of neutral mucins, acidic mucins and glycogen.

3) Histochemical reactions applied to the chronic prostatitis show presence of neutral and acidic mucins as the major components, whereas sulfated mucins are found at very few cellular sites. Two types of acini are identified in the tissue. Appearance of some acini is found to be normal but their mucin contents are reduced when compared with mucins of acini of normal and healthy subjects. The result shows presence of only neutral mucins in moderate concentration and sialomucins in weak concentration. The hyperplastic acini found at various regions show the presence of neutral mucins in moderate concentration, carboxymucins in traces, but some hyperplastic acini show the presence of sulfated mucins in their apocrine secretion. The secretory elements found in various acini also show presence of neutral mucins in high concentration and acidic mucins (sialomucins) in traces.

The ducts, small and large, distributed in this prostatic tissue show the presence of only neutral mucins in moderate concentration and sialomucins in weak concentration.

The stroma found in the region of hyperplastic acini, as well as in the region of normal appearing acini, shows the presence of neutral and acidic mucins in weak to moderate concentration and traces of sulfomucins, whereas muscle fibres of the stroma show the presence of neutral mucins alongwith glycogen and traces of sialomucins.

The blood vessels distributed in the stroma are affected showing obliteration in some regions. The histochemical results for such blood vessels revealed the presence of neutral mucins in intense to moderate concentration, sialomucins in weak concentration and sulfomucins in traces, but the blood vessels undergoing obliteration show presence of only neutral mucins in moderate concentration in their wall.

4) The prostatic tissue with acute nonspecific prostatitis with abscesses reveals the presence of less concentration of neutral mucins in the normal acini, whereas their secretion shows the presence of both neutral and acidic mucins. The necrotic acini show less concentration of neutral mucins, while their secretion shows the presence of only neutral mucins in weak to moderate concentration. Thus the secretion of

necrotic acini shows loss of mucins. This loss is evident in the case of acidic mucins than in the case of neutral mucins.

In this affected prostatic tissue the infiltration of inflammatory cells in the stroma is observed. These inflammatory cells show the presence of neutral mucins, small amount of glycogen and acidic mucins, while some of the inflammatory cells show traces of sulfomucins.

The stroma in this prostatic disorder reveals more or less normal pattern of distribution of mucopolysaccharides. It shows the presence of neutral mucins, glycogen, acidic mucins (sialomucins) and sulfomucins.

The duct system of this prostatic tissue shows somewhat different pattern of mucin contents as compared to the normal prostatic duct system. The duct shows the presence of only neutral mucins and absence of acidic and sulfated mucins, while the smooth muscle fibres of the stroma show presence of only neutral mucins with traces of glycogen.

5) Various histochemical reactions applied to the glandular adenocarcinoma of prostatic tissue reveal the presence of only neutral mucins in normal looking and affected acini, while the secretion of both these acini shows the presence

of moderate concentration of neutral mucins and carboxy mucins (sialomucins) in traces. Corpora amylacea found in some acini shows the presence of neutral mucins in moderate concentration, carboxy mucins (sialomucins) in small amount and sulfomucins in traces.

The glandular tumor cells found in this affected prostate show the presence of only neutral mucins and absence of acidic and sulfomucins.

The duct system in the adenocarcinoma shows the presence of neutral mucins in less concentration with traces of acidic mucins, while the stroma with connective tissue shows the presence of neutral as well as carboxy mucins. The muscle fibres of stroma show the presence of small amount of glycogen in addition to the neutral mucins.

6) The Anaplastic carcinoma of the prostate in the present investigation reveals the following results with various histochemical reactions. The normal appearing acini show the presence of neutral as well as acidic mucins, but the affected acini show partial loss of both the types of mucins indicating presence of moderate to weak concentration of neutral mucins and traces of acidic mucins. The secretion is found to be decreased in affected acini as compared to the secretion of normal appearing acini in this tissue. The secretion

in this pathological disorder contains neutral mucins and at some places mixture of neutral and acidic mucins.

Histologically the Anaplastic carcinoma in the present investigation shows three different types of cells, viz., transitional epithelium, inflammatory cells and tumor cells. The histochemistry of these cells reveals the presence of neutral, acidic and sulfated mucins in the transitional epithelium, the presence of neutral and sialomucins in the inflammatory cells and neutral, and acidic mucins with traces of glycogen in the tumor cells. The neutral mucins are found more in the tumor cells than in the remaining types of cells; this increase may be due to the presence of glycogen in the tumor cells.

The ducts present in the stroma of normal appearing acinar region and tumor region show similar results with various histochemical reactions. The duct wall and epithelium shows the presence of only neutral mucins in moderate concentration. The stroma in this prostatic disorder shows the presence of neutral mucins in moderate concentration, acidic mucins (sialomucins) in weak concentration and traces of sulfomucins, while the smooth muscle fibres of the stroma show the presence of less concentration of neutral mucins with glycogen.

The blood vessels of the tumor region also show diversion from the normal structure and they histochemically show the presence of neutral mucins in moderate concentration and sialomucins in weak

to traces.

A critical evaluation of the literature on prostate included in the introductory chapter shows that the prostate gland in normal and under various prostatic disorders has been mainly studied for proteins, enzymes, lipids and inorganic ions, but very few research workers have reported about the mucin contents and their distribution, especially in the abnormal prostate. The presence of fructose moiety as a carbohydrate component in the anterior lobe of rat prostate has been shown by Davies and Mann (1947 a), Lutwak and Mann (1951). Absence of glycogen in the rat prostate is reported (Takkar and Kamboj, 1970) and it is also reported in bull (Sajonski et al., 1972). On the other hand the presence of glycogen has been reported in the prostate of dog (Gerber, 1961), rabbit (Schantz, 1964) and in wombat (Brooks et al., 1978). Similarly Rodger and Ian (1980) demonstrated the glycogen and N-acetyl glucosamine in the prostate of Australian and American marsupials. The presence of glycogen in prostate tissue is also found in the present investigation.

Bischof and Gerhard (1982) showed age-dependent changes in the carbohydrate pattern of human prostate epithelium. The histochemical studies show the presence of PAS-positive and diastase-resistant material in the prostate of dog (Arcadi, 1952), ram (Aitken, 1955), boar (Aitken, 1960) and bull (Stallcup, 1969). Gupta and Yashwant Singh (1982) observed the saliva-resistant and PAS-positive material

in the intracellular region of the goat prostate and also showed moderate alcianophilia in the mucous alveoli.

The presence of acidic mucins in the prostate has been reported by a number of research workers. Acid mucins have been studied in the prostate of dog (Arcadi, 1952), deer (Aughey, 1969), rat and man (Preto-Parvis et al., 1966; Pasqualucci and Macha, 1968; Leutert and Jahn, 1970). Miraglia et al. (1970) in marmoset and Glyal and Mathur (1974) in H.auratus collaris prostate demonstrated the presence of sialic acid. Seasonal variations leading to depletion in prostatic glycogen, sialic acid and neutral mucins are shown in the quiescent period of some bats (Pawar, 1976; Vibhute, 1980; Fartade, 1981).

Tsukise et al. (1986) observed weak to strong positive histochemical reactions for complex carbohydrates in secretory epithelium of prostate showing the presence of neutral and acidic mucins. Further, Tsukise and Yamada (1984) studied the complex carbohydrates of the secretory epithelium of goat prostate and showed the presence of three types of secretory epithelial cells which contain neutral and acidic carbohydrates. Variations in the carbohydrates after castration and after hormone administration have been worked out by many workers. Chierego and Fabris (1951) in dog and Singhal (1968) in rat showed that testosterone increases glycogen content of prostate, whereas, Bose and Kar (1968) reported that castration in monkey results in the increase in the prostatic sialic acid. Cyproterone

acetate administration resulted in the increase in sialic acid content of prostate of rat (Rajlaxmi, 1972).

A review of literature on recent work related to the mucin content of prostate under different pathological disorders shows very scanty information about the mucopolysaccharide distribution. Levine and Foster (1964) have shown the presence of some mucicarminophilic material in the significant number of well differentiated carcinomas of prostate. Histochemical study of Franks et al. (1964) showed that alcian blue positive mucins occur commonly in the cells and acini of both latent and overt prostatic cancers, but rarely in the normal gland or in BPH. Similarly, in the case recorded by Sika and Buckley (1964) the acini contain variable amounts of PAS-positive and mucinocarminophilic substance, but no mucin can be demonstrated in the cells. Further, Franks et al. (1964) showed that the colloid cancers produce large quantities of alcian blue positive, sialic acid containing mucins in which sialic acid residues are sulfated. These extensive mucinous tumors also contain nonsulfated mucins. Patel et al., (1981) studied a case of mucin secreting adenocarcinoma of prostate with very high acid-phosphatase level. Villary and Napoli (1984, 1985) reported less concentration of acidic mucins in the glandular lumen of atypical epithelial hyperplasia, but in well differentiated adenocarcinoma acidic mucins are found in large concentration.

Histochemical study by Sugiyama (1985) showed presence

of neutral and acidic carbohydrates in prostate tumor, further he showed that BPH cell basement membrane, cytoplasm of the epithelium and cell interstitium contain chondroitin B and hyaluronic acid. 1,2 Glycol group of neutral complex carbohydrates in the interstitium of the prostatic cancer are shown to exist in smaller amount than those in BPH.

Thus the available literature in earlier years of mucopolysaccharides of the prostate shows that they are only studied for their mucin content in normal mammals including man, but during recent years it seems that the prostate gland is mainly studied for its qualitative as well as quantitative variations in the mucin secretion by different cellular structures of affected prostate and to evolve the relation between the mucin secretion and its diagnostic value for the identification of prostatic disorders. Among such research workers, the work of Frank et al. (1964) shows that alcian blue positive mucins occur commonly in the cells and acini of both latent and overt prostatic cancers, but rarely in the normal gland or in BPH. Further they showed that colloid cancers produce large quantities of alcian blue-positive, sialic acid containing mucins, in which sialic acid residues are sulfated and on this basis they differentiate this tumor from the other tumors as mucinous tumor. The characteristic feature of this mucinous tumor is that the entire tissue gets converted into mucin secreting cells. Such type carcinomas are named as mucinous adenocarcinomas (Ashley, 1980). Villary

and Napoli (1984, 1985) studied a diagnostic value of acid mucins in the prostatic neoplasm and reported weak positive material in the epithelial cells of hyperplasia but more frequent and abundant material in the neoplasm of well differentiated adenocarcinoma. According to these scientists the acid mucin secretion is useful in confirming the presence of cancer in equivocal cases and for quicker identification of mucinous microcarcinoma. In the present investigation somewhat different rsults are observed as compared to the above cited references. In the chronic prostatitis and in acute nonspecific prostatitis with abscesses, the mucin contents are depleted than the mucins of normal prostate. This depletion is evident in the case of neutral mucins and acidic mucins in the affected acini and secretion, but stroma and muscle fibres revealed less alterations. Thus these two noncancerous diseases of prostate selectd in the present investigation show loss of mucins. Similarly, studies on mucin content and their concentration in the adenocarcinoma and anaplastic carcinoma show depletion in neutral and acidic mucins in affected acini, secretion and ducts, whereas the inflammatory cells and tumor cells show presence of neutral mucins in moderate concentration, sialomucins in weak concentration and sulfated mucins in traces. These results, however support the earlier observations by Sugiyama (1985) who studied the histchemistry of complex carbohydrates in prostatic tumor and showed the presence of neutral. and acidic carbohydrates. Further with the help of immunohistochemical study of BPH he showed that the cell basement membrane, the cytoplasm of epithelium and the cell

interstitium contain chondroitin B and hyaluronic acid. 1,2 Glycol group of neutral complex carbohydrates are shown to exist in small amount in the interstitium of prostatic cancers than those in the BPH. In addition the prostatic cancer cell cytoplasm shows the presence of chondroitin sulfate A, C and hyaluroic acid.

A critical review of other chemical constituents of prostate included in the introductory chapter shows that inhibin levels increase in BPH by ten-fold in comparison to the normal and cancerous tissue (Sheth et al., 1981). The presence of Keratin is found in the metaplastic squamous epithelium (Friedmann et al., 1985), in micro-carcinoma and atypical hyperplasia (Battaglia et al., 1985), in normal and BPH (Kitajima et al., 1986), in normal, BPH and carcinoma (Kuwahara et.al., 1987) and in the histological sections of normal, hyperplastic and neoplastic prostate (Purnell et.al., 1987).

The acid phosphatase activity in normal and in the abnormal prostate is studied by many research workers. The prostatic acid phosphatase activity in normal and hyperplastic prostate is uniform at apical portion of glandular epithelium and it is localized in the microvilli lining, prostatic and vesicular bodies of apical cell regions. The neoplastic prostatic tissue reveal more intense and uniform staining of tumor cells and of the glandular epithelium of well differentiated adenocarcinoma, on the other hand less intense and more variable staining is seen in neoplastic cells of moderately and poorly differentiated adenocarcinoma (Mori and Choei, 1985).

Zundervan et.al., (1986) demonstrated the localization of secretory prostatic acid phosphatase in human hyperplastic prostatic epithelium containing α-glycosidase and β-galactosidase. Loor et al. (1981) reported that the activity of prostatic acid phosphatase in prostatic cancer is about 25% of that in normal prostate and BPH.

Seaman and Winell (1959) observed a high degree of esterase activity in prostatic cancer cells of mature dogs. Mizutani et al. (1986) observed five times higher 5α-reductase activity in BPH than in prostatic cancer in man. Ronquist et al. (1984) reported 50 to 90 per cent decrease in the prostatic fucosyl transferase activity in the prostatic cancer. While the prostate specific antigen is found to be increased in prostatic cancer (Fuse et al.,, 1986), Calli and Mori (1967) demonstrated reduction in the total lipids in the adenomatous prostate tissue, but a significant increase is observed in the phospholipid contents indicating enhanced biosynthetic activity in this pathological tissue. Zn level increases in the typical canine hyperplasia while prostatic secretion of men with prostatitis shows absence of Zn (Tunn et al., 1979).

The above mentioned discussion on various metabolites in the prostate under pathological conditions shows that either these chemicals are uniformly distributed or they show decrease, especially under malignancy. From the present investigation now it can be said that not only the enzymes, lipids, and Zn, but also the mucin

content of prostatic tissue shows either uniform distribution or decrease in concentration in the chronic prostatitis, adenocarcinoma, anaplastic carcinoma and abscesses. This decrease is mainly evident in the case of neutral and acidic mucins in the epithelium of the acini. Thus on this basis some criteria for diagnosis of above prostatic disorders can be evolved.

Relation Between BPH and Cancer and Other Prostatic Disorders:

The exact relationship of hyperplasia to prostatic cancer is difficult to determine, but the histopathological characters of BPH apparently represent a precancerous condition (but it is not firmly established yet). Studies in this relation by Edwards et al., (1953) indicate that cancer and prostatic hyperplasia are associated more frequently. The data presented by them also indicate that the cases of latent cancer predominate among large prostate and that the more voluminous the hyperplastic gland, the more likely it is to contain an acclute cancer. Nearly 50 to 60 per cent of the patients with prostatic cancer also have nodular hyperplasia. The hyperplasia is common among the adults over 45 years of age, but carcinoma is not so common, though the hyperplasia and carcinoma occur within the same mass of tissue. According to Lewis (1950), Moore (1944), and Franks (1956) these two disorders, viz., hyperplasia and carcinoma probably represent distinct and separate disorders

of prostate, as the prostatic cancer arises from the outer true or main glands, whereas hyperplasia affects mainly the inner mucosal and submucosal glands of the prostate. In this regard, in the present investigation, not from the point of histopathological alterations, but from the point of view of mucin histochemistry, some relation can be shown to exist in these two disorders. From the observations (Table No. 7) it is clear that in the normal prostate and BPH with prostatitis studied in the present investigation the acini and their secretion contain higher concentrations of neutral mucins, and sialomucins and traces of sulfomucins. The other disorders selected in this investigation also show the presence of hyperplastic acini. When the mucin content of these hyperplastic acini is compared with the mucins of BPH, then decrease in mucin content (more evident in sialic acid) is seen. Thus the hyperplastic acini found in acute nonspecific prostatitis with abscesses, chronic prostatitis, adenocarcinoma and anaplastic carcinoma show decrease in their mucin content. These observations suggest that when the hyperplastic acini of affected prostate show the decrease in the mucin content than that found in the BPH and normal prostate then it can be said that such affected prostate is definitely associated not only with BPH, but also with some additional abnormality. This abnormality may be acute nonspecific prostatitis with abscesses or malignancy. Thus study of mucopolysaccharides in prostatic disorders can be used as one of the clues to evolve the relationship between BPH and other prostatic disorders. Of course, further detailed investigation

TABLE NO. 7

Comparative account of mucopolysaccharides found at major histological structures of human normal prostate and prostate under different pathological disorders.

Mucopolysaccharides	Normal	BPH	Chronic Prostatitis	Prostatitis with Abscesses	Adenocarci-noma	Anaplastic Carcinoma
			ACINI			
Glycogen	(-) Absent	(-) Absent	(-) Absent	(-) Absent	(-) Absent	(-) Absent
Neutral mucins	(+++) Intense	(++to +++) Moderate to Intense	(++) Moderate	(+) Weak	(+) Weak	(++) Moderate
Acid mucins (sialic acid)	(++) Moderate	(+) Weak	(+) Weak	(-) Absent	(-) Absent	(±) Traces
Sulfated mucins	(+) Weak	(±) Traces	(-) Absent & (±) Traces in some	(-) Absent	(-) Absent	(-) Absent
			SECRETION			
Glycogen	(-) Absent	(-) Absent)	(-) Absent	(-) Absent	(-) Absent	(-) Absent
Neutral mucins	(++++) High	(++++) High	(++to +++) Moderate intense	(++) Moderate	(++to +) Moderate to weak	(+) weak
Acidic mucins (Sialic acid)	(+++) Moderate	(++ to +++) Moderate to intense	(+) Weak	(-) Absent	(+) Weak	(±) Traces
Sulfated mucins	(+) Weak	(+) Weak	(-) Absent	(-) Absent	(-) Absent	(-) Absent
			STROMA			
Glycogen	(+) Weak	(+) Weak	(-) Absent	(+) Weak	(-) Absent	(±) Traces
Neutral mucins	(+++) Intense	(+++) Intense	(++) Moderate	(++) Moderate	(+) Weak	(++) Moderate
Acidic mucins (Sialic acid)	(+) Weak	(+) Weak	(++) Moderate	(++) Moderate	(+) Weak	(+) Weak
Sulfated mucins	(±) Traces	(±) Traces)	(+) Weak	(±) Traces	(-) Absent	(±) Traces

is needed for the firm establishment of such relationship.

SUMMARY AND CONCLUDING REMARKS

A critical analysis of the literature on the prostate gland shows that though the histology and histochemistry of the normal prostate and the prostate under pathological disorders has been studied, very little literature exists about the mucopolysaccharide distribution in the normal prostate and the alterations in the mucopolysaccharides in different prostatic disorders. The study of only some special types of cancers (mucin microcarcinoma) has shown that normal acinar cells of the prostate get modified and transformed into mucin secreting neoplasmic cells Therefore, the present investigation was undertaken to understand the alterations and distribution of mucins in the prostate under some of the pathological disorders. The prostatic disorders viz., BPH with prostatitis, chronic prostatitis, acute nonspecific prostatitis with abscesses, adenocarcinoma and anaplastic carcinoma of the prostate are selected and their mucopolysaccharide contents are investigated by employing various histochemical techniques.

The investigations have been carried out in the following manner:

(1) To study the histological structure of human normal prostate and the prostate under different pathological disorders.

(2) To find out histopathological differences in the prostate glands selected for the present investigation.

(3) To find out the distribution and localization of various muco-substances in normal and prostate under different pathological conditions in man.

(4) To study the variations in the distribution and localization of various mucosubstances in the human prostate glands selected for the present investigation.

(5) To find out whether these variations in the distribution and localization of mucosubstances bear any relationship with the significance in early diagnosis of prostatic disorders.

The observations and conclusions derived therefrom are summarized below:

1) Histological study of normal prostate using H-E technique shows presence of glandular elements, smooth muscles and fibrous tissue. The prostatic acini and tubules are invested by limiting fibromuscular stroma propria that follows all the irregularities of the glandular elements. Immediately outside the stroma propria the extensive supporting framework of the prostate is continued as fibrous tissue containing irregularly interlacing strands and bundles of smooth muscles.

Histochemical reactions employed for the study of

mucopolysaccharides show the presence of neutral mucins in intense to high concentration, acidic mucins inmoderate and sulfomucins in weak concentration. The acinar secretion contains high concentration of neutral mucins, moderate concentration of acidic mucins and weak concentration of sulfomucins. The stroma shows the presence of neutral mucins (intense) acidic mucins and glycogen in weak concentration. The muscle fibres show presence of weak concentration of neutral mucins and traces of acidic mucins and glycogen. The duct wall and epithelium show moderate concentration of neutral mucins, weak concentration of sialic mucins and traces of glycogen./

2) In Benign prostatic hyperplasia (BPH) with prostatitis the histological structure of the prostate shows proliferation of both stroma and epithelium which results in symmetrical or nodular localized enlargement of the gland. The acini and ducts increase in size and number. The proliferation is regular and symmetrical. The stroma in hyperplasia closely invest the acinar wall and contains smooth muscle fibres, it also shows area of infarction adjacent to which the acini are lined with metaplastic squamous epithelium. Corpora amylacea is found in some of the acini. The secretory activity in BPH is normal.

The histochemical results obtained for mucopolysaccharide show that in BPH the acini contain neutral mucins (moderate to intense) acidic mucins (sialomucins) weak, and traces of sulfomucins, while the secretion shows the presence of neutral mucins (high

concentration), acidic mucins (sialic acid) moderate concentration and sulfomucins (weak). The corpora amylacea occasionally found shows moderate concentration of neutral and sialomucins and absence of sulfomucins. The stromal components exhibit presence of neutral mucins (intense), sialic acid (weak), glycogen (weak) and sulfated mucins (traces). The ducts found in the stromal and acinar region reveal the presence of neutral mucins (intense to moderate), carboxy mucins (weak), and sulfomucins (weak). The important feature of BPH in this investigation is that some of the functional acini are lined with metaplastic epithelium. Histochemically the metaplastic epithelium shows three types of cells:

i) Cells elaborating neutral mucins,

ii) Cells elaborating mixture of neutral and acidic mucins,

iii) Cells elaborating only sulfated acidic mucins.

3) Histopathologically the tissue of chronic prostatitis is characterized by focal hyperplasia in the acini, the acini being lined by cuboidal epithelium instead of columnar epithelium. The acini and ducts are destroyed at places and they are replaced by an exudate of plasma cells, microphages and eosinophils. Large area of tissue shows proliferating fibrous stroma. The cells in the acini are with hypertrophid nuclei. The blood vessels are destroyed and obliterated.

The histochemical reactions show the presence of neutral mucins (moderate), and carboxy mucins (traces) in the hyperplastic acinar epithelium, and the basement membrane, but some of the hyperplastic epithelium shows presence of sulfated mucins in the apocrine region. The secretion of the hyperplastic acini shows presence of moderate to intense concentration of neutral mucins and traces of acidic mucins. The stroma contains neutral mucins (weak to moderate), acidic mucins (weak) and sulfated mucins (traces), while the muscle fibres show the presence of glycogen, neutral mucins and acidic mucins. The wall of the normal blood vessel shows the presence of neutral mucins (moderate to intense), sialomucins (weak) and sulfomucins (traces), whereas the obliterating blood vessel wall shows presence of only neutral mucins.

4) The tissue sections of the acute nonspecific prostatitis with abscesses stained with H-E technique show the presence of necrotic and destroyed acinar epithelium. The lumen of these acini is also filled with necrotic substance. The stroma shows diffused, dense and acute inflammatory cell infiltration, prodominantly composed of polymorphs, forming many microabscesses. At some places the stroma also shows blood spaces.

The histochemical reactions show the presence of only neutral mucins (weak concentration) in the necrotic acini and absence of acidic mucins, while the secretion of these acini shows less concentration of mucins than the mucins of normal prostatic secretion. The

loss of mucins in the necrotic secretion is more evident in the case of acidic mucins than in the neutral mucins. The inflammatory cells found in stroma contain neutral mucins (moderate), glycogen, acidic mucins (weak) and sulfomucins (traces). The muscle fibres found in stroma show the presence of neutral mucins and glycogen.

5) Adenocarcinoma of the prostate tissue, histopathologically, shows presence of tumor composed of glandular cells arranged in adenoid cysts and streaks. Occasionally some normal prostatic acini are also seen. The glandular tumor cells show clear and eosinophilic cytoplasm containing round, hypertrophid and hyperchromatic nuclei. The stroma becomes thick due to increased tumor glandular tissue.

Histochemically the normal appearing acini occasionally found in tumor region show the presence of only neutral mucins (weak) and absence of sialomucins and sulfomucins, whereas secretion shows weak to moderate concentration of neutral mucins, weak concentration of acidic mucins, and absence of sulfomucins. Similarly the stroma which is thick in the neighbouring region of tumor growth shows presence of neutral and acidic mucins (weak concentration) and absence of glycogen and sulfomucins. Corpora amylacea found in the normal appearing but dilated acini shows presence of neutral mucins (moderate), sialomucins (weak) and sulfomucins (traces). The glandular tumor cells of adenocarcinoma show the presence of only neutral mucins in weak concentration.

6) Histopathological observations of Anaplastic carcinoma show the prostate tissue mainly consisting of tumor beneath the strip of transitional epithelium. The normal appearance of prostate is totally lost, because of the infiltration of tumor cells forming sheets and clusters in the stroma and in the inter-acinar region. The tumor cells show hyperchromatic nuclei and vacuolated, eosinophilic cytoplasm. The stroma also shows infiltration of inflammatory cells. At some places reduced but normal appearing functional acini are observed. The tumor cells also grow over the wall of the blood vessels found in the tumor region.

Histochemical techniques show the presence of neutral mucins (weak to moderate) acidic mucins (traces) in the affected acini, whereas secretion shows presence of mixture of neutral and acidic mucins (weak to moderate). The transitional epithelium invaginated from the wall of prostatic urethra shows the presence of two types of cells:

1) Cells containing only neutral mucins (moderate),
2) Cells containing mixture of neutral and acidic mucins.

The inflammatory cells found in the stromal region show the presence of neutral mucins in the majority of the cells, and sialomucins in some of the cells. The tumor cells exhibit the presence of neutral mucins (moderate), acidic mucins and glycogen (traces). These cells also show increased PAS activity than that of the inflammatory

and transitional epithelial cells. The ducts show only neutral mucins (moderate) whereas stroma indicates the presence of neutral mucins (moderate), sialomucins (weak) and sulfomucins (traces). Muscle fibres show the presence of neutral mucins (weak) and glycogen. The blood vessels found in the tumor region show the presence of neutral mucins (moderate) and sialomucins (trace).

A cursory glance at review and observations in the present investigation brings out the following conclusions:

(1) The normal human prostate histologically shows presence of well developed, active glandular elements and contains high to intense concentrations of neutral mucins, acidic mucins and traces of sulfomucins with glycogen in the smooth muscle fibres only.

(2) BPH with prostatitis shows slight changes in the histological structure from that of normal prostate. BPH tissue shows presence of hypertrophid, dilated acini and metaplastic epithelium, but no any change is observed in the mucin secretion in BPH; it shows almost resemblance with the mucin secretion of normal prostate.

(3) Chronic prostatitis, though, shows hyperplastic acini, it differs histopathologically from normal prostate and BPH. The histochemical analysis in this disorder shows decrease in neutral mucins than that found in the normal prostate or BPH. This decrease

is especially noted in the acini and stroma.

(4) Acute nonspecific prostatitis with abscesses shows characteristically different histopathological structure from that of the other prostatic disorders. The characters described in the present investigation will be helpful in identification of the prostatitis with abscesses. Histochemically this tissue shows loss of neutral mucins, sialic acid and sulfomucins at acini, secretion and very slight decrease of mucins is observed in the stromal components. The loss of the mucins in this disorder is more evident than that found in the chronic prostatitis. This will give additional clue to identify this prostatic disorder.

(5) Thus the histopathological characters described in the present investigation will help in the diagnosis and confirmation of the chronic prostatitis and acute nonspecific prostatitis with abscesses.

(6) Two cases of malignancy studies represent different histopathological structures. The histological as well as histochemical observations described in the present investigation will help in distinguishing between glandular adenocarcinoma and anaplastic carcinoma of human prostate. The histochemical analysis of these two disorders show decrease in mucins at normal appearing histological structures. This decrease in mucins especially in the sialic acid content (absent in glandular carcinoma and traces in the anaplastic carcinoma) will help in early diagnosis of malignancy.

(7) It is reported by some scientists that the BPH and carcinoma are generally associated with each other and BPH leads to carcinoma, but it is not observed in each and every case of BPH. From the present investigation it is found that when acini in BPH show decrease in mucin contents to large exrtent, one can suspect that probably BPH is going to convert in to malignancy.

(8) BPH showing metaplastic epithelium sometimes may be misdiagnosed as a malignant tissue, as the histopathological structure mimics that of the squamous epithelium carcinoma of prostate. But from the present investigation it can be said that both these disorders can be very well differentiated from each other on the basis of mucin contents. The squamous epithelial carcinoma show uniform distribution of neutral mucins but in metaplasia there are three types of cells elaborating neutral mucins, mixture of both neutral and acidic mucins and sulfated mucins respectively.

Concluding Remarks

The aims and objectives of the present investigation were to study the histopathology and the mucopolysaccharides in the prostate under some of the pathological conditions and to compare it with that of the normal prostate, to give some additional histopathological and histochemical clues for identification of the particular prostatic disorder and to compare the results obtained in the present investigation with the existing literature. It is hoped that the aims and objectives

of the present investigation have satisfactorily been achieved.

The author is fully aware of the shortcomings during the tenure of the present investigation. The author had to depend only on light microscopic observations, also within the limitations of the laboratory only specific histochemical methods have been carried out to localize the mucosubstances. The approximate staining intensities by visual estimation such as trace, poor, weak, moderate, intense and high, may indicate roughly the relative amounts of mucosubstances in different histological sites of prostate under investigation.

While concluding the author feels that the histochemical and histopathological confirmations made in the present study will be justified with a similar work using additional biochemical, immunohistochemical and other recent techniques including the use of electron microscope.