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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.

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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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HYPERHOMOCYSTEINEMIA AS A CAUSE OF ERECTILE DYSFUNCTION

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Abstract.

Hyperhomocysteinaemia (elevated blood levels of the amino acid homocysteine) attracted the interest of researchers in the middle of the 20th century. At first, Butz and du Vigneaud in 1932 described a disorder of methionine metabolism in children, which was manifested by homocysteinuria (homocysteine is not normally detected in the urine).

In 1962 Cavan and Neil found that homocysteinuria in children is associated with a defect in cystathione-B-synthase and manifests early development of atherosclerosis.

It is quite possible that these facts would have remained unnoticed by the medical

community had it not been for further research by Kilmer McQuilley, a professor in the Department of Pathology at Harvard Medical School.

The scientist suggested that while high concentrations of homocysteine could damage blood vessels in young people, it was likely that lower concentrations of homocysteine, acting over a longer period of time, could cause cardiovascular disease in adults. Subsequent studies enabled him to formulate the "homocysteine" theory of atherosclerosis and to publish its main points in 1969.

Hyperhomocysteinaemia in young men has been shown to cause damage to the endothelium of blood vessels, and consequently males face the consequent equally global problem of developing erectile dysfunction.

Erection is a state regulated by a neurovascular process, characterized by blood filling of the cavernous bodies, provided by neural and humoral mechanisms occurring at different levels of the nervous system.

Erectile dysfunction (ED) refers to the inability to achieve and maintain an erection at a level necessary to ensure satisfactory sexual intercourse. Although ED is not life-threatening, it is a serious psychological and physiological problem, and it has now been shown to correlate the quality of intimate life with general health and even with life expectancy. In the USA alone, ED is reported in 20-30 million men, and the prevalence of these disorders increases with age.

Methods: A study of the homocysteine level of multidisciplinary hospital patients was used as the main marker. The work used laboratory and statistical research methods, as well as analysis and synthesis methods.

Conclusions: Using patient analyses, laboratory and statistical data, it has been shown that hyperhomocysteinaemia is one of the molecular mechanisms in the development of erectile dysfunction.

Key words. Homocysteine, methionine, hyperhomocysteinaemia, erectile dysfunction, guanidylase, protein kinase, asymmetric dimethylarginine.

Introduction.

There are factors such as diet (methionine-rich foods: dairy, meat: coffee), lifestyle (smoking, alcoholism), disease, use of medications, and many others that contribute to elevated homocysteine levels in the human body. This condition leads to impaired erectile function of the penis, and consequently to further infertility, to deep depression.

There are many factors that affect homocysteine levels in the blood:

Smoking: causes a decrease in the levels of vitamins (B6, B1) in the blood due to exposure to cyanide in cigarette smoke. Each cigarette smoked in a day increases homocysteine levels by 1% in women and 0.5% in men, in addition, hyperhomocysteinaemia has the highest correlation with arterial hypertension and smoking.

Coffee: caffeine can inhibit methionine synthase. Among men aged 40-43 who drink more than 6 cups of strong coffee a day, the concentration of homocysteine in the blood is 19% higher than in non-drinkers: in women - by 28%.

Alcohol: excessive consumption in alcoholics significantly reduces the content of vitamin B6 in blood plasma and folate in erythrocytes: in addition, ethanol inhibits the activity of methionine synthase in the liver, contributing to an increase in the concentration of homocysteine in plasma. Deficiency of pyridoxine, cobalamin and folate may be increased, for example, by parasitisation of *Helicobacter pylori*, which in case of low effectiveness of oral therapy requires parenteral administration of drugs, as well as confirmation of microbial parasitisation, which hampers absorption of drugs [1-10].

Results.

Homocysteine (Heys) is a sulphur-containing amino acid that is an intermediate product of methionine metabolism. If methionine metabolism is disturbed, excessive amounts of methionine accumulate in the body, which leads to the development of many pathological processes. This article will consider the role of Heys in the development of erectile dysfunction in men aged 35 years and older.

Remethylation of homocysteine to methionine is catalysed by the cytoplasmic enzyme methionine synthase (MTR). Methylcobalamin, a derivative of vitamin B12, is required for the enzyme to function. Methionine synthase catalyses the remethylation of homocysteine into methionine through a reaction in which methylcobalamin acts as an intermediate carrier of the methyl group. In this process, cobalamin is oxidised, and the MTR enzyme is rendered inactive. The function of the enzyme can be restored during the methylation reaction with the participation of the enzyme methionine synthase reductase (MTRR). The donor of the methyl group in this case is the activated form of methionine - S-adenosylmethionine, which

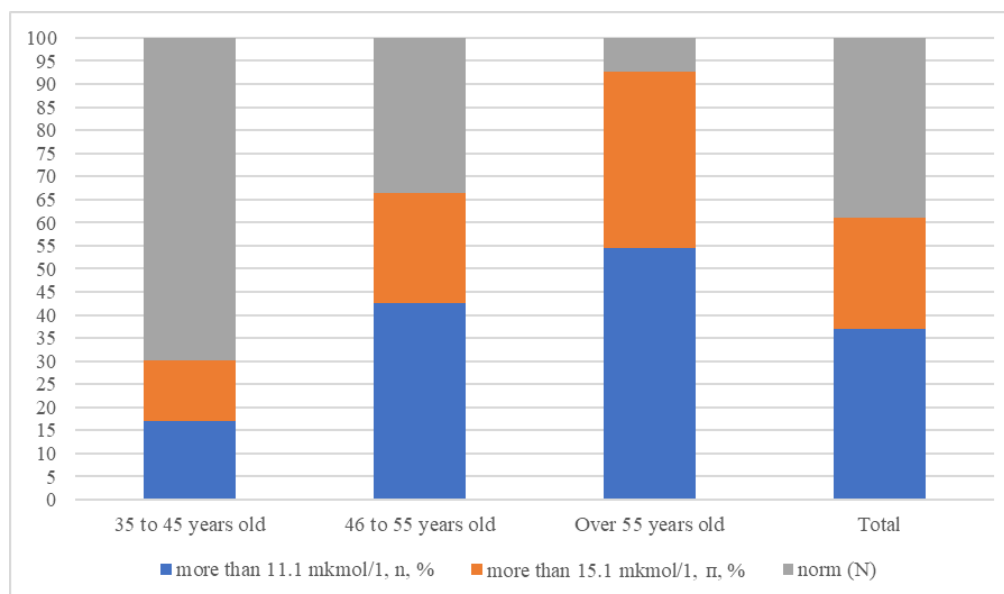


Figure 1. Patient groups by age and homocysteine level.

Table 1. Patient groups by age.

Group	n	Number of patients with Hyperhomocysteinaemia	
		more than 11.1 mkmol/l, n, %	more than 15.1 mkmol/l, n, %
35 to 45 years old	70	49 (70)	19 (27)
46 to 55 years old	80	70 (87,5)	8 (10)
Over 55 years old	55	15 (27)	30 (54)
Total	205	134 (65)	57 (27)

is also used for methylation of other compounds: DNA, RNA, proteins and phospholipids [7].

A key role in the synthesis of methionine from homocysteine is played by the enzyme 5,10- methylenetetrahydrofolate reductase (MTHFR), which reduces 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate, which carries the methyl group required for homocysteine remethylation [9,10]. The metabolic consequence of folic acid deficiency is an increase in homocysteine levels. Genetic defects in the production of enzymes that catalyse the transition of folic acid into its active form, which is necessary for remethylation of homocysteine into methionins, have also been identified.

The MTHFR gene is localised on the short arm of chromosome 1 (1p36.3) and consists of 11 exons. The length of the entire coding region is about 1980 nucleotide pairs. The most studied is mutation C677T of the MTHFR gene, associated with the substitution of cytosine for thymine at position 677, causes the substitution of alanine for valine (p.Ala222Val) in the catalytic domain of the enzyme protein, leading to a 70% decrease in its activity in the homozygous variant for the polymorphic allele, and in heterozygous genotypes - by 35%. Homozygosity for the C677T allele leads to a significant increase in the level of homocysteine, especially against the background of low plasma folate content. The decrease in the activity of this enzyme is one of the important causes of homocysteine accumulation in the body [8].

Penile erection is regulated neurogenically, psychogenically and hormonally. All of these mechanisms contribute to the release of NO as a key mediator by vascular endothelium

through stimulation of non-adrenergic, non-cholinergic nerves. NO is released by endothelin and neurons in penile tissue and binds to soluble guanylate cyclase to increase the production of 3',5-cyclic guanosine monophosphate (cGMP), which activates protein kinase G to form a cGMP/PCG complex that causes relaxation of smooth muscle in the corpora cavernosa, followed by a large arterial blood flow, which represents the fundamental mechanism of penile erection [7].

In excessive amounts, homocysteine is able to block endothelial NO synthases, reduces nitric oxide production, is also able to induce the activity of 3-hydroxy-3-methylglutaryl-CoA reductase, which leads to an increase in cholesterol and its deposition in the intima of blood vessels, which in turn contributes to a decrease in blood flow. It also increases asymmetric dimethylarginine (ADMA), an endogenous nitric oxide inhibitor.

Having analysed scientific papers, monographs and using laboratory data of patients of a multidisciplinary organisation 3 groups were formed.

The first group included men aged 35 to 45 years (70), the second group 46 to 55 years (80), and the third group men over 55 years (55).

In the course of the work, it was accepted to use the classification according to serum homocysteine level: moderate (mild) from 11 to 15 $\mu\text{mol/l}$; Medium from 15.1 to 20 mkmol/l ; High more than 20.1 mkmol/l . No patients with levels greater than 20.1 mkmol/l was identified during the study.

The laboratory data of the patients showed that 125 men out of 205 - ti were found to have sexual dysfunction. 80 men (64%)

had Heys levels between 11 and 15 mkmol/l; 45 men (36%) between 15.1 and 20 mkmol/l; and 0 men (0%) had homocysteine levels over 20.1 mkmol/l. Also, there was a correlation between age and serum homocysteine levels.

Conclusion.

Thus, hyperhomocysteinaemia is an important factor in the pathogenesis of not only cardiovascular pathology, but also erectile dysfunction. Confirmation of this is the determination of homocysteine content in the blood of patients in a multidisciplinary hospital. Results: 125 men out of 205 have been diagnosed with sexual dysfunction. In 80 men (64%) - the level of Heys in the range of 11 - 15 $\mu\text{mol/l}$; in 45 men (36%) within 15.1-20 $\mu\text{mol/l}$; in 0 men (0%) - the level of homocysteine over 20.1 $\mu\text{mol/l}$. allow not to exclude the involvement of hyperhomocysteinemia in the development of erectile dysfunction. There is also a relationship between age and serum homocysteine level. One of the most important tasks today is to find biomarkers to predict the course of erectile dysfunction, as homocysteine level determination is an indirect confirmation criterion. Further study of homocysteine can help clarify the role of the vascular component in the pathogenesis of the disease, identify the effect of increased concentration of homocysteine on the pathological process, and develop therapeutic tactics in treatment.

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