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Transformation of the Human Prostate Gland in Early Neonatal Period to Later Childhood Period of Development

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Morphometric parameters of the acini of human prostate glands and epithelium, lining gland was carried out from the neonatal period to the second childhood. For the first time, the end pieces of the prostatic glands and their lumens at different age periods according to their lobular structure of the prostate are described. Changes in the sizes of the end pieces of the glands, the gaps of the terminal sections of the glands and their epithelial cells from the early neonatal period to the late childhood age period are described. Histological differences were found in the prostate between different lobules. In the postnatal period, canalization of the ductal system of the prostate glands proceeds through apoptosis and polarization of epithelial cells. In the formed acini of the prostate glands, pronounced changes occur during the children's age periods that correspond to the functions of the organ.

Key words: prostate, epithelium, glands, epithelial cord, apoptosis

Introduction

The genital system of boys, including the prostate, is morphologically formed by the time of birth and its transformations are aimed at further morphofunctional development, which is in the period of 20-45 years, and the age of 41-45 years is considered the beginning of significant involutional changes. Probably this is a reason that all previously conducted studies of the morphogenesis of the prostate glands were performed mainly in the man prostates during mature age and older one. It is widely known that a malignant neoplasm, including the prostate cancer, occurs due to the re-awakening of development processes that occur during organogenesis. The formation of prostatic ducts from epithelial cords and their further transformation into the acini of human prostate glands continues in the postnatal period of prostate development. Clarification of the appearance timing and formation of various structures is important for monitoring the proper development of an organ. There are not many studies of the structural organization of the human prostate glands in its various lobules during the birth period and childhood. Many issues of prostate morphology from birth and throughout childhood are unclear.

The aim of this study was to determine the morphometric parameters of epithelial cords, prostatic ducts, and acini of human prostate glands and their lining epithelium and gland shape in all prostate structural lobules of boys during perinatal and childhood periods of development.

Material and methods

The studies were performed on 36 prostates of boys aged from the first day of life to 13 years (**Table 1**), which were obtained in accordance with the law of the Republic of Belarus no. 55-3 "On the Burial and Funeral Business," as amended by act no. 2/2235 from September 1, 2015. The independent Ethics committee of Vitebsk State Medical University approved the study (Protocol No. 2 of May 7, 2018). Material was collected within 12 hours after death. An organocomplex was removed from the pelvic cavity (bladder, prostate, seminal vesicles, rectum) and its preparation was performed with the release of the prostate. Histological sections were prepared with a Leica RM 2125 RT rotary microtome (Germany), and stained with hematoxylin-eosin and fuxelin according to Hart. Stained preps were examined with a Leica DM 2000 microscope (Germany) equipped with a camera adapter at a total magnification of 100×, 200×, and 400×. Micrographs of the study areas were obtained with a Leica D-LUX 3 digital camera (Germany). The micrographs of the prostate glands were processed with the use of the Image Fiji software using the set of standard tools [4] and plugins that make it possible to change the sharpness and contrast of images and allow smoothing, removal of "noise," and separation of a color image into the color channels. Then, using the Trianable Weka Segmentation plugin, the images were segmented, and their binary masks were obtained. All processed images were calibrated using a standard object micrometer. The morphometric study included the measurements of acini, the acinar lumen areas, and the epithelium height in the inferoposterior, inferolateral, superomedial lobules of the right and left lobes of the prostate. We used the morphological method of verification of apoptotic cells on stained histological preps using the criteria of apoptosis as recommended by Skibo [5]. Statistical hypotheses were tested using Statistica 10.0 and Microsoft Excel 2007 software. The statistical homogeneity of the samples was tested using the nonparametric ANOVA procedures (Kruskal–Wallis test for multiple comparisons). When statistical heterogeneity of several samples was found, subsequent identification of heterogeneous groups was performed using the Mann–Whitney U test and Dunn's post hoc test with Bonferroni adjustment. The critical level of significance was $p < 0.05$.

Table 1. Distribution of the study material according to age groups

Age period	Early neonatal	Later neonatal	Infancy	Early childhood	First late childhood	Second late childhood
	1-7days	8-28 days	1 month- 1 year	1-3 years	4-7 years	8-12 years
Number of cases studied	7	3	9	5	4	8

Results and discussion

In the neonatal and infancy periods, epithelial cords with cleft like lumens, epithelial tubules with lumens of different size and shape, prostatic ducts and acini of human prostate glands were found in all prostatic areas (**Fig. 1**). The epithelial cords are multicellular structures formed by tightly adjoining epithelial cells bounded by the basal membrane. Epithelial cells in the cords contained large nuclei and showed no signs of polarity relative to the basal membrane. In some epithelial cells with changes in the morphology of nuclei and cytoplasm were detected characteristics of apoptosis (**Figs. 2, 3**). In all detected epithelial cords between epithelial cells were present cleft like lumens due to the loss of cell–cell contacts [5]. In infants, epithelial cords were detected up to 3 months of age.

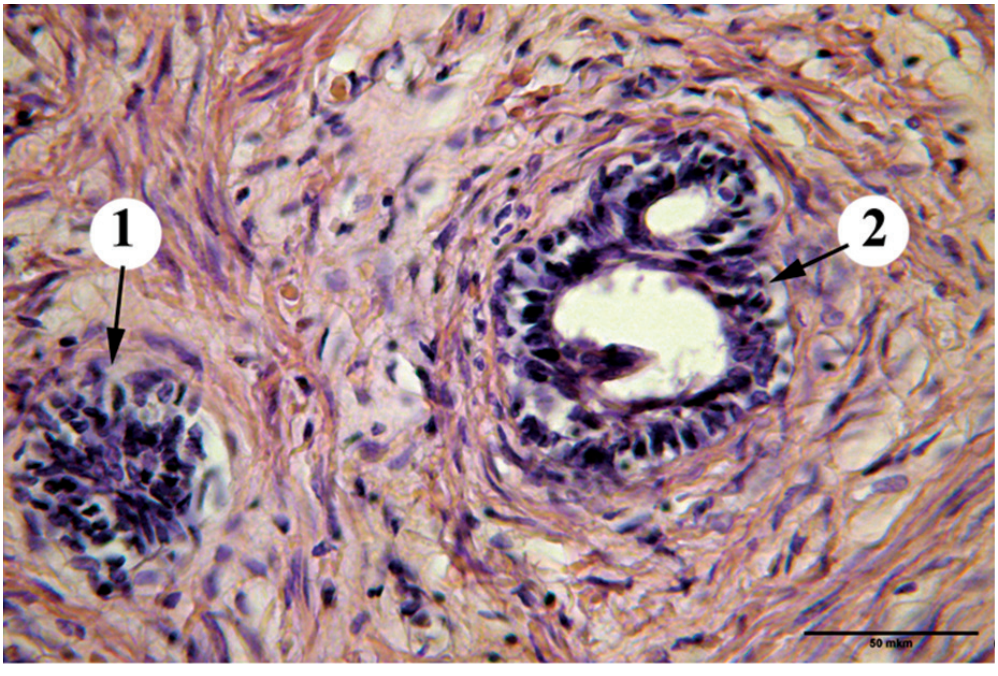

Fig. 1. Prostate preparation of a boy (27 days old). Staining with hematoxylin and eosin. 1) Epithelial cord with epithelial cells tightly adjoining each other. Epithelial cells contain large nuclei without signs of polarization. 2) Epithelial cells of the acini of human prostate glands with basally located nuclei. × 400.

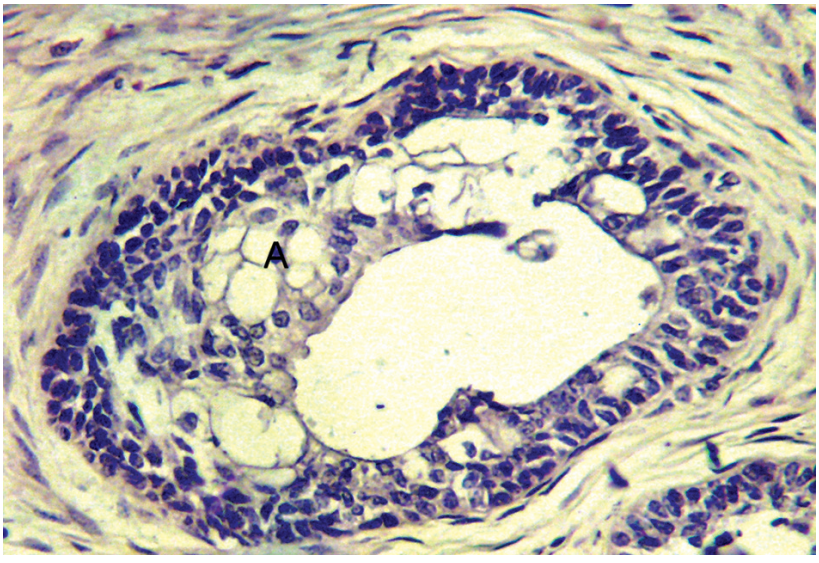

Fig. 2. Prostate preparation of a newborn boy (2 days old). Staining with hematoxylin and eosin. A – conglomerates of apoptotic cells in the prostatic ductal lumens. The epithelial tubules contained epithelial cells with changes in the morphology of nuclei and cytoplasm characteristic of apoptosis: chromatin margination, pyknosis in nuclei, changes in the cytoplasm staining pattern, and gaps between individual epithelial cells due to the loss of cell–cell contacts. × 200.

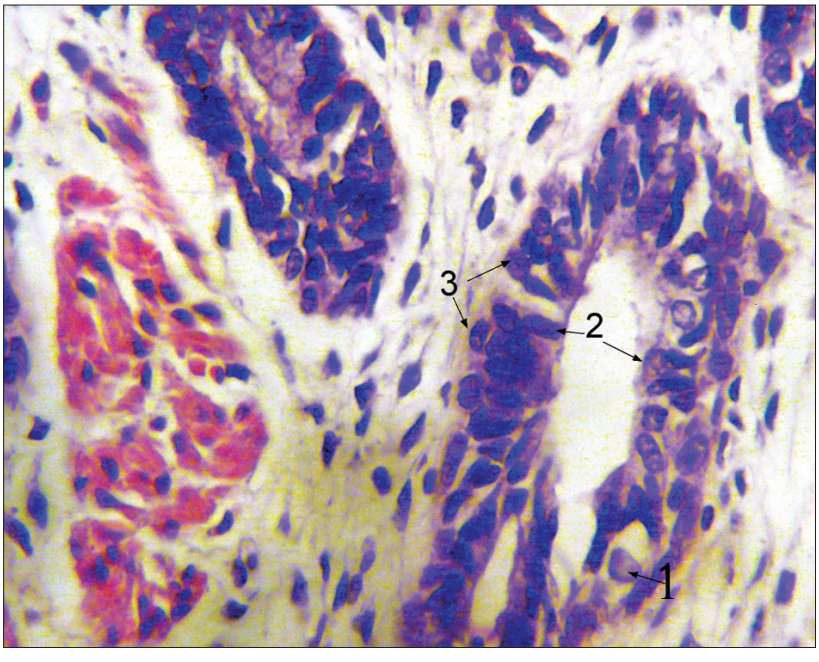

Fig. 3. Prostate preparation of a boy (11 days old). Staining with hematoxylin and eosin. 1. Cell with signs of karyopyknosis of the nucleus and cleared cytoplasm (apoptotic cells). 2. Cubic epithelial cells of prostatic duct. 3. Basal epithelial cells. × 200.

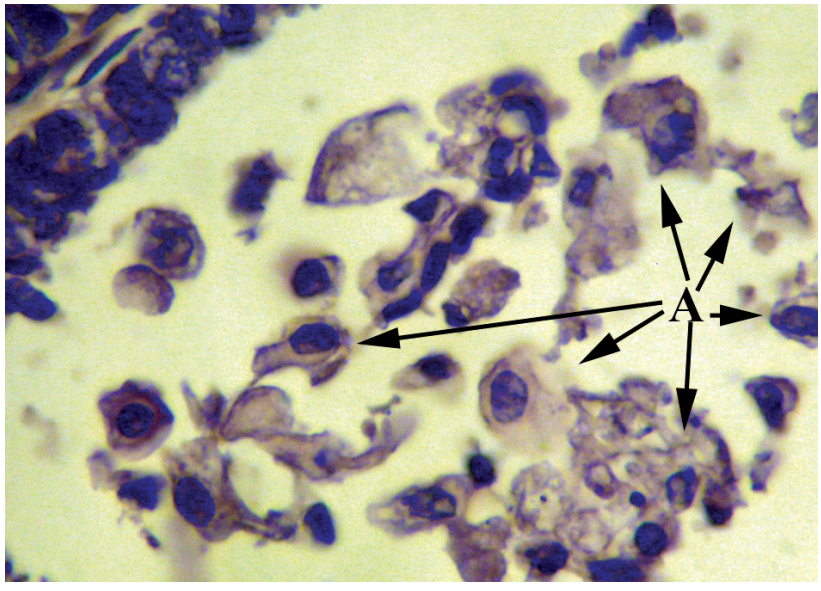

Fig. 4. Prostate preparation of a newborn boy (11 days old). Staining with hematoxylin and eosin. A – conglomerates of apoptotic cells in the prostatic ductal lumens. × 400.

Probably, the canalization of the ductal system of the prostate glands occurring in the neonatal periods [6,7] continues in the postnatal period. Prostatic ducts and acini of human prostate glands, were lined with double-layered epithelium with basally located nuclei. In prostatic ducts located closer to the prostatic part of the urethra, conglomerates of apoptotic cells were observed (**Fig. 4**). This statement is not consistent with the opinion of some authors who claim that remnants of metaplastic cells and / or debris are found inside the prostatic ducts [8]. Starting from infancy, the structure of the glands was studied in place of the definitive inferoposterior, inferolateral, superomedial lobules, which was not possible in the neonatal period. In infancy in competition with the neonatal periods the acinar area and the height of the epithelium lining the acini decreases in all structural prostatic lobules ($p \leq 0.05$) (**Table 2**). The height of the epithelium of the acini significantly increased in early childhood in comparison with the infancy ($p \leq 0.05$) and does not change in other children's age periods ($p > 0.05$). The acinar lumen area of the prostatic glands decreases in all structural lobules of the prostate in early childhood in comparison with the infancy ($p \leq 0.05$) and does not change in other children's age periods ($p > 0.05$) (**Fig. 5**). The results of our studies are consistent with the data of researchers who claim that the prostate develops to a large extent immediately after birth, and then remains relatively inactive until puberty [3, 8]. There is an opinion that in some children's age periods in the prostate there are no histological differences between different lobules [3].

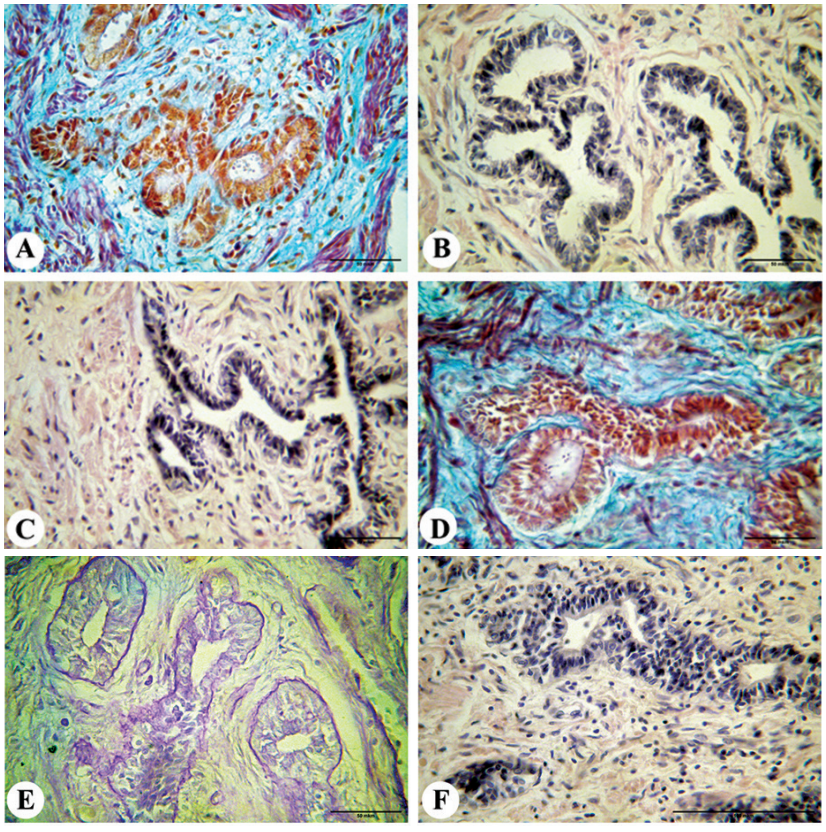

Fig. 5. Prostate preparation of boys at different ages. **A** – Prostate preparation of a boy (1 month old) in the superomedial lobule. Staining according to Heidenhain; **B** – Prostate preparation of a boy (4 months old) in the inferolateral lobule. Staining with hematoxylin and eosin; **C** – Prostate preparation of a boy (2 years old) in the inferolateral lobule. Staining with hematoxylin and eosin; **D** – Prostate preparation of a boy (3 years old) in the posterolateral lobule. Staining according to Heidenhain; **E** – Prostate preparation of a boy (8 years old) in the posterolateral lobule. Staining according to Ritter – Oleson; **F** – Prostate preparation of a boy (11 years old) in the superomedial lobule. Staining with hematoxylin and eosin. Scale bars 50 μm.

We detected that in the superomedial lobule of the prostate of infants, the acinar area, acinar lumen area, height of their epithelium statistically differed from the inferolateral and inferoposterior lobules ($p \leq 0.05$) and did not statiastically differ between the inferolateral and inferoposterior lobules ($p > 0.05$) (**Tables 3,4,5**). The differences among the lobules were "smoothed out" in early childhood and were not detected in the first childhood ($p > 0.05$). In the second childhood, differences in lobules for all studied parameters ($p \leq 0.05$) were revealed among the superomedial and inferolateral lobules and the superomedial and inferoposterior lobules.

Table 2. Prostate gland size in neonatal, infancy, and childhood periods M (1st Qu; 3rd Qu, μm).

		Epithelium height, μm	Acinar area, μm^2	Acinar lumen area, μm^2
Early neonatal		12,5(9,4;16,4)	5002(3390;7484)	24(150;551)
Late neonatal		14,8*(11,9;18,1)	5136*(2751;10072)	852*(465;1425)
Infancy	SM	8,2*(6,58;10,6)	3055*(1694;5554)	823(414;1501)
	IP	10,0 *(8,0;12,9)	4242* (2406;7786)	1029(518;1876)
	IL	10,2 *(8,2;13,1)	3856*(2188;7089)	1061(528;1918)
Early childhood	SM	9,5*(7.1;13.8)	3712*(2049;6858)	508*(204;1099)
	IP	11,4* (8,9;14)	4793(2719;8812)	585*(406;1035)
	IL	10,1 (7,8;13)	4300(2444;7934)	541*(249;1058)
First late childhood	SM	11,1(8,3;12,3)	4529*(2500;8366)	534(214,8;1154)
	IP	10,9 (8,3;16,2)	5752*(3263;10575)	597(305;1164)
	IL	10,6 (8,3;13,7)	5346*(3030;9839)	658(449;1129)
Second late childhood	SM	11,4 (9,0;13,0)	4330(23988;7951)	238(145;417)
	IP	11,6 (9,0;15,0)	5942(33714;10924)	392(213;749)
	IL	16,9*(13,0;25,0)	5453(3091;10026)	389*(223;749)

* – the critical level of significance was $p < 0.05$
SM – superomedial lobule, IP – inferoposterior lobule, IL – inferolateral lobule

Table 3. Comparison of the height of the epithelium among lobules within the age group (adjusted for multiple comparisons).

Options for comparison	Compared groups	p
Infancy	IL-IP	0,32
	IL-SM	<0,001*
	IP-SM	<0,001*
Early childhood	IL-IP	0,6486
	IL-SM	<0,0115*
	IP-SM	<0,0172*
First later childhood	IL-IP	0,2343
	IL-SM	0,1234
	IP-SM	0,1818
Second later childhood	IL-IP	<0,0161*
	IL-SM	<0,001*
	IP-SM	<0,001*

* – the critical level of significance was $p < 0.05$

Table 4. Comparison of the acinar area among lobules within the age group (adjusted for multiple comparisons).

Options for comparison	Compared groups	p
Infancy	IL-IP	0,0703
	IL-SM	<0,0030*
	IP-SM	<0,001*
Early childhood	IL-IP	0,119675
	IL-SM	<0,0259*
	IP-SM	<0,001*
First later childhood	IL-IP	0,1765
	IL-SM	0,6529
	IP-SM	0,3342
Second later childhood	IL-IP	0,19592
	IL-SM	<0,001*
	IP-SM	<0,001*

* – the critical level of significance was $p < 0.05$

Table 5. Comparison of the acinar lumen area among lobules within the age group (adjusted for multiple comparisons).

Options for comparison	Compared groups	p
Infancy	IL-IP	0,6897
	IL-SM	<0,0032*
	IP-SM	<0,006*
Early childhood	IL-IP	0,2534
	IL-SM	0,5392
	IP-SM	0,1686
First later childhood	IL-IP	0,2787
	IL-SM	0,1175
	IP-SM	0,4129
Second later childhood	IL-IP	<0,001*
	IL-SM	<0,001*
	IP-SM	0,9386

* – the critical level of significance was $p < 0.05$

Conclusions

In the postnatal period, the processes of canalization of the ductal system of glands occur in the prostate by apoptosis and polarization of epithelial cells. In the formed acini of the prostate glands, pronounced changes occur during the children's age periods that correspond to the functions of the organ.

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