MODERN MEDICINE AND PRACTICE
http://innovatus.es/index.php/ejmmp
EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE
Vol. 4 No. 2 (Feb - 2024) EJMMP ISSN: 2795-921X

Endometriosis, Pathophysiology and Pathomorphology

Varsha Gopakumar Nair

Lecturer of Physiology Department of the Samarkand State Medical University

Chetan Ram

Lecturer of Physiology Department of the Samarkand State Medical University

Sarkisova Victoria

Lecturer of Physiology Department of the Samarkand State Medical University

Raxmanov Otabek Rasulovich

Kimyo international University, Tashkent

Abstract. Endometriosis is a chronic disease characterized by the benign growth of hormone-dependent tissue, morphologically similar to the endometrium, outside the uterine mucosa. Endometriosis is diagnosed in 10% of women of childbearing age; it ranks third in the structure of gynecological morbidity.

Key words: endometrioid heterotopia cells, xenobiotic metabolism, eotaxin, glycodelin, interleukins (IL) 1, 6, 8, transdermal growth factor β (TGF-β).

In women suffering from chronic pelvic pain, endometriosis is detected in 71% of cases, in case of infertility - with a frequency of 30–45%, and the combination of chronic pelvic pain syndrome and infertility is caused by endometriosis in 84% of cases. The relevance of the problem of endometriosis is determined not only by its high prevalence. Despite the large number of studies, to date there is no single classification or consensus on the criteria for clinical diagnosis, which entails the emergence of a variety of approaches in the management of patients. This diversity is also facilitated by the existence of several theories of pathogenesis, which make it possible to justify the development of certain treatment methods. One of the first to emerge was the implantation theory, which considers the possibility of the development of endometriosis from viable endometrial cells displaced into the thickness of the uterine wall or transferred retrogradely, through the fallopian tubes, into the abdominal cavity during menstruation. Experimental studies have revealed the ability of endometrial implants to invade the subperitoneal space extremely quickly [2]. The theory has been confirmed by such clinical facts as an increased incidence of endometriosis in the presence of difficulties in the outflow of menstrual blood in women with malformations of the genital organs, as well as a higher (60%) frequency of left-sided ovarian lesions, due

to the location of the mesentery of the sigmoid colon and the accumulation of retrogradely transferred cells in left half of the pelvis [3]. It is known that the likelihood of endometriosis recurrence sharply decreases after endometrial ablation [4]. Consequently, any therapeutic effect that leads to a decrease in proliferative processes and reduces the viability of endometrial cells is justified from the standpoint of preventing both endometriosis itself and its relapses. As an alternative hypothesis, almost simultaneously with the implantation one, a metaplastic theory was put forward, suggesting the possibility of metaplasia of the embryonic peritoneum or coelomic epithelium. The metaplastic theory explains the occurrence of endometriosis in places significantly removed from the abdominal cavity, but to date, having not been rejected, it has not found experimental confirmation. Classic theories of the origin of endometriosis cannot explain the main cause of the disease, namely: why endometrial cells do not die, but continue to exist and function outside their natural habitat? Obviously, the following conditions are necessary for the development of endometriosis: an increased ability of ectopic cells to survive and, on the other hand, the inability of invaded tissues to ensure the destruction of these cells. In the search for the reasons that determine these conditions, theories were born that explain different aspects of the pathogenesis of endometriosis. Endometriosis is considered a disease with a hereditary predisposition. Cytogenetic studies reveal structural and quantitative changes in several chromosomes in endometrioid heterotopia cells, reflecting genomic instability as a characteristic feature of the disease [5]. Interestingly, the chromosomal region associated with the development of endometriosis is home to several genes responsible for the regulation of the mitotic cell cycle. Thus, the severity and prevalence of endometriosis correlate with a decrease in TOB1 expression and the disappearance of p53 tumor suppressor genes [6, 7]. In general, the genetic concept considers endometriosis as the result of abnormal functioning of three classes of genes: those involved in xenobiotic metabolism, those mediating inflammatory responses and regulating the action of steroids [8]. The inflammatory response in the body is inextricably linked to the immune response, and this has given rise to research that continues to this day. Changes in cellular immunity in endometriosis are expressed in the suppression of T-cell immunity and activation of polyclonal B cells. Macrophages accumulating in the peritoneal fluid of patients with endometriosis initiate a cascade of reactions that involve chemokines, cytokines and growth factors [8]. With external endometriosis, there are significant changes in the activity of proteases and protease inhibitors in the peritoneal fluid [9]. The consequence of this is a change in apoptosis with a decrease in the activity of cathepsins and an increase in the activity of their inhibitors, and an increase in the invasive potential of the endometrium itself due to an increase in the activity of plasmin, one of the main disintegrators of the intercellular matrix. As a result, endometrial cells entering the peritoneal fluid with altered properties do not undergo apoptosis and penetrate into the peritoneal cover. It has been established that with endometriosis in the peritoneal fluid the content of complement, eotaxin, glycodelin, interleukins (IL) 1, 6, 8, transdermal growth factor β (TGF-β), vascular endothelial growth factor (VEGF) and some other factors increases, including while the concentration of endothelial growth factor (EGF), fibroblast growth factor (FGF), interferon-γ, IL-2, -4, -12 decreases [10]. Cytokines serve as mediators of intercellular interactions, regulate hematopoiesis, immune response, and cell cycle in various tissues. IL-1 induces the synthesis of prostaglandins, stimulates fibroblast proliferation, collagen accumulation and fibrinogen formation, i.e. processes that contribute to the fibrosis and adhesion formation characteristic of endometriosis. At the same time, in patients with endometriosis, polymorphism of genes associated with a decrease in fibrinolysis is detected, therefore, the formation of adhesions turns out to be not so much a result of the functioning of heterotopias,

but rather a consequence of gene and immune damage that underlies the occurrence of endometriosis. Along with cytokines, macrophages participate in increasing the synthesis of prostaglandins. Excessive concentrations of prostaglandins in tissues and in the systemic circulation are responsible, like cytokines, for the clinical symptoms of endometriosis - pain, infertility, menstrual dysfunction [8]. From a clinical point of view, understanding the processes associated with the inflammatory reaction and the immune response allows us to search for treatment methods that reduce the severity of inflammation and correct the immune status. Growth factors, the content of which changes in endometriosis both in the peritoneal fluid and in tissues, not only reflect the activation of macrophages, but also have a powerful effect on the balance of the processes of cell proliferation and apoptosis. Along with SERF and TGF-β, increased expression of insulin-like growth factor 1 (IGF-1) is found in endometriotic lesions, while the concentration of binding proteins in endometriotic heterotopias is reduced compared to normal endometrium. At the same time, proliferation is supported by proto-oncogenes, for example, oncoprotein C-myc, high expression of which is found in endometrioid heterotopias. Along with an increase in proliferative activity in endometrioid cells, the processes of apoptosis weaken, which, together with the characteristics of the immune response (weakening T-cell immunity), creates the prerequisites for the survival of implants outside the uterine mucosa [11]. In addition to increased viability, endometrioid heterotopia cells have a high invasive ability. It is likely that this ability to invade, which is also characteristic of normal endometrial cells, is due to increased expression of matrix metalloproteinases (MMPs). The role of MMPs and tissue metalloproteinase inhibitors in the pathogenesis of endometriosis is being actively studied [12]. MMPs stimulate angiogenesis, i.e. serve as an additional factor in the neovascularization of endometrioid implants together with FGF, IL-6, IL-8 and SERF [8]. The ways of external, including medicinal, influence on autocrine and paracrine regulation and intercellular interaction are realized through the hormonal control system. All described processes, mediated by cytokines, growth factors, and other biologically active substances, depend on the concentration and cyclic fluctuations of steroid hormones. It is this dependence that underlies the pathogenesis and becomes the basis for prescribing therapy for endometriosis. The hormone dependence of endometriosis should not be understood primitively as a standard reaction to excess estrogen and progesterone deficiency. It should be taken into account that among the genetic determinants of the disease there is also an altered response to steroid hormones. Endometrioid heterotopias are less sensitive to hormones than normal endometrium, this is confirmed by a decrease in the expression of estradiol and progesterone receptors, which is directly dependent on the degree of distance of the lesion from the uterus. Moreover, genetically determined abnormalities of the progesterone receptor are observed in endometriosis [13]. With a decrease in sensitivity to progesterone, endometrioid heterotopias have the ability to locally synthesize estrogens, which is evidenced by the presence of increased expression of aromatase. Thus, with endometriosis, a precedent is created for not a systemic, but a tissue hormonal imbalance, with a shift in emphasis towards proliferative estrogen influences. Thus, endometriosis is a genetically determined disease, which is based on abnormalities in intracellular processes and intercellular interactions, creating conditions for the survival and development of endometrial cells outside the uterine mucosa. It follows from this that the only radical method of treating endometriosis can be considered the removal of not only endometrioid heterotopias, but also the endometrium itself as a potential “supplier” of relapses; It is no coincidence that endometriosis is the third most common cause of hysterectomy [14]. But such an approach should have good reasons for use in women of reproductive age, since it deprives them of the opportunity to perform

childbearing and provokes the emergence of various somatic and psychological, and sometimes social problems [15]. All other treatment methods, surgical and conservative, can only claim a temporary effect, and therefore require a thoughtful, individual choice, which should have the characteristics of the clinical symptoms of the disease as the main starting point. The clinical picture of endometriosis is characterized by pain, infertility, and menstrual irregularities. The presence and severity of symptoms do not correspond much to the visualized severity of the process, which once again confirms the opinion that the formation of symptoms is predominantly influenced not only and not so much by the heterotopias themselves, but by inflammatory, immune, endocrine and other pathophysiological features that lead to the appearance of both heterotopias and symptoms of endometriosis. Pelvic pain in endometriosis is varied, depending more on the localization of the process than on the degree of its spread. Premenstrual/menstrual increased pain is a characteristic, but not strictly obligatory, sign of endometriosis. Assessment of the severity of pain is always subjective, but nevertheless, it is the subjective idea of severe, moderate or mild pain that forms the basis for the choice of patient management tactics. Objectification of the severity of a pain symptom is valuable in the process of monitoring the effect of therapy, and it is recommended to use visual analogue scales. Menstrual irregularities in patients with endometriosis are represented by various types of abnormal uterine bleeding (AUB) - metrorrhagia, menorrhagia, menometrorrhagia. Although AUB in endometriosis is inferior to pain in terms of significance, from the standpoint of a violation of the quality of life, it is often they that become the main reason for visiting a doctor, especially with the development of anemia in patients with menorrhagia. Infertility accompanies edometriosis in approximately half of all cases. The cause-and-effect relationship between these two conditions is not completely clear. It is likely that endometriosis itself can cause infertility, leading to the development of adhesions in the pelvis, a secondary disorder of the ovulatory function of the ovaries, which is especially true with prolonged pelvic pain, which decompensates the central mechanisms of regulation of the menstrual cycle. But the pathophysiological features of endometriosis may be equally significant in violations of the processes of fertilization, transport and implantation of the fertilized egg [16]. In this case, it is appropriate to say that infertility develops in parallel with endometriosis. One of the factors in the pathogenesis of infertility can be considered significant electrolyte shifts in the peritoneal fluid observed in endometriosis, since they lead to disruption of the processes of migration of male gametes along the female reproductive tract, reducing sperm motility [9]. Whatever the underlying cause of infertility, we have to admit that, as with pelvic pain, there is no connection between the severity of the process and impaired fertility. Finally, again, regardless of the extent of the spread of the pathological process, there is an asymptomatic course of endometriosis, which presents particular difficulties in choosing the optimal tactics for managing patients. The problem of choice is complicated by the fact that endometriosis is often combined not only with infertility, but also with uterine fibroids, endometrial hyperplastic processes, diffuse fibrocystic mastopathy, which have many common pathogenetic characteristics. The classical methods of treating uterine fibroids, endometriosis and endometrial hyperplastic processes are surgical interventions, which in no way solve all the patient's problems with combined gynecological pathology [17]. Despite its limited effectiveness, organ-preserving surgical tactics are recognized today as the leading method of treating endometriosis. At the same time, we must be aware that the elimination of endometrioid heterotopias is an independent goal in the treatment of endometriosis, but not in the treatment of patients with endometriosis. If the doctor, as he generally should, wants to deal not with the disease, but with the patient, he will first of all solve the problems that bother her, such as pain, menstrual dysfunction, infertility. An

integrated approach to solving the patient's problems involves the participation of both surgical and suppressive hormonal treatment, and the share of this participation, as well as the choice of hormone therapy method, will vary significantly in individual cases. Hormone therapy for endometriosis includes antigonadotropins (danazol), gonadoliberin hormone agonists (GnRH), progestins, and combined oral contraceptives (COCs). Danazol suppresses the release of gonadotropic hormones of the pituitary gland, blocks estradiol receptors in the ovaries, increases the level of free testosterone in the blood, thus inducing a hypoestrogenic and hyperandrogenic state, which leads to regression of endometrioid heterotopias. The high androgenic activity of antigonadotropins causes a number of side effects, including a negative effect on fat and carbohydrate metabolism, weight gain, hirsutism and other manifestations of androgen-dependent dermopathy. Progestins used to treat endometriosis: dydrogesterone (Duphaston), medroxyprogesterone acetate (Provera, Depo-Provera), linestrenol (Orgametril), norethisterone (Norkolut, Primolut-nor), levonorgestrel-releasing intrauterine system (Mirena) - inhibit the growth of endometrioid tissue, cause decidualization of the endometrium and its atrophy. In large doses, they inhibit the secretion of gonadotropins and estrogens, promoting the development of amenorrhea. The effectiveness of progestins against endometriosis depends on the dose and regimen. Low doses of progestins used in a cyclic regimen are well tolerated, but their effectiveness is low. Highly effective progestin regimens have a number of disadvantages that reduce their tolerability. These include: long-term restoration of fertility after using prolonged forms, breakthrough bleeding, weight gain, edema, adverse metabolic reactions (impaired glucose tolerance, changes in the blood lipid spectrum). GnRH agonists were originally developed as drugs with greater activity and duration of action compared to endogenous GnRH. However, it turned out that long-term continuous administration of GnRH agonists provides only a short-term increase in the level of gonadotropins, and then the synthesis and secretion of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) decrease. This paradoxical effect, called "desensitization," has proven useful in the treatment of many hormone-dependent gynecological diseases. In addition to the pituitary gland, GnRH receptors are found in a number of tissues, including the ovaries, endometrium and cells of malignant tumors of the ovaries and mammary glands; therefore, the action of GnRH agonists is not limited to the central component, but also has a local character. Thus, activation of apoptosis processes in endometrioid heterotopias under the influence of GnRH agonists was detected. The complex effect on the organs of the reproductive system leads to a state of "medical pseudomenopause" and atrophy of the endometrium, ectopic endometrial glands and stroma, which ultimately helps eliminate pain and reduce the prevalence of endometrioid lesions in 75–92% of patients [17–19]. The advantages of this type of therapy include the absence of progestogenic and androgenic effects, including a negative effect on the lipid spectrum of the blood. GnRH agonists can be recommended without restrictions and provide an additional therapeutic effect for uterine fibroids, polycystic ovary syndrome, and mastopathy. Dyslipidemia, increased blood clotting and any diseases/conditions associated with the risk of thrombosis and thromboembolic complications are also neither a contraindication nor a reason for caution when prescribing these drugs. At the same time, hypoestrogenism induced by taking GnRH agonists becomes the basis for a number of side effects, such as hot flashes, headache, fatigue, insomnia, depression, sweating, vaginal dryness, weakened libido, decreased bone mineral density leading to osteopenia and osteoporosis. The side effects of therapy sometimes interfere so significantly with the quality of life that the patient is ready to choose the resumption of endometriosis symptoms over them. Additional administration of add-back therapy helps

improve tolerability. In general, GnRH agonists are rightfully considered one of the most effective and safe treatments for endometriosis [19, 20]. The therapeutic effectiveness of COCs for endometriosis is determined by its gestagenic component. Progestins in COCs reduce cell proliferation and induce apoptosis in endometrioid heterotopias. Ethinyl estradiol, the second component of COCs, serves two purposes. First, it provides endometrial stability, which minimizes the likelihood of breakthrough bleeding. Secondly, the presence of estrogen potentiates the action of progestin, apparently due to an increase in the concentration of intracellular progesterone receptors. The clinical advantages of the method lie in its good tolerability and the presence of positive effects useful in the treatment of patients with endometriosis. Thus, low-dose contraceptives help reduce menstrual blood loss, as well as the severity of dysmenorrhea [21]. The positive effect on these two common gynecological problems increases women's adherence to this treatment method. It is believed that endometriosis is associated with a slight increase in the likelihood of ovarian cancer, and another positive effect of COCs is a reduction in this likelihood to values comparable to the population. Having once been first-line drugs in the treatment of endometriosis, COCs subsequently remained for quite a long time in the shadow of newer and highly effective methods of hormonal treatment, but the synthesis of new progestins has returned interest in them. Of course, the most promising COC currently containing dienogest (Janine) is currently the most promising for the treatment of endometriosis. Dienogest successfully combines the properties of members of the 19-nortestosterone family and progesterone derivatives, and has progestogenic and antiandrogenic effects. A feature of dienogest is its metabolic neutrality, which is especially important when planning long-term treatment. The ability of the drug to have a pronounced peripheral antiproliferative effect turned out to be clinically significant.

This antiproliferative effect of dienogest involves more than a progesterone-like effect. Dienogest has the additional ability to normalize intracellular signaling systems and suppress angiogenesis, proven experimentally. Realizing its effect through gene expression, the formation of specific proteins, cytokines and growth factors, dienogest leads to an increase in the processes of apoptosis simultaneously with a decrease in the proliferative activity of endometrioid heterotopia cells. In the practice of treating endometriosis, oral contraceptives should be recommended for daily use, without pauses or withdrawal bleeding. At the beginning of the 21st century, a concept was published, the essence of which is as follows. Fundamental changes in the role of a woman in society and her lifestyle require a revision of the medical interpretation of monthly ovulation and menstruation. Ovulation, significant fluctuations in hormone levels throughout the cycle and menstruation are not only unnecessary, but also pose health risks, increasing the likelihood of ovarian cancer (continuous ovulation theory) and the risk of anemia, arthritis, bronchial asthma, dysmenorrhea, endometriosis, uterine fibroids and premenstrual syndrome [22]. Long-acting COC regimens are much more effective in reducing the risk and preventing gynecological diseases compared to standard 21-day regimens [23]. In a number of prospective studies, women with endometriosis and persistent dysmenorrhea (persisting despite cyclic use of oral contraceptives) reported a significant reduction in symptoms with daily, continuous use. The undoubted advantage of COCs over other types of hormonal therapy is the possibility of long-term, many-year use, which is very important for endometriosis. So, the goal of treating endometriosis is to relieve the patient of symptoms that bring suffering; therefore, the choice of management tactics primarily depends on the characteristics of the clinical symptoms of the disease. Surgical treatment, according to consensus, is indicated for women with

a combination of endometriosis and infertility. Obviously, heterotopically located endometrial tissue has a stimulating effect on the functional activity of peritoneal macrophages, which entails disruption of conception, implantation and pregnancy. This determines the feasibility of surgical treatment, which is confirmed by an increase in the frequency of spontaneous conception by 20% [16]. After surgery, it is desirable to restore fertility as quickly as possible, often using assisted reproductive technologies. Postoperative suppressive hormonal therapy is not carried out or its minimum course is recommended, preceding the fertility restoration program. The undisputed indication for surgery is severe chronic pelvic pain. Not so certain, but also quite reasonable, is surgical intervention for moderate pelvic pain. Postoperative hormone therapy in such situations is necessary not only to prevent relapses, but also due to its own analgesic potential. Severe pain is usually associated with deep invasive endometriosis; its pathogenesis involves pro-inflammatory cytokines (tumor necrotizing factor - TNF), IL-6, chemokines, products of immunocompetent cells (CCL2, CCL3, CCL5, etc.), which exert their influence as a direct inflammatory pain reaction, and indirectly by increasing the pain sensitivity of neuronal cells [24, 25]. The process of transmitting the pain signal induced by these factors involves genes, the expression of which, as studies show, is modulated by GnRH agonists and progestins, probably through the suppression of ONF and IL-6 [26]. For severe pelvic pain, the choice is usually made between GnRH agonists, progestins used in a continuous regimen and an adequate dose (for example, medroxyprogesterone acetate 50 mg per day), danazol. The drugs demonstrate comparable effectiveness in relieving pain symptoms [27], but differ greatly in side effects [28], and it is the expected tolerability of adverse reactions that should be taken into account when choosing a method of drug treatment.

Literature :

Kurbonova G. A., Lapasova Z. K. CURRENT VIEWS ON IRON DEFICIENCY ANAEMIA IN PATIENTS WITH CARDIOVASCULAR DISEASE //The American Journal of Medical Sciences and Pharmaceutical Research. – 2022. – Т. 4. – №. 03. – С. 59-64.

Khidirovna L. Z. et al. Significance of Syndrome Teetering in Development of Residual Pain Syndrome in Patients Operated for Lumbar Osteochondrosis //Texas Journal of Multidisciplinary Studies. – 2022. – Т. 6. – С. 59-63.

Sherali K., Zebiniso L., Gulbahor K. Features Of Anthropometric Indicators Of Children Of The First Year Of Life Born Of Mothers In The State Of Hypothyrozis //The American Journal of Medical Sciences and Pharmaceutical Research. – 2020. – Т. 2. – №. 09. – С. 64-68.

Хакимова Л., Лапасова М., Лапасова З. The use of innovative learning methods in high educational establishments as a stage of implementation of improving the quality of the educational process //Общество и инновации. – 2022. – Т. 3. – №. 1/S. – С. 121-125.

Khidirovna L. Z. Primary and Secondary Hyperalgesia //Scholastic: Journal of Natural and Medical Education. – 2023. – Т. 2. – №. 5. – С. 99-104.

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.

Лапасов С. Х. и др. Инновационные подходы в диагностике язвенной болезни у взрослых в первичном звене здравоохранения: обзор литературы //Здоровье, демография, экология финно-угорских народов. – 2018. – №. 4. – С. 68-72.

Khidirovna L. Z. et al. Significance of Syndrome Teetering in Development of Residual Pain Syndrome in Patients Operated for Lumbar Osteochondrosis //Texas Journal of Multidisciplinary Studies. – 2022. – Т. 6. – С. 59-63.

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.

Sarkisova V. ASPECTS OF THE STATE OF THE AUTONOMIC NERVOUS SYSTEM IN HYPOXIA //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 977-982.

Vladimirovna S. V. Epidemiology, Theories Of The Development, Conservative And Operative Treatment Of The Endometriosis //The Peerian Journal. – 2023. – Т. 15. – С. 84-93.

Vladimirovna S. V. About the Causes of Endometrial Hyperplasia and Forms of Endometrial Hyperplasia //Global Scientific Review. – 2023. – Т. 12. – С. 25-32.

Sarkisova V., Xegay R. Causes, Diagnosis, Conservative And Operative Treatment Of Uterine Myoma //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 198-203.

Саркисова В. В. Патогенетические отношения артериальной гипертензии и сопротивления инсулина //IQRO. – 2023. – Т. 2. – №. 1. – С. 727-731.

Vladimirovna S. V. PATHOGENETIC RELATIONSHIPS OF ARTERIAL HYPERTENSION AND INSULIN RESISTANCE //IQRO. – 2023. – Т. 2. – №. 1. – С. 685-691.

Sarkisova V., Regina X. РОЛЬ БРАДИКИНИНА В ПРОТЕКАНИИ ОСНОВНЫХ ЖИЗНЕННЫХ ПРОЦЕССОВ //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 587-593.

Sarkisova V., Numonova A., Xegay R. Аспекты Состояния Вегетативной Нервной Системы При Гипоксии //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 228-231.

Sarkisova V., Alvi I. THE PROBLEM OF COMORBIDITY OF AFFECTIVE DISORDERS AND PERSONALITY DISORDERS //Science and innovation. – 2023. – Т. 2. – №. D5. – С. 170-177.

Sarkisova V. et al. BIPOLAR AFFECTIVE DISORDER (BAR) //Science and innovation. – 2023. – Т. 2. – №. D5. – С. 165-169.

Sarkisova V. et al. CYTOKINE PROFILE IN PATIENTS WITH GRANULOMATOSIS WITH POLYANGIITIS (WEGENER'S) //Science and innovation. – 2023. – Т. 2. – №. D11. – С. 336-343.

V. Sarkisova, Z. Lapasova, F. Shernazarov, O. Rakhmanov INFLAMMATORY DISEASES OF THE PELVIC WOMEN ORGANS // SAI. 2023. №D11. URL: https://cyberleninka.ru/article/n/inflammatory-diseases-of-the-pelvic-women-organs (дата обращения: 31.01.2024).

Шерназаров Фаррух,Шерназаров Самандар,Курбаниязова В.Е.,Виктория Саркисова Владимировна. (2023). Клиническое значение микробиоты кишечника у новорожденных с геморрагической болезнью. IQRO , 2(2), 867–877. Retrieved from http://wordlyknowledge.uz/index.php/iqro/article/view/893

V. Sarkisova, I. Alvi THE PROBLEM OF COMORBIDITY OF AFFECTIVE DISORDERS AND PERSONALITY DISORDERS // SAI. 2023. №D5. URL: https://cyberleninka.ru/article/n/the-problem-of-comorbidity-of-affective-disorders-and-personality-disorders (дата обращения: 31.01.2024).

Саркисова В., Абдурахманова К. Роль гормональных препаратов в терапии гиперпластических процессов эндометрия и в частности при миоме матки //Журнал вестник врача. – 2014. – Т. 1. – №. 1. – С. 167-168.

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.

Sarkisova V., Xegay R. Causes, Diagnosis, Conservative And Operative Treatment Of Uterine Myoma //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 198-203.

Sarkisova V., Numonova A., Xegay R. АНТИБИОТИКОРЕЗИСТЕНТНОСТЬ ИЛИ БОРЬБА С ГЛОБАЛЬНОЙ УГРОЗОЙ XXI ВЕКА //Science and innovation. – 2022. – Т. 1. – №. D8. – С. 232-241.

Sarkisova V. et al. CYTOKINE PROFILE IN PATIENTS WITH GRANULOMATOSIS WITH POLYANGIITIS (WEGENER'S) //Science and innovation. – 2023. – Т. 2. – №. D11. – С. 336-343.

Vladimirovna S. V. et al. TORCH-Complex //Scholastic: Journal of Natural and Medical Education. – 2023. – Т. 2. – №. 6. – С. 183-187.

Vladimirovna S. V. et al. NEUROIMMUNOLOGICAL MECHANISMS OF THE FORMATION OF CHRONIC PAIN SYNDROME //EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE. – 2024. – Т. 4. – №. 2. – С. 45-49.

Vladimirovna S. V. et al. HYPOXIA AND ASPHYXIA //EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE. – 2024. – Т. 4. – №. 2. – С. 37-44.

Vladimirovna S. V. et al. TORCH-Complex //Scholastic: Journal of Natural and Medical Education. – 2023. – Т. 2. – №. 6. – С. 183-187.

Sarkisova, Z. Lapasova, F. Shernazarov, O. Rakhmanov INFLAMMATORY DISEASES OF THE PELVIC WOMEN ORGANS // SAI. 2023. №D11. URL: https://cyberleninka.ru/article/n/inflammatory-diseases-of-the-pelvic-women-organs (дата обращения: 12.02.2024).