EPITHELIAL GROWTH OF THE PROSTATE IMPLANTED BY LAZARENKO'S METHOD

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UDC 612.617.014.2 :612.6.02

The prostate gland of rabbits of different ages was implanted into intact and castrated homologous recipients.

The results showed that the biological powers of the prostatic ephithelium do not diminish with age, and there is only an increase in the number of highly differentiated cells. Epithelium of the glands implanted into castrated animals does not undergo glandular differentiation.

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Information in the literature on reactivity, plasticity, and the genetic nature of the prostatic epithelium is conflicting [1, 3, 4, 8, 9]. Investigations of organs implanted by Lazarenko's method showed that this method reveals most completely the biological powers of the tissues [5]. Only the sexually mature rabbit prostate has been studied by this method, and even so its histochemical characteristics have not been determined [3, 4, 6, 7].

In the present investigation the morphogenetic powers of the prostatic epithelium were studied at various stages of ontogenetic development and their relationship to the hormonal background was examined.

EXPERIMENTAL METHOD

Two series of experiments were carried out on 60 male chinchilla rabbits kept on a mixed diet. In series I, the prostate of animals of different age groups (1-2 and 5-6 months and 2 years after birth) was implanted into sexually mature rabbits aged 6 months. In series II the prostate of rabbits of the same age groups was implanted into castrated recipients (castration was performed 2 weeks before cultivation). Cultivation was carried out by Lazarenko's method [5].

Altogether 200 implanted glands were studied at stages of between 1 and 60 days of the experiment. Material was collected always at the same time of day, fixed in Carnoy's fluid, 10% formalin, or Zenker-formol by Maximov's method, and embedded in paraffin wax. Serial sections cut to a thickness of 5-6 μ were stained with Mayer's hematoxylin and eosin and with azan by Heidenhain's method.

Histochemical reactions were carried out for RNA with methyl green – pyronine by Brachet's method, ribonuclease control, for DNA by Feulgen's method, for glycogen and neutral mucopolysaccharides by the PAS reaction according to McManus and Hotchkiss (amylase and pepsin controls), for acid mucopolysaccharides with colloidal iron by Hale's method and by Steedman's method (testicular and streptococcal hyaluronidase controls), and for keratin by an acid solution of basic brown by Shubich's method. Total nucleic acids were detected by staining with gallocyanin by Einarson's method.

EXPERIMENTAL RESULTS

In both series of experiments the tissues cultivated in a focus of aseptic inflammation passed through a series of successive states of depression, activation and growth, organogenesis and functional differentiation, followed by regression of the newly formed structures.

Depending on the age of the donor, the period of depression lasted from 12 to 24 h and was expressed histologically by preservation of the original state of the cultivated tissues, as a result of injury to the tissue during mincing and to the disturbed conditions of nutrition. Intensive accumulation of granules of

Department of Histology and Embryology, Tyumen Medical Institute (Presented by Academician V. N. Chernigovskii). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 66, No. 10, pp. 84-88, October, 1968. Original article submitted July 16, 1967.

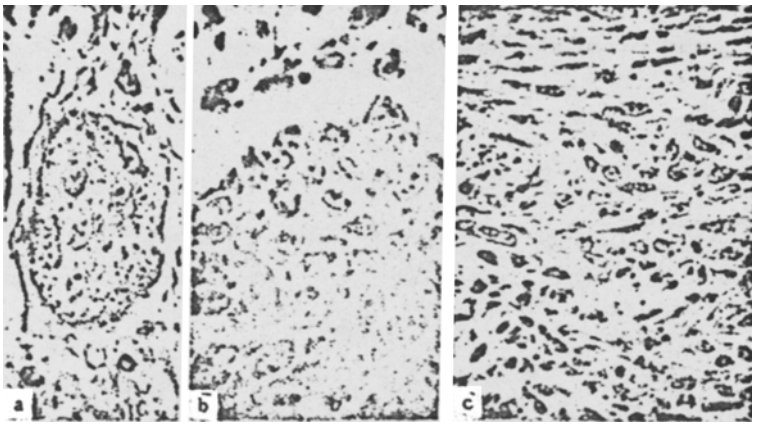

Fig. 1. Protective differentiation of prostatic epithelium cultuvated in vivo. a) Accumulation of glycogen in cells of an indifferent epithelial band. Donor, rabbit aged 1 month; recipient, rabbit aged 6 months. PAS reaction according to McManus and Hotchkiss. Objective 90, ocular 7; b) RNA granules in epithelial bands, 1 day after implantation. Donor, rabbit aged 1 month; recipient, rabbit aged 6 months. Methyl green – pyronine according to Brachet. Objective 90, ocular 7; c) stratified epithelial layer, 10 days after implantation. Donor, rabbit aged 5 months; recipient, rabbit aged 6 months. Einarson's gallocyanin. Objective 60, ocular 7.

glycogen, RNA, and acid mucopolysaccharides took place in the epithelial cells (Fig. 1a, b). Toward the end of the 1st day the implanted tissue fragments became saturated with exudative fluid and progressive degenerative changes were found in them. Most epithelial cells of the sexually immature prostate (rabbits aged 1-2 months) were activated and were proliferating within the fragment itself. At the edge of the implanted fragment the activated epithelium was unfolding into a flat sheet and invading the depth of the fibrin. At this stage numerous mitoses were found. Tissue cells injured during mincing or located in the deep zone of the implanted fragments showed degenerative changes.

In the implanted glands taken from sexually mature and old animals, most of the secretory cells of the terminal portions and highly differentiated cells of the efferent ducts matured abortively, died, and became detached into the lumen. Cells at the stage of intermediate differentiation showed signs of dedifferentiation (depolymerization of carbohydrate-protein complexes was demonstrated histochemically) and along with the cambial cells underwent progressive changes just as in the case of implantation of prostatic tissue from young donors. These progressive and degenerative changes lasted up to 4 days in these experiments.

Epithelial bands ingrowing into the fibrin joined up with the newly formed connective tissue proliferating in the intercelloidin spaces. Proliferating foci of epithelium, on reaching the surface of the celloidin fragments, formed eliminating stratified layers, initially without any clearly defined vertical anisomorphism. This was confirmed by the even distribution of structural materials (RNA, glycogen, acid mucopolysaccharides) throughout the layer.

Deeply growing bands [2] developed from the layers thus formed and branched repeatedly. In some parts of the implanted gland, where active inflammation persisted for a long time, a picture of infiltrative growth appeared.

As the inflammation subsided (6, 8, and 10 days of the experiment), organogenesis and functional differentiation of the regenerating epithelial tissues began to take place in the glands implanted in the experiments of series I.

The centrally situated cells in some of the epithelium bands matured abortively and died. In other epithelial bands the lumen of the acini was formed by a redistribution of the cells.

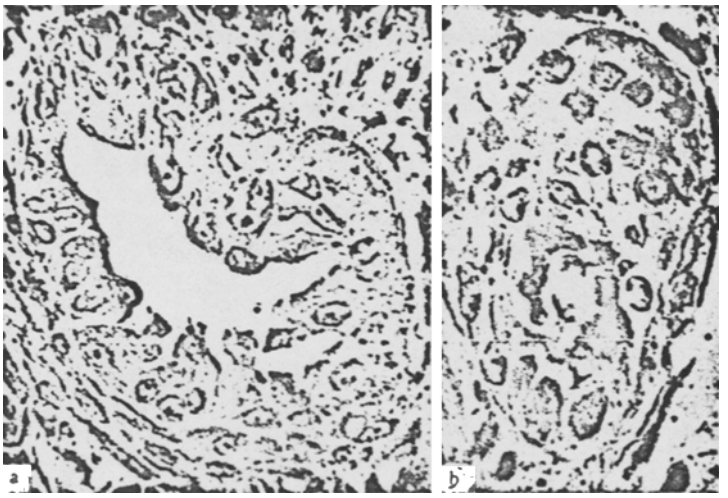

Fig. 2. Functional differentiation in prostates implanted into intact and castrated recipients. a) Apocrine secretion in newly formed terminal division, 10 days after implantation; donor, rabbit aged 2 months; recipient, rabbit aged 5 months. PAS reaction according to McManus and Hotchkiss (treated with amylase). Objective 90, ocular 7; b) stratified epithelial cyst with atypical keratinization of cells of apical layer, 12 days after implantation. Donor, rabbit aged 5 months; recipient, castrated rabbit aged 6 months. Stained with acid solution of basic brown by Shubich's method. Objective 90, ocular 7.

Structures resembling cysts were formed, lined initially with stratified epithelium. The lumen of these structures was filled with homogeneous contents giving a positive reaction with colloidal iron and alcian blue. The reaction was prevented by testicular hyaluronidase and weakened by streptococcal hyaluronidase. This suggests that the contents of the first generation of acini included chondroitin sulfate-C and hyaluronic acid.

As maturation of the connective tissue proceeded, the epithelial lining of the first generation of acini was converted into pseudostratified and, eventually, into a double-layered epithelium.

Cells of the newly formed acini underwent glandular differentiation. From the stage of 10 days they showed atypical function of apocrine type (Fig. 2a). Cells of the epithelium lining the newly formed acini were of different types. Some cells contained large number of granules of RNA and glycogen uniformly distributed throughout the cytoplasm, and acid mucopolysaccharides at the borders between the cells, i.e., they were cambial cells. Others showed a polar distribution of glycogen and RNA (apical zone) and gave a negative reaction for acid mucopolysaccharides.

The cytoplasm of cells of the first type contained a PAS-positive substance in the apical zone. The intensity of the PAS reaction in these cells fell after treatment with pepsin, or extraction of lipids with hot methanol-chloroform, but was not reduced by salivary amlyase. The PAS-positive substances of these cells evidently contained mucoproteins and lipoproteins.

The eliminating epithelial layers developed vertical amisomorphism without signs of keratinization (Fig. 1c).

All the changes described above except glandular differentiation of the proliferating epithelium took place in implanted glands cultivated in castrated recipients.

At the site of the epithelial bands (in the experiments of series II) cysts were formed, lined with simple cubical, pseudostratified, and in some cases stratified squamous epithelium. In the cysts lined with stratified squamous epithelium the cytoplasm of the apical layers gave a positive reaction for keratin, indicating atypical keratinization (Fig. 2b).

The newly formed structures in the implanted glands in the experiments of both series I and series II showed regression and disappeared completely by the 60th day.

Analysis of the results shows that with increasing age the biological powers of the prostatic epithelium do not diminish, and there is simply an increase in the number of highly differentiated and specialized cells. This explains the different prognosis for the prostatic epithelium at successive stages of ontogenesis.

The absence of glandular differentiation in prostate glands implanted into castrated animals demonstrates that conversion of the epithelium is dependent on the hormonal balance of the recipient and the determinants of the epithelium of the urogenital sinus from which the prostate arises.

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