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Influence of Various Factors on the Morphofunctional Characteristics of the Epididymis

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Abstract: The morphological equivalents of the negative influence of various damaging factors are basically similar, which indicates the presence of a nonspecific response mechanism to the action of unfavorable factors formed during evolution. Despite a significant number of works devoted to the morphology of the epididymis (testis), many aspects of the morphofunctional, molecular and biochemical transformations occurring in the epididymis still remain poorly studied and require further in-depth study.

Keywords: epididymis (testis); epididymal duct; main cells; basal cells; spermatozoa.

Impaired fertility is associated with the influence of many factors, and various disorders of the histophysiology of the epididymis (testis) play a significant role in impaired fertility. There is a significant number of studies showing the negative impact of various chemicals on the histophysiology of the epididymis (testis). For example, the destructive influence of dioxin [41], bisphenol [54, 69], toluene [9, 62], epichlorohydrin (the raw material of epoxy resins) [8], and furan [47] on the histophysiology of the epididymis (testis) has been shown. There is evidence of the adverse effects of electromagnetic radiation from cell phones [5]. A negative effect on the epididymis of herbicides [48] and insecticides [26] has been revealed. The toxic effect of herbicides and insecticides led to swelling and vacuolization of epithelial cells of the epithelium. Epithelial cells showed signs of apocrine secretion; the number and size of lysosomes in the cells increased. At the same time, the contractility of the muscle membrane myocytes deteriorated. In the lumen of the epididymis, the number of abnormal and immobile spermatozoa increased. The authors believe that these toxicants indirectly affect the structures of the epididymis through their toxic effect on Leydig cells [26, 48].

M. Ahmed et al. [24] based on the analysis of ultrastructural changes in the epithelial cells of the epididymis of rats (Rattus) showed the negative effect of an extract of the Boswellia papyrifera F. (frankincense) plant used as an incense. It was revealed that destructive changes affect all types of epithelial cells of the epididymis. In epithelial cells, a decrease in size and destructive changes were observed in mitochondria, the Golgi complex, and both types of EPS. A comparative analysis of the effects of a sweetener (molasses obtained from sugar cane) and refined sugar on the reproductive potential of male rats (Rattus) showed destructive changes in the epididymis in rats receiving both products at a dose of 7.9 g/kg per day. Against the background of a decrease in the level of androgens in rats, the proportion of abnormal spermatozoa in the epididymis increased [61]. When rats (Rattus) are exposed to the cytostatic drug vincristine, a number of dose-dependent changes occur in the epithelium of the appendage. These changes included an increase in the number of cells with an abnormal arrangement of cell nuclei in the apical zones, numerous protrusions of the apical surface of cells into the lumen, an increase in lysosomes and multivesicular bodies in the cytoplasm [27, 30]. The use of the aromatase inhibitor letrozole increases the number of cells entering apoptosis in the epithelium of the appendage [63]. The action of valproic acid, which is part of drugs used to treat neurological disorders, leads, against the background of a decrease in androgen content, to a significant decrease in the weight of the epididymis and sperm content in it [17, 46]. When podophyllotoxin (better known in pharmacology as condylin) is administered to sexually mature male rats (Rattus), changes in the structural organization of the epididymis are observed. Against the background of increased production by cells of tumor necrosis factor α (TNF-α) and a number of pro-apoptotic proteins: caspase-3, caspase-8, caspase-9 and cytochrome C, an increase in apoptosis in the

epithelium of the appendage was noted [17]. When exposed to gossypol (a glucoside-like compound found in cotton seeds), hypertrophy of epithelial cells occurred, especially in the epididymal duct.

The main cells lost microvilli, and the number of vesicles in the apical zone of the cells increased. At the same time, an increase in immobile and abnormal spermatozoa was noted in the epididymal duct; many were deprived of heads. It has been shown that during puberty, the rat epididymis (Rattus) was particularly sensitive to the effects of gossypol [32, 37]. In experimental hyperhomocysteinemia, mitochondrial dysfunction developed in the epithelial cells of the epididymis, which was reflected in the form of a sharp decrease in succinate dehydrogenase activity, a decrease in carnitine, and lactate accumulation [14, 15]. A negative effect of cigarette smoke on the accessory sex glands and epididymis in male rats (Rattus) exposed to cigarette smoke for a long time was revealed [22].

The authors found that exposure to cigarette smoke caused swelling of the appendage tissue and an increase in destructive changes in the epithelium of the appendage. Administration of ethanol to rats (Rattus) significantly reduced the content of carnitine in the tissues of the epididymis, acetylcarnitine, glycerylphosphorylcholine and sialic acid, indicating its adverse effect on the synthesis of these secretory products. At the same time, there was a decrease in the motility and fertilizing ability of sperm, which indicated a violation of the maturation of sperm in the epididymis. All of these changes returned to normal after ethanol administration was discontinued, indicating temporary effects of ethanol [68]. Administration of flutamide (an antitumor agent, antiandrogen) significantly reduced the number of basal cells in the epithelium of the appendage [27].

Under conditions of experimental diabetes (induced by a single intraperitoneal injection of streptozotocin in prepubertal and mature rats), the concentrations of testosterone, androgen binding protein, sialic acid, glycerylphosphorylcholine and carnitine in the tissues of the epididymis are significantly reduced, indicating its adverse effect on the secretory activity of the epididymis. Diabetes negatively affects sperm maturation, which may be associated with a decrease in the bioavailability of testosterone and epididymal secretory products [21]. Exposure to arsenic, cadmium, lead and mercury affects the morphology and function of the mouse epididymis (Mus) [52]. Exposure to these chemical elements reduces the weight of the epididymis, the motility and number of sperm, and damages the sperm structures inside the epididymal duct. These changes are exacerbated with increasing exposure time and with exposure to higher doses.

The presented data show that species differences in the morphofunctional organization of the epithelium of the epididymis (testis) are insignificant. This indicates the manifestation of the principle of parallelism in the evolutionary dynamics of the epithelium of the appendage. The use of the rat epididymis as an object for experimental models in the studies of most scientists compensates for the impossibility of a comprehensive study of this issue in in vivo conditions in mature men suffering from infertility. The morphological equivalents of the negative influence of various damaging factors are basically similar, which indicates the presence of a nonspecific response mechanism to the action of negative factors formed during evolution. It must be recognized that, despite the ongoing research, many aspects of the morphofunctional, molecular and biochemical transformations occurring in the epididymis (testis) still remain poorly understood and require further in-depth study.

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