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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 შედეგის 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.

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PECULIARITIES OF IMMUNE STATUS IN THE PRESENCE OF SECONDARY IMMUNODEFICIENCY OF INFECTIOUS AND NON-INFECTIOUS ORIGIN IN WOMEN OF REPRODUCTIVE AGE

Lytvynenko M.V¹, Antonenko P.B¹, Lobashova K.G¹, Kashchenko O.A¹, Bondarenko A.V², Bondarenko O.V³, Gargin V.V^{2,3*}.

¹Odessa National Medical University, Odessa, Ukraine.

²Kharkiv National Medical University, Kharkiv, Ukraine.

³Kharkiv International Medical University, Kharkiv, Ukraine.

Abstract.

Summary: The design of studies on the immune system does not have gender peculiarities, but the information about the higher frequency of pathology of the female reproductive system in the presence of immunodeficiency condition determines the purpose of this study, namely, to identify the features of immune status in the presence of secondary immunodeficiency of infectious (i.e., HIV infection, AIDS stage) and non-infectious origin (alcohol dependence syndrome) and their combination in women of reproductive age.

Materials and methods: The material for the study of cellular and humoral immunity was a lymphocyte suspension obtained by centrifugation of peripheral blood (taken within 12 hours after death) in women of reproductive age with HIV infection (AIDS stage), alcohol dependence syndrome and their combination. Immunological examination included the determination of quantitative indicators of cellular immunity using monoclonal antibodies: T-lymphocytes (CD3) and their main subpopulations of T-helper cells (CD4), cytotoxic lymphocytes (CD8), CD4/CD8 immunoregulatory index; as well as indicators of humoral immunity: B-lymphocytes (CD19) and immunoglobulins of the main classes (IgA, IgG, IgM). Additionally, interleukins IL-6 and IL-10 were studied to determine the parameters of the cytokine profile.

Results: The study indicates (Table 1) that the number of leukocytes and lymphocytes in the group of deceased women with alcohol dependence syndrome was $3.6 \pm 0.38 \times 10^9$ /l and $0.82 \pm 0.35 \times 10^9$ /l; in deceased women with HIV/AIDS, these indicators were reduced – $2.9 \pm 0.03 \times 10^9$ /l and $0.39 \pm 0.04 \times 10^9$ /l, respectively; and in deceased women with combined pathology (AIDS and alcohol dependence syndrome), they were reduced even more intensively – $2.7 \pm 0.04 \times 10^9$ /l and $0.35 \pm 0.06 \times 10^9$ /l ($p < 0.01$). Compared to the control group – $5.22 \pm 0.4 \times 10^9$ /l and $1.73 \pm 0.21 \times 10^9$ /l – the number of leukocytes and lymphocytes was reduced in all study groups. In the group of deceased women with alcohol dependence syndrome, significant impairments in the proliferative activity of T-lymphocytes (CD3) and their subpopulation (CD4), as well as B lymphocytes (CD19) and natural killer cells (CD16) were found compared to the group of healthy individuals. Thus, in the control group, the percentage, and absolute values of CD3 were $60.37 \pm 4.2\%$ and $1.04 \pm 0.05 \times 10^6$ /l, and in women suffering from chronic alcoholism, they were statistically significantly lower – $49.1 \pm 3.1\%$ and $0.42 \pm 0.08 \times 10^6$ /l, respectively, $p < 0.01$. The same tendency was found when comparing the values of T-helper cells (CD4) in the control group ($44.2 \pm 2.9\%$ and $0.76 \pm 0.13 \times 10^6$ /l) and in deceased patients suffering from chronic alcoholism ($33.7 \pm 4.6\%$ and $0.28 \pm 0.23 \times 10^6$ /l), $p < 0.01$.

Conclusions: Secondary immunodeficiencies of infectious and non-infectious origin in women (in particular, those formed in HIV/AIDS, alcohol dependence syndrome and their combination) are characterized by negative changes in the cellular and humoral components of the immune system, as evidenced by the presence of transient immunodeficiency, activation of cytolytic and auto aggressive reactions. As a result of these processes, systemic and organ pathology develops, in particular, weakening of the body's resistance to various infections and pathological changes in organs and tissues, which may be one of the links in the development of pathological processes in internal organs and tissues.

Key words. Secondary immunodeficiency, infection, HIV/AIDS, addiction, chronic alcoholism, immune system.

Introduction.

Secondary immunodeficiency states (SIDS) are much more common than primary immunodeficiencies [1,2], and are the result of many factors that can affect an organism with a healthy immune system: infectious agents, medications, metabolic disorders, environmental conditions, and bad habits [3,4]. These SIDSs are clinically manifested by an increased frequency or unusual complications of common infections and sometimes opportunistic infections [5,6]. Secondary immunodeficiencies have a wide range of manifestations depending on the severity of external damaging effects and the susceptibility of the body [7,8].

Secondary immunodeficiency can be defined as a transient or persistent impairment of the function of immune system cells or tissues caused by factors outside the immune system [1,9]. Over the past five decades, the most studied secondary immunodeficiency is the acquired immunodeficiency syndrome (AIDS) caused by human immunodeficiency virus (HIV) infection [10,11].

SIDS is characterized by an acquired decrease in the number and/or function of immune cells. The most common type of SIDS is a decrease in antibody levels that occurs as a result of an underlying disease or as a side effect of medication. Paradoxically, immunodeficiencies initially attributed to secondary causes may partially be the result of an underlying primary immunodeficiency [12,13], which requires more detailed study. In particular, studies on the initial clinical manifestations of a confirmed immunodeficiency state indicate that most patients have a history of infection, but focusing solely on manifestations centered on infection might lead to overlooking patients who initially had other manifestations, such as immune dysregulation [14,15]. Among the diseases that can lead to the development of SIDS, HIV/AIDS and chronic alcoholism are the most common [16,17]. The combination

of these two pathologies is particularly dangerous [18,19]. Usually, the design of studies on the immune system does not have gender specifics [20,21], but information on the higher frequency of pathology of the female reproductive system in the presence of immunodeficiency condition [22,23] determines the purpose of this study, namely to identify the features of immune status in the presence of secondary immunodeficiency of infectious (we chose HIV/AIDS) and non-infectious origin (alcohol dependence syndrome) and their combination in women of reproductive age.

Materials and Methods.

We formed four groups of cases of women who died due to craniocerebral injuries (accidental causes). The group of secondary immunodeficiency of infectious origin consisted of 25 women with HIV infection, AIDS stage. HIV infection was verified by enzyme-linked immunosorbent assay (ELISA) with confirmation by western blot method. The group of secondary immunodeficiency of non-infectious origin consisted of 25 deceased women with alcohol dependence syndrome. The main feature of these women was the presence of alcoholic cirrhosis of the liver, as well as the relevant anamnestic data established during the interview of relatives. A group of 30 deceased women with a combination of HIV/AIDS and alcohol dependence syndrome was also formed. The fourth group was the control group, which consisted of 30 women who died of diseases not related to alcohol abuse, pathology of the reproductive system without concomitant HIV infection (those who died as a result of accidents). Tobacco smoking, contraceptive use (oral contraceptive pills), age at first sexual intercourse, somatic pathology, and number of pregnancies were not considered, as the principle of randomization was used in the recruitment of groups.

The material for the study of cellular and humoral immunity was a lymphocyte suspension obtained by centrifugation of peripheral blood (taken within 12 hours after death) on a ficoll-verigraphin density gradient (density 1.077 g/cm³). Immunoglobulins of classes A, M, and G were determined by enzyme-linked immunosorbent assay using Hema test systems (Ukraine). The content of IL-6 and IL-10 cytokines in the patients' serum was determined by enzyme-linked immunosorbent assay using diagnostic kits (R&D Diagnostics Inc., USA), the sensitivity of the test systems being 4-5 pg/ml. To accomplish this, peripheral blood (5 ml) was taken with a syringe from the femoral vein of a deceased woman or the ventricles of the heart, centrifuged at 3000 rpm in the cold for 10 minutes. The serum was poured into 0.5 ml into an epidural tube, frozen and stored at -76°C until use; hemolyzed sera were not used [24]. The amount of cytokines was calculated by constructing a calibration curve using a computer program and expressed in pg/ml.

Immunological examination included the determination of quantitative indicators of cellular immunity using monoclonal antibodies: T-lymphocytes (CD3) and their main subpopulations of T-helper cells (CD4), cytotoxic lymphocytes (CD8), CD4/CD8 immunoregulatory index; as well as indicators of humoral immunity: B-lymphocytes (CD19) and immunoglobulins of the main classes (Ig A, Ig G, Ig M) [25,26]. Additionally, interleukins

IL-6 and IL-10 were studied to determine the parameters of the cytokine profile. The CD68 marker, a transmembrane glycoprotein macrophage marker (sialomycin), which is expressed on the surface of macrophages, neutrophils, monocytes, basophils, dendritic cells, and some B-lymphocytes, was determined.

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 by Student-Fisher t-test in representative samples) were used. The criterion for statistical reliability of the findings was considered to be $p < 0.01$.

Results and Discussion.

The study shows (Table 1) that the number of leukocytes and lymphocytes in the group of deceased women with alcohol dependence syndrome was $3.6 \pm 0.38 \times 10^9 / l$ and $0.82 \pm 0.35 \times 10^9 / l$; in those who died with HIV/AIDS, these indicators were reduced – $2.9 \pm 0.03 \times 10^9 / l$ and $0.39 \pm 0.04 \times 10^9 / l$, respectively; and in cases with combined pathology (AIDS and alcohol dependence syndrome), they were reduced even more intensively – $2.7 \pm 0.04 \times 10^9 / l$ and $0.35 \pm 0.06 \times 10^9 / l$ ($p < 0.01$). Compared with the control group – $5.22 \pm 0.4 \times 10^9 / l$ and $1.73 \pm 0.21 \times 10^9 / l$ – the number of leukocytes and lymphocytes was reduced in all study groups.

Immunological parameters obtained during the study of all groups and the control group are shown in Table 1. In the group of deceased women with chronic alcoholism, significant impairments in the proliferative activity of T-lymphocytes (CD3) and their subpopulation (CD4), B-lymphocytes (CD19) and natural killer cells (CD16) were found compared to the control group. Thus, in the control group, the percentage, and absolute values of CD3 were $60.37 \pm 4.2\%$ and $1.04 \pm 0.05 \times 10^6 / l$, and in deceased women with alcohol dependence syndrome, they were statistically significantly lower – $49.1 \pm 3.1\%$ and $0.42 \pm 0.08 \times 10^6 / l$, respectively, $p < 0.01$. The same tendency was found when comparing the values of T-helper cells (CD4) in the control group ($44.2 \pm 2.9\%$ and $0.76 \pm 0.13 \times 10^6 / l$) and in the group of deceased with alcohol dependence syndrome ($33.7 \pm 4.6\%$ and $0.28 \pm 0.23 \times 10^6 / l$), $p < 0.01$, Table 1.

The effect of HIV/AIDS on the immune system is characterized not only by a decrease in the total number of T-lymphocytes due to the subpopulation of CD4-lymphocytes, but also by the suppression of CD4 cell function. The CD4 counts in these deceased women ($25.3 \pm 2.2\%$) were statistically significantly lower not only than in the control group ($44.2 \pm 2.9\%$), but also lower than in the group with alcohol dependence syndrome ($33.7 \pm 4.6\%$), $p < 0.01$, Table 1. The lowest values of helper T-lymphocytes (CD4) – $23.4 \pm 1.4\%$ – were observed in the last group of HIV/AIDS and alcohol dependence syndrome. This might be due to comorbid disorders.

In all groups, there was a significant increase in cytotoxic T-suppressor (CD8), which in the control group was $15.3 \pm 1.2\%$, in the group with alcohol dependence syndrome – $18.3 \pm 0.7\%$, in those with AIDS – $23.2 \pm 1.6\%$, $p < 0.01$, Table 1. It should be noted that despite a significant increase in this indicator in percentage terms, its absolute values, on the contrary, decrease,

Table 1. Immunologic parameters in deceased women with HIV/AIDS, alcohol dependence syndrome, HIV/AIDS and alcohol dependence syndrome and in the control group ($M \pm m$).

Immunological parameters – relative (%) and absolute numbers ($\times 10^6 / l$) ⁶	Control group, n=30	Group with alcohol dependence syndrome, n=25	Group with HIV/AIDS, n=25	Group with HIV/AIDS and alcohol dependence syndrome, n=30
White blood cells, g/l	5,22±0,4	3,6±0,38	2,9±0,03	2,7±0,04
	p ₁₋₂ <0.01 p ₁₋₃ <0.01 p ₁₋₄ <0.01	p ₂₋₃ <0.01 p ₂₋₄ <0.01	p ₃₋₄ <0.01	
Lymphocytes, %.	32,9±3,3	23,3±2,3	13,4±0,04	13,2±1,2
	p ₁₋₂ <0.01 p ₁₋₃ <0.01 p ₁₋₄ <0.01	p ₂₋₃ <0.01 p ₂₋₄ <0.01		
Lymphocytes g/l	1,73±0,21	0,82±0,35	0,39±0,04	0,35±0,06
	p ₁₋₂ <0.01 p ₁₋₃ <0.01 p ₁₋₄ <0.01	p ₂₋₃ <0.01 p ₂₋₄ <0.01		
CD3 T-lymphocytes, %.	60,37±4,2	49,1±3,1	48,7±3,3	47,1±3,1
	p ₁₋₂ <0.01 p ₁₋₃ <0.01 p ₁₋₄ <0.01			
T-lymphocytes CD3 $\times 10^6 / l$,	1,04±0,05	0,42±0,08	0,19±0,03	0,16±0,04
	p ₁₋₂ <0.01 p ₁₋₃ <0.01 p ₁₋₄ <0.01	p ₂₋₃ <0.01 p ₂₋₄ <0.01		
CD4 T-helper cells, %.\	44,2±2,9	33,7±2,6	25,3±2,2	23,4±1,4
	p ₁₋₂ <0.01 p ₁₋₃ <0.01 p ₁₋₄ <0.01	p ₂₋₃ <0.01 p ₂₋₄ <0.01		
CD4 T-helper cells $\times 10^6 / l$, ⁶	0,76±0,13	0,28±0,23	0,11±0,02	0,09±0,01
	p ₁₋₂ <0.01 p ₁₋₃ <0.01 p ₁₋₄ <0.01	p ₂₋₃ <0.01 p ₂₋₄ <0.01		
T-cytotoxic CD8, %.	15,3±1,2	18,3±0,7	23,2±1,6	23,8±1,6
	p ₁₋₂ <0.01 p ₁₋₃ <0.01 p ₁₋₄ <0.01	p ₂₋₃ <0.01 p ₂₋₄ <0.01		
T-cytotoxic CD8, $\times 10^6 / l$ ⁶	0,26±0,04	0,19±0,03	0,09±0,02	0,08±0,01
	p ₁₋₂ <0.01 p ₁₋₃ <0.01 p ₁₋₄ <0.01	p ₂₋₃ <0.01 p ₂₋₄ <0.01		
Immunoregulatory index, CD4/CD8	2,93±0,05	1,83±0,04	1,09±0,07	1,04±0,04
	p ₁₋₂ <0.01 p ₁₋₃ <0.01 p ₁₋₄ <0.01	p ₂₋₃ <0.01 p ₂₋₄ <0.01	p ₃₋₄ <0.01	
CD16 killers, %.	17,5±0,6	15,5±0,9	13,2±2,3	9,3±2,1
	p ₁₋₂ <0.01 p ₁₋₃ <0.01 p ₁₋₄ <0.01	p ₂₋₃ <0.01 p ₂₋₄ <0.01	p ₃₋₄ <0.01	
Killers CD16 $\times 10^6 / l$ g/l	0,25±0,03	0,12±0,04	0,05±0,01	0,04±0,01
	p ₁₋₂ <0.01 p ₁₋₃ <0.01 p ₁₋₄ <0.01	p ₂₋₃ <0.01 p ₂₋₄ <0.01		
B-cells, %.	12,2±2,9	23,5±1,8	27,1±1,5	28,2±1,8
	p ₁₋₂ <0.01 p ₁₋₃ <0.01 p ₁₋₄ <0.01	p ₂₋₃ <0.01 p ₂₋₄ <0.01		
B cells $\times 10^6 / l$ ch	0,21±0,05	0,19±0,03	0,11±0,02	0,09±0,03
	p ₁₋₂ <0.01 p ₁₋₃ <0.01 p ₁₋₄ <0.01	p ₂₋₃ <0.01 p ₂₋₄ <0.01		

CD68, %.	22,3±3,4	15,2±1,9	10,4±1,1	10,1±1,2
	p ₁₋₂ <0.01 p ₁₋₃ <0.01 p ₁₋₄ <0.01	p ₂₋₃ <0.01 p ₂₋₄ <0.01		
CD68, x10 ⁶	0,38±0,05	0,13±0,04	0,05±0,01	0,04±0,01
	p ₁₋₂ <0.01 p ₁₋₃ <0.01 p ₁₋₄ <0.01	p ₂₋₃ <0.01 p ₂₋₄ <0.01		

Note: n – number of women who died; p – significance level of the difference between the indicators.

Table 2. Serum levels of immunoglobulins and cytokines in deceased women with HIV/AIDS, alcohol dependence syndrome, HIV/AIDS and alcohol dependence syndrome as well as the control group (M±m).

Immunological parameters	Control group, n=30	Group with alcohol dependence syndrome, n=25	Group with HIV/AIDS, n=25	A group with a combination of HIV/AIDS and alcohol dependence syndrome, n=30
IgA, g/l	1,78±0,04	3,4±0,06	3,9±0,3	4,1±0,27
	p ₁₋₂ <0.01 p ₁₋₃ <0.01 p ₁₋₄ <0.01	p ₂₋₃ <0.01 p ₂₋₄ <0.01		
IgM, g/l	1,2±0,05	1,5±0,04	1,8±0,07	2,0±0,33
	p ₁₋₂ <0.01 p ₁₋₃ <0.01 p ₁₋₄ <0.01	p ₂₋₃ <0.01 p ₂₋₄ <0.01		
IgG, g/l	13,8±2,3	18,4±2,8	27,3±3,1	26,8±2,9
	p ₁₋₂ <0.01 p ₁₋₃ <0.01 p ₁₋₄ <0.01	p ₂₋₃ <0.01 p ₂₋₄ <0.01		
IL-6, pg/ml	3,7±0,11	7,5±1,4	28,5±6,2	19,1±1,3
	p ₁₋₂ <0.01 p ₁₋₃ <0.01 p ₁₋₄ <0.01	p ₂₋₃ <0.01 p ₂₋₄ <0.01	p ₃₋₄ <0.01	
IL-10, pg/ml	6,4±0,13	9,9±2,1	10,7±1,4	11,2±2,1
	p ₁₋₂ <0.01 p ₁₋₃ <0.01 p ₁₋₄ <0.01			

Note: n – number of patients; p – level of significance of the difference between the indicators.

as there is a prominent statistically significant decrease in the number of leukocytes in the blood of deceased women of all groups, p<0.01, Table 1.

The values of natural killer cells (CD16) in all groups were significantly lower than in the control group without pathology. In all groups, there was a decrease in the cytotoxic activity of killer cells and cell-mediated cytotoxicity (Table 1).

Alcohol consumption is stressful for the body and causes the formation of an adaptation syndrome. The mechanisms that underlie this complex process lead to a violation of not only the population and subpopulation composition of cells, but also their activation potential, in particular, there is a violation of the production of antibodies by B-lymphocytes (CD19). The percentage of B-lymphocytes in patients with chronic alcoholism is increased (23.5±1.8%) compared to the control group (12.2±2.9%), p<0.01, Table 1. However, it was found that in comparison with the control group, in the group of deceased women with alcohol dependence syndrome, the content of immunoglobulins of classes A (3.4±0.06 g/l), G (18.4±2.8 g/l) and M (1.5±0.04 g/l) in the blood serum was

statistically significantly increased, Table 2. It should be noted that according to the literature, patients with alcoholism have impaired hemolytic activity of complement, changes in the content of C1, C3 and C4 components of the complement system, and increased levels of circulating immune complexes [27,28]. Thus, chronic alcohol abuse contributes to the emergence of a significant tension of the immune system, which, responding to constant external stimuli (alcohol intoxication), exhausts its reserves, which leads to the emergence of an immunodeficiency state. Significant violations of immunological parameters in the group with alcohol dependence syndrome revealed in the course of the study give reason to believe that one of the fundamental factors in the pathogenesis of alcoholism should be considered a violation of immune mechanisms in response to alcohol as the main etiological agent. It can be assumed that ethanol, in the case of excessive consumption, can act as a "pathogen", introducing serious changes and disorders in both the mechanisms of innate and adaptive immunity, and subsequently in the body systems as a whole.

A significant increase in the percentage and decrease in the absolute number of B-lymphocytes (CD19) was observed in the deceased with HIV/AIDS. This figure is $27.1 \pm 1.5\%$ and $0.11 \pm 0.02 \times 10^6 /l$ compared to the control group ($12.2 \pm 2.9\%$ and $0.21 \pm 0.05 \times 10^6 /l$), $p < 0.01$. In the group with combined pathology, B-cell indices are $28.2 \pm 1.8\%$ and $0.09 \pm 0.03 \times 10^6 /l$. In deceased women with AIDS, the content of immunoglobulin A (3.9 ± 0.3 g/l) and IgG (27.3 ± 3.1) is twice higher than in the control group, respectively (1.78 ± 0.04 g/l, 13.8 ± 2.3 g/l), $p < 0.01$, Table 2. The amount of IgM in women with AIDS (1.8 ± 0.07 g/l) is also statistically significantly higher than in the control group (1.2 ± 0.05 g/l), but not as pronounced as the levels of immunoglobulins A and G. In the group with combined pathology (AIDS and alcohol dependence syndrome), immunoglobulin levels are also significantly higher than in the control group and higher than in the group of deceased women with alcohol dependence syndrome, Table 2. Thus, a significant decrease in the absolute number of CD4-T helper cells and CD8 cytotoxic T-lymphocytes, accompanied by hyperproduction of IgG and IgA in deceased women with combined pathology (AIDS and alcohol dependence syndrome), can be treated as evidence of a redistribution of the cellular immune response to the humoral response, which is unable to provide protection against HIV/AIDS and opportunistic infections.

Chronic alcohol intoxication leads to a change in the functional state of almost all neurotransmitter systems of the body and is accompanied by serious disorders of neuroimmune interactions, which is expressed not only in an increase in the number of immunoglobulins of all classes, but also in the production of anti-inflammatory and proinflammatory cytokines. IL-10 production increases already at the stage of episodic alcohol consumption, as well as intracellular synthesis of IL-6. The content of proinflammatory – IL-6 (7.5 ± 1.4 pg/ml) and anti-inflammatory – IL-10 (9.9 ± 2.1 pg/ml) cytokines in the serum of the deceased with alcohol dependence syndrome was statistically significantly different from the control group (3.7 ± 0.11 pg/ml and 6.4 ± 0.13 pg/ml).

In deceased women with HIV/AIDS, the content of IL-6 was 28.5 ± 6.2 pg/ml, and IL-10 – 10.7 ± 1.4 pg/ml. High levels of IL-6 indicate a weakening of the functional activity of type I T-helper cells. Elevated levels of IL-6 affect the regulatory disorganization of the immune system, which reduces the differentiation and activity of cytotoxic T lymphocytes and their participation in antiviral and antibacterial immunity. The data obtained on cytokine dysregulation showed that increased levels of IL-6 and IL-10 affect the regulatory disorganization of the immune system and may affect the differentiation and activity of cytotoxic T-lymphocytes and their participation in antiviral and antibacterial immunity. In the pathogenesis of HIV infection and AIDS, cytokine imbalance is central to the pathogenesis and affects the strength of the immune system's response to specific viral antigens. The cytokine network is involved in almost all stages of virus-cell interaction. Imbalance of cytokines contributes to the virus infection of CD4 cells, leading to the progression of immunosuppression and further development of opportunistic infections in patients with HIV, AIDS stage.

Recently, it has been established that adhesion molecules, in particular macrosialin (CD68) and integrin, which can act as coreceptor molecules and interact with ligands of the intercellular adhesion marker (CD54), make a certain contribution to the interaction of viruses with T-lymphocytes, monocytes and macrophages [29]. In patients with AIDS, there is a dysfunction of monocyte cells (in particular, decreased chemotaxis and cytotoxicity).

There is evidence that an increase in the incidence of autoimmune and infectious diseases, and impaired tissue regeneration in alcoholics is a consequence of dysfunction of the immune system. The immune system, as well as the nervous and endocrine systems, is an integrative system and interacts with them normally; in case of pathologies that lead to compensated and uncompensated dysfunctions of these organs, a cascade of secondary trophic disorders occurs and, as a result, a new cycle of organ dysfunctions develops.

Described processes could be detected important link in transformation of inflammatory reaction in different tissue [30-32] and in persons with harmful addiction or genetic predisposition especially [33-35]. But organs of female genital system could be defined as most defined target for such changes in immunity [36,37], where development of neoplastic processes have been characterized especial frequency [38-40]. Our results accords described before changes in cellular and humoral immunity [41,42] in patients with SIDS, that should be taken into account considering unfavorable situation with female health [43], peculiarities of carrying such patients [44] and deontological features [45]. Our data are important for understanding that among women with immunodeficiency and women without immunodeficiency, recurrent loneliness is significantly more common among women with immunodeficiency regarding genital system, and women with immunodeficiency had significantly fewer children [46,47]. Sexual dysfunction, lubrication dysfunction and genital pain dysfunction are significantly more common in women with immunodeficiency compared to women without immunodeficiency; but no differences are seen in menopausal characteristics [46,48].

Thus, the studies have shown that chronic alcohol intoxication leads to statistically significant impairment of cellular immunity in the subjects, namely: impaired proliferative activity of T- and B-lymphocytes; cytolytic activity of natural killer cells. changes in the population composition of blood cells, which is expressed by a decrease in the percentage of CD4 T-lymphocytes (helpers) in the peripheral blood, an increase in CD8 T-lymphocytes and an increase in the percentage of CD19 B-lymphocytes. increase in the peripheral blood of immunoglobulins of all classes, interleukins IL-6 and IL-10.

HIV infection, the AIDS stage, leads to even more serious changes in the state of the immune system: inhibition of T-helper cells, reduction of T-lymphocyte functionality; cytolytic activity of natural killer cells. an increase in the number of B-lymphocytes, impairment of their functional capabilities; a significant increase in the peripheral blood of immunoglobulins of all classes, interleukins IL-6 and IL-10.

Conclusions.

Secondary immunodeficiencies of infectious and non-infectious origin in women (in particular, those formed in HIV infection, alcohol dependence syndrome and their combination) are characterized by negative changes in the cellular and humoral components of the immune system, as evidenced by the presence of transient immunodeficiency, activation of cytolytic and autoaggressive reactions. As a result of these processes, systemic and organ pathology develops, in particular, weakening of the body's resistance to various infections and pathological changes in organs and tissues, which may be one of the links in the development of pathological processes in internal organs and tissues.

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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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