

## Current Views about the Morphofunctional Characteristics of the Epididymis

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**Abstract:** This article discusses current ideas about the morphofunctional characteristics of the epididymis (testis). It should be noted that the structure of the sections of the epididymis and their topography have specific differences.

**Keywords:** morphology, epididymis, testis, tubules.

The epididymis (testis) is a paired organ of the male reproductive system that serves for the maturation, accumulation and promotion of sperm. The epididymis (testis) consists of a head, body and tail. The epididymis (testis) consists of the efferent tubules, which arise from the rete testis, and the epididymal duct. When entering the epididymis, the efferent tubules are strongly twisted, forming from 6 to 10 conical lobules, the pointed apices of which extend from the mediastinum of the testicle. The expanding bases form the head of the appendage. Each conical lobule is formed by a twisted efferent tubule, 15–20 cm long. At the base of the cone of the epididymis, the efferent tubules open into the epididymal duct, which forms the body and tail of the epididymis. The cones are separated from each other by thin connective tissue septa with a large number of blood vessels [1, 2, 4, 6, 16]. It should be noted that the structure of the sections of the epididymis and their topography differ among species [17, 19]. For example, in the epididymis of the testis of a cat (*Felis catus* L.), based on an analysis of the microscopic structure of various parts of the epididymis, 8 zones are distinguished. Zones I and II correspond to the head of the appendage, III–VII – to the body and VIII – to the tail [15]. There are even more detailed divisions into departments, for example, only in the proximal part of the mouse epididymis there are 5 segments (divisions) [22, 29].

B. Stadler et al. [19] distinguish 19 sections (segments) in the rodent testicular epididymis, and 9 in the human epididymis. The wall of the efferent tubules and duct of the epididymis is formed by three membranes - mucous, muscular and adventitial. The mucous membrane of the epididymis is represented by the epithelium and the lamina propria. The efferent tubules of the epididymis in most mammals are lined with multirow epithelium. However, in humans, multirowing is observed only in certain areas of the epithelium of the efferent tubules, and most areas of the epithelial layer are lined with single-layer columnar epithelium. The epididymal duct is lined with multirow columnar epithelium [2, 6, 16]. The study of epithelial cells of the appendage has been carried out by many authors, however, there is still no generally accepted classification of these cells. There is no unity of views both in educational and scientific literature. The number of cell types identified by different authors in the epithelium of the appendage varied to several. This is due both to different methodological approaches and to species differences in the epithelial lining of the epididymis (testis) of the studied objects. Thus, in the textbook “Histology, Embryology, Cytology” edited by E.G. Ulumbekova and Yu.A. Chelyshev [10] in the epithelium of the efferent tubules of the epididymis there are tall cylindrical cells equipped with cilia and low cubic cells with a folded surface with microvilli. The epididymal duct contains tall cylindrical and basal (intercalary) cells. In the literature of Yu.I. Afanasyev and N.A. Yurina [1] in the epithelium of the epididymis there are columnar epithelial cells containing stereocilia and intercalated cells (however, differences in the structure of the epithelium between the efferent tubules and the epididymal duct are not described). In “Histology Guide,” ed. R.K. Danilov [16] in the epithelium of the efferent tubules there are 3 types of cells - ciliated, basal (intercalated) and non-ciliated cells. In the epithelium of the epididymal duct there are 2 types of cells - main and basal. In the textbook R.K. Danilova and T.G. Borovoy “Histology,

embryology, cytology” [11] in the efferent tubules of the epididymis, two types of cells are distinguished - tall ciliated epithelial cells and low cells with microvilli. In the epididymal duct, these authors distinguish columnar (containing stereocilia) and intercalated epithelial cells.

According to Terminologia Histologica (2009) and Terminologia Embryologica (2014) [2, 6], in the single-layer columnar epithelium of the efferent tubules of the appendage, 2 types of cells are distinguished - cubic microvillous epithelial cell and columnar ciliated epithelial cell.

In the multirow epithelium of the epididymal duct in humans (*Homo sapiens* L.), the following types of cells are distinguished: chief cells (epithelial cells with stereocilia) and basal cells (basal epithelial cells) [2, 6]. Salet V.M.J. et al. [16] in the epithelial lining of the epididymal duct of a cat (*Felis domestica* L.) identified 3 types of epithelial cells: 1) main (cylindrical in shape), predominant in the epithelial layer and found throughout the epithelium of the epididymis; 2) basal (being poorly differentiated, immature); 3) apical (intermediate between the first two types of cells).

According to W.G. Breed [33], in the epithelium of the epididymal duct of the jerboa mouse (*Notomys alexis* L.) 3 types of cells are detected - main, light and basal. The main cells of the epithelium of the epididymis (testis) The ciliated cells of the epithelium of the efferent tubules contain cilia on their apical surface, and between the bases of the cilia there are numerous microvilli. The flickering of the cilia promotes the movement of sperm from the efferent tubules to the epididymal duct. Receptors for androgens, estrogens, prolactin, and angiotensin II have been identified in the nuclei of ciliated cells [12, 28, 29]. Expression of the  $3\beta$ -HSD protein was detected in ciliated cells [29]. Although the general plan of organization of ciliated cells is similar in all species, a number of features stand out. For example, ciliated cells of the epididymis of the donkey (*Equus asinus* L.) contain apically located pigment inclusions in the cytoplasm [29]. Unciliated cells of the efferent tubules take part in the processes of reabsorption of substances from the lumen of the tubule. This is indicated by numerous microvilli on the apical surface of cells, a large number of lysosomes, osmiophilic granules and vesicles in the apical part of the cytoplasm [4, 16].

The main cells in the epithelium of the epididymal duct are highly prismatic cells. Their height in the initial section of the epididymal duct in humans (*Homo sapiens* L.) ranges from 60–80  $\mu\text{m}$ ; in the direction from the body to the tail of the epididymis, their height decreases. The nucleus of the main cell is oval or elongated, with uneven contours, located in the basal part of the cell. One or more nucleoli are detected in the nucleus. In the cytoplasm of cells, granular and agranular endoplasmic reticulum and the Golgi complex are well developed. In the apical part of the cytoplasm, PAS-positive granules [19], numerous vesicles and lysosomes are detected. On the apical surface of the main cells there are stereocilia (immobile microvilli) [35], having a height of up to 25  $\mu\text{m}$  in the initial section of the epididymal duct; in the region of the tail of the epididymis, their height ranges from 5–10  $\mu\text{m}$ . Stereocilia differ from typical micropiles in their larger size, as well as in the absence of the villin protein and the expression of alphaactinin. Androgen and estrogen receptors have been identified in the chief cells, and the concentration of these receptors increases during the reproductive season. This, for example, was established in a study of the seasonal dynamics of the morphofunctional characteristics of the epididymis of the sand rat (*Psammomys obesus*) [5]. At the same time, androgen markers were detected in the apical part of the cytoplasm of the main cells, and androgen markers were detected in the apical part of the cytoplasm of the main cells and in their nuclei. In castrated animals, markers of androgen and estrogen receptors were practically not detected.

Among the chief cells, two types are distinguished (typical chief cells and chief cells containing a large number of mitochondria). Distinctive features of the second type of main cells, in addition to a large number of mitochondria, are higher activity of hydrolytic and redox enzymes, as well as a higher content of estrogen receptors [4, 16, 29].

Chief cells are the main type of cells in the tubules of the epididymis, constituting up to 80% of the epithelial layer; it is these cells that secrete specific androgen-dependent proteins in the secretion of the epididymal tubules and reabsorb substances from the lumen of the tubules. Aldosterone, biogenic amines, and components of the renin-angiotensin system take part in the regulation of reabsorption [4,

16, 17]. Basal (intercalated) cells of the epithelium of the epididymal duct are low, pyramidal or round cells located between the basal areas of the main cells. They have light cytoplasm, are poor in organelles, are poorly differentiated cells, and provide the process of physiological and reparative regeneration of the epithelial layer [4, 16, 17].

Using the marker cytokeratin-5, it was shown that basal cells in the epididymis of the rat (*R. norvegicus* B.) are absent at birth. They gradually appear retrogradely from the vas deferens and tail of the epididymis to the initial segments of the epididymis. At the beginning of differentiation, basal cells contact the lumen, and their nucleus is located at the same level as that of neighboring epithelial cells, then the nucleus of the basal cell moves to the basal part [6, 7]. Basal epithelial cells of the rat epididymis (*R. norvegicus* B.) exhibit stem cell properties [13]. To isolate a highly purified population of basal cells, the authors used integrin $\alpha$ -B. Microarray analysis revealed that the expression levels of 552 genes were higher in basal cells compared to other cell types. Among these genes, 45 were expressed at high levels (these highly expressed genes encode proteins involved in cell adhesion, cytoskeletal function, ion transport, cell signaling, etc.). Thus, basal cells may represent the epididymal stem cell population. In addition to the above cells, macrophages and various types of lymphocytes are always present in the epithelium of the epididymis. Immunocompetent cells are of particular importance. Immunohistochemical studies have proven that these cells are helper lymphocytes (CD4+) or cytotoxic killers (CD8+) [17, 34]. Each section of the epididymis (testis) has its own unique function: the head and body receive and conduct immature and maturing forms of sperm, in which the flagellum remains spirally twisted, while the caudal section accumulates mature, fertile sperm with active motile and straight flagella [4, 16, 17].

The muscular layer of the epididymal duct (testis) thickens in the distal direction. Near the vas deferens in the muscular layer there are 2 layers of smooth myocytes - the internal circular and the external longitudinal. The contractile activity of smooth myocytes is higher in the proximal region compared to the distal region [4]. The regulation of contractions of smooth myocytes is carried out by mediators of the sympathetic division of the autonomic nervous system, as well as oxytocin [6, 9]. The smooth myocytes of the caudal epididymis respond most actively to the action of oxytocin. Based on experimental data on the role and significance of oxytocin in the regulation of the contractile activity of myocytes of the epididymal muscularis, drugs based on oxytocin may be a promising option for the treatment of ejaculatory disorders [29]. The adventitial membrane of the epididymal duct is similar to that of the efferent ducts; it contains numerous vessels and nerve endings. Spermatozoa developing in the lumen of the epididymal tubules and immunocytes circulating in the vessels separate the hemato-epididymal barrier. This barrier includes the endothelium of the hemocapillaries, muscle (myoid) cells in the wall of the epididymal tubules, the basement membrane of the epithelium and intercellular contacts between epithelial cells [3, 17].

Damage to the structural components of the blood-epididymal barrier leads to the development of infertile conditions and the formation of sperm granulomas [3, 18]. Damage to the epididymal epithelium can be caused by increased seminal fluid pressure (obstructive damage), as well as by external factors such as bacterial infection, chemical agents and drugs [18]. Only during transit through the epididymis do sperm finally mature, acquire motility and the ability to fertilize an egg [3, 34]. According to G.A. Cornwall [34], the importance of understanding the role of the epididymis in sperm maturation is determined by the fact that 40% of infertile men with idiopathic infertility have precisely this type of disorder [3].

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