GYNECOMASTIA - AS AN IMPORTANT ISSUE IN MODERN MEDICINE

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Abstract. *Gynecomastia is an enlargement of the mammary glands in men, which is more often bilateral and less often unilateral. In the presence of pronounced unilateral gynecomastia and suspicious palpation results, it becomes necessary to exclude breast cancer. Children of both sexes have breast tissue.*
Keywords: *testostheron, estradiol, galactorrhea, leidigoma, hypercomastia.*

The development of mammary glands depends on androgenic and estrogenic stimulations. With the predominance of estrogenic influences, when the activity of androgens is low, the development and differentiation of breast tissue occurs, and, conversely, when the androgenic activity is higher than the estrogenic, the mammary glands remain underdeveloped. In adult men, the molar ratio of testos- theron / estradiol in plasma is approximately 300/1. A slight deviation from this value towards a decrease in the level of androgens or an increase in the content of estrogens can stimulate the proliferation of previously inactive breast tissue and lead to the development of gynecomastia. Gynecomastia also develops when the function of androgen receptors is impaired. In such cases, both normal and elevated levels of androgens can lead to the development of gynecomastia. Prolactin stimulates lactation, but it plays a secondary role in the development of breast tissue. At the same time, if an excess of prolactin leads to the development of endocrine hypogonadism, gynecomastia and galactorrhea develop. Testicular tumors (leidigoma, embryonic carcinoma, teratocarcinoma, chorioncarcinoma, combined tumor) directly or through an increase in HCG secretion lead to an increase in the production of estrogens by Leydig cells. With chronic diseases (cirrhosis of the liver, hyperthyroidism), with a number of pathological conditions (for example, renal insufficiency) and with the use of certain drugs, gynecomastia can develop against the background of normal levels and the ratio of androgens and estrogens. The reason for the development of gynecomastia in such cases is not yet clear. The cause of gynecomastia cannot be found out in about 50% of men. Such forms of gynecomastia are considered idiopathic. Gynecomastia often develops in boys at puberty (at the age of 14), but after 2-3 the year disappears. The development of obesity is accompanied by more pronounced gynecomastia, which persists longer. Physiological gynecomastia is a small increase in the mammary glands that occurs in newborns, adolescents and elderly men. In newly born boys, maternal estrogens penetrating through the placenta lead to hyperplasia of breast tissue, which does not last long and spontaneously regresses. Adolescent hypercomastia is often considered a variant of the norm and it does not require treatment. Palpation of the mammary glands reveals a certain amount of glandular tissue in about 40% of adolescent boys. In some cases, the proliferation of glandular tissue occurs, which leads to a more pronounced increase in the mammary glands and creates discomfort in patients of a psychological nature. However, the cause of pronounced gynecomastia in the young may be endocrine or systemic diseases, so in such cases it is necessary to conduct an examination of the patient. To exclude pathology, it is necessary to examine the basal levels of testosterone, estradiol, LH and FSH. At the same time, it is important to assess the

degree of general androgenization of the patient, because with simple adolescent gynaecomastia, there are no permanent hormonal shifts. Usually, adolescent gynecomastia develops after the onset of puberty, and the presence of gynecomastia without other signs of puberty may be a consequence of endocrine disease (in most cases, a hormone-producing tumor). Adolescent gynecomastia regresses spontaneously, but in some cases it may persist, then it is called persistent adolescent gynecomastia. In this case, endocrine or any general diseases cannot be detected, patients note the development of gynaecomastia only in adolescence, and in the future it does not progress. Senile gynecomastia. With age, the incidence of gynecomastia increases, which is associated with an increase in the ratio of estrogens / androgens. During this period, the proliferation of breast tissue is associated with a number of common diseases (renal or hepatic insufficiency), taking certain medications, for example, spironolactone or veroshpiron (a competitive aldosterone antagonist), digoxin, angiotensin-converting enzyme inhibitors and cytotoxic compounds (Morley et al., 1990). When painful gynecomastia occurs, a rapidly progressive enlargement of the mammary glands occurs. In such cases, it is necessary to differentiate gynecomastia with breast cancer. Breast cancer occurs in men aged 50-70 years and accounts for 1% of all cases of breast cancer. It is also necessary to exclude paraneoplastic, or HCG- producing bronchial cancer, as well as para-neoplastic tumors of the testicles, liver, adrenal glands or gastrointestinal tract. Gynecomastia can be observed in all conditions in which there is a lack of androgen production or a violation of their action. With Klinefelter syndrome, gynecomastia develops in combination with small dense testicles. Proliferation of glandular tissue is also observed in Kallmann syndrome, idiopathic hypogonadotropic hypogonadism, Reifen- Stein syndrome, X-linked spinal and bulbar muscular atrophy, pro- interstitial-scrotal hypospadias with pseudovaginal. Excessive secretion of estrogens in the gonads or adrenal glands or their formation from androgens on the periphery also lead to the development of gynaecology. Primary estrogen-producing tumors of the testicles (from Leydig or Sertoli cells) and adrenal glands (especially cancer) are rare, but they should be remembered when conducting differential diagnosis of gynecomastia. Increased production of estrogens is also observed when stimulated by an increased amount of chorionic gonadotropin. The source of HCG formation can be testicular teratomas, chorioncarcinomas and embryonic carcinomas, as well as extra-gonadal tumors, especially of the lungs and liver (Meschede D., Behre H.M., Nieschlag E., 2005). It is known that estrone and estradiol are formed from androgens androstenedione and testosterone under the action of the aromatase enzyme. There is a rare hereditary form of gynecomastia associated with increased activity of the aromatase enzyme. With this form of mastopathy, the levels of androgens in the blood may be within normal values, but the rate of their conversion into estrogens increases. In some cases, the acceleration of the conversion of androgens into estrogens may exceed the norm in 10 times. The cause of this pathology is unknown, the disease is inherited as an autosomal dominant or X-linked trait (Belkovitz et al., 1985). It is believed that increased conversion of androgens into compounds with estrogenic properties may occur in breast tissue. It is possible that in men with gynecomastia, there is an increase in the sensitivity of the mammary gland vascular tissue to estrogenic influences. This could explain some cases of familial gynecomastia. 1/3 of men with hyperthyroidism develop gynaecomastia, which is associated with an increase in the production of estrogens in untreated hyperthyroidism. An increase in the level of estrogens is accompanied by an increase in the formation of globulin binding sex steroids in the liver, which leads to a decrease in the level of free, biologically active testosteron . It is assumed that it is the deviation of the androgen/estrogen ratio from the norm that

leads to the development of obvious gynecomastia. With congenital hyperplasia of the adrenal cortex (insufficiency of the enzyme 21- hydroxylase) and androgen-secreting tumors of the adrenal cortex , the level of androstenedione is increased and, accordingly, the amount of estrogen produced may increase, since androstenedione is a substrate of the aromatase enzyme. Chronic liver and kidney diseases can also be accompanied by gynecomastia. In some cases, changes in the androgen/estrogen ratio are detected in such patients. Many medications can affect the ratio of androgens/estrogens, which leads to the development of gynecomastia. However, in some cases it is not possible to establish exactly what exactly they caused the development of this disease. The effect of drugs that cause the development of gynecomastia is diverse, but some of them disrupt the synthesis of testosterone. Thus, drugs with antitumor effect disrupt the synthesis of testosterone, which is a non- specific phenomenon of their general toxicity. Ciproterone-atse- tat, a drug used in the treatment of hyper- androgenia, acts on androgen receptors and blocks them. The antifungal drug ketoconazole has an inhibitory effect on the production of androgens in the adrenal glands. Estrogens and similar substances that contribute to the development of gynecomastia can enter the body both with food and through the skin (from cosmetics). Tumors of the mammary glands in men are rarely detected. Unilateral breast enlargement in men is a stage in the development of bilateral gynecomastia, but in these cases it is necessary to exclude the presence of a tumor (O'Hanlon et al., 1995). Androgen and estrogen receptors are found in breast cancer tissue in most cases, but their presence seems to have only a small diagnostic, therapeutic and prognostic value (Pich et al., 1999). Many men with breast cancer have BRCA2 gene mutations, which suggests the existence of a genetic predisposition to this disease (Csokay et al., 1999). In the literature, there are descriptions of cases of breast cancer in men with androgen receptor gene mutations (Wooster et al., 1992). Any asymmetric, painful and dense swelling in the area of the periarticular circle should cause oncological alertness in the doctor and requires referral of the patient for examination, including taking a biopsy of material from this area. The use of the following drugs and drugs leads to the development of gynecomastia in men (Meschede D. et al., 2005) (Meschede D. et al., 2005): amphetamines, antitumor agents, calcium channel blockers, cimetidine, diazepam, digitalis, estrogens, flutamide, human chorionic gonadotropin, angiotensin-converting enzyme inhibitors, isoniazide, ketoconazole, marijuana, methyldopa, metronidazole, opiates and opioids, penicillamine, reserpine, spironolactone, tricyclic anti- depressants. Laboratory tests are prescribed depending on the form of gynecomastia. If gynecomastia is adolescent or senile, poorly expressed and does not progress, then there is no need to conduct a thorough examination of the patient. We can limit ourselves to the study of the levels of LH, FSH, estradiol and testosterone (Bowers et al., 1998). With more pronounced gynecomastia, there is a need to study the concentration of testosterone, estradiol, SHBG, LH, FSH, prolactin, TSH, β-hCG, alphafetoprotein, as well as the determination of liver and kidney function. In some cases, hormone levels are examined in dynamics, DNA analysis and karyotyping are performed. It is necessary to find out whether the patient took pharmaceutical or narcotic drugs, as well as alcohol. Clinical examination of a patient with gynaecology includes, first of all, palpation of the mammary glands. Palpationally, it is possible to detect a certain amount of glandular tissue in many men. However, it is difficult to establish the presence of pathology in such cases and the clinical assumption of the presence of gynecomastia often remains subjective. First of all, it is necessary to differentiate gynecomastia from lipomastia. Obese men often have deposits of fatty tissue on their breasts. It is possible to establish the presence of lipomastia or gynecomastia by palpation,

but this can only be clarified during ultrasound. As already noted above, gynecomastia is often one- sided or more pronounced on one of the sides. The reasons for this asymmetry have not been established. The degree of gynecomastia is assessed in accordance with the stages of development of the mammary glands according to Tanner (Meschedi D. et al., 2005): stage 1: prepubescent mammary glands (glandular tissue is not palpable); stage 2: the beginning of development (mammary glands are detected during examination, glandular tissue is palpated, periarticular circles increase); stages 3 and 4: further enlargement of the mammary glands (at stage 3, the periarticular circles do not rise above the surface, at stage 4 they rise); stage 5: mature mammary glands (outlines and proportions characteristic of adults, near- nipple circles no longer rise above the surface). When examining patients with gynecomastia, it is necessary not only to conduct a study of the mammary glands, but also to pay attention to the degree of virilization, the presence of symptoms such as a weakening of libido or potency, general lethargy, and the absence of pronounced hairiness in the chin area.

REFERENCES

1. Sarkisova V., Xegay R., Numonova A. ENDOCRINE CONTROL OF THE DIGESTION PROCESS. GASTROINTESTINAL ENDOCRINE CELLS //Science and innovation. – 2022. – T. 1. – №. D8. – C. 582-586.
2. Sarkisova V. ASPECTS OF THE STATE OF THE AUTONOMIC NERVOUS SYSTEM IN HYPOXIA //Science and innovation. – 2022. – T. 1. – №. D8. – C. 977-982.
3. Sarkisova V. et al. ESSENTIAL ROLE OF BRADIKININ IN THE COURSE OF BASIC LIFE PROCESSES //Science and innovation. – 2022. – T. 1. – №. D8. – C. 576-581.
4. Sarkisova V., Xegay R. CAUSES, DIAGNOSIS, CONSERVATIVE AND OPERATIVE TREATMENT OF UTERINE MYOMA //Science and innovation. – 2022. – T. 1. – №. D8. – C. 198-203.
5. Джуманов Б. и др. Применение инструментальных методов исследование в диагностике острого аппендицита у беременных //Журнал проблемы биологии и медицины. – 2014. – №. 1 (77). – С. 9-12.
6. Саркисова В., Джуманов Б., Исроилова Г. Анализ репродуктивного и соматического здоровья женщин, госпитализированных по поводу гиперплазии эндометрия и маточных кровотечений //Журнал вестник врача. – 2014. – Т. 1. – №. 01. – С. 169-170.
7. Саркисова В., Абдурахманова К. Роль гормональных препаратов в терапии гиперпластических процессов эндометрия и в частности при миоме матки //Журнал вестник врача. – 2014. – Т. 1. – №. 01. – С. 167-168.
8. Sarkisova V., Regina X. РОЛЬ БРАДИКИНИНА В ПРОТЕКАНИИ ОСНОВНЫХ ЖИЗНЕННЫХ ПРОЦЕССОВ //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 587-593.
9. Sarkisova V., Numonova A., Xegay R. АНТИБИОТИКОРЕЗИСТЕНТНОСТЬ ИЛИ БОРЬБА С ГЛОБАЛЬНОЙ УГРОЗОЙ XXI ВЕКА //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 232-241.
10. Sarkisova V., Numonova A., Xegay R. АСПЕКТЫ СОСТОЯНИЯ ВЕГЕТАТИВНОЙ НЕРВНОЙ СИСТЕМЫ ПРИ ГИПОКСИИ //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 228-231.

11. Саркисова В., Абдурахманова К. Астено-вегетативные нарушения, оценка качества жизни у женщин климактерического возраста с гиперпластическими процессами в матке //Журнал вестник врача. – 2014. – Т. 1. – №. 01. – С. 163-166.
12. Vladimirovna S. V. Epidemiology, Theories Of The Development, Conservative And Operative Treatment Of The Endometriosis //The Peerian Journal. – 2023. – Т. 15. – С. 84-93.
13. Vladimirovna S. V. et al. Analysis of Women's Reproductive and Somatic Health, Hospitalized for Endometrial Hyperplasia and Uterine Bleeding //Eurasian Medical Research Periodical. – 2023. – Т. 17. – С. 91-96.
14. Vladimirovna S. V. About the Causes of Endometrial Hyperplasia and Forms of Endometrial Hyperplasia //Global Scientific Review. – 2023. – Т. 12. – С. 25-32.
15. Vladimirovna, S. V. ., Safoyevna, K. D. ., Anvarovna, S. L. ., & Olegovna, X. R. . (2023). Hyperplastic Processes of the Endometrium: Issues of Ethiopathogenesis, Clinic, Diagnosis, Treatment. *Scholastic: Journal of Natural and Medical Education*, *2*(3), 72–77.
16. Vladimirovna, S. V. ., K. D. . Safoyevna, S. L. . Anvarovna, and X. R. . Olegovna. “Hyperplastic Processes of the Endometrium: Issues of Ethiopathogenesis, Clinic, Diagnosis, Treatment”. *Scholastic: Journal of Natural and Medical Education*, vol. 2, no. 3, Mar. 2023, pp. 72-77,
17. Vladimirovna, S. V. ., Shoukatovna, I. M. ., Ulugbekovna, R. F. ., & Olegovna, X. R. . (2023). Adenomyosis as an Independent Unit of Dysfunction of the Endometrium and Uterine Myometrium. *Scholastic: Journal of Natural and Medical Education*, *2*(3), 85–91.
18. Vladimirovna, S. V. ., I. M. . Shoukatovna, R. F. . Ulugbekovna, and X. R. . Olegovna. “Adenomyosis As an Independent Unit of Dysfunction of the Endometrium and Uterine Myometrium”
19. Саркисова Виктория Владимировна. (2023). Патогенетические отношения артериальной гипертензии и сопротивления инсулина. *IQRO JURNALI*, *2*(1), 727–731.
20. Саркисова Виктория Владимировна. “Патогенетические отношения артериальной гипертензии и сопротивления инсулина”. *IQRO JURNALI*, vol. 2, no. 1, Mar. 2023, pp. 727-31,
21. Sarkisova Victoria Vladimirovna. (2023). PATHOGENETIC RELATIONSHIPS OF ARTERIAL HYPERTENSION AND INSULIN RESISTANCE. *IQRO JURNALI*, *2*(1), 685–691.
22. Sarkisova Victoria Vladimirovna. “PATHOGENETIC RELATIONSHIPS OF ARTERIAL HYPERTENSION AND INSULIN RESISTANCE”. *IQRO JURNALI*, vol. 2, no. 1, Mar. 2023, pp. 685-91,
23. Vladimirovna S. V. ABOUT THE CAUSES OF ENDOMETRIAL HYPERPLASIA AND FORMS OF ENDOMETRIAL HYPERPLASIA //ResearchJet Journal of Analysis and Inventions. – 2022. – Т. 3. – №. 11. – С. 66-72.
24. Vladimirovna, S. V. (2022). ABOUT THE CAUSES OF ENDOMETRIAL HYPERPLASIA AND FORMS OF ENDOMETRIAL HYPERPLASIA. *ResearchJet Journal of Analysis and Inventions*, *3*(11), 66-72.
25. Sarkisova V., Xegay R., Numonova A. ENDOCRINE CONTROL OF THE DIGESTION PROCESS. GASTROINTESTINAL ENDOCRINE CELLS //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 582-586.

26. Sarkisova, V. (2022). ASPECTS OF THE STATE OF THE AUTONOMIC NERVOUS SYSTEM IN HYPOXIA. *Science and innovation*, *1*(D8), 977-982.
27. Sarkisova, V., Mavlyanova, U., Xegay, R., & Numonova, A. (2022). ESSENTIAL ROLE OF BRADIKININ IN THE COURSE OF BASIC LIFE PROCESSES. *Science and innovation*, *1*(D8), 576-581.
28. Sarkisova, V., & Xegay, R. (2022). CAUSES, DIAGNOSIS, CONSERVATIVE AND OPERATIVE TREATMENT OF UTERINE MYOMA. *Science and innovation*, *1*(D8), 198-203.
29. Джуманов, Б., Абдурахманова, К., Саркисова, В., & Абдухакимов, Т. (2014). Применение инструментальных методов исследование в диагностике острого аппендицита у беременных. *Журнал проблемы биологии и медицины*, (1 (77)), 9-12.
30. Саркисова, В., Джуманов, Б., & Исроилова, Г. (2014). Анализ репродуктивного и соматического здоровья женщин, госпитализированных по поводу гиперплазии эндометрия и маточных кровотечений. *Журнал вестник врача*, *1*(01), 169-170.
31. Sarkisova, V., & Regina, X. (2022). РОЛЬ БРАДИКИНИНА В ПРОТЕКАНИИ ОСНОВНЫХ ЖИЗНЕННЫХ ПРОЦЕССОВ. *Science and innovation*, *1*(D8), 587-593.
32. Саркисова, В., & Абдурахманова, К. (2014). Роль гормональных препаратов в терапии гиперпластических процессов эндометрия и в частности при миоме матки. *Журнал вестник врача*, *1*(01), 167-168.
33. Shodiyeva D., Shernazarov F. ANALYSIS OF THE COMPOUNDS PROVIDING ANTIHELMITIC EFFECTS OF CHICHORIUM INTYBUS THROUGH FRACTIONATION //Science and innovation. – 2023. – Т. 2. – №. D2. – С. 64-70.