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## **ТИББИЁТДА ЯНГИ КУН НОВЫЙ ДЕНЬ В МЕДИЦИНЕ NEW DAY IN MEDICINE**

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Научно-реферативный,  
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## THE INFLUENCE OF VARIOUS FACTORS ON TESTICLE FUNCTION AND MORPHOLOGY

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### ✓ Resume

*The male reproductive system is a separate topic for long discussions and is currently characterized by a higher morbidity and mortality rate and, accordingly, a shorter life expectancy than a woman, as an equal participant in the reproductive process. Changes in the environment (pollution), various chemical and physical factors affect the normal functioning of the male reproductive system. In this regard, the reproductive system is a "mirror" (highly sensitive) of the body, and the nature of reactions to various factors here is not unique. This review presents information on the influence of various factors on the morphology of testicular tissue.*

**Keywords:** testis, rats, reproductive health, morphology, seminiferous tubules.

## ВЛИЯНИЕ РАЗЛИЧНЫХ ФАКТОРОВ НА ФУНКЦИЮ И МОРФОЛОГИЮ ЯИЧЕК

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### ✓ Резюме

*Мужская репродуктивная система является отдельной темой для долгих дискуссий и в настоящее время характеризуется более высокой заболеваемостью и смертностью и, соответственно, более короткой продолжительностью жизни, чем у женщины, как равноправного участника репродуктивного процесса. Изменения окружающей среды (загрязнение), различные химические и физические факторы влияют на нормальное функционирование мужской репродуктивной системы. В этом отношении репродуктивная система является «зеркалом» (высокочувствительным) организма, и характер реакций на различные факторы здесь не является уникальным. В данном обзоре представлена информация о влиянии различных факторов на морфологию ткани яичек.*

**Ключевые слова:** яички, крысы, репродуктивное здоровье, морфология, семенные канальцы.

## MOYAK FUNKTSIYASI VA MORFOLOGIYASIGA TURLI OMILLARNING TA'SIRI

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**Kalit so'zlar:** moyak, kalamushlar, reproduktiv salomatlik, morfologiya, urug' kanalchalari.

## Relevance

Changes in the environment (pollution), various chemical and physical factors affect the normal functioning of the male reproductive system. In this regard, the reproductive system is a "mirror" (highly sensitive) of the body, and the nature of reactions to various factors is not specific here [12]. The male reproductive system is a separate topic for long discussions and is currently characterized by a higher morbidity and mortality rate and, accordingly, a shorter life expectancy than a woman, as an equal participant in the reproductive process [11]. Of all the organs of the male reproductive system, the testicles and epididymis are called universal experimental organs, where the influence of factors of various levels can be quickly and accurately studied for initial reports and long-term results. In addition, according to modern concepts, the epididymis is an accessory sex gland, in which the final maturation and accumulation of mature spermatozoa occurs [9]. Baymurodov R.R. in his studies (2021) studied the morphological changes in the testicles and epididymis during irradiation. In the era of scientific and technological progress, among all pollution, radioactive pollution, the sources of which are not only natural factors, but also, to a greater extent, anthropogenic activity, is considered especially dangerous [2]. The effects of ionizing radiation significantly disrupt the integrity of structures in the cells of various tissues of the body and the balance of metabolism that maintains homeostasis. The development of radiation-biochemical effects is most pronounced in radiosensitive tissues of the body, including spermatogenic epithelial tissues. Morphometry of the testicles showed uneven changes in their weight, length and thickness in postnatal ontogenesis. Comparison of the growth rate of body weight and length with the weight and volume of the testicles shows that with an increase in their volume, body weight increases more than length. The weight of the testicles increases 1.16 times faster than body weight, and a high rate of testicular growth is observed at the age of 90 days. In the experiment, all anatomical indicators of the testicles lag behind the control indicators. Radiation, which negatively affects the morphological structure of the testicles, leads to a delay in all morphometric parameters, including the thickness of the white layer and spermatogenic epithelium. The delay is more pronounced in white rats at 180 days of age and less pronounced at 360 days of age. This is due to the activation of the body's protective and compensatory mechanisms, which is more pronounced in groups receiving ASD-2f. With chronic radiation sickness, puberty is delayed. This is manifested by disturbances in the stages of spermatogenesis, changes in the cells of the spermatogenic line and a delay in the lumen of the seminiferous tubules. In white rats in the control group, quantitative changes are observed in Leydig cells at the age of sexual maturity (90 days), characterized by a sharp increase in their number by 11.2 times, and by puberty (360 days) this figure increases by 1.4 times compared to the period of sexual maturity. In all experimental groups, the number of Leydig cells, as well as their diameter, is lower than in the control group. Chronic radiation sickness has a negative effect on the vascular system of the testes and seminiferous tubules, where the diameter of arterioles and venules, as well as the diameter of the seminiferous tubule curvature, decreases more under the influence of radiation than under the influence of ASD-2f and in comparison with the control group [2].

Up to 58% of pathologies leading to infertility in adult men begin in childhood and adolescence. In some cases, significant violations occur in the early stages of sexual formation and intrauterine development [1]. Hypoxia is one of the main factors that provoke the disruption of the processes of adaptation to extrauterine life. Most complications of pregnancy (preeclampsia), somatic and infectious diseases of the pregnant woman, the effects of adverse factors are accompanied by oxygen deficiency in the organs and tissues of the fetus [4]. It is known that hypoxia has a negative effect on all systems of the growing organism, especially the central nervous and cardiovascular systems. Antenatal damage to the reproductive system is also important, since the consequences of this damage can be irreversible and can lead to impaired testicular function in the postpartum period and the subsequent development of primary infertility. Palatov T.M. According to (2017), morphological studies of fetal testes taken from mothers with a pathological course of pregnancy revealed structural changes in the spermatogenic epithelium of the fetus, the structure of which corresponds to the structure of the fetus at a gestational age of 20 weeks and older. 14-16 weeks, which indicates a delay in fetal development. Intrauterine hypoxia has a destabilizing effect on the processes of proliferation and differentiation of the spermatogenic epithelium, which is manifested in a decrease in the number of cells in the lumen of the testicular tubules with increasing gestational age. Recently, reports of cases of testicular pathology in COVID-19 have appeared, which are becoming increasingly reliable. Postmortem studies of human testes have shown that SARS-CoV-2 infections lead to testicular inflammation, edema, and sperm degeneration due to infiltration of CD3+ and CD68+ immune cells, similar to severe acute respiratory syndrome (SARS). In a study by M. Yang et al. (2020), pathological examination of testes revealed Leydig and Sertoli cell death in patients who died of COVID-19 [16].

Various studies have shown that testicular biopsies from infertile patients with COVID-19 show signs of an autoimmune inflammatory process characterized by lymphocytic infiltration of testicular tissue, combined with varying degrees of sclerosis. In addition, in many cases, angiodysplasia and recalibration of testicular vessels with dystrophic changes in the parenchyma were noted. It is also important that, along with inflammatory processes, signs of stenotic microangiopathy have been identified in testicular tissues after COVID-19, which contributes to the development of secondary ischemic-hypoxic damage to cells and a decrease in their secretory function [15].

Numerous experimental studies and clinical observations have revealed a high probability of inheriting various pathological changes resulting from prenatal stress from the mother [6]. It is known that prenatal stress causes a complex of various micro- and ultrastructural morphological, neurochemical, endocrine, metabolic changes in offspring, which are consolidated in postnatal life (the phenomenon of intrauterine programming of diseases). At the same time, prenatal stress causes long-term disorders in offspring, primarily in the neuroendocrine regulation of reproduction and the hormonal adaptation system. At the same time, prenatal stress is usually caused by various extragenital diseases of the mother, among which type 1 diabetes occupies a special place. The prevalence of this pathology is observed everywhere, including in women of childbearing age [7].

According to a review of the literature, there is a close paracrine relationship between Leydig cells and Sertoli cells. In particular, Sertoli cells have been shown to secrete a number of peptides that act on Leydig cells. Sertoli cells have been shown to secrete inhibin, activin, and insulin-like growth factor 1, which increase the expression of luteinizing hormone receptors in Leydig cells, thereby activating steroidogenesis. At the same time, under the influence of follicle-stimulating hormone of the pituitary gland, Sertoli cells produce alpha and beta growth factors that suppress testosterone secretion by Leydig cells. It is known that hyperglycemia, which develops when  $\beta$ -cells of the islets of Langerhans are damaged, ultimately leads to disturbances in the intravascular hemodynamics of various organs and systems, which in turn leads to the development of hypoxia. At the same time, glucose and lactate serve as the main energy substrates for germ cells. However, the ability of germ cells to utilize glucose is very low, and lactate is their main energy substrate and a key factor in the survival of these cells in hypoxic conditions [8]. The lactate supplier for germ cells is Sertoli cells. It is logical to assume that a decrease in the concentration of sustentocytes in the offspring of female rats with experimental type 1 diabetes mellitus will ultimately lead to lactate deficiency. According to the studies of Palatova T.V. (2022), during pathological pregnancy in women with impaired uteroplacental blood circulation, chronic intrauterine hypoxia, morphofunctional changes in the testicular tissue of the fetus were found, manifested in an increase in the stroma and atrophy of the organ parenchyma, which is manifested by a decrease in the diameter of the tubules and the number of cells in them, dystrophy of the spermatogenic epithelium, a decrease in proliferative potential and increased apoptotic activity. There is a correlation between the gestation period and the parenchymal-stromal index in the tissues of the fetal testicles, which decreases with chronic intrauterine hypoxia. Chronic hypoxia and the developing morphofunctional changes in the human fetal testes are accompanied by the development of hormonal dysfunction, a factor confirmed by a decrease in the expression of androgen receptors and an increase in the expression of estrogen receptors with an increase in vasculoendothelial expression, which can subsequently lead to pathology of reproductive function in adulthood. Morphological changes in the testes of newborn rats, developing in conditions simulating intrauterine hypoxia in rats, consist of dystrophic changes in spermatogenic epithelial cells, peritubular edema, a decrease in the diameter of the tubules, a decrease in proliferative activity and fibroblast growth factor function against the background of increased apoptotic activity of the spermatogenic epithelium [9].

Several studies have investigated the relationship between sperm quality, changes in testicular structure, dysregulation and the presence of stress factors, increased or decreased testicular temperature, exposure to various radiation and chemicals, and brain injury. The decline in male fertility, especially with advancing age, is associated with lifestyle choices and environmental factors, which play a significant role in fertility and its consequences for future populations, making it a major public health issue. Thus, lifestyle changes through education, environment, nutrition/exercise, and a structured program of psychological support, combined with the use of antioxidants, can prevent infertility and therefore help families improve their quality of life and their chances of conceiving, increasing or optimizing the likelihood of spontaneous conception. [10].

Reproductive health can be influenced positively or negatively by many factors, such as paternal age, exercise, obesity, nutrients, caffeine, testicular temperature, clothing, mobile phones, and reactive oxygen species (ROS) damage, which have an impact on quality of life. In addition, an altered balance between the antioxidant system and oxidative stress can determine poor fertilization/embryonic development,



miscarriage, and birth defects. Exposure to elevated testicular temperatures can impair fertility by altering sperm parameters (count, motility, and morphology) and disrupting the integrity of sperm membranes. Scrotal temperature reflects testicular temperature, and its thermoregulation is a major protective mechanism [13]. High temperatures promote increased production of ROS, which subsequently damage the sperm plasma membrane and lead to deterministic DNA fragmentation of nuclear and mitochondrial genomes, cellular damage, and apoptosis. Animal studies have shown that an increase in testicular temperature of 1–1.5°C results in reduced testicular size, reduced sperm production, abnormal shape, and reduced motility. Heat stress can affect testicular cells, especially mature spermatocytes and spermatids with high mitotic rates. Studies in rats have shown that hyperthermia affects spermatozoa by inducing DNA damage and apoptosis through intrinsic or extrinsic pathways. This results in reduced in vivo and in vitro fertilisation. The following changes were observed in the testes of experimental rats during cold exposure: morphologically, the seminiferous tubules are characterized by a straight shape and a narrowing of their diameter due to a decrease in the width of the epitheliospermatogenic layer in them. Swelling of the intertubular stroma was also observed. Leydig cells located in the interstitial tissue are mainly round or process-shaped, located singly or near the vessels. Spermatogenic cells are mainly represented by spermatogonia and primary spermatocytes. These testes may show impaired generative and excretory function [16].

The effect of prolonged light stress (light desynchronization) affects the reproductive and endocrine parts of the testes of white male rats. Swelling of the interstitial tissue is visually recorded; morphometric analysis reveals a significant increase in the cross-sectional area (4.3%) and diameter (1.5%) of the convoluted seminiferous tubules, which is accompanied by a decrease in such indicators as the thickness of the epitheliospermatogenic layer (12.3%) and the number of spermatids (2.6%) and spermatogonia (5.3%), as well as a decrease in the number of Leydig cells (7.1%). Under stress of various etiologies in rats, there is a disruption in the hypothalamic-pituitary system, which leads to an imbalance in the synthesis of releasing factors and, as a result, to the production of gonadotropic hormones (FSH and LH) of the anterior pituitary. This leads first to stimulation of testosterone synthesis, which manifests itself in the number of spermatids, i.e. stimulation of spermatogenesis, and then to a decrease in its secretion, which is characterized by a decrease in the quantitative content of spermatogonia, spermatids, i.e. suppression of spermatogenesis is observed [17].

The male testicular system is very sensitive to the effects of xenobiotics. Various toxic substances can accumulate in the testicles, which leads to impaired spermatogenesis, changes in the qualitative and quantitative parameters of spermatozoa. In rats, intoxication with the herbicide 2,4-DA, changes are observed in the white layer of the testicle: collagen fibers are loosely arranged due to cracks of various sizes, some of the fibers are destroyed, some fibers have a tortuous course, blood vessels are hyperemic. On the edge of the testicle, near the white layer, the convoluted tubules are very freely located. In the peripherally located tubules, destructive and necrotic foci are detected, resulting from the necrosis of many of their cells. Sometimes, detachment of the spermatogenic epithelium is observed in the inner part of the tubules. As a result, the number of cells in the spermatogenic epithelium decreases, gaps appear, many cells lose contact with the sustentocytes, and syncytia disappear. In the convoluted tubules located in the center, an increase in the size of the cell nuclei during the growth and proliferation stages is noted. Many nuclei are in a state of karyopycnosis. In some convoluted tubules, the cells are hypertrophied and have an oxyphilic color. The use of complex analysis using light-optical and ultrastructural methods made it possible to observe the relationship between the spermatogenic epithelium and sustentocytes in the testicles of rats. In the process of spermatozoa formation, a change in shape, chromatin distribution in the nucleus, and the formation of an acrosome are observed. During the formation of the bundle, microtubules and numerous mitochondria are formed. When animals are poisoned with xenobiotics, similar profound irreversible changes have been observed in the stroma, endocrine apparatus, vascular system, and spermatogenic epithelium. Changes in the microstructure of the gonads were observed in the testes of rats exposed to a single dose of G-irradiation. The spermatogenic epithelium of the compressed seminiferous tubules of rats is a very sensitive tissue to a single dose of ionizing radiation of animals at doses of 0.5 and 1.0 Gy, which is manifested by clear morphological changes in its structure 3 days after irradiation. In the experimental group of rats exposed to 90 days of radiation, the diameter of the curved seminiferous tubules was 4% smaller than in the control group, and their cross-sectional area was 6%. In addition, the height of the spermatogenic epithelium decreases by 7%, the diameter of the seminiferous tubule lumen by 9%, the weight of the testicles by 4%, the length of the testicles by 4%, the thickness of the testicles by 3%, and the volume of the testicles by 6%. The number of Leydig cells decreases by 8% and their volume by 3% [14].

## Conclusion

Reproductive health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity in all matters relating to the reproductive system, its functions and processes. Among the medical and biological factors, congenital malformations of the reproductive system, primary diseases and their complications are the main ones. Of all the organs of the male reproductive system, the testicles and epididymis are universal experimental organs, where the influence of factors at various levels can be studied quickly and accurately for long-term results.

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