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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 ВИНТИ 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 ВИНТИ 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. Корректур авторам не высылаются, 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 computer-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 საქურაღებოლ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დაიცვათ 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 შედეგების 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 ფხიხლებში 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.

Yaomin Luo, Xin Chen, Enhao Hu, Lingling Wang, Yuxuan Yang, Xin Jiang, Kaiyuan Zheng, Li Wang, Jun Li, Yanlin Xu, Yinxu Wang, Yulei Xie. TRANSCRIPTOME ANALYSIS REVEALED THE MOLECULAR SIGNATURES OF CISPLATIN-FLUOROURACIL COMBINED CHEMOTHERAPY RESISTANCE IN GASTRIC CANCER.....	6-18
Abramidze Tamar, Bochorishvili Ekaterine, Melikidze Natela, Dolidze Nana, Chikhelidze Natia, Chitadze Nazibrola, Getia Vladimer, Gotua Maia, Gamkrelidze Amiran. RELATIONSHIP OF ALLERGIC DISEASES, POLLEN EXPOSURE AND COVID-19 IN GEORGIA.....	19-26
Ibtisam T. Al-Jureisy, Rayan S. Hamed, Ghada A. Taqa. THE BIO-STIMULATORY EFFECT OF ADVANCE PLATELET RICH FIBRIN COMBINED WITH LASER ON DENTAL IMPLANT STABILITY: AN EXPERIMENTAL STUDY ON SHEEP.....	27-31
Amandeep Singh, Navnath Sathe, Kanchan Rani, Saumya Das, Devanshu J. Patel, Renuka Jyothi R. IMPACT OF MOTHER'S HYPOTHYROIDISM ON FETAL DEVELOPMENT AND OUTCOMES: A SYSTEMATIC REVIEW.....	32-36
Sevil Karagül, Sibel Kibar, Saime Ay, Deniz Evcik, Süreyya Ergin. THE EFFECT OF A 6-WEEK BALANCE EXERCISE PROGRAM ON BALANCE PARAMETERS IN FRAILTY SYNDROME: A RANDOMIZED CONTROLLED, DOUBLE-BLIND, PROSPECTIVE STUDY.....	37-42
Zainab Suleiman Erzaq, Fahmi S. Ameen. COMPARISON BETWEEN PCR STUDY AND ELISA STUDY AMONG PATIENTS WITH DIARRHEA.....	43-47
Igor Morar, Oleksandr Ivashchuk, Ivan Hushul, Volodymyr Bodiaka, Alona Antoniv, Inna Nykolaichuk. THE INFLUENCE OF THE ONCOLOGICAL PROCESS ON THE MECHANICAL STRENGTH OF THE POSTOPERATIVE SCAR OF THE LAPAROTOMY WOUND.....	48-51
Lyazzat T. Yeraliyeva, Assiya M. Issayeva, Malik M. Adenov. COMPARATIVE ANALYSIS OF MORTALITY FROM TUBERCULOSIS AMONG COUNTRIES OF FORMER SOVIET UNION.....	52-57
Rana R. Khalil, Hayder A.L. Mossa, Mufeda A. Jwad. MITOFUSIN 1 AS A MARKER FOR EMBRYO QUALITY AND DEVELOPMENT IN RELEVANCE TO ICSI OUTCOME IN INFERTILE FEMALES.....	58-61
Geetika M. Patel, Nayana Borah, Bhupendra Kumar, Ritika Rai, V. K. Singh, Chandana Maji. MEDITERRANEAN DIET AND ITS IMPACT ON THE ILLNESS CHARACTERISTIC OF YOUTH WITH IRRITABLE BOWEL CONDITION.....	62-66
Ketevan Arabidze, Irakli Gogokhia, Khatuna Sokhadze, Nana Kintsurashvili, Mzia Tsiklauri, Tamar Gogichaishvili, Iamze Tabordze. THE EVALUATION OF THE RISK OF COMPLICATIONS DURING MULTIMODAL AND OPIOID ANESTHESIA IN BARIATRIC SURGERY AND ABDOMINOPLASTY.....	67-71
Hadeer Sh Ibrahim, Raghad A Al-Askary. MARGINAL FITNESS OF BIOACTIVE BULKFILL RESTORATIONS TO GINGIVAL ENAMEL OF CLASS II CAVITIES: AN IN VITRO COMPARATIVESTUDY.....	72-79
Lobashova O.I, Nasibullin B.A, Baiazitov D.M, Kashchenko O.A, Koshelnyk O.L, Tregub T.V, Kovalchuk L.Y, Chekhovska G.S, Kachailo I.A, Gargin V.V. PECULIARITIES OF THE ORGANS OF THE REPRODUCTIVE SYSTEM OF WOMEN OF REPRODUCTIVE AGE WITH LIVER DYSFUNCTION UNDER THE INFLUENCE OF EXOGENOUS POLLUTANTS.....	80-86
Victoriia Ivano. EXPLORING NEONATAL HEALTH DISPARITIES DEPENDED ON TYPE OF ANESTHESIA: A NARRATIVE REVIEW.....	87-93
Omar B. Badran, Waleed G. Ahmad. THE COVID-19 PANDEMIC LOCKDOWN'S IMPACT ON ROUTINE CHILDHOOD VACCINATION.....	94-98
Valbona Ferizi, Lulëjeta Ferizi Shabani, Merita Krasniqi Selimi, Venera Bimbashi, Merita Kotori, Shefqet Mrasori. POSTNATAL CARE AMONG POSTPARTUM WOMEN DURING HOSPITAL DISCHARGE.....	99-104
Devanshu J. Patel, Asha.K, Amandeep Singh, Sakshi Vats, Prerana Gupta, Monika. A LONGITUDINAL STUDY OF CHILDHOOD SEPARATION ANXIETY DISORDER AND ITS IMPLICATIONS FOR ADOLESCENT PSYCHOPATHOLOGY.....	105-111
Kachanov Dmitrii A, Artsygov Murad M, Omarov Magomed M, Kretova Veronika E, Zhur Daniil V, Chermoew Magomed M, Yakhyaev Adam I, Mazhidov Arbi S, Asuev Zaurbek M, Bataev Ahmed R, Khasuev Turpal-Ali B, Rasulov Murad N. COMPARATIVE ANALYSIS OF THE EFFECTS OF SOME HEPATOPROTECTORS IN EXPERIMENTALLY INDUCED MAFLD IN ADULT WISTAR RATS.....	112-115
Nada J Alwan, Raghad A Al-Askary. EVALUATION OF INTERFACIAL ADAPTATION BETWEEN VARIOUS TYPES OF FIBER POSTS AND RESIN CEMENTS USING	

MICRO CT: AN IN VITRO COMPARATIVE STUDY.....	116-121
Anish Prabhakar, Vinod Mansiram Kapse, Geetika M. Patel, Upendra Sharma. U.S, Amandeep Singh, Anil Kumar. EMERGING NATIONS' LEARNING SYSTEMS AND THE COVID-19 PANDEMIC: AN ANALYSIS.....	122-127
Tereza Azatyan. THE STUDY OF SPATIAL REPRESENTATIONS OF CHILDREN WITH DIFFERENT DEGREES OF INTERHEMISPHERIC INTERACTION.....	128-132
Sefineh Fenta Feleke, Anteneh Mengsit, Anteneh Kassa, Melsew Dagne, Tiruayehu Getinet, Natnael Kebede, Misganaw Guade, Mulat Awoke, Genanew Mulugeta, Zeru Seyoum, Natnael Amare. DETERMINANTS OF PRETERM BIRTH AMONG MOTHERS WHO GAVE BIRTH AT A REFERRAL HOSPITAL, NORTHWEST ETHIOPIA: UNMATCHED CASE- CONTROL STUDY.....	133-139
Himanshi Khatri, Rajeev Pathak, Ranjeet Yadav, Komal Patel, Renuka Jyothi. R, Amandeep Singh. DENTAL CAVITIES IN PEOPLE WITH TYPE 2 DIABETES MELLITUS: AN ANALYSIS OF RISK INDICATORS.....	140-145
Mukaddes Pala. ExerciseandMicroRNAs.....	146-153
Zurab Alkhanishvili, Ketevan Gogilashvili, Sopia Samkharadze, Landa Lursmanashvili, Nino Gvasalia, Lika Gogilashvili. NURSES' AWARENESS AND ATTITUDES TOWARDS INFLUENZA VACCINATION: A STUDY IN GEORGIA.....	154-159
Aveen L. Juma, Ammar L. Hussein, Israa H. Saadon. THE ROLE OF COENZYME COQ10 AND VITAMIN E IN PATIENTS WITH BETA-THALASSEMIA MAJOR IN BAGHDAD CITY POPULATION.....	160-162
Merve Karli, Basri Cakiroglu. ADRENAL METASTASIS OF BILATERAL RENAL CELL CARCINOMA: A CASE PRESENTATION 12 YEARS AFTER DIAGNOSIS.....	163-165
Manish Kumar Gupta, Shruti Jain, Priyanka Chandani, Devanshu J. Patel, Asha K, Bhupendra Kumar. ANXIETY SYNDROMES IN ADOLESCENTS WITH OPERATIONAL RESPIRATORY CONDITIONS: A PROSPECTIVE STUDY.....	166-171
Mordanov O.S, Khabadze Z.S, Meremkulov R.A, Saeidyan S, Golovina V, Kozlova Z.V, Fokina S.A, Kostinskaya M.V, Eliseeva T.A. EFFECT OF SURFACE TREATMENT PROTOCOLS OF ZIRCONIUM DIOXIDE MULTILAYER RESTORATIONS ON FUNCTIONAL PROPERTIES OF THE HUMAN ORAL MUCOSA STROMAL CELLS.....	172-177
Nandini Mannadath, Jayan. C. EFFECT OF BIOPSYCHOSOCIAL INTERVENTION ON BEAUTY SATISFACTION AFTER STAGED SURGERY AMONG ADOLESCENTS WITH ORAL FACIAL CLEFTS.....	178-182
Bhupendra Kumar, Sonia Tanwar, Shilpa Reddy Ganta, Kumud Saxena, Komal Patel, Asha K. INVESTIGATING THE EFFECT OF NICOTINE FROM CIGARETTES ON THE GROWTH OF ABDOMINAL AORTIC ANEURYSMS: REVIEW.....	183-188
Musheghyan G.Kh, Gabrielyan I.G, Poghosyan M.V, Arajyan G.M. Sarkissian J.S. SYNAPTIC PROCESSES IN PERIAQUEDUCTAL GRAY UNDER ACTIVATION OF LOCUS COERULEUS IN A ROTENONE MODEL OF PARKINSON'S DISEASE.....	189-195
Bhupendra Kumar, Barkha Saxena, Prerana Gupta, Raman Batra, Devanshu J. Patel, Kavina Ganapathy. EFFECTS OF SOCIAL ESTRANGEMENT ON YOUNG PEOPLE'S MATURATION: A REVIEW OF THE RESEARCH.....	196-202
Mordanov O.S, Khabadze Z.S, Meremkulov R.A, Mordanova A.V, Saeidyan S, Golovina V, Kozlova Z.V, Fokina S.A, Kostinskaya M.V, Eliseeva T.A. COMPARATIVE SPECTROPHOTOMETRY ANALYSIS OF ZIRCONIUM DIOXIDE WITH THE CUBIC AND TETRAGONAL PHASE AFTER ARTIFICIAL AGING.....	203-210
Mohammed Abidullah, Sarepally Godvine, Swetcha Seethamsetty, Geetika Gorrepati, Pradeep Koppolu, Valishetty Anuhya, Sana vakeel. EFFECT OF GOAL-ORIENTEDPATIENT CENTRIC HEALTH CARE PROFESSIONAL INTERVENTION ON BLOOD GLUCOSE CONTROL INTYPE 2 DIABETES MELLITUSANDLEVEL OF PATIENT SATISFACTION.....	211-217

PECULIARITIES OF THE ORGANS OF THE REPRODUCTIVE SYSTEM OF WOMEN OF REPRODUCTIVE AGE WITH LIVER DYSFUNCTION UNDER THE INFLUENCE OF EXOGENOUS POLLUTANTS

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Abstract.

Introduction: The widespread use of chemicals by modern society and the prevalence of harmful habits (alcoholism, tobacco smoking, drug addiction) leads to an unnaturally high intake of exogenous pollutants in the human body, which can cause damage to internal organs, including the reproductive system. The aim of this study was to determine the peculiarities of the reproductive system of women of reproductive age with liver dysfunction under the influence of exogenous pollutants, namely, due to harmful working conditions and tobacco smoking.

Materials and methods: Estimation of activity of liver enzymes was determined by the level of activity of alanine aminotransferase, aspartate aminotransferase, and gamma-glutamyl transaminase. The first group (control group) included women with no changes in liver enzyme activity and no history of harmful working conditions or bad habits. The second group (comparison group) – women with no history of harmful working conditions and bad habits, but with laboratory data showing changes in liver enzyme activity. The third group included women who have been working with harmful substances for more than 10 years. The fourth group included women who have smoked for more than 10 years. Changes in objective indicators of women's reproductive system have been studied (vaginal discharge, elasticity of the vaginal wall, epithelial integrity, mucous membranes moistness, pH of the vaginal contents, cytological type, vaginal contents) for all groups.

Results: Gynecologic examination and evaluation revealed changes indicating the presence of candidiasis and bacterial vaginosis (caused by anaerobic microbiota) in women who worked in harmful working conditions and smoked, both with and without signs of inflammation. During the objective examination, changes in vaginal discharge were observed in women. Only in 20% of women with smoking habits and 10% of women with harmful working conditions there was no vaginal discharge, while in the control group, such women were the majority. In the group with signs of impaired liver function, the absence of discharge was observed in 30% of women. According to the results of cytological studies, a quarter of women who smoked and one in five women who worked

in hazardous conditions had estrogen deficiency, apparently as a result of dysregulation disorders under the influence of pollutants. The inflammatory or cytolytic type of smear, which is a consequence of restructuring, was observed in most women from the smoking group. Also, in the two study groups, there was an increase in the number of cases of fungal or Gardnerella vaginal lesions.

Conclusions: Disorders of the genital organs in women under the influence of exogenous pollutants are associated with hepatic and endocrine disorders. Obviously, the mechanisms of formation of the pathological condition cause these disorders, and since women working in harmful conditions and smoking have more developed gynecological manifestations, they have more developed symptoms. Inflammatory changes have been revealed in the cervix for up to 30% of women with the influence of xenobiotics. The relationship between the activity of liver enzymes and epithelial integrity has been revealed as the most significant correlation in study parameters ($r=0.71$ for alanine aminotransferase and epithelial integrity).

Key words. Genitals, liver, vaginal smear cytology, xenobiotic, pollutant, addiction.

Introduction.

The widespread use of chemicals by modern society and the prevalence of harmful habits (alcoholism, tobacco smoking, drug addiction) leads to an unnaturally high intake of exogenous pollutants in the human body [1,2], which can cause damage to internal organs, including the reproductive system [3,4]. According to Barker's hypothesis, environmental exposure at an early age (especially in the prenatal period) [5] can permanently affect health and vulnerability to disease in adulthood [6,7]. Therefore, changes in the female reproductive system can have adverse consequences not only concerning the woman's body, but also her descendants [5,8]. In the context of the demographic crisis in Europe and Ukraine, the effects of xenobiotics are gaining social significance [9].

The liver, with its multifunctional purpose, is one of the first organs to experience the effects of xenobiotics (i.e. chemical compounds that are foreign to the human body). A wide range of different medications and xenobiotics can damage the epithelium of the bile ducts and cause inflammatory diseases of the latter (cholangiopathies), from transient cholestasis to

vanishing bile duct syndrome, sclerosing cholangitis with the development of biliary fibrosis and cirrhosis [10].

Simultaneously, we have to consider liver and reproductive system in interaction with multifaceted bidirectional fashion [11]. Sex steroid signaling influences hepatic endobiotic and xenobiotic metabolism and contributes to the pathogenesis of functional and structural disorders of the liver. In turn, liver function affects the reproductive axis via modulating sex steroid metabolism and transport to tissues via sex hormone-binding globulin [11]. The liver senses the body's metabolic status and adapts its energy homeostasis in a sex-dependent fashion, a dimorphism signaled by the sex steroid milieu and possibly related to the metabolic costs of reproduction. Sex steroids impact the pathogenesis of non-alcoholic fatty liver disease, including development of hepatic steatosis, fibrosis, and carcinogenesis. Consistent with sex-dimorphic preclinical findings, androgens promote hepatic steatosis and dysglycemia in women, whereas endogenous estradiol appears protective in both men and women [11].

Animal models of liver damage caused by xenobiotics provide important insights into the molecular mechanisms of xenobiotic-induced cholangiopathies and biliary fibrosis, including primary biliary cirrhosis and primary sclerosing cholangitis. For people living in Ukraine, common sources of xenobiotics are harmful working conditions and harmful habits [12,13], including tobacco smoking [14-16]. Given that liver dysfunction can be detected by determining enzyme activity and primary changes in the female reproductive system by cytological examination respectively, we decided to set the aim of this study to determine the peculiarities of the reproductive system of women of reproductive age with liver dysfunction under the influence of exogenous pollutants, namely, due to harmful working conditions and tobacco smoking.

Materials and Methods.

The material of the research is the data obtained during the examination of women who came to see a gynecologist to the consultative polyclinic of the Ukrainian Research Institute of Medical Rehabilitation and Balneology of the Ministry of Health of Ukraine. The study was conducted in accordance with the principles of the World Medical Association's Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects" (amended in October 2013). Written informed consent was obtained from all patients who participated in the study. Women who had pathological changes in the genital system (polyps, adenomyosis, leiomyoma, fibroids) diagnosed by ultrasound were excluded from this study. Contraceptive use (oral contraceptive pills), age at first sexual intercourse, somatic pathology, and number of pregnancies were not taken into account, as the principle of randomization was used in the recruitment of groups.

Changes in the activity of liver enzymes were determined by the level of activity of alanine aminotransferase, aspartate aminotransferase, and gamma-glutamyl transaminase. The patients were divided into follows groups. The first group (control group) included women with no changes in liver enzyme activity and no history of harmful working conditions or bad habits (20 people). The second group (comparison group)

– women with no history of harmful working conditions and bad habits, but with laboratory data showing changes in liver enzyme activity (20 people). The third group included women who have been working with harmful substances for more than 10 years (20 people). The harmful substances were presented as one from list: heavy metal, pesticide chemicals, formaldehyde. The fourth group included women who have smoked for more than 10 years (20 people). The ultrasound or clinical data have not detected any hepar pathology in all groups, so changes of enzymes could be recognized or as preclinical, or as temporary changes. The average age of women in all groups was 31-33 years (from 29 to 39 years).

Each of the women underwent examinations, which included: collecting complaints, anamnesis, objective, and additional methods of examination - a routine gynecological speculum examination of the vaginal mucosa, cervix, the nature of the discharge, its color, the presence of small hemorrhages.

The cellular material for liquid cytology was transferred with a cytobrush into a liquid storage medium (CITOSCREEN system), which was sent to the laboratory, where thin-layer cytological preparations were prepared using special equipment [17]. As a result of a series of procedures (separation of cellular material from the brush, determination of the density of the cell suspension, further dilution according to the density group, centrifugation, and automatic application of the cell suspension to glass), preparations were obtained in which the cells were a uniform monolayer.

Vaginal swabs were examined for bacterial microbiota. A cytological examination of vaginal swabs was performed to determine the percentage of epithelial cells, which allowed to assess the value of estrogens in the body and the possible level of atrophy. The acidity (pH) of the vaginal environment was evaluated using indicator strips. An ultrasound examination of the pelvic organs was also performed.

Statistical processing of the data was performed using the Statistica for Windows 8.0 software package. Methods of descriptive statistics (determination of numerical characteristics of variables - arithmetic mean (M), mean sampling error (m), determination of the reliability of differences (p), which were tested via the Student-Fisher t-test in representative samples) were used. Correlation between indicators was assessed using Spearman's correlation coefficient (r). The difference in values between comparative indicators was considered significant at $p < 0.05$.

Results.

When analysing changes in liver enzymatic activity among the two groups of women exposed to xenobiotics, we found a higher enzyme activity, and while in the comparison group this could be explained by the presence of a pathological process in the liver, which was detected later, no reasons for the increase in enzyme activity in the two study groups were found, which allows us to link the effect of exposure to harmful occupational factors or smoking on the functional activity of the liver. The digital parameters are shown in Table 1.

Ovarian and menstrual cycle disorders (menstrual delay) in the control group were observed in only one of the women. This was due to the presence of a follicular cyst, which was

Table 1. Activity of liver enzymes.

Enzyme	Group 1 - control group, no changes in liver enzyme activity (N=15)	Group 2 - comparison group - no information on xenobiotics with changes in liver enzyme activity (N=15)	Group 3 - women with harmful working conditions for more than 10 years (N=15)	Group 4 - women with more than 10 years of smoking experience (N=15)
Alanine aminotransferase, U/l	24.2±1.1	59.1±2.5*	61.5±2.8*	62.4±3.3*
Aspartate aminotransferase, U/l	24.8±1.2	57.7±2.7*	59.1±3.6*	59.3±2.3*
Gamma-glutamyl transaminase, U/l	21.4±1.3	73.9±3.4*	75.7±3.9*	72.4±2.4*

Note: * - significant difference with the control group ($p < 0.05$).

confirmed by ultrasound. Among the women in the comparison group, 6 patients had abnormal uteruses. In the group with harmful working conditions, there were 9 such women, and in the group of smokers - 11 women.

Gynecologic examination and evaluation revealed changes indicating the presence of candidiasis and bacterial vaginosis (caused by anaerobic microbiota) in women who worked in harmful working conditions and smoked, both with and without signs of inflammation. During the objective examination, changes in vaginal discharge were observed in women. Only in 20% of women with smoking habits and 10% of women with harmful working conditions there was no vaginal discharge, while in the control group, such women were the majority. In the group with signs of impaired liver function, the absence of discharge was observed in 30% of women. Data on objective indicators established during the examination of women are presented in Table 2.

Correlation between activity of liver enzymes and indicators of gynaecological data is presented in Table 3.

According to the results of cytological studies, a quarter of women who smoked and one in five women who worked in hazardous conditions had estrogen deficiency, apparently as a result of dysregulation disorders under the influence of pollutants. The inflammatory or cytolytic type of smear, which is a consequence of restructuring, was observed in most women from the smoking group. Also, in the two study groups, there was an increase in the number of cases of fungal or Gardnerella vaginal lesions.

Discussion.

Much of what is known about the harmful effects of tobacco use on health has been derived from epidemiologic studies conducted over the past half century [18,19]. These studies have clearly established that tobacco use, especially smoking of manufactured cigarettes, causes the majority of lung, oropharyngeal, laryngeal, and esophageal cancers, as well as approximately one-third of all pancreatic, kidney, bladder, and cervical cancers [18,20]. More recent evidence also suggests that smoking causes liver cancer. However, information about the similarity of mechanisms leading to changes in the liver and cervix, their relationship or sequence remains an open question [21,22]. Similar questions regarding the links of pathogenesis relate to the impact of harmful working conditions.

The structure of morbidity among women of reproductive age in Ukraine is characterized by a high frequency of pathological processes that affect the ability to give birth to a healthy child. Among these diseases, inflammatory processes,

neoplasms, hyperplastic and atrophic changes, malformations, and dys hormonal disorders are common, and these processes are usually links in the chain of pathogenesis of malignant neoplasms. The triggering mechanisms and etiologic factors are not always possible to establish. At the same time, in Ukraine, the presence of regions with a polluted environment has been established, whose residents are more likely to suffer from the development of pathological processes of the genital system. One of the conditions for the presence of pollutants is work with harmful substances. Another condition is the presence of bad habits accompanied by the intake of xenobiotics into the body, which is observed, in particular, in tobacco smoking.

Such substances affect liver function, but the possibility of pathological changes in internal organs has long been debated. Recent studies indicate that they are carcinogenic not only to the target organs but also to other ones. The mechanisms of correction of possible damage remain a gap in preventive medicine, and our study shows that pathological changes are formed in the female reproductive system earlier than the first complaints emerge, which, against the background of the rather low level of reproductive health of the female population in Ukraine, may be the basis for the development of preventive measures and further work on the evaluation of the effectiveness of the use of corrective medications [23,24].

The information on the effect of xenobiotics on cervical tumor transformation is less known, but previously published results show higher proliferative activity of the cervical epithelium and transformation of the apoptotic process in such women [25,26]. Some synthetic estrogens and chemical environmental pollutants that have estrogenic properties, also known as xenoestrogens, mimic natural estrogens and bind to estrogen receptors (ER) and therefore desensitize the latter or reduce the number of receptors available for binding [27].

Changes in blood cellular parameters can be one of the triggers not only of the adverse effects of pollutants, but also a marker of the risk of developing concomitant pathology. In this case, the complex of changes is characteristic of a complex transformation in the whole body in the case of xenobiotic exposure triggers a complex cascade of cellular interactions, one of the stages of which is the morphological restructuring of the cervical epithelium, which is manifested by an inflammatory type of smear, coilocytosis, the presence of bi- and multinucleated cells, keratinocytes with cytoplasmic amphophilia, and, most importantly, changes in the architecture of cervical epithelial cells [25,26].

Despite the availability of information on the relationship between disorders of estrogen synthesis and the morphological

Table 2. Changes in objective indicators of women's reproductive system, n (%).

Indicators.	Group 1 - control group, no changes in liver enzyme activity (N=20)	Group 2 - comparison group - no information on xenobiotics with changes in liver enzyme activity (N=20)	Group 3 - women with harmful working conditions for more than 10 years (N=20)	Group 4 - women with more than 10 years of smoking experience (N=20)
<i>Vaginal discharge</i>				
missing	14(70%)	6(30%)	2(10%)	4(20%)
scanty, superficial, yellow		3(15%)	4(20%)	4(20%)
scanty, superficial, white	6(30%)	5(25%)	4(20%)	4(20%)
moderate, white, crumbly		5(25%)	5(25%)	5(25%)
gray, foamy		3(15%)	5(25%)	3(15%)
<i>Elasticity of the vaginal wall</i>				
missing			1(5%)	1(5%)
weak			5(25%)	4(20%)
moderately reduced	1(5%)	5(25%)	13(65%)	14(70%)
normal	19(95%)	15(75%)	1(5%)	1(5%)
<i>Epithelial integrity</i>				
petechiae, bleeding			1(5%)	2(10%)
bleeding on contact		1(5%)	4(20%)	3(15%)
thinning	2(10%)	4(20%)	11(55%)	10(50%)
intact	18(90%)	15(75%)	4(20%)	5(25%)
<i>Mucous membranes moistness</i>				
severe dryness, inflammation			1(5%)	5(25%)
pronounced dryness, no inflam-n		1(5%)	3(15%)	3(15%)
Minimal	1(5%)	2(10%)	3(15%)	9(45%)
Moderate	2(10%)	3(15%)	9(45%)	2(10%)
Normal	17(85%)	14(70%)	4(20%)	1(5%)
<i>pH of the vaginal contents</i>				
4.0-4.4 (normal)	19(95%)	13(65%)	4(20%)	2(10%)
4.4-5.0 (mild atrophy, bact. vag-s)	1(5%)	4(20%)	10(50%)	8(40%)
5.1-5.5 (moderate atrophy)		3(15%)	3(15%)	4(20%)
5.5 and more (pronounced atrophy, cytolytic type)			3(15%)	6(30%)
<i>Cytological examination</i>				
Type I - significant estrogen deficiency (mainly parabasal cells with round nuclei, leukocytes)			4(20%)	5(25%)
Type II - moderate estrogen deficiency (among the parabasal cells there are individual cells of the intermediate layer, leukocytes)		2(10%)	6(30%)	5(25%)
Type III - minor estrogen deficiency (mainly cells of the intermediate layer, sometimes superficial)	1(5%)	2(10%)	3(15%)	
Type IV - normal estrogen values (mainly well-defined cells of the surface layer with a small nucleus)	19(95%)	15(75%)	3(15%)	
Inflammatory type - cells of all layers of the epithelium with a large number of leukocytes, the presence of cocci		1(5%)	2(10%)	6(30%)
Cytolytic type - destroyed cells, naked nuclei			2(10%)	4(20%)
<i>Microscopy of vaginal contents</i>				
Mostly lactobacilli	19(95%)	15(75%)	9(45%)	4(20%)
"Key" cells, Gardnerella vaginalis, anaerobic flora		3(15%)	4(20%)	7(35%)
Fungi of the Candida genus	1(5%)	2(10%)	7(35%)	9(45%)

Table 3. The relationship between activity of liver enzymes and indicators of gynaecological data taking into account the Spearman's correlation coefficient (*r*).

Enzyme	Vaginal discharge	Elasticity of the vaginal wall	Epithelial integrity	Mucous membranes moistness	pH of the vaginal contents	Cytological type	Vaginal contents
Alanine aminotransferase	0.35	0.41	0.71	0.39	0.34	0.44	0.70
Aspartate aminotransferase	0.34	0.39	0.64	0.38	0.36	0.48	0.66
Gamma-glutamate transaminase	0.27	0.44	0.63	0.47	0.29	0.54	0.65

and functional state of the liver, the sequence of pathological changes remains unclear [28,29], and numerous experimental studies have been conducted to establish the pathogenesis of these changes. It has been established that estrogen treatment in early menopause protects against the development of metabolic syndrome and pathological processes in the liver, and a longer reproductive period is significantly associated with a decrease in the prevalence of metabolic syndrome [30,31]. However, our study suggests that primary changes are quite likely to occur in the liver. In any case, targeted therapy will require a better understanding of the mechanisms by which estrogen signalling exerts its protective effect [28].

However, it is most likely that pollutants have simultaneous effects on the liver and reproductive organs, given that several factors play a role in altered imprinting: the environmental agents involved, their doses, stage of exposure, duration of exposure, just one or several chemicals involved, the history of previous exposure [32], the role of genetic and epigenetic factors [6,33].

Given the close relationship between pollutants, hepatic metabolism and reproductive functions in women, pollutant-induced metabolic dysfunctions may be of particular importance for the liver of a woman, reducing sex differences in the prevalence of non-alcoholic liver disease. The intake of environmental pollutants disrupts the endocrine system and can disrupt the programming of liver metabolism [34-36].

As we have wrote above sex steroids impact the pathogenesis of non-alcoholic fatty liver disease, including development of hepatic steatosis, fibrosis, and carcinogenesis [11]. Described in our results correlation between liver dysfunction and abnormalities in female reproductive organs could be characterized consequences not only with feedback mechanism reaction but and inadequate changes in situations which require recruiting its efforts, for example in vaccination [37,38], changes of immune status [39], infectious pathology [40], endocrine [41] and respiratory [42] pathology. In female reproductive system it could be predisposing unfavourable course of neoplastic process [43]. Contamination of environment could play additional role in such processes [13,44]. Preservation of sufficient endogenous estradiol production could be crucial as protective mechanism in such conditions [11]. So, correlation between alanine aminotransferase and epithelial integrity ($r=0.71$), between alanine aminotransferase and vaginal contents ($r=0.70$) should be researched more detail with detection of order in that changes that look unclear now.

Our results accords described before inflammatory changes in cellular and humoral immunity [45,46], that should be taken into account considering unfavourable situation with female health and deontological features [47]. Our data are important for understanding that among women with influence of pollutants with significantly more common pathological changes among such women regarding genital system. Connection and possible interaction of hepar disturbance with sexual dysfunction, lubrication dysfunction and genital pain dysfunction require more detail future research with involvement of specialist of different fields.

Conclusion.

Disorders of the genital organs in women under the influence of exogenous pollutants are associated with hepatic and endocrine disorders. Obviously, the mechanisms of formation of the pathological condition cause these disorders, and since women working in harmful conditions and smoking have more developed gynecological manifestations, they have more developed symptoms. Inflammatory changes have been revealed in cervix for up to 30% women with influence of xenobiotic. The relationship between activity of liver enzymes and epithelial integrity has been revealed as most significant correlation in study parameters ($r=0.71$ for alanine aminotransferase and epithelial integrity).

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Conflict of interest statement.

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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