GEORGIAN MEDICAL NEWS

ISSN 1512-0112

N0 10 (331) Октябрь 2022

ТБИЛИСИ - NEW YORK

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

Monthly Georgia-US joint scientific journal published both in electronic and paper formats of the Agency of Medical Information of the Georgian Association of Business Press. Published since 1994. Distributed in NIS, EU and USA.

GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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Содержание:

GEORGIAN MEDICAL NEWS
No 10 (331) 2022

ULTRASTRUCTURAL FEATURES OF THE REARRANGEMENT OF CELLS OF THE HEMATOTESTICULAR BARRIER AND SPERMATOGENIC EPITHELIUM OF THE RATS TESTICLES AFTER INTRODUCTION OF HIGH DOSES OF PREDNISOLONE

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Abstract.

A feature of recent decades is the gradual increase in the level of male infertility, one of the important causes of which, of course, is endocrine dysfunction of various origins. Therefore, the aim of the study was to establish the features of the rearrangement of the testicle's cellular elements of white rats with the introduction of high doses of prednisolone. An ultrastructural study was carried out on 42 male rats. It has been established that long-term introduction of high doses of prednisolone promotes the activation of spermatogenesis with a progressive increase in immature forms of germ cells and a simultaneous decrease in the specific number of mature spermatozoa. Activation of spermatogenesis occurs against the background of increased blood circulation in the testicles with an increase in the blood supply to their vessels, especially in the early period (7-14 days from the start of use), which may be a consequence of the direct effects of prednisolone stimulating blood circulation. In the long term (14-28 days) there is a decrease in the throughput of small arteries and arterioles against the background of venous stasis, as well as the rate of activation of spermatogenesis, which may be a reaction to the overload of the capillary bed of the testicles and cause further development of organ's ischemia with it.

Key words. Ultrastructure, testicles, spermatogenesis, hemocapillaries, prednisolone.

Introduction.

Infertile marriages today represent not only a medical and biological problem, but also a social and demographic problem [1-4]. Moreover, a feature of recent decades is the gradual growth of the male component of this pathological process, one of the important causes of which, of course, is endocrine dysfunction of various genesis. [2,3].

At the same time, research conducted in recent years shows that with long-term use of hormonal drugs, according to the physiological principle of "negative feedback", the production of own hormones by endocrine glands is suppressed. In particular, in many patients with the introduction of high doses of glucocorticoids, dysfunctions from the side of the sexual sphere were noted: menstrual cycle disorders in women, development of impotence in men [5].

It should also be taken into account that an important role in establishing the mechanisms of the development of various pathological processes is assigned to the study of the nature of the blood supply of organs and systems, since the state of the vascular system, including the testicles, is decisive for their structure and function and is one of the priority tasks of modern morphological science [6-9].

Materials and Methods.

Experiments were conducted on 42 male rats, which were daily intramuscularly injected prednisone (a synthetic glucocorticoid) at the rate of 0.4 mg/kg, which is the maximum single daily dose. The material for the ultrastructural study was taken 1, 3, 7, 14 and 28 days after the introduction of the drug, as well as from animals of two control groups (the initial group - control I and the 28-day observation group - control II, which was injected with a physiological solution in volume, similar to prednisolone).

Pieces of testicular tissue were fixed in a 2.5-3% solution of glutaraldehyde with an active reaction medium of pH 7.2-7.4 prepared on Millonig's phosphate buffer. After 50–60 minutes, the fixed material was transferred to a buffer solution and washed for 20–30 minutes. Post fixation was carried out with a 1% solution of osmium tetroxide in a phosphate buffer of pH 7.2-7.4 for 60 minutes, after which dehydration was carried out in alcohols and acetone and poured into a mixture of epoxy resins with araldite. Semi-thin sections with a thickness of 1-2 μm were made using an ultramicrotome LKB -3 (Sweden), stained with a solution of methylene blue. Ultrathin sections were contrasted with 1% aqueous solution of uranyl acetate and lead citrate according to the Reynolds method and studied in an EM-125K electron microscope.

Animals were removed from the experiment by intraperitoneal injection of large doses of concentrated sodium thiopental.

All experimental studies were carried out in compliance with the principles of bioethics set in the Declaration of Helsinki and the Law of Ukraine "On the Protection of Animals from Cruelty" (No. 1759-VI dated 15.12.2009).

Results and Discussion.

According to the results of our preliminary histological studies, it was established that as the drug was injected, activation of spermatogenesis occurred. In the lumen of the convoluted tubules, the number of germ cells increased significantly, especially due to their immature forms (spermatogonia and spermatocytes). At the same time, the number of mature forms of spermatozoa decreased. The detected changes took place against the background of increased blood flow in the vessels of the testicles.

The ultrastructural study made it possible to penetrate more deeply into the morphogenetic mechanisms of the phenomena that occurred at the same time. Already one day after the introduction of high doses of prednisolone, the content of fat inclusions in Leydig cells, against the background of a decrease in the number of hormonal granules, mitochondria, and tubules

of the endoplasmic reticulum, increased significantly. In the nuclei of such cells, a margination of condensed chromatin was observed, with its predominant localization near the karyolemma, which acquired uneven contours.

Certain changes were also observed in the cells of the spermatogenic epithelium. If spermatogonia and spermatocytes showed signs of increased functional activity in the form of an increase in the number of organelles and tubules of the granular and smooth endoplasmic reticulum, then dystrophic changes were more characteristic of spermatids. In particular, they had blurred contours of the nuclear cover, missing tail tubes. Mitochondria lost the orderliness of cristae with a decrease in their density. As a result of the destruction of organelles, vacuoles were formed in their place.

As for the hemomicrocirculatory bed, there was an increase in its blood supply against the background of a decrease in capillary permeability. This was confirmed by the frequency of detection of shaped elements (both individual erythrocytes and their small clusters), as well as the morpho functional state of the endotheliocytes of their walls. The nuclei of such cells were enlarged and exploded into the lumen of micro vessels, which led to compression and deformation of erythrocytes. Condensation of heterochromatin lumps near the karyoplasm indicated an increase in the functional activity of cells (Figure 1). In the cytoplasm, the number of organelles near the nuclear location increased, and its electron density increased. Due to swelling, the basement membrane thickened.

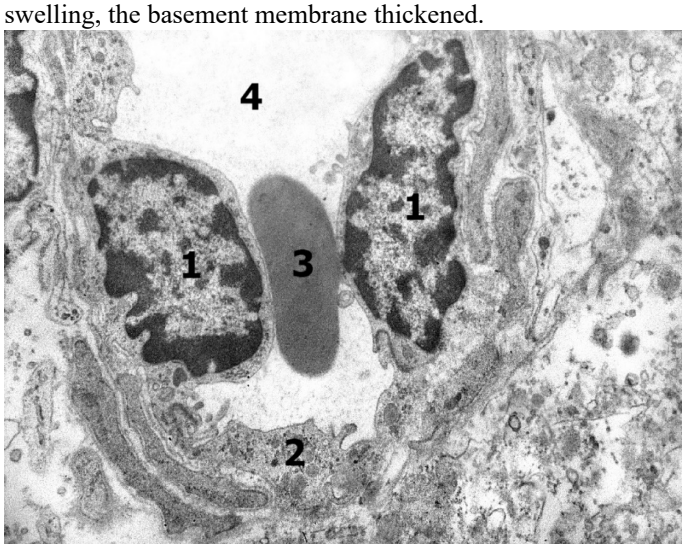

Figure 1. *Ultrastructure of a hemocapillary in a rat testicle one day after the introduction of a high dose of prednisolone. x 12000. Endotheliocyte nuclei – 1, endotheliocyte cytoplasm – 2, deformed erythrocyte in capillary lumen – 3, capillary lumen – 4.*

After three days of experimental observation, the ultrastructural changes in the cellular elements of the testicles of white laboratory rats detected in the previous term gradually increased. In particular, along with dystrophic changes, signs of increased functional activity were noted in endocrinocytes. The nuclei of such cells were somewhat enlarged in size, their karyoplasm looked enlightened, and euchromatin was diffusely located over the entire area of the nucleus. Cytoplasm of cells due to swelling also looked enlightened. In it, along with vacuoles of various sizes that arose at the sites of destroyed organelles, it was possible to observe the presence of hormonal granules and a cluster of small-sized rather electron-dense mitochondria.

As for the supporting cells of Sertoli, their ultrastructure did not undergo special changes. The blood-testicular barrier also retained its three-layered structure. Along with Sertoli cells, spermatogonia in various morpho functional states were found.

Structural changes in other germ cells deepened somewhat. In particular, in spermatids, a decrease in the electron density of their nuclei was noted, and the contours of the tail tubes were blurred. Disorganization of cristae was noted in mitochondria. As a result of the destruction of organelles, vacuoles were formed.

Changes in the hemomicrocirculatory channel were especially noticeable. The nuclei of endotheliocytes and especially their cytoplasm was swollen due to which the nuclei exploded into the lumen of capillaries and the area of the cytoplasm on the sections increased, which led to a significant narrowing of the microvessels lumen, which practically did not exceed the diameter of erythrocytes. As a result, the surface of erythrocytes intimately touched the luminal surface of endotheliocytes cytomembranes.

The seven-day period of experimental observation made it possible to establish the further development of ultrastructural changes, which were quite clearly visible in the interstitial endocrinocytes of Leydig in the form of dystrophic phenomena in the cytoplasm with the destruction of cell organelles with the formation of vacuoles of various sizes and shapes in the enlightened cytoplasm, as well as the destruction of mitochondrial cristae with the formation of voids with preserved contours of organelles (Figure 2).

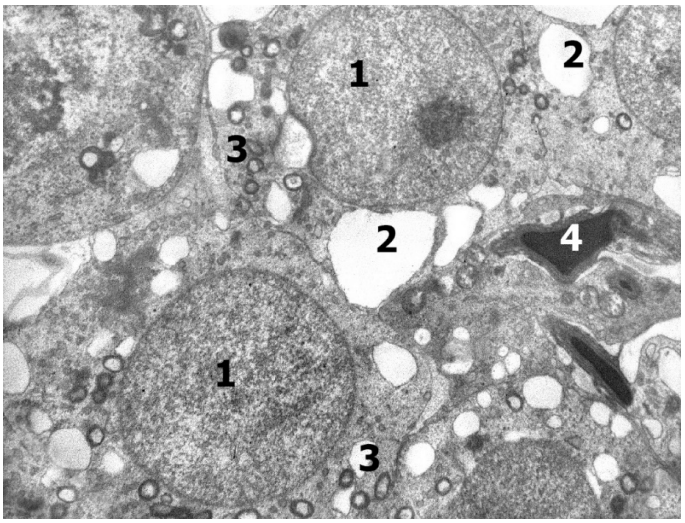

Figure 2. *Ultrastructure of a rat testicle seven days after introduction of high doses of prednisolone. x 9000. Nuclei of interstitial Leydig endocrinocytes – 1, vacuoles – 2, mitochondria with destroyed cristae – 3, deformed spermatids – 4.*

The nuclei of endocrinocytes were in different morphofunctional states. At the same time, in some cases, the cariolem was clear and gave the nuclei a rounded shape, in other cases, its contours were blurred and indistinct, with the formation of intussusceptions. The content and arrangement of

chromatin were different: from diffuse to the formation of lumps of different sizes and intensity of staining.

Sertoli supporting cells continued to remain unchanged. They had an elongated nucleus and rested on the basement membranes. The basement membranes themselves were slightly thickened, had uneven contours, and in some places with fibration.

From the side of spermatogonia, there was an increase in their functional activity with an increase in the number of organelles, especially mitochondria. At the same time, in some cases, spermatogonia with pronounced destructive changes were found.

As for other germ cells, the subsequent disruption of the spermatids structure attracted attention. They were characterized by different degrees of formation of covers, as well as the absence or deformation of tail tubes.

The consequences of the hemodynamic rearrangement of the hemocapillary channel were somewhat special. The latter testified to stagnation as a result of a decrease in the permeability of microvessels against the background of arterial inflow activation.

Hemocapillaries had a narrowed lumen due to protrusion of the swollen nuclei of endotheliocytes. The karyolema of the endotheliocyte nuclei formed intussusceptions, which gave their contours a jagged shape. Thin strips of cytoplasm extended from the nuclei to both sides. A small number of organelles with near nuclear localization was noted. The lumen of microvessels was often filled with formed elements of blood. Moreover, their accumulation resembled coin columns, and the erythrocytes of which they consisted were often deformed and lost their spherical and disk-like shapes due to compression (Figure 3).

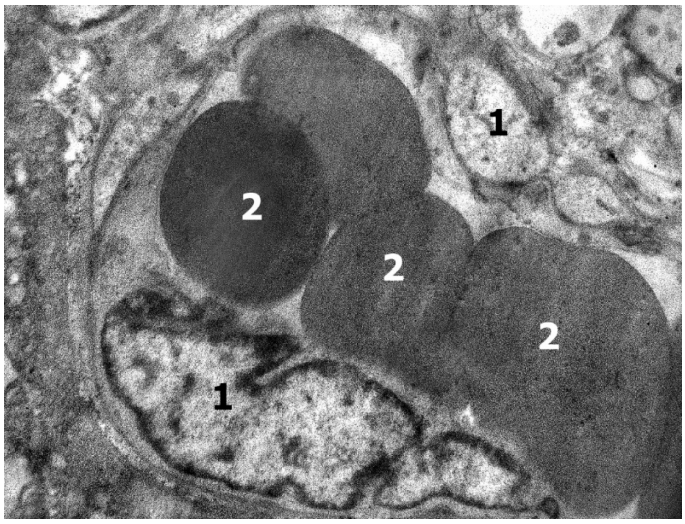

Figure 3. *Ultrastructure of the hemocapillary of a rat testicle seven days after introduction of high doses of prednisolone. x12000. Nuclei of endotheliocytes – 1, erythrocytes – 2.*

The fourteenth day of experimental observation was characterized by the maximum development of morphofunctional changes, which were detected in earlier periods, and which gradually increased. In particular, as regards interstitial Leydig endocrinocytes, dystrophic phenomena continued to increase in them, which was confirmed by an increase in the number and size of vacuoles, as well as mitochondria with destroyed cristae. The near-nuclear localization of vacuoles was characteristic, which in such cases were quite large electron-transparent voids surrounded by a thin membrane with uneven contours, that sometimes led to deformation of the contours of the nuclei themselves.

During this observation period, spermatogonia continued to increase their morphofunctional activity. This was evidenced by an increase in the size of their nuclei with marginalization of partially condensed chromatin. The number and lumen of tubules and cisterns of smooth and granular endoplasmic reticulum increased. A relatively significant number of fat inclusions and polysomes were found in the cytoplasm. The cytoplasm itself increased its electron density. Most of the organelles occupied a near-nuclear position (Figure 4).

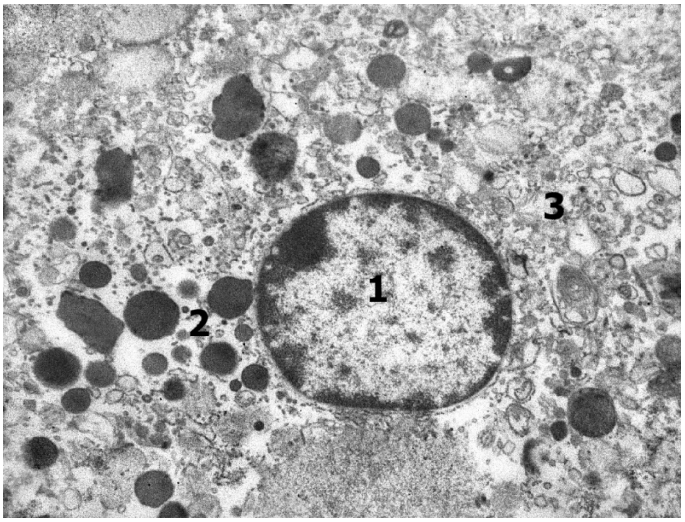

Figure 4. *Ultrastructure of a rat testicle fourteen days after introduction of high doses of prednisolone. x12000. Nucleus of spermatogonia - 1, fat inclusions and mitochondria - 2, cisterns and tubules of the endoplasmic reticulum - 3.*

At the same time, Sertoli supporting cells and their nuclei acquired a flattened appearance, being located on thinned basement membranes.

Spermatocytes continued to remain completely unformed and often deformed and with fragmented nuclei. Tails in most cases were not identified.

Hemomicrocirculation disorders became especially intense. In comparison with the 7-day period of observation, microvessel congestion was observed not only against the background of narrowing of the capillaries lumen due to the swelling of the endotheliocytes nuclei, but also against the background of expanded lumens of microvessels in which the formed elements of blood often formed into figures resembling "coin columns" . Cytoplasm of endotheliocytes, which formed the wall of such hemocapillaries, was elongated thin strips. The basement membrane under such endotheliocytes was also thinned and destructed here and there.

In the final stage of the experiment, on the 28th day from its beginning, the signs of hemodynamic disorders of a stagnant

nature drew attention first of all. This was confirmed not only by the state of the hemomicrocirculatory channel, but also by the state of venules and small veins. At the same time, the cytoplasm of endotheliocytes stretched into thin strips, although the cell nuclei protruded in the direction of the lumen, which indicates their functional activity. Local detachment of endotheliocytes from their basement membranes was observed due to subendothelial edema (Figure 5).

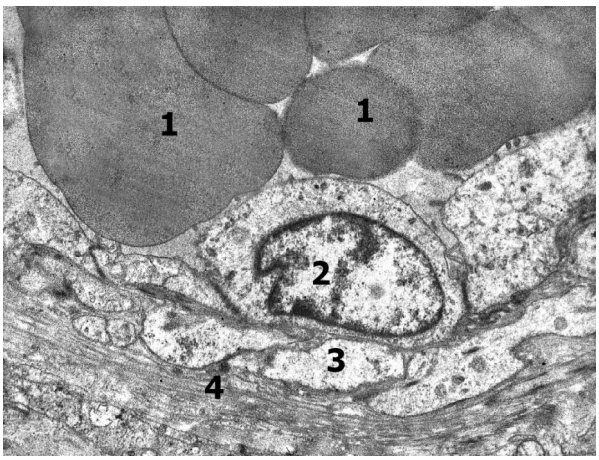

Figure 5. *Ultrastructure of the hemocapillary of a rat testicle twenty-eight days after introduction of high doses of prednisolone. x12000. Erythrocytes – 1, endotheliocyte nucleus – 2, zones of subendothelial edema – 3, basement membrane – 4.*

Sertoli supporting cells and Leydig interstitial endocrinocytes also attracted attention, which were distinguished by the condensation of heterochromatin with its predominantly perikaryolemma localization. The cytoplasm of such cells looked dark due to an increase in its electron density, which, together with a decrease in the number of organelles and a simultaneous increase in the number of vacuoles, may be evidence of a decrease in the functional activity of such cells, or even their possible presence in the stage preceding apoptosis, that is, the natural death of cells (Figure 6).

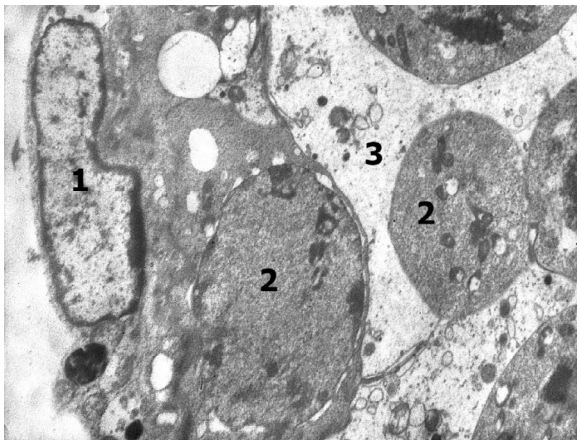

Figure 6. *Ultrastructure of a rat testicle twenty-eight days after introduction of high doses of prednisolone. x12000. Cell nucleus – 1, Leydig interstitial endocrinocyte nucleus – 2, spermatogonia cytoplasm – 3.*

Clear signs of apoptosis activation of Leydig cells were especially pronounced in certain places. The cytomembrane of such cells lost its structure, due to which their contours were uneven. In some places, due to defects in the cytomembrane, part of the cytoplasm together with organelles leaked into the intercellular space. Whole fragments of different sizes were separated from the cell. The nuclei of such cells became markedly pyknotic. Their karyolemma formed deep invaginations, which separated the nuclei into almost separate parts. Condensed heterochromatin occupied a peripheral position. A decrease in functional activity was evidenced by an intense increase in the electron density of the cytoplasm and a significant expansion of tubules and cisterns of the endoplasmic reticulum, which took on the appearance of "rosettes". As a result, the cells became "dark" in appearance (Figure 7).

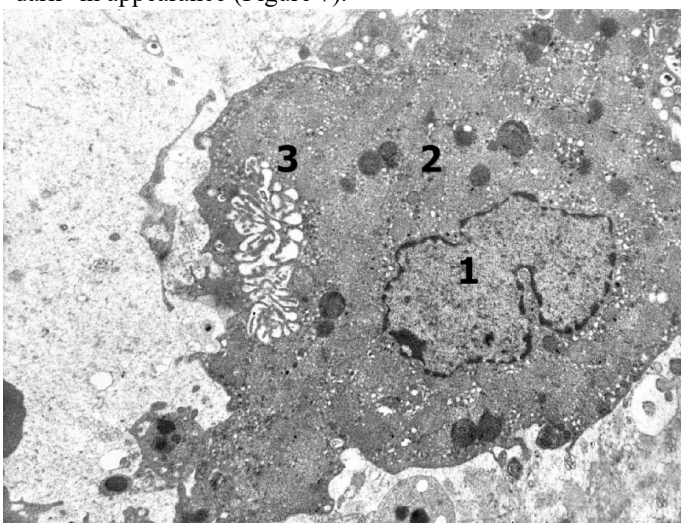

Figure 7. *Ultrastructure of a rat testicle twenty-eight days after introduction of high doses of prednisolone. x12000. Nucleus of a cell with invaginates of different depths - 1, cytoplasm of Leydig interstitial endocrinocyte - 2, expanded tubules and cisterns of the endoplasmic reticulum - 3.*

As for the spermatocytes, a significant part of them continued to remain completely unformed, often with deformed nuclei and without clearly defined tails.

Thus, the data we obtained about the structural and functional changes in the parenchyma of the testicles and their blood vessels fully correspond to modern ideas about the nature of hormonal influences on the sexual sphere and may be a consequence of the development of side effects of prednisolone [10-12]. This can be attributed to an increase in the functional activity of the spermatogenic epithelium against the background of increased blood vessel filling. At the same time, the mineralocorticoid effect of prednisolone can lead to the development of arterial hypertension, which in the future in the complex can be the cause of the development of organ's ischemia with a violation of its functional capacity [13].

As for the morphofunctional rearrangement of the cells of testicles spermatogenic epithelium at experimental animals, when using high doses of prednisolone, this process is noticeably

activated with simultaneous qualitative and quantitative deviation from the norm due to a significant increase in immature forms and a decrease in the specific weight of mature spermatozoa, that, together with progressive ischemia, can be cause of infertility [14]. Such dynamics of changes may be the result of simultaneous potentiating and competing effects on the morphofunctional state of Leydig interstitial endocrinocytes and the circulatory system.

Conclusions.

1. Long-term introduction of high doses of prednisolone to white rats promotes the activation of spermatogenesis with a progressive increase in immature forms of germ cells and a simultaneous decrease in the specific number of mature spermatozoa as a result of prednisolone's potentiating and at the same time competing with the hormonal function of interstitial endocrinocytes.
2. Activation of spermatogenesis occurs against the background of increased blood circulation of the testicles with increased blood filling of their vessels, especially in the early period (7-14 days from the start of use), which may be a consequence of the direct blood circulation-stimulating effects of prednisolone.
3. In the long term (14-28 days), there is a decrease in the permeability of small arteries and arterioles against the background of venous stasis, as well as the rate of activation of spermatogenesis, that can be a reaction to overloading of the hemomicrocirculatory channel of the testicles and cause further development of organ's ischemia with its functional insufficiency.

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РЕЗЮМЕ

УЛЬТРАСТРУКТУРНЫЕ ОСОБЕННОСТИ ПРЕСТРОЙКИ КЛЕТОК ГЕМАТОТЕСТИКУЛЯРНОГО БАРЬЕРА И СПЕРМАТОГЕННОГО ЭПИТЕЛИЯ ЯИЧЕК КРЫС ПРИ ВВЕДЕНИИ ВЫСОКИХ ДОЗ ПРЕДНИЗОЛОНА

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Особенностью последних десятилетий является постепенное возрастание уровня мужского бесплодия одной из важных причин которого, безусловно, является эндокринная дисфункция разного генеза. Поэтому целью исследования было установление особенностей перестройки клеточных элементов яичек белых крыс при введении высоких доз преднизолона. Ультраструктурное исследование проведено на 42 крысах-самцах. Установлено, что длительное введение высоких доз преднизолона способствует активации сперматогенеза с прогрессирующим увеличением незрелых форм половых клеток и одновременное уменьшение удельного количества зрелых сперматозоидов. Активация сперматогенеза происходит на фоне усиления кровообращения яичек с увеличением кровенаполнения их сосудов, особенно в раннем периоде (7-14 сутокотначалаприменения), что может являться следствием непосредственных стимулирующих кровообращение воздействий преднизолона. В отдаленные сроки (14-28 сутки) происходит снижение пропускной способности мелких артерий и артериол на фоне венозного застоя, а также темпов активации сперматогенеза, что может быть реакцией на перегрузку капиллярного русла яичек и вызвать в дальнейшем развитие ишемии органа с его.

Ключевые слова: ультраструктура, яички, сперматогенез, гемокапилляры, преднизолон.

SUMMARY

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A feature of recent decades is the gradual increase in the level of male infertility, one of the important causes of which, of course, is endocrine dysfunction of various origins. Therefore, the aim of the study was to establish the features of the rearrangement of the testicles cellular elements of white rats with the introduction of high doses of prednisolone. An ultrastructural study was carried out on 42 male rats. It has been established that long-term introduction of high doses of prednisolone promotes the activation of spermatogenesis with a progressive increase in immature forms of germ cells and a simultaneous decrease in the specific number of mature spermatozoa. Activation of spermatogenesis occurs against the background of increased blood circulation in the testicles with an increase in the blood supply to their vessels, especially in the early period (7-14 days from the start of use), which may be a consequence of the direct effects of prednisolone stimulating blood circulation. In the long term (14-28 days) there is a decrease in the throughput of small arteries and arterioles against the background of venous stasis, as well as the rate of activation of spermatogenesis, which may be a reaction to the overload of the capillary bed of the testicles and cause further development of organ's ischemia with it.

Key words: ultrastructure, testicles, spermatogenesis, hemocapillaries, prednisolone.