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The Ultrastructure of Rhesus Monkey Prostate

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Summary. An ultrastructural study of immature and mature rhesus monkey prostate is described and a comparison is made with human tissue. The immature gland consists of largely undifferentiated epithelium showing little or no secretory activity. The mature gland exhibits the general characteristics of prostates of the other species studied. Columnar epithelial cells and undifferentiated basal cells are observed. The two lobes of the gland show several differences, the caudal lobe being rich in secretory granules, with the cranial lobe consisting of taller vacuolated cells. The description provides a basis for comparison with ultrastructural changes produced during in vivo and in vitro experimentation and with characteristics of normal and diseased human prostate.

Key words: Monkey - Prostate - Ultrastructure.

A zonal interpretation of the human prostate has been described by McNeal (15) in which the parenchyma of the gland is subdivided into a central zone, forming the greater part of the base, and a peripheral zone caudal to this. Anatomical similarity between the parenchyma of the human gland, as described by McNeal, and the cranial and caudal entities of the simian prostate have been found (1), suggesting that the monkey may be a useful model for further study of prostatic function, biochemistry and endocrinology.

Whereas several biochemical and ultrastructural studies have been performed on both normal and diseased human prostates (2, 3, 9), relatively few investigations have been made on the monkey prostate. In this study, the ultrastructure of immature and mature Macaque prostate is described to characterise the normal tissue of the caudal and cranial lobes. This provides a basis for comparison with cellular changes resulting from alterations in endocrine status produced in vivo, in organ culture and with diseased tissue. The study also provides a comparison with the reported ultrastructural appearance of the different zones of human tissue.

MATERIALS AND METHODS

Two adult (approximately 10 years) and two immature (approximately 2 years) rhesus monkeys (Macaca mulatta) were used in the study. The animals were anaesthetised and the prostates removed by open surgery during the course of a complete study of the reproductive tract. The lobes of both mature and immature animals were well defined and easily separated. They were prepared for both histological and electron microscopical examination.

Small portions (5-10 c.mm) of the caudal and cranial lobes of each animal were dissected out and briefly immersed in 3% glutaraldehyde in 0.1 M phosphate buffer (pH 7.4). After the tissue had been cut into 1 mm cubes fixation was continued for a period of 3 h. The specimens were washed overnight in 0.1 M phosphate buffer (Sorenson's pH 7.4). The tissue was dehydrated in a graded series of alcohols, immersed in propylene oxide and embedded in araldite epoxy resin. Ultrathin sections of tissue were cut using glass knives on a Cambridge-Huxley ultramicrotome. Sections for light microscopy were stained with toluidine blue and borax, while ultrathin sections were

collected on unsupported copper grids. The sections were stained with uranyl acetate and lead citrate and examined in an AEI EM6B electron microscope.

RESULTS

Immature Prostate

The tissue from both lobes consisted of abundant fibromuscular stroma containing small, round, undifferentiated acini (Figs. 1 and 2). The cranial epithelial cells contained both pale and dark nuclei, while those of cells from the caudal lobe were predominantly pale. The epithelial cells were cuboidal in shape and there was a stroma : epithelium ratio of approximately 2 : 1. There was a higher frequency of developed lumina in the acini of the cranial lobe.

The cranial and caudal lobe tissues were similar in ultrastructural appearance (Figs. 3-6). The acini were surrounded by orderly layers of smooth muscle cells distal to a layer of collagen fibres and fibroblasts. The cells contained large irregularly shaped nuclei with a fine granular matrix and peripherally located heterochromatin (Fig. 5). Nucleoli were often prominent while many round or rod-shaped mitochondria occupied the cytoplasm around the nucleus. Small amounts of granular endoplasmic reticulum consisting of flattened parallel profiles were present while moderate numbers of free ribosomes were observed in the cytoplasm. The Golgi complex was scarce and was composed of small round vesicles and flattened lacunae. Secretory vacuoles and granules were rarely observed and where lumina were present there were no microvilli and very little or no secretion. In many cells there were large numbers of glycogen particles. The plasma membrane between adjacent cells was often interdigitated and intercellular spaces were observed (Figs. 3, 6). Cilia were occasionally observed protruding between cells (Fig. 6) and many centrioles were visible. Desmosomes were very prominent between developing cells with abundant tonofilaments extending into the cytoplasm. Moderate numbers of fibres were observed in the cytoplasm of many cells. There was a high level of micropinocytosis activity along the basement membrane (Fig. 4) while the basal lamina was single and continuous (Fig. 5). Attached hemidesmosomes occurred along the length of the membrane.

In general the acini were composed of largely undifferentiated and partially polarised immature cells. In many acini there was no clear definition between secretory epithelium and basal cells in either lobe, while in others this difference became clear.

Mature Prostate

Histologically the mature Macaque prostate consisted of fibromuscular stroma and large round acini lined by pseudostratified columnar epithelium (Figs. 7 and 8). There was a stroma : epithelium ratio of approximately 1 : 1. The epithelial cells of the caudal lobe had pale nuclei and a granular cytoplasm (Fig. 7). The acini of the cranial lobe (Fig. 8) were more irregularly shaped and lined by appreciably taller cells than those of the caudal lobe. The cytoplasm in the cranial lobe had a vacuolated appearance and both pale and dark nuclei were observed.

The arrangement of the stroma in ultrathin sections of mature rhesus monkey prostate was similar to that of the immature animal. The acini were surrounded by collagen fibres proximal to fibroblast and smooth muscle cell layers. Many blood vessels and unmyelinated nerve fibres were observed in the stroma. The prostatic acini of each lobe consisted of columnar epithelial cells and basal cells (Figs. 9-12). In general the mature tissue appeared degenerate compared with the immature prostate.

i) Caudal Lobe. In the mature caudal lobe the columnar cells generally contained pale, round, basally situated nuclei with a granular matrix and peripheral heterochromatin (Fig. 9). Many round mitochondria were observed in the basal portion of the cells, while moderate amounts of granular endoplasmic reticulum, consisting of short narrow lacunae with ribosomes disposed along the membrane, were present in the supranuclear region (Fig. 10). Moderately developed Golgi apparatus consisted of flattened saccules in parallel arrays and small round vesicles. An outstanding feature of these cells was the large number of electron dense secretory granules, observed throughout the supranuclear region and particularly towards the apex of the cells. Many secretory vacuoles and lysosomes were also concentrated near the lumina and the latter was often filled with secretory products (Fig. 9). Microvilli were observed in moderate numbers at the apex of the glandular cells with well formed junctional complexes in this region. Desmosomes were common apically but were less common towards the base of the cells. There was evidence of both merocrine and apocrine secretion.

Flattened or trilateral basal cells occurred at intervals around the periphery of the acini interposed between the bases of the epithelial cells (Figs. 9 and 10) but never extending to the

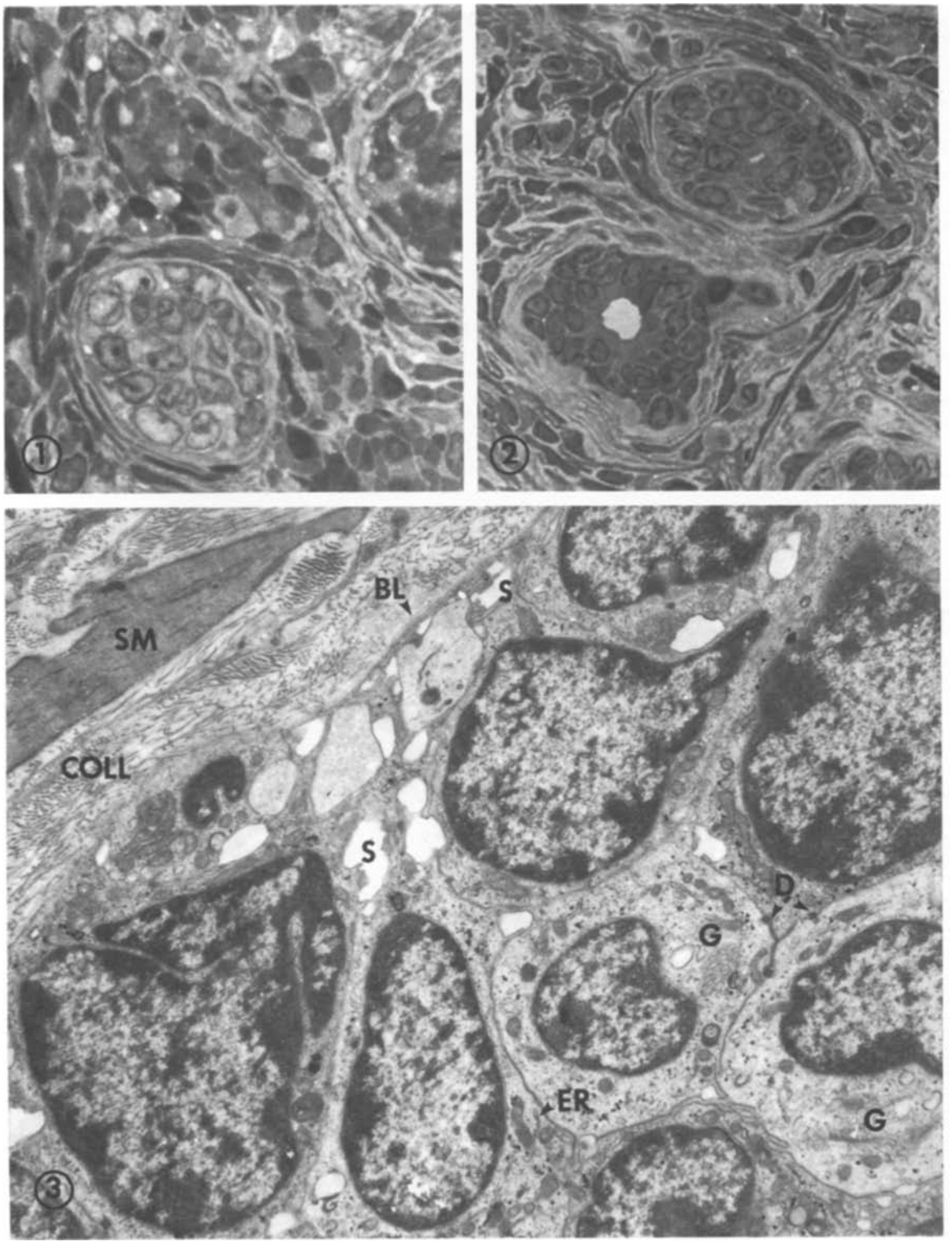

Fig. 1. Immature caudal prostate. Acini are in a ratio 1 : 2 with the stroma and contain undifferentiated pale cells. Toluidine blue stained, 1 µm thick. (x 841)

Fig. 2. Immature cranial prostate. Similar appearance to caudal lobe but with greater frequency of developed lumina. Toluidine blue stained, 1 µm thick. (x 850)

Fig. 3. Immature caudal prostate showing undifferentiated cells. Golgi apparatus (G) is undeveloped as is the endoplasmic reticulum (ER). SM = smooth muscle; COLL = collagen; BL = basal lamina, D = desmosomes; S = intercellular spaces with cytoplasmic projections. (x 10.300)

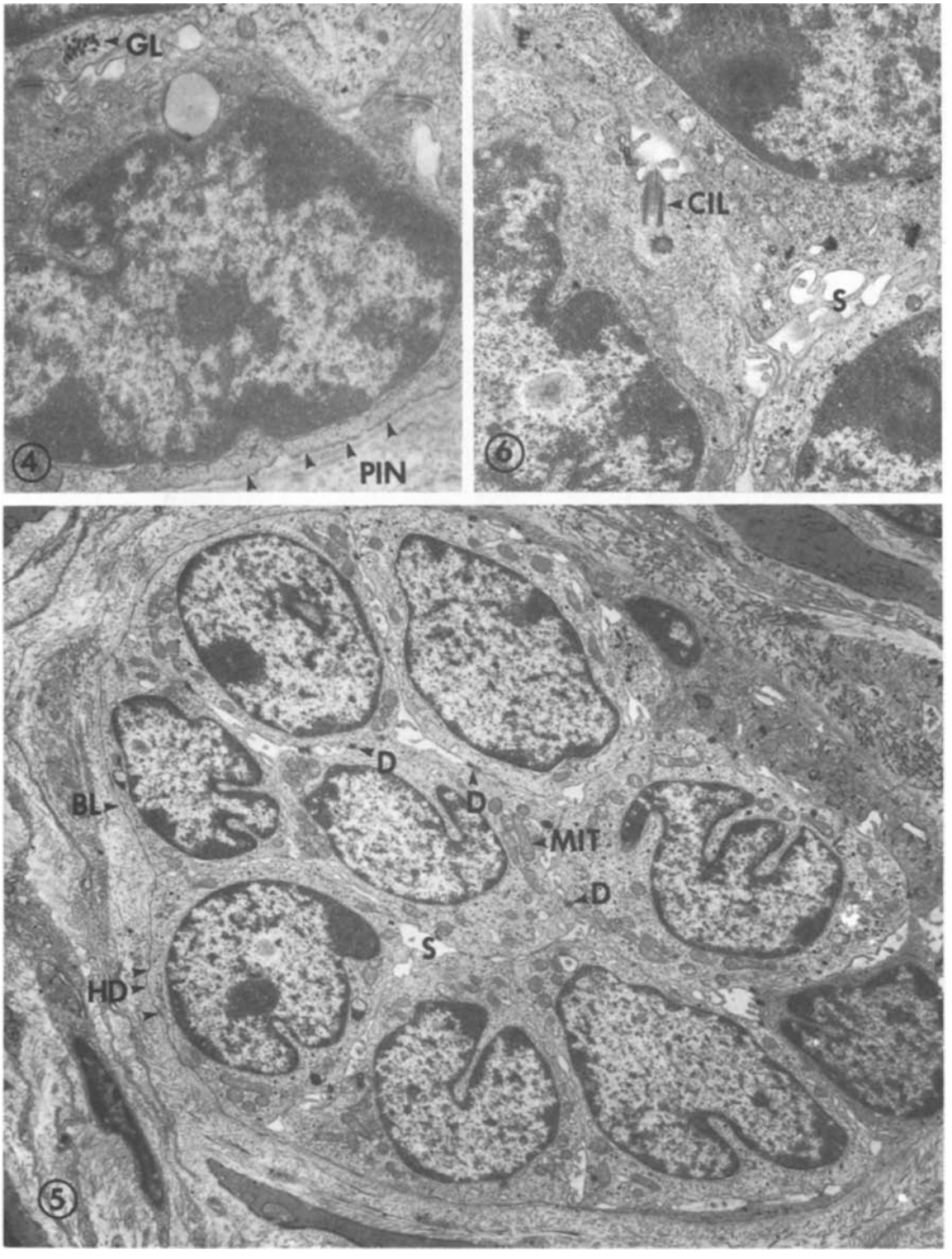

Fig. 4. Immature caudal prostate. Abundant micropinocytosis (PIN) is found at the basement membrane of basal cells GL = glycogen. (x 17.000)

Fig. 5. Immature cranial prostate showing largely undifferentiated cells with irregular nuclei and frequent desmosome (D) attachment. MIT = mitochondria; S = intercellular spaces; BL = basal lamina; HD = hemidesmosomes. (x 5.615)

Fig. 6. Immature cranial prostate exhibiting a cilium (CIL) protruding between adjacent cells. S = intercellular space with cytoplasmic projections. (x 10.850)

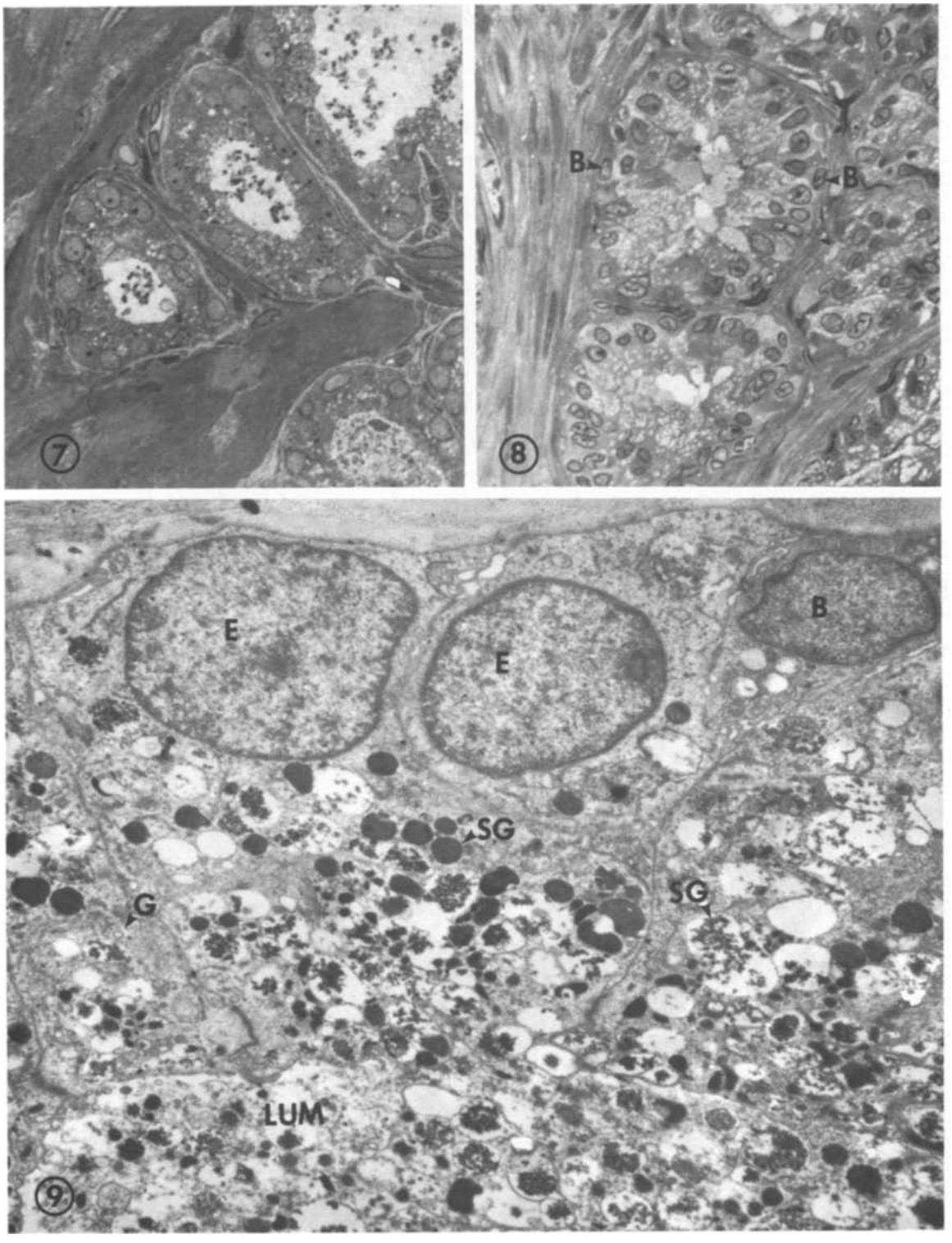

Fig. 7. Mature caudal prostate showing pseudostratified columnar epithelium with active secretion. Acinus : stroma ratio is 1 : 1. Toluidine blue staining, 1 μm thick. (x 750)

Fig. 8. Mature cranial prostate indicating high columnar cells with vacuolated cytoplasm. Basal cells (B) are evident. Toluidine blue staining, 1 μm thick. (x 655)

Fig. 9. Mature caudal prostate. Epithelial cells (E) are replete with secretory granules (SG). Golgi apparatus (G) is not highly developed. Basal cells (B) exhibit no secretion. The lumen (LUM) is filled with secretory products. (x 7.500)

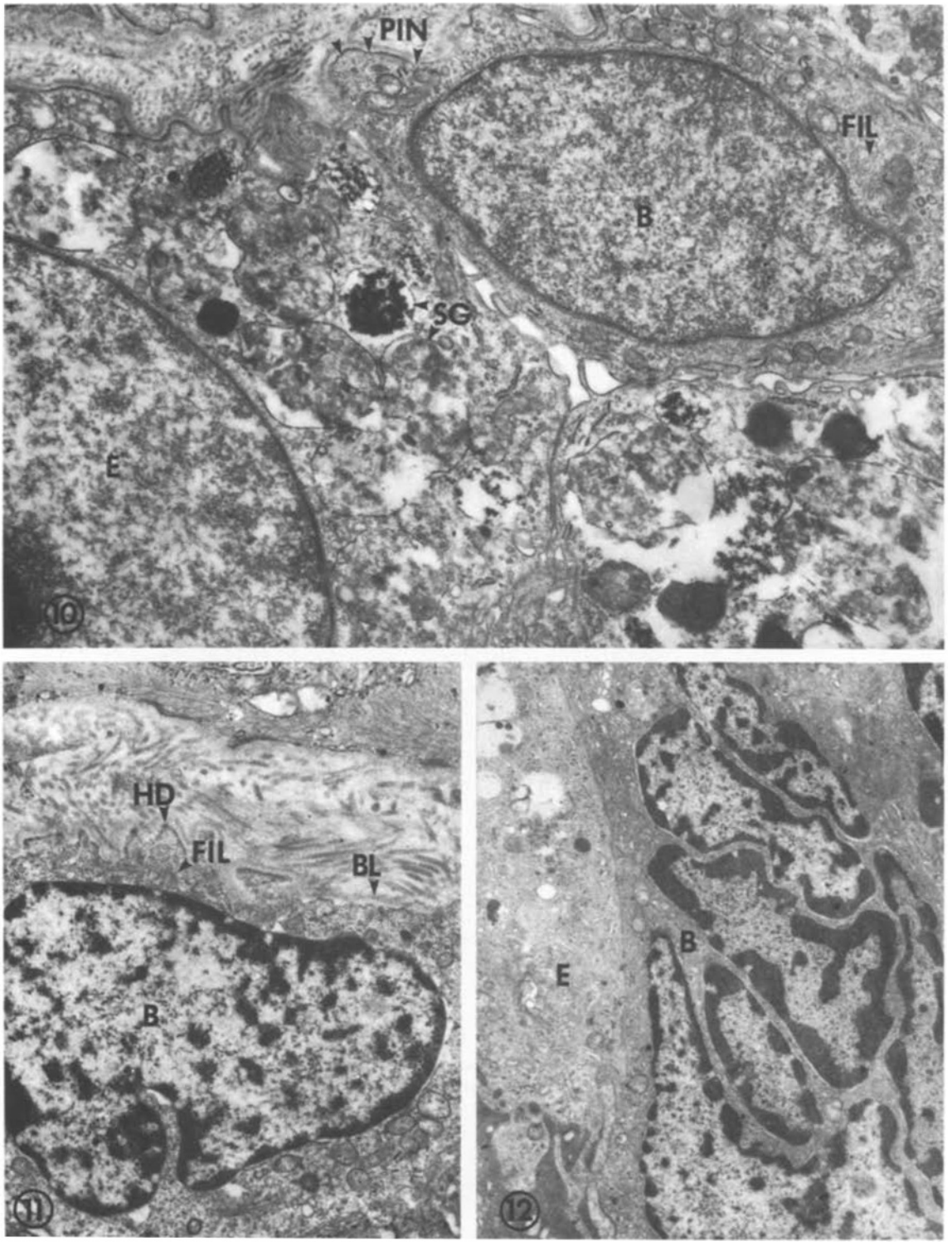

Fig. 10. Mature caudal prostate showing adjacent basal (B) and epithelial (E) cells. Filaments are evident in the basal cells while secretory granules (SG) almost fill the epithelial cell cytoplasm. Micropinocytosis (PIN) is confined to basal cells. (x 15.950)

Fig. 11. Mature cranial prostate. Basal cell (B) exhibiting hemidesmosomes (HD) along the basement membrane and cytoplasmic filaments (FIL). The basal lamina (BL) is single and continuous, while the basement membrane sometimes projected into the stroma. (x 12.250)

Fig. 12. Mature cranial prostate showing highly indented nuclei in the basal region with little cytoplasmic development. E = epithelial cell; B = basal cell. (x 12.750)

lumen. The basal plasma membrane and that of the glandular cells were interdigitated and desmosomes were often observed. A large portion of each basal cell was occupied by the nucleus following the shape of the cell outline. The cytoplasm contained many round mitochondria, while the Golgi complex was poorly developed, consisting only of a few flattened cisternae and small vesicles. Only a few, short, parallel profiles of granular endoplasmic reticulum were observed, while free ribosomes were more concentrated than in the epithelial cells. Micropinocytosis was common at the plasma membrane of the basal cells in contact with the basal lamina (Fig. 10) but was rarely seen basally in the columnar cells. Tonofilaments were also frequently present in the basal cell cytoplasm (Fig. 10) but not often seen in the glandular cells. Occasional cilia were observed.

In general the basal cells were similar in appearance to the cells of the immature prostate.

ii) Cranial Lobe. The epithelial cells of the cranial lobe, although taller, had a similar organisation to those of the caudal lobe. The basally positioned nuclei were irregular in shape and showed marked indentations (Fig. 12). Both pale and dark nuclei were seen. The nucleoli were often prominent and dark heterochromatin was frequently seen at the periphery of the nuclei. The endoplasmic reticulum and Golgi apparatus were similar in situation and extent to the caudal cells, although the lacunae of the Golgi apparatus were slightly dilated. Many elongated mitochondria were seen around the nucleus and large numbers of empty secretory vacuoles were present towards the apex of the cells. In contrast to the caudal lobe relatively few secretory granules were present. Many interdigitations were observed between the cells. The basal cells in this region of the prostate (Fig. 11) were similar in characteristics to the other lobe, although nuclei were often darker and more irregular in shape. The basement membrane of the cranial lobe acini was often more infolded than that of the caudal lobe (Fig. 11) and extensive cytoplasmic projections into the stroma were sometimes observed with high numbers of hemidesmosomes attaching to basal cells. The basal lamina was single and regular.

DISCUSSION

The rhesus monkey prostatic acinus has the general characteristics of that of other species studied e. g. man, rat and dog (4, 6, 10). Columnar and basal cell types were observed, the former having basally situated nuclei with mitochondria and granular endoplasmic reticulum, secretory vacuoles and secretory granules situated towards the apex of the cells. The basal cells were similar in ultrastructural appearance to those of the rat, dog and human (17, 22). The cilia observed in the mature and immature tissue corresponded to those found in basal cells of rat and human prostate (8, 22) while glycogen found in the immature monkey was similar to that seen in basal cells of dog prostate (22). These basal cells were essentially undifferentiated with relatively large nuclei and absent secretory processes.

There were a number of features similar to those seen in human prostatic tissue. Large numbers of secretory vacuoles were observed in the columnar cells as have been previously described in human acini (3, 10). Short narrow profiles of granular endoplasmic reticulum were present in Macaque columnar cells as have also been shown in human prostate (3, 10) unlike the extensive quantities of endoplasmic reticulum found in other species (6, 11). The presence of two types of secretion, apocrine and merocrine, in prostatic tissue has also been demonstrated in both human and rat prostate (4, 6).

In the rhesus monkey the cranial and caudal lobes are distinct and show both physiological and anatomical differences (19, 24). They are also ultrastructurally different. The caudal lobe, which has been shown to selectively concentrate zinc in the baboon (20), contains many electron dense secretory granules, with the cranial lobe acini being rich in secretory vacuoles. The zinc rich lateral lobe of rat prostate also contains many secretory granules as does the dog prostate (22). The differences in granules from the caudal and cranial lobes of the monkey prostate may represent a difference in secretory products from the two regions of the prostate, as has been observed in the rat.

In view of differences in the nomenclature of the subdivisions of the human prostate up to the present time, there is difficulty in comparing the findings of this study with those of Fisher and Sieracki (10), who noted no major ultrastructural differences between juxta-urethral and more peripheral parenchyma, and with those who found basal cells to be less frequent in the periurethral tissue (3). The obvious anatomical separation between the two lobes of the monkey prostate is not seen in the human gland, although histological differences have been demonstrated together with a variable susceptibility to disease (15, 21).

The epithelium of the immature prostate was largely undifferentiated with few cytoplasmic organelles and little or no secretion. It was similar to the prepubertal human prostate, the latter however having been found by Zondek and Zondek (25), to show rather more secretion in

the periurethral region than was seen in either the cranial or caudal lobe of the immature monkey. A striking number of similarities occurred between the undifferentiated cells of the immature monkey prostate and those reported in cases of metaplasia in the human gland (13). As with man there is a strong androgen dependency of the monkey prostate for growth and development (7).

The basal cells of the mature prostate were also similar in many respects to the epithelial cells of the immature gland. These basal cells are considered to be potential precursors of epithelial cells as has been described in both rat (23) and dog (22). They are not likely to act as myoepithelial cells, as suggested in the mouse ventral prostate by Rowlatt and Franks (18) since the acini are extensively lined with contractile smooth muscle cells. Organ culture experiments in vitro (5) have clearly indicated the proliferative capacity of the basal cells and their role as potential precursors to secretory cells. Whereas they may develop from the immature prostate into differentiated epithelium in the mature gland, they appear also to be stimulated in mature animals to proliferate under conditions adverse to normal epithelial cell maintenance (23). This is supported by the observations of Karpas and Moumgis (12) on the latent potential of basal cells to proliferate in human prostate and by the apparent lack of androgenic control of benign prostatic hyperplasia in vitro (14, 16).

From the ultrastructural study above it is apparent that several similar characteristics exist between the previously reported human prostate (4, 10) and that of the Rhesus monkey. In the results of subsequent experiments the cell types of both lobes are seen to react individually to manipulation of hormonal status, the most significant alterations occurring at the ultrastructural level. These observations suggest that the monkey may be a suitable model for further study of prostatic function, biochemistry and endocrinology.

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