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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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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:

Erkin Pekmezci, Murat Türkoğlu.
URTICA DIOICA EXTRACT DOWNREGULATES THE GENE EXPRESSION OF 5A-RII IN HACAT CELLS: POSSIBLE IMPLICATIONS AGAINST ANDROGENIC SKIN DISEASES……..…….....……6-9

Anoop Karthika, Kowmudi Gullapalli, Krishnaveni Nagappan, Manohar Dronavajjula, Anilakumar Kandangath Raghavan, Ramalingam Peraman.
RESPONSE SURFACE METHODOLOGY ASSISTED ULTRAPERFORMANCE LIQUID CHROMATOGRAPHIC METHOD OPTIMIZATION FOR THE SIMULTANEOUS ESTIMATION OF SIX FAT-SOLUBLE VITAMINS IN TABLET DOSAGE FORM USING A DEVELOPED AND VALIDATED UPLC-Q-TOF/MS METHOD…….....10-22

M. Aghajanyan, M. Sargsyan.
COMPARATIVE ASSESSMENT OF ATHLETES' AUTONOMIC REACTIVITY BY HRV INDICATORS IN FUNCTIONAL TESTS OF VARIOUS DIRECTIONS…….....……23-28

Pilishvili O, Chkhaidze Z, Jinchveladze D, Dzamukashvili M, Khodeli N.
"EX VIVO" MACHINE PRESERVATION OF THE ABDOMINAL ORGANS OF A PIG…….....……..29-35

Olha Yakovleva, Oleh Hoina-Kardasevich, Nataliia Shcherbeniuk.
EFFICACY OF OSSEIN-HYDROXYAPATITE COMPLEX AS A PHARMACOLOGICAL CORRECTOR OF BONE LOSS (REVIEW)…….....……..36-40

Drobinska Nataliia, Abrahamovych Orest, Abrahamovych Maryana, Ivanochko Ruslana, Chemes Viktoriia.
CHARACTERISTICS OF CALCIUM-PHOSPHORUS METABOLISM AND BONE TURNOVER INDICATORS IN PATIENTS WITH LIVER CIRRHOSIS AND THEIR DIAGNOSTIC VALUE FOR ASSESSING BONE STRUCTURES DISORDER……....……..41-48

Reem H Mohammad, Muhammad A Al Kattan.
SMOKING JEOPARDIZED MITOCHONDRIAL FUNCTION VITIATING LIPID PROFILE…….....……..49-51

Margarita Vrej Sargsyan.
SPECIFICITIES OF THE COURSE OF SUBCLINICAL HEPATITIS AMONG YOUNG ADULTS WITH ACUIE GLOMERULONEPHRITIS…….....……..52-56

ChigogidzeM, PagavaZ, Taboridze I, Lomia N, Saatashvili G, Sharashidze N.
ASSESSMENT OF CORONARY COLLATERAL CIRCULATION PREDICTORS AMONG PATIENTS WITH ACUTE CORONARY SYNDROME IN POPULATION GEORGIA…….....……..57-64

Zahraa S. Thabit, Harith Kh. Al-Qazaz.
HEALTH-RELATED QUALITY OF LIFE AMONG PATIENTS WITH OSTEOARTHRITIS: A CROSS-SECTIONAL STUDY…….....65-70

Nurkina Dinara Almatovna, Baimuratova Mayrash Aushatovna, Zhussupbekova Lazzat Ibrashevna, Kodaspayev Almat Turysbekovitch, Alimbayeva Saira Hamidzhanovna.
ASSESSMENT OF RISK FACTORS OF MYOCARDIAL INFARCTION IN YOUNG PERSONS…….....……..71-77

Zoryana Bilous, Orest Abrahamovych, Maryana Abrahamovych, Oksana Fayura, Anhela Fedets.
CHARACTERISTICS OF THE AUTONOMIC NERVOUS SYSTEM STATE, ASSESSED BY THE HEART RATE VARIABILITY STUDY IN CIRRHOTIC PATIENTS WITH SYNTROPIC CARDIOMYOPATHY AND ITS EATURES DEPENDING ON THE QT INTERVAL DURATION…….....……78-82

Tchernev G, Lozev I, Pidakev I, Kordeva S.
KARAPANDZIC FLAP FOR SQUAMOUS CELL CARCINOMA OF THE LOWER LIPP: POTENTIAL ROLE OF NITROSAMINES IN EPROSARTAN AS CANCER TRIGGERING FACTORS…….....……83-85

Skobska O.Ye, Zemskova O.V, Lisianyi O.M, Andrieiev S.A, Levcheniuk S.V, Khinikadze Mirza.
CLINICAL-AND-FUNCTIONAL ASSESSMENT OF THE EARLY POSTOPERATIVE OUTCOME OF SURGICAL TREATMENT OF PATIENTS WITH VESTIBULAR SCHWANNOMA…….....……..86-93

Vladyslava Kachkovska, Anna Kovchun, Viktor Kovchun, Ivan Klisch, Olha Marchuk, Iryna Dudchenko, Lyudmyla Prystupa.
ER22/23EK AND TTH111I POLYMORPHISMS IN THE GLUCOCORTICOID RECEPTOR GENE IN PATIENTS WITH BRONCHIAL ASTHMA WITH REGARD TO THE AGE OF ONSET…….....……94-97

S.B.Imamverdiyev, E.C.Qasımov, R.N.Naghıyev.
COMPARATIVE RESULTS OF MODERN EXAMINATION METHODS IN EARLY DIAGNOSIS OF BLADDER CANCER, DETERMINATION OF THE DEGREE OF INVASION AND SELECTION OF RADICAL TREATMENT TACTICS……..……98-102

Baidurin S.A, Akhmetzhanova Sh.K, Ilmalieva A.Zh, Sagyndykova G.Zh, Orazbekova A.B.
MYELODYSPLASTIC SYNDROME: DIAGNOSIS, TREATMENT AND PROGNOSIS (LITERATURE REVIEW)…….....……103-107

Popovych T, Zaborovskyy V, Baryska Ya, Pohoryelova Z, Maslyuk O.
THE NATURE AND FEATURES OF SURROGACY AS AN ASSISTED REPRODUCTIVE TECHNOLOGY….....…108-112

Tagiyeva Fakhriya Alamdar.
PECULIARITIES OF LIPID EXCHANGE IN PREGNANT WOMEN WITH OBESITY…….....…113-115

ML Touré, G Carlos Othon, SM Diallo, TH Baldé, SD Barry, MM Konaté, F Sakadi, FD Kassa, A Kourouma, JM Kadji, M Diakité, A Sakho, MT Diallo, S Condé, V Millimono, D Camara, H Madandi, TM Diallo, E-Lamah, FA Cisse, A Cissé.
EPILEPTIC SEIZURES REVEALING STURGE WEBER'S DISEASE IN A TROPICAL ENVIRONMENT: STUDY OF EIGHT CASES…….....……..116-124

Makhlynets NP, Prots HB, Pantus AV, Ozhogan ZR, Plaviuk LYu.
THE EXISTENCE OF A FUNCTIONAL MATRIX IN THE DEVELOPMENT OF THE FACIAL SKELETON IN CHILDREN…….....……..125-132

Zaitsev A.V, Ilenko-Lobach N.V, Boychenko O.M, Ilenko N.M, Krutikova A.D, Ivanitskyi I.O, Bublii T.D, Kotelevska N.V.
INTEGRAL METHOD FOR ASSESSING THE EFFICIENCY OF DENTAL CARIES PREVENTION…….....…133-136

I. Ye. Herasymiuk, O.M. Herman, O.P. Ilkiv.
ULTRASTRUCTURAL FEATURES OF THE REARRANGEMENT OF THE CELLS OF THE HEMATOTESTICULAR BARRIER AND THE SPERMATOGENIC EPITHELIUM OF THE RATS TESTICLES DURING THE SUDDEN WITHDRAWAL OF PREDNISOLONE AFTER ITS LONG-TERM INTRODUCTION IN HIGH DOSES….....137-141

ML Touré, G Carlos Othon, A Touré, M Diakité, K Condé, DF Kassa, F Sakadi, D Camara, S Conde, V Millimono, MS Diallo, SM Diallo, JM Kadji, E-Lamah, FA Cisse, A Cissé.
GAYET WERNICKE'S ENCEPHALOPATHY AFTER COVID-19 IN ELDERLY SUBJECTS IN TROPICAL ENVIRONMENTS: STUDY OF SIX (6) OBSERVATIONS IN CONAKRY…….....……142-146

Uwe Wollina.
EROSIVE PUSTULAR DERMATOSIS OF THE SCALP (EPDS) – A CASE SERIES AND SHORT REVIEW….....147-152

GEORGIAN MEDICAL NEWS
No 1 (334) 2023

ULTRASTRUCTURAL FEATURES OF THE REARRANGEMENT OF THE CELLS OF THE HEMATOTESTICULAR BARRIER AND THE SPERMATOGENIC EPITHELIUM OF THE RATS TESTICLES DURING THE SUDDEN WITHDRAWAL OF PREDNISOLONE AFTER ITS LONG-TERM INTRODUCTION IN HIGH DOSES

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Abstract.

With long-term use of hormonal drugs, according to the principle of "negative feedback", the production of own hormones by the endocrine glands is inhibited. With sudden withdrawal, in particular, of glucocorticoids, there are processes that threaten the development of secondary adrenal insufficiency.

The purpose of the study: to establish the peculiarities of the reconstruction of the cellular elements of the testicles of white rats after the withdrawal of high doses of prednisolone. An ultrastructural study was performed on 60 male rats. It has been established that the sudden withdrawal of prednisolone after long-term introduction in high doses causes changes in the body that can be characterized as a state of "acute hypocorticism." At the same time, further progression of the dystrophic-destructive processes that occurred during the preliminary long-term introduction of the drug occurs. The most pronounced such changes were observed up to 7 days after cancellation. Then their intensity decreased, and by the 14th day signs of regenerative processes appeared, which gradually increased. Therefore, by the 28th day of the experiment, the ultrastructure of the cellular elements of the testicles was almost completely restored, which may be evidence of the high compensatory and regenerative ability of animals of this species, which must be taken into account when extrapolating the results to humans.

Key words. Ultrastructure, testicles, spermatogenesis, capillaries, prednisolone, hypocorticism.

Introduction.

Clinical and experimental studies conducted in recent years show 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 sexual sphere were noted: menstrual cycle disorders in women, development of impotence in men [1]. Such dysfunctions in men can be a direct consequence of morphological changes in the structural components of the blood-testicular barrier and the spermatogenic epithelium of the testicles [2,3].

At the same time, it has been established that with sudden withdrawal of glucocorticoids, reverse processes occur, which threaten the development of secondary adrenal insufficiency [4,5]. Morphological changes in the testicles that occur at the same time can also be the reason for the development of infertility [6,7]. Therefore, further research is needed to establish the ultrastructural mechanisms of such changes.

Material and Methods.

Experiments were conducted on 60 rats, which were daily intramuscularly administered prednisolone (synthetic glucocorticoid) at the rate of 0.4 mg/kg, which is the maximum single daily dose. Material for morphological and morphometric studies was taken from 30 rats - 1, 3, 7, 14 and 28 days after drug administration, and from another 30 rats - 1, 3, 7, 14 and 28 days after its withdrawal. The control group consisted of 9 intact animals.

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), and they were 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 accordance with the principles of bioethics set forth 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.

Based on the results of the research, it was established that the long-term introduction of high doses of prednisone 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 the potentiating and at the same time competing action of prednisone with the hormonal function of interstitial endocrinocytes.

Activation of spermatogenesis occurs against the background of increased blood circulation of the testicles with the expansion of the lumen and increased blood filling of vessels of all calibers, 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.

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 can be a reaction to overloading the hemomicrocirculatory bed of the testicles and cause further development of ischemia of the organ with its functional insufficiency.

Certain features of the structural reorganization of rat testicular tissues were also established after the sudden withdrawal of prednisolone after its long-term introduction in large doses. If 1 day after the withdrawal of special ultrastructural differences in the cellular elements of the testicles from rats with a 28-day introduction of the drug were not detected, then already on the 3rd day, significant differences were observed, which at the ultrastructural level were manifested by pronounced destructive changes. In particular, Leydig endocrinocytes were distinguished by a noticeable decrease in the number of organelles. Vacuoles of various sizes were formed in their place. A small number of mitochondria that could still be differentiated lost their cristae and had a hollow appearance.

Quite often, vacuoles acquired particularly large sizes, occupying most of the area of the cytoplasm. At the same time, the condensation of heterochromatin, especially in the near karyolemma zone, led to the deformation of the nucleus with the formation of near karyolemma voids (Figure 1).

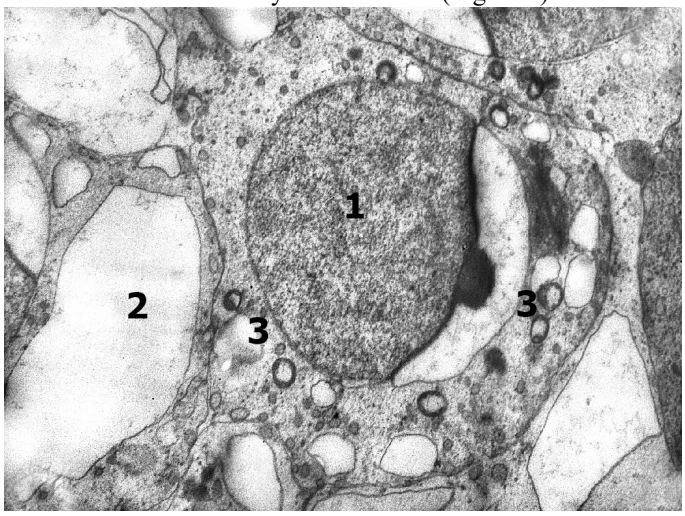

Figure 1. *Ultrastructure of the rat testicle three days after the sudden withdrawal of prednisolone after its previous long-term introduction in large doses. x 12,000. Leydig interstitial endocrinocyte nucleus – 1, vacuoles – 2, mitochondria with destroyed cristae – 3.*

Pronounced condensation of chromatin was also observed in the nuclei of spermatids. In them, the thickness of the cytoplasm surrounding the nucleus decreased. At the same time, Sertoli cells looked somewhat enlarged due to the expansion of the cytoplasmic area. Although the noticeable decrease in the number of organelles in them attracted attention (Figure 2).

The number of spermatocytes significantly decreased most of which continued to remain incompletely formed.

Ultrastructural changes from the side of the hemomicrocirculatory channel were especially noticeable. First of all, the anemia of the micro vessels attracted attention, although their lumen remained quite wide. At the same time, the endotheliocyte nuclei looked pyknotically deformed with condensation of heterochromatin. As a result of their stretching along the periphery, the cytoplasm of cells became thinner, in the perinuclear zone, the cytolemma formed numerous pseudopodia, and the number of organelles decreased in the cytoplasm. Basal membranes looked thickened and homogenized in places (Figure 3).

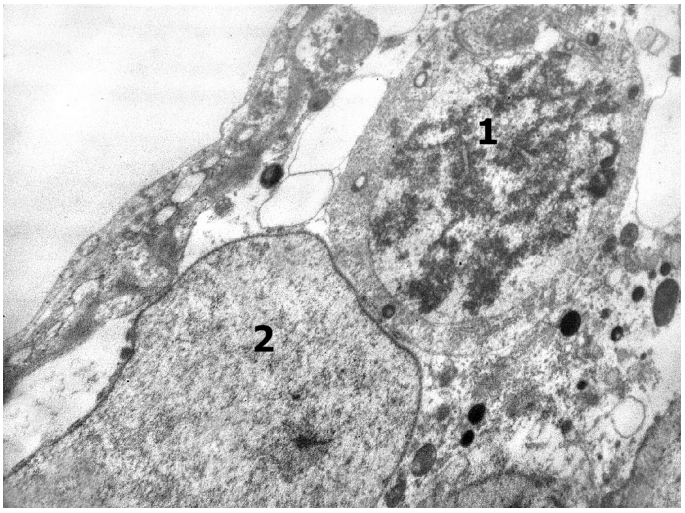

Figure 2. *Ultrastructure of the testicle of a rat three days after the sudden withdrawal of prednisolone after its previous long-term introduction in large doses. x 12,000. Spermatid nucleus – 1, Sertoli cell – 2.*

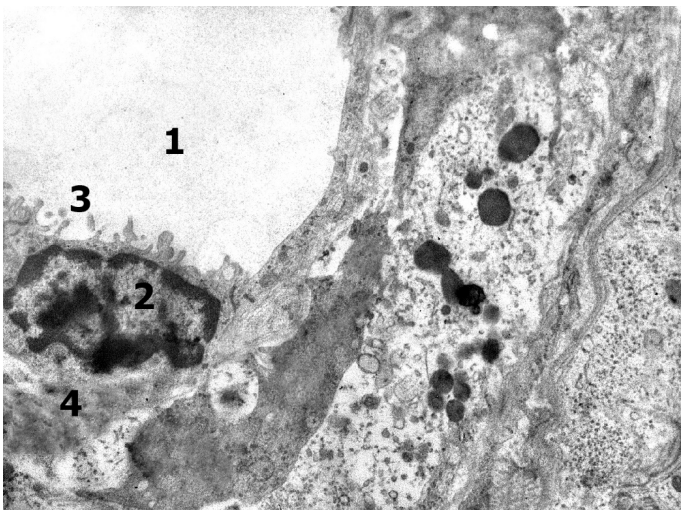

Figure 3. *Ultrastructure of the testicle of a rat three days after the sudden withdrawal of prednisolone after its previous long-term introduction in large doses. x 12,000. Capillary lumen – 1, endotheliocyte nucleus – 2, pseudopodia – 3, homogenized area of basement membrane – 4.*

Destructive changes in cellular elements became even more pronounced on the 7th day after withdrawal of prednisolone administration. In Leydig endocrinocytes, further reduction in the number of organelles continued with the formation of vacuoles of various sizes in their place. A small number of mitochondria, which were still not completely destroyed, lost their cristae and had the appearance of small-sized cavities with preserved external contours. At the same time, lumps of condensed chromatin occupied the central position in the nuclei. The majority of spermatocytes were deformed with a disturbed structure (Figure 4).

Sometimes almost completely destroyed cellular elements of the testicles came into view, which were areas of homogenized tissue with the remains of individual fragments of certain cells or their destructured fragments (Figure 5).

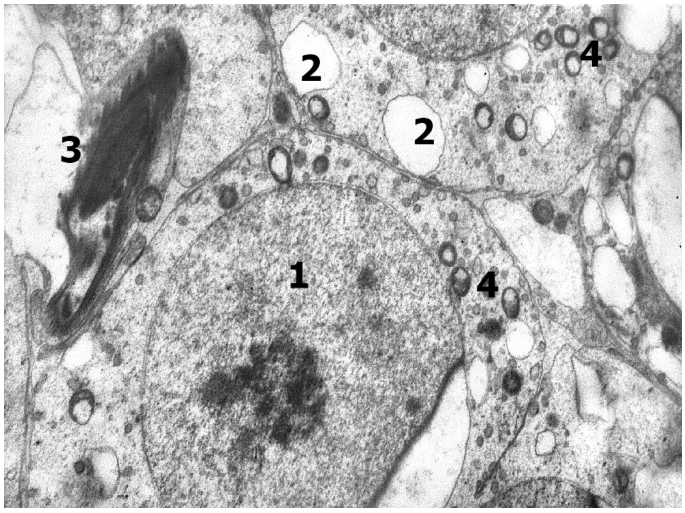

Figure 4. *Ultrastructure of the testicle of a rat seven days after the sudden withdrawal of prednisolone after its previous long-term introduction in large doses. x 12,000. interstitial Leydig endocrinocyte nucleus – 1, vacuoles – 2, spermatocyte – 3, mitochondria with destroyed cristae – 4.*

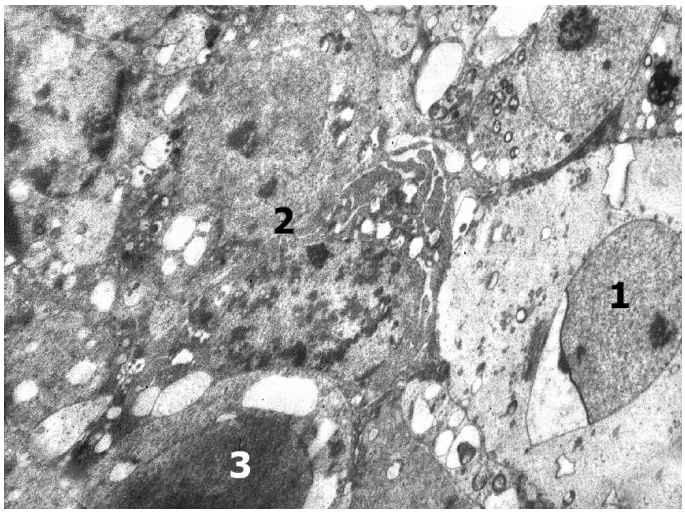

Figure 5. *Ultrastructure of the testicle of a rat seven days after the sudden withdrawal of prednisolone after its previous long-term introduction in large doses. x 9,000.*

The nucleus of an interstitial Leydig endocrinocyte – 1, destructively homogenized cells of the spermatogenic epithelium – 2, the nucleus of a spermatid with vacuoles in the cytoplasm – 3.

Certain changes were also observed from the side of the hemomicrocirculatory channel. The lumen of capillaries slightly narrowed compared to the previous period of observation, continuing to remain, however, still quite wide and many times exceeding the diameter of single erythrocytes, which were sometimes found in micro vessels. Endotheliocytes had elongated peripheral parts and thickening in the central parts due to the location of the nuclei here. Condensation of heterochromatin was observed in the nuclei with its predominant near karyolemma localization. White-nucleated areas of the cytolemma continued to form numerous pseudopodia.

The results of an ultrastructural study on the 14th day after the withdrawal of prednisolone indicated a certain stabilization of dystrophic-destructive changes, and sometimes regenerative processes in the cellular elements of testicles of experimental animals. Against the background of still quite pronounced vacuolization of the cytoplasm of interstitial Leydig endocrinocytes and the absence of cristae in the mitochondria, the nuclei of such cells again acquired a clear rounded shape and were evenly filled with diffuse euchromatin, which can be considered a sign of the restoration of their functional activity (Figure 6).

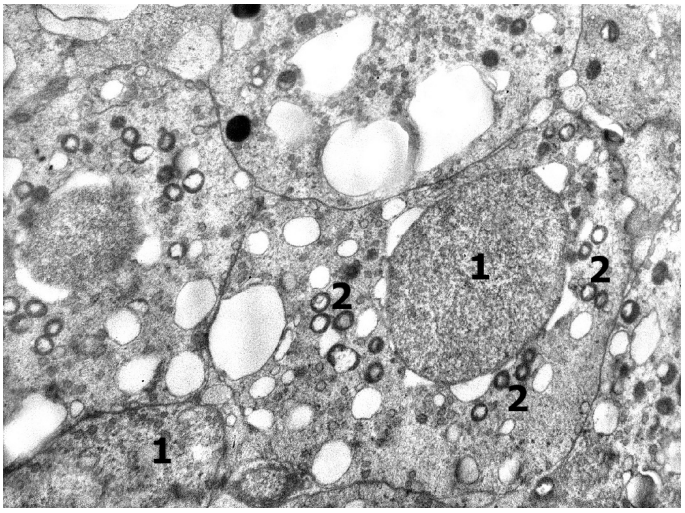

Figure 6. *Ultrastructure of the testicle of a rat fourteen days after the sudden withdrawal of prednisolone after its previous long-term administration in large doses. x 12,000. Interstitial Leydig endocrinocyte nucleus – 1, mitochondria with destroyed cristae – 2.*

As for the cells of the spermatogenic epithelium, they were in different morpho-functional states and at different stages of maturation. In particular, as regards spermatocytes, the nuclei of some of them had a typical spindle-like shape, while others, on the contrary, were deformed and increased in size. In some cases, the formation of tails could be observed. In the cytoplasm, it was sometimes possible to observe an increase in the number of organelles, in particular, mitochondria with clear contours of cristae, as well as various inclusions. Covers formed around the cores. However, a significant part of spermatocytes still retained signs of immaturity (Figure 7).

On the side of the hemomicrocirculatory channel, a pronounced narrowing of the lumen of capillaries was observed due to the thickening of the lateral parts of the cytoplasm of endotheliocytes and the increase in the size of their holes, which led to a decrease in the throughput of these micro vessels (Figure 8).

However, with an increase in the number of organelles in the cytoplasm, the endotheliocyte nuclei were pyknotically deformed with scalloped contours of the karyolemma, condensed heterochromatin in the form of lumps accumulated near the nuclear envelope, which can collectively indicate the functional stress of these cells. The number of pseudopodia decreased in the perinuclear zones of the cytoplasm. At the same time, the basal membranes were thickened.

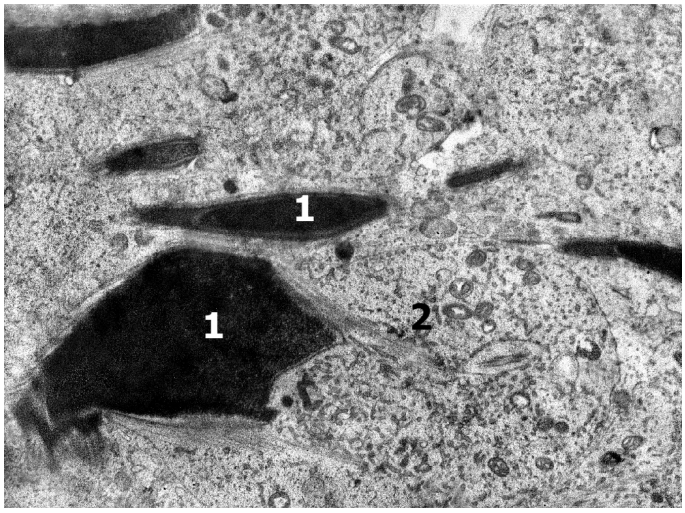

Figure 7. *Ultrastructure of the testicle of a rat fourteen days after the sudden withdrawal of prednisolone after its previous long-term introduction in large doses. x 12,000. Spermatocyte nucleus - 1, organelles in spermatocyte cytoplasm - 2.*

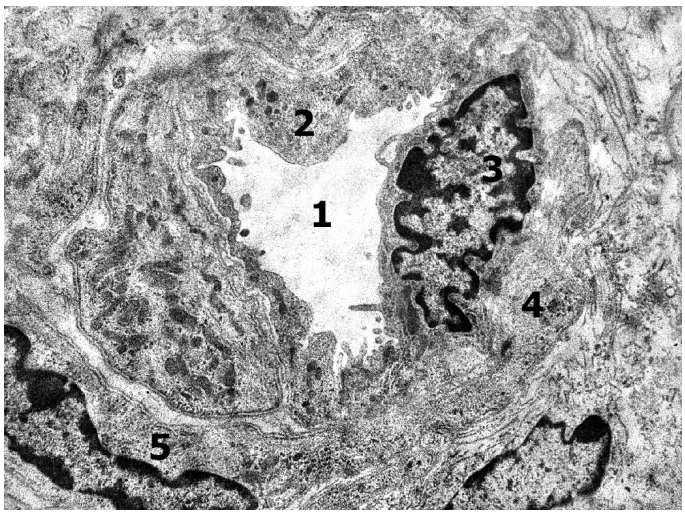

Figure 8. *Ultrastructure of the testicle of a rat fourteen days after the sudden withdrawal of prednisolone after its previous long-term introduction in large doses. x 12,000. Capillary lumen – 1, endotheliocyte cytoplasm with organelles – 2, endotheliocyte nucleus – 3, basement membrane – 4, Sertoli cell nucleus – 5.*

Further observation showed that in the testicles of white laboratory rats in the period from 14 to 28 days after the sudden withdrawal of prednisolone after its previous long-term introduction in large doses, the regenerative processes grow quite intensively and progressively. Thus, on the 28th day of observation, during the ultrastructural study, a significant majority of interstitial Leydig endocrinocytes, supporting Sertoli cells, as well as all cells from the generation of the spermatogenic epithelium had a normal structure and were in a moderately active morpho functional state. Although, along with that, there were cells with one or another degree of dystrophic-degenerative changes. The structural organization of the capillaries was also without peculiarities, the lumen of which sometimes contained individual blood cells. However, sometimes there were capillaries with a narrowed lumen due to swelling and an increase in the size of the nuclei of the endotheliocytes of their walls.

Thus, according to the results of an ultrastructural study, it was established that the sudden withdrawal of prednisolone after its previous long-term introduction in high doses causes changes in the body that can be characterized as a state of "acute hypocorticism." At the same time, there is further development and progression of dystrophic-destructive processes that occurred during the previous long-term introduction of high doses of prednisolone [8,9]. Therefore, in the early period after the sudden withdrawal of prednisolone, the probability of infertility is even greater than with its long-term administration. The most pronounced such changes were observed up to the 7th day after the withdrawal of the drug. Then their intensity decreased, and by the 14th day there were even signs of regenerative processes that gradually increased. Therefore, by the 28th day of the experiment, the ultrastructure of the cellular elements of the testicles was almost completely restored, which can be evidence of the high compensatory and regenerative ability of animals of this species, which must be taken into account when extrapolating the obtained results to humans.

All these processes took place against the background of remodeling of the hemomicrocirculatory channel. Initially, a decrease in the blood filling of the capillaries was noted while maintaining their expanded lumen, and then the narrowing of the latter due to the functional activation of endotheliocytes. Such microvascular reactions can also occur under conditions of hypocorticism as a result of sharp dehydration of the body from the loss of sodium and chloride ions with urine and a decrease in their absorption in the intestines. A decrease in the volume of circulating blood at the same time leads to a decrease in blood pressure [10]. To maintain central and systemic pressure, the body reacts accordingly with organ ascending vasoconstriction with a decrease in the capacity of organ blood vessels, including the testicles. That is, with the sudden withdrawal of prednisone in the bloodstream of the testicles, reverse processes occur to those observed during its long-term introduction [4,5].

Conclusion.

1. Sudden withdrawal of prednisolone after its previous long-term introduction in high doses leads initially to reverse vascular reactions, followed by the development of ascending vasoconstriction and a decrease in the permeability of the blood vessels of the testicles (up to 14 days after the withdrawal of prednisolone), which is accompanied by a decrease in the blood filling of capillaries, the progression of dystrophic-destructive changes in the cellular elements of the spermatogenic epithelium and can be the reason for the development of infertility.

2. Subsequently, there is a partial recovery of the morpho-functional state of the parenchyma of the testicles and their blood vessels, which under such conditions can be evidence of the high compensatory and regenerative ability of animals of this species, although even on the 28th day after the withdrawal of prednisone, cells with one or another degree of destructive changes in intracellular organelles.

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РЕЗЮМЕ

У Л Ь Т Р А С Т Р У К Т У Р Н Ы Е ОСОБЕННОСТИ ПРЕСТРОЙКИ КЛЕТОК ГЕМАТОТЕСТИКУЛЯРНОГО БАРЬЕРА И СПЕРМАТОГЕННОГО ЭПИТЕЛИЯ ЯИЧЕК КРЫС ПРИ ПРИ ВНЕЗАПНОЙ ОТМЕНЕ ПРЕДНИЗОЛОНА ПОСЛЕ ЕГО ДЛИТЕЛЬНОГО ВВЕДЕНИЯ В ВЫСОКИХ ДОЗАХ

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При длительном применении гормональных препаратов по принципу «отрицательной обратной связи» угнетается выработка собственных гормонов эндокринными железами. При внезапной отмене, в частности глюкокортикоидов, происходят процессы, угрожающие развитием вторичной недостаточности надпочечников Морфологические изменения возникающие при этом в яичках могут быть причиной бесплодия.

Цель исследования: установление особенностей перестройки клеточных элементов яичек белых крыс после отмены введения высоких доз преднизолона. Ультраструктурное исследование проведено на 60 крысах-самцах. Установлено, что внезапная отмена преднизолона после его длительного введения в высоких дозах вызывает изменения в организме, которые можно охарактеризовать как состояние «острого гипокортицизма». При этом происходит дальнейшее прогрессирование дистрофически-деструктивных процессов, возникших при предварительном длительном введении препарата. Наиболее выражено такие изменения наблюдались до 7 суток после отмены. Затем интенсивность их уменьшалась, а к 14-м суткам возникали признаки регенераторных процессов, которые постепенно нарастали. Поэтому к 28-м суткам эксперимента почти полностью восстанавливалась ультраструктура клеточных элементов яичек, что может быть свидетельством высокой компенсаторной и регенераторной способности животных данного вида, которые нужно учитывать при экстраполяции результатов на человека.

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