

12. Swe N. N., Sendhilnathan S., van Den Berg M., Barr C. Over ground walking and body weight supported walking improve mobility equally in cerebral palsy: a randomised controlled trial. *Clin Rehabil.* 2015. Vol. 29, No. 11. P. 1108-1116.

DOI: <https://doi.org/10.1177/0269215514566249>

13. The efficacy of functional gait training in children and young adults with cerebral palsy: a systematic review and meta-analysis / A. T. C. Booth et al. *Dev Med Child Neurol.* 2018. Vol. 60, No. 9. P. 866-883. DOI: <https://doi.org/10.1111/dmcn.13708>

14. Verschuren O., Peterson M. D., Balemans A. C. J., Hurvitz E. A. Exercise and physical activity recom-

mendations for people with cerebral palsy. *Dev Med Child Neurol.* 2016. Vol. 58, No. 8. P. 798-808. DOI: <https://doi.org/10.1111/dmcn.13053>

15. Willerslev-Olsen M., Petersen T. H., Farmer S. F., Nielsen J. B. Gait training facilitates central drive to ankle dorsiflexors in children with cerebral palsy. *Brain.* 2015. Vol. 138, No. 3. P. 589-603.

DOI: <https://doi.org/10.1093/brain/awu399>

16. Willoughby K. L., Dodd K. J., Shields N. A systematic review of the effectiveness of treadmill training for children with cerebral palsy. *Disabil Rehabil.* 2009. Vol. 31. P. 1971-1979.

DOI: <https://doi.org/10.3109/09638280902874204>

The article was received
2020.09.23



UDC 618.14-002:618.177]-073.432.19

<https://doi.org/10.26641/2307-0404.2020.4.221395>

O.M. Makarchuk,
O.M. Ostrovska,
Okolokh Onieka Gibson,
I.K. Orishchak,
A.R. Cheredarchuk

ENDOMETRIAL STATE IN WOMEN WITH UTERINE FACTOR OF INFERTILITY AT THE STAGE OF PRECONCEPTIONAL CARE ACCORDING TO SONOGRAPHY AND DOPLEROMETRY DATA

*Ivano-Frankivsk National Medical University
Halytska str. 2, Ivano-Frankivsk, 76018, Ukraine*

*Івано-Франківський національний медичний університет
вул. Галицька, 2, Івано-Франківськ, 76018, Україна
e-mail: o_makarchuk@ukr.net*

Цитування: *Медичні перспективи.* 2020. Т. 25, № 4. С. 114-121

Cited: *Medicni perspektivi.* 2020;25(4):4-

Key words: *infertility, uterine factor, echostructure of the endometrium, chronic endometritis, preconceptional diagnosis*

Ключові слова: *безпліддя, матковий фактор, ехоструктура ендометрія, хронічний ендометрит, прекоцепційна підготовка*

Ключевые слова: *бесплодие, маточный фактор, эхоструктура эндометрия, хронический эндометрит, прекоцепционная диагностика*

Abstract. *Endometrial state in women with uterine factor of infertility at the stage of preconceptional care according to sonography and doplerometry data. Makarchuk O.M., Ostrovska O.M., Okolokh Onieka Gibson, Orishchak I.K., Cheredarchuk A.R. In recent years, the number of cases of uterine factors infertility is constantly growing. Unfortunately, the analysis of scientific works is characterized by the lack of data on the improvement of the diagnostic algorithm and the expediency of accentuating the significance of the preconceptional stage. The purpose of this study was to develop sonographic criteria for endometrial readiness for implantation at the stage of preconceptional care in women with uterine factor infertility. The first group included 80 women with uterine factor infertility, the second group (40 women) consisted of patients who entered the IVF program for the first time. The control group consisted of 30 women with normal fertility. Studies of the structure of the endometrium, myometrium and ovarian tissue were performed on a Voluson 760, on the 4th-6th days of the menstrual cycle (according to the*

International Endometrial Tumor Analysis (IETA) – consensus of ultrasound description of endometrial changes) and on the 20th-24th days of the cycle. To assess the indirect signs of chronic endometritis the echographic criteria developed by V.N. Demidov et al. were used. The sonographic diagnosis was verified during morphological and immunohistochemical examination. The most common menstrual disorders in women with uterine factor infertility were algodysmenorrhea – 33.3%, algohypomenorrhea – 22.2%, hypoopsomenorrhea – 64.4%. Thinning of the endometrium was significantly more often observed in the group with uterine factor of reproductive disorders; one third of patients (33.8%) had dyschronosis of the endometrial echotexture; heterogeneity of M-echo with a predominance of hyperechoic areas was diagnosed in 41.3% of cases. Hyperechogenic inclusions in the basal layer, multiple structures of a linear nature and increased echogenicity were revealed in every fifth patients and hypoechoic uterine contour – in 47.5% of cases. The most significant odds ratio associated with IVF failures and early reproductive loss was found in patients with endometriosis (OR – 5.85; 95% CI: 1.32-13.32), synechiae (OR – 2.27; 95% CI: 0.96-10.16) and polyps (OR – 2.48; 95% CI: 0.84-11.36). It was possible to distinguish the following criteria of functional readiness of the endometrium for implantation: endometrial thickness was more than 8 mm, compliance with the echostructure phase of the menstrual cycle, homogeneity of M-echo, absence of hyper- and hypoechoic inclusions, and full hemodynamics in the vascular pool of the pelvis.

Реферат. Стан ендометрія в жінок з матковим фактором безпліддя на етапі прекоцепційної підготовки за даними сонографії та доплерометрії. Макарчук О.М., Островська О.М., Околюх Оніека Гібсон, Оріщак І.К., Чередарчук А.Р. В останні роки відмічена тенденція до зростання частки маткових чинників безпліддя. Аналіз наукових робіт розчаровує відсутністю даних щодо удосконалення діагностичного алгоритму, доцільності акцентуації значущості прегравідарного етапу. Метою цього наукового дослідження стала розробка сонографічних критеріїв готовності ендометрія до імплантації на етапі прекоцепційної підготовки в жінок з матковим фактором безпліддя. У першу групу увійшли 80 жінок з матковим фактором безпліддя, другу групу (40 жінок) склали пацієнтки, які вперше вступали до програми IVF. Контрольну групу склали 30 жінок з нормальною фертильністю. Дослідження структури ендометрія, міометрія та тканини яєчників виконували на апараті Voluson 760, на 4-6 день менструального циклу (згідно з International Endometrial Tumor Analysis (IETA) – консенсусу ехографічного опису змін ендометрія) та на 20-24 дні циклу. Для оцінки опосередкованих ознак хронічного ендометриу використовували ехографічні критерії, розроблені В.Н. Демидовим та співав., а також сонографічний діагноз верифікували в ході морфологічного та імуногістохімічного дослідження. Найбільш поширеними порушеннями менструальної функції в жінок з матковим фактором безпліддя стали альгодисменорея – 33,3%, альгогіпоменорея – у 22,2%, гіпоопсоменорея – 64,4%. Витончення ендометрія достовірно частіше відмічено в групі з матковим фактором репродуктивного нездоров'я, у третини (33,8%) дисхроноз ехоструктури ендометрія, неоднорідність М-ехо з переважанням гіперехогенних ділянок – у 41,3% спостережень. Гіперехогенні включення в базальному шарі, множинні структури лінійного характеру та підвищеної ехогенності зафіксовані в кожній п'ятій пацієнтки, а гіпоехогенний контур матки – у 47,5% спостережень. Найбільш значуще відношення шансів, що слід пов'язати із невдачами при проведенні програми IVF та ранніми репродуктивними втратами, визначено в пацієнток з ендометріозом (OR - 5,85; 95% CI: 1,32-13,32), синехіями (OR - 2,27; 95% CI: 0,96-10,16) та поліпами (OR - 2,48; 95% CI: 0,84-11,36). Вдалося виділити такі критерії функціонального щодо готовності до імплантації ендометрія, а саме: товщина ендометрія більше 8 мм, відповідність ехоструктури фазі менструального циклу, однорідність М-ехо, відсутність гіпер- та гіпоехогенних включень, а також повноцінна гемодинаміка в судинному басейні малого таза.

In recent years, the number of cases of uterine factors infertility is constantly growing which many authors associate with the widespread use of intrauterine contraception, a negative tendency to increase the frequency of abortion, invasive manipulations including diagnostic endoscopy [1, 8, 10]. Antibacterial resistance and the evolution of the microbial factor in recent decades also play an important role, which has led to the development of asymptomatic obscure forms of the inflammatory process, as well as changes in immunological, metabolic and hormonal homeostasis [5, 8, 10, 11].

In recent decades, endometriometric pathology occupies a leading place in the structure of gynecological morbidity and is included in the list of important factors of reproductive failure, pain synd-

rome, uterine bleeding, etc. [1, 3, 8, 13]. Despite numerous randomized trials, nowadays there is no consensus on the impact of intrauterine pathology and surgery on reproductive outcomes. However, it is undeniable that the state of the endometrium and uterine cavity, the latent course of the inflammatory process, possible endocrine and immunological disorders, as well as anatomical factors, have a negative impact on implantation processes, leading to reproductive health disorders [2, 3, 8, 10, 11, 13].

It should be noted that the frequency of uterine factor in the genesis of female infertility according to domestic and foreign authors is from 25-42% to 46-67%, and more than half of the cases happen during the reproductive age [3]. Uterine pathology, hyperplastic processes and endometrial polyps,

fibroids, intrauterine synechiae occur in 21–47% of cases in women suffering from infertility, including failed IVF attempts [2, 13]. According to Rudakova E.B. et al. in 54% of cases, female infertility is accompanied by pathological changes in the uterus; endometrial dysfunction was diagnosed in 41% of women [9, 13], so when examining patients with infertility or habitual miscarriage it is important to assess the uterine cavity and endometrium [2, 5, 10]. The success of implantation in IVF programs, as well as the probability of miscarriage, significantly depends on the state of the endometrium, especially endometrial receptivity [4, 7, 12, 15, 16]. Endometrial receptivity disorder is considered to be one of the most significant factors in failed IVF attempts and early reproductive loss [4, 12, 15, 16]. According to N. Ledee-Bataile [14] and other literature sources, 2/3 of implantation failures are associated with inadequate endometrial receptivity [1, 6, 7, 8].

However, the lack of a single concept of the pathogenesis of implantation insufficiency in the case of uterine infertility factors, the feasibility of studying the mechanisms of formation and relationship of pathological processes of the endometrium, which underlie macro- and microscopic disorders of its function, substantiation of the complex analysis which would consider features of the structure and function of the uterine mucous membrane, optimization of sound treatment approaches, require the implementation of this research. The analysis of scientific works reveals the lack of emphasis on the need to improve the diagnostic algorithm, the feasibility of restoring the reproductive health of this group of women after treatment and underlining the importance of the preconceptional stage.

According to many researchers, further progress of scientific research is impossible without a comprehensive detailed approach to the assessment of the endometrial condition [10, 12, 13] which requires optimization of the diagnostic algorithm to characterize its organic and functional capacity (using both invasive and non-invasive methods) and the correction of pathological changes, if it is possible [12].

Non-invasive endometrial evaluation involves transvaginal ultrasonography and 3D ultrasonography, transvaginal color Doppler mapping in combination with pulsed Doppler and ultrasound, and, if necessary, magnetic resonance imaging. In the preclinical diagnosis of uterine factor infertility, especially endometrial hyperplastic processes, polypoid, etc. the ultrasound plays the most important role, as the interpretation of the obtained characteristics (thickness, structure) in relation to its real condition (degree of maturity, receptivity)

activity of the cytokine component and growth factors) determine the readiness for implantation and is extremely important for the establishment of the "implantation window", the optimal time of embryo transfer, hormonal and drug support during pregnancy, which ultimately determines the tactics, pathogenetic treatment and successful preconceptional care. [2, 7, 10, 12].

Objective interpretation and a comprehensive approach to ultrasound characteristics of the endometrium, the use of three-dimensional ultrasound and Doppler allow us to assess the volume of the endometrium and uterine body, the state of the vascular network, to measure blood flow parameters in vessels with hypo- and hypervascularization or avascular areas. Indirect signs that may indicate chronic endometritis, which underlies, according to most researchers, endometrial receptivity disorders, are changes in the sources of basal layer fibrosis, thinning and asymmetry of the anterior and posterior walls in two-dimensional ultrasound and vascularization disorders [2, 10, 12].

In this regard, the development of sonographic criteria for endometrial readiness for implantation at the stage of preconception in women with uterine factor infertility is important for practical gynecology and reproductive medicine, which is the purpose of this study.

MATERIALS AND METHODS OF RESEARCH

The first main group included 80 women with uterine factor infertility. The second main group (40 women) consisted of first-time IVF patients. The control group consisted of 30 women with normal fertility who had already given birth and applied for a preventive examination. Women of the compared groups were comparable in age, the average age was 31.8 ± 3.4 years, most of them had an ovulatory menstrual cycle, and every second patient had a habitual miscarriage, failed IVF attempts in the anamnesis and early reproductive loss. The proportion of patients with a history of unsuccessful IVF attempts was 32.5%. The information obtained during the previous study was entered into an individual observation map and supplemented, if necessary, by informal interviews and questionnaires, which allowed obtaining social characteristics of surveyed women regarding their age, social and family status, menstrual function, gynecological and somatic diseases, etc. All examined women underwent ultrasound examination of the pelvic organs in the cycle preceding the IVF program or pregnancy planning. Examination of the structure of the endometrium, myometrium and ovarian tissue was performed on a Voluson 760, on the 4th-6th days of the menstrual cycle (according to the International Endometrial

Tumor Analysis (IETA) – consensus of ultrasound description of endometrial changes) and on the 20th-24th days of the cycle, using an abdominal frequency sensor 3.5 MHz and vaginal sensor with a frequency of 5 MHz according to the conventional method: review transabdominal scan followed by transvaginal detailing of the uterine structure, ovaries and assessment of the degree of the endometrial vascularization, biometrics, ovaries, including two-dimensional ultrasound and Doppler. To assess the indirect signs of chronic endometritis the echographic criteria developed by V.N. Demidov et al. was used [3]. The diagnosis of probable chronic endometritis, made with the help of sonography, was usually verified during morphological and immunohistochemical examination. For statistical processing of the obtained data, file tables were applied using the program "Statistica 6", with the calculation of average relative values and errors ($M \pm m$), ($P \pm m$), Fisher-Student test (t) and the significance of differences (p-value, the differences were considered significant at $p < 0,05$).

RESULTS AND DISCUSSION

Menstrual disorder was observed in 45 (56.3%) patients of the first group and 17 (42.5%) – in the second main group, while in the control group menstrual disorders were found in only 4 people (13.3%), that is, the share is 2.3-3.2 times smaller against groups of patients with infertility. The most common menstrual disorders in women with uterine infertility were algodysmenorrhea, revealed in 15 (33.3%) patients; algohypomenorrhea was present in the history of 10 women (22.2%), which is twice as common as in women of the second group. Patients with uterine factor infertility are also characterized by a significant proportion of hypoopsomenorrhea (64.4%), the number of diagnosed cases is many times higher than in women who gave birth and in those who applied for reproductive technology for the first time. The identified features of the menstrual cycle in patients of both study groups suggest a low index of reproductive health in this category of patients, and the relationship of menstrual disorders with dysfunction of the hypothalamic-pituitary-ovarian axis and decreased activity of the endocrine system in general cause impaired immunological resistance and depression of local factors of local immunity of the genital mucosa [8]. In addition, menstrual dysfunction as a symptom of uterine pathology is evidence of hormone-dependent processes (fibroids, endometrial hyperplasia, etc.) and can be seen as a marker of increased risk of implantation disorder and miscarriage.

Analytical studies revealed that a group of patients with uterine factor infertility factor had

suffered from various childhood infections, chronic diseases of the tonsils, diseases of the genitourinary tract, endocrine and dysmetabolic dysfunction (diffuse toxic goiter, hypothyroidism and obesity) that accumulated symptoms of reproductive disorders.

The most common uterine pathologies in patients of the first group were adenomyosis and endometriosis (49 cases (61.3%)), uterine fibroids (29 people (36.3%)), endometrial hyperplasia and polyps (19 cases (23.8%)), and synechiae of the uterine cavity (19 women (23.8%)). In the second main group, uterine pathology is represented in a smaller proportion, mainly due to endometrial hyperplasia and polyposis (10.0%), adenomyosis and endometriosis (27.5%), dysfunctional uterine bleedings were revealed in 32.5% of cases. Statistically significant differences between the main groups were found in such clinical conditions as endometriosis, uterine fibroids, polyps and synechiae of the uterine cavity ($p < 0.05$). The most significant odds ratio in patients with endometriosis (OR – 5.85; 95% CI: 1.32-13.32), synechiae (OR – 2.27; 95% CI: 0.96-10.16) and polyps (OR – 2.48; 95% CI: 0.84-11.36), which should be associated with IVF program failures and early reproductive loss.

According to the results of the research, the following factors that significantly reduce reproductive potential and increase the risk of implantation failures when using IVF programs were found: menstrual disorder (odds ratio – 2.43), endometriosis (odds ratio – 3.69), fibroids (odds ratio – 4.27), endometrial polyps (odds ratio – 6.28) and synechiae of the uterine cavity (odds ratio – 5.38), high index of somatic pathology (odds ratio – 1.48) and metabolic and endocrine dysfunction (odds ratio – 2.31).

Taking into account the high index of somatic and gynecological morbidity, as well as timely diagnosis of uterine factors allow expanding the diagnostic algorithm and forming sono-morphological criteria for endometrial readiness for implantation.

One of the most important sonographic parameters that characterizes the condition of the endometrial component is the thickness of the endometrium, which in patients of both major groups was significantly less than in women who have already performed their reproductive function, but in women with uterine factor infertility, these data were most indicative. In the first phase of the cycle – on the 6th-8th day, the thickness of the endometrium in both main groups was 5.2 ± 2.2 mm and 5.5 ± 2.1 mm, respectively, against 7.0 ± 2.6 mm in the control group. In the second phase of the menstrual cycle – on the 20th-24th day the indicators in the first group were 7.9 ± 2.6 mm, in the second group – 8.2 ± 2.3 mm, in the control group – 11.1 ± 3.1 mm.

The least endometrial thickness was observed in patients with polyps and synechiae of the uterine cavity, with cases of reproductive loss and failed IVF attempts in the history.

The data obtained by us as a result of this stage of scientific research confirm the search for negative effects of endometrial thinning on the consequences of in vitro fertilization programs and increasing the proportion of miscarriages. In addition, according to a number of authors, a decrease in endometrial thickness may be an echographic sign of chronic endometritis, as prolonged inflammation and mucosal trauma during diagnostic and therapeutic interventions contribute to significant thinning of the uterine mucosa and hyperplasia of connective tissue elements.

It should be noted that the ultrasound image of the endometrium, corresponding to the day of the menstrual cycle, as the most frequent sonographic marker of endometrial potential failure, was only in one third of patients of the first main group (27-33.8%), while in women with physiological fertility it was observed only in isolated cases (2.5%).

The uterine cavity was dilated in 11 cases (13.8%) in the first main group and in 3 (7.5%) women of the second group, and the limits of dilation ranged from 0.3 mm to 0.8 mm, with episodes of asymmetric distribution, that meets the sonographic criteria for signs of chronic endometritis according to V.N. Demidov et al. [1, 3]. M-echo heterogeneity with a predominance of hyperechoic sites was observed in 33 cases (41.3%) in patients with a history of miscarriage and failed IVF attempts and in 11 (27.5%) women in the second group, while in patients with preserved fertility this ultrasound feature was not observed.

High proportion of more than half of the examined patients of the first main group of sonographic picture of heterogenous myometric structure, expansion of its cavity to 0.3 or more due to fluid content, irregular thickening of the endometrium, the presence of areas of increased or decreased echogenicity of the medial structure of the uterine body as well as hyperechogenic structures of the basal layer of the endometrium suggest the likelihood of chronic endometritis.

In addition, according to the sonographic study, M-echo formations of different echogenicity with clear contours, sometimes with cystic inclusions and deformation of the mid-hyperechogenic M-echo line, which should be considered as signs of polyps, were found.

Hyperechogenic inclusions, both single and multiple, were detected in 21 cases (26.3%) in the history of reproductive loss, 19 (23.8%) women had visualized multiple structures of a linear nature and

increased echogenicity, and a slightly smaller proportion of such sonographic changes were observed in women who first applied to the clinic of reproductive medicine because of primary infertility – 3 cases (7.5%).

Hypoechoic contour of the uterus was observed in 38 women (47.5%) of the first main group, a slightly lower percentage (in 11 people – 27.5%) was diagnosed in the second group.

Varicose veins of the parametrium were found in 33 people (41.3%) with frequent reproductive losses and uterine infertility, in patients who applied to the clinic of reproductive medicine for the first time these sonographic signs were diagnosed 1.5 times less often, however in women with preserved fertility, the visualization of this pathology did not differ significantly from the indicators of the second group. Having used the A.E. Volkov's criteria of ultrasound classification of varicose veins of the pelvis [2] the diameter of varicose veins, which did not exceed 10 mm, was noted in the study, in some cases there was a combination of varicose veins of the parametrium and visualization of the hypoechoic contour of the uterine cavity.

The above-mentioned sonographic signs of probable chronic endometritis were not revealed in 14 patients (17.5%) with uterine factor infertility and in 17 (42.5%) women who first applied to the clinic of reproductive medicine because of infertility, as well as in 8.7 % in the case of preserved fertility.

According to the results of Doppler blood flow in the right and left uterine arteries and subjective assessment of the degree of vascularization of blood flow in the myometrium and subendometrial area, the reduced visualization of myometrial vessels in the second phase of the menstrual cycle was revealed. It should be mentioned that radial arteries are visualized in 53.8% of cases, basal – in 48.8%, spiral – in 23.8% of cases ($p < 0.05$), and the final diastolic blood flow rate was significantly lower than in women of the control group, which is evidence of the severity of dyscirculatory disorders on the background of a long-term inflammatory process in women with uterine factors of reproductive disorders. Our results are comparable with the existing scientific notations on the increase in the proportion of hemodynamic disorders in the vascular pool of the small pelvis in the case of chronic inflammatory process of the endometrium, which is morphologically represented by capillary network deficiency, stroma fibrosis with sclerosis of the spiral arteries, formation of multiple vessels of capillary type and clinically represented by endometrial hypoplasia for the period of the "implantation

window" with a decrease in hemodynamic parameters in the uterine vessels [2, 9].

According to the results of a comprehensive assessment of the obtained indicators of 2D ultrasound and Doppler at the stage of preconceptional care it was possible to identify the following functional criteria in terms of the endometrial readiness for implantation, namely: endometrial thickness greater than 8 mm, correspondence of echostructure to the phase of the menstrual cycle, homogeneity of M-echo, absence of hyper- and hypoechoic inclusions, as well as full-fledged hemodynamics in the vascular pool of the small pelvis.

CONCLUSIONS

1. Signs of probable chronic endometritis were more often visualized in women with a history of uterine infertility, frequent reproductive losses, and failed IVF attempts, indicating a decisive role for uterine factors in the genesis of infertility.

2. Analysis of echosonographic signs of probable chronic endometritis suggested that endometrial thinning was significantly more common in groups of women with uterine factor of reproductive disorders than in patients who first applied for IVF,

and in one third of such patients (33.8 %) the echostructure of the endometrium did not correspond to the phase of the menstrual cycle; the heterogeneity of M-echo with a predominance of hyperechoic areas was observed in 41.3% of cases, which is obviously a consequence of invasive interventions in the anamnesis. Hyperechogenic inclusions in the basal layer, multiple structures of a linear nature and increased echogenicity were recorded in one in five patients, and hypoechoic uterine contour – in 47.5% of cases.

3. Thus, a comprehensive study using sonographic criteria can increase the informativeness and accuracy of diagnosis of predictors of endometrial implantation failure, which is especially important in IVF programs. And the formed sonographic criteria of the ability of the endometrium for implantation can be clarified and expanded in the list in the course of further research, it is also possible to improve the algorithm of preconceptional care.

Conflict of interests. The authors declare no conflict of interest.

REFERENCES

1. Borys EN, Suslykova LV, Kaminskyi VV. [Optimization of preparation of morphofunctional endometrial structure in assisted reproductive technology programs]. *Reproduktivnaia endokrinologiya*. 2015;1:60-63. Ukrainian. doi: <https://doi.org/10.18370/2309-4117.2015.21.60-63>
2. Volkova EYu, Korneeva IE, Silant'eva ES. [The role of uterine hemodynamics in assessing of endometrial receptivity]. *Problemy reproduktivnoi meditsiny*. 2012;2:57-62. Russian. Available from: <https://www.mediasphera.ru/issues/problemy-reproduktivnoi/2012/2/downloads/ru/031025-72172012213>
3. Demidov VN, Gus AI. [Pathology of the uterus cavity and endometrium]. *VMK: prakticheskoe posobie*; 2001. Russian. Available from: http://med-vvolske.ru/docs/2018_04_06/-R8BsDQTR36K6saGAZHKK9iaFe.pdf
4. Serova OF, Tamazyan GV, Sovaev NI, Trifonova IA, Eliseev EN. [The clinical significance of the morphological and functional state of the endometrium in reproductive disorders]. *Voprosy ginekologii, akusherstva i perinatologii*. 2010;4:43-48. Russian. Available from: <http://www.phdynasty.ru/katalog/zhurnaly/voprosy-ginekologii-akusherstva-i-perinatologii/2010/tom-9-nomer-4/10195>
5. Korobko OM. [The role of a comprehensive study of the uterine cavity in improving the effectiveness of female infertility treatment after unsuccessful attempts at assisted reproductive technologies]. *Zdorove zhenshchiny*. 2011;9:163-4. Ukrainian. <https://med-expert.com.ua/ua/publishing-activity-uk/zdorove-zhenshchiny-publishing-activity-uk/>
6. Kotsabyn NV, Makarchuk OM. [Role of the endometrium functional state as a leading factor in the successful implantation of a fertilized egg]. *Arkhiv klinichnoi medytsyny*. 2014;2:8-10. Ukrainian. Available from: https://issuu.com/glvysnyk.if.ua/docs/akm__2_2014
7. Leviashvili MM, Demura TA, Mishieva NG, Fayzullina NM, Nazarenko TA, Kogan EA. [Endometrial receptivity assessment in patients with unsuccessful in vitro fertilization programs]. *Akusherstvo i ginekologiya*. 2012;4:65-69. Russian. Available from: <https://aig-journal.ru/articles/Ocenka-receptivnosti-endometriya-u-pacientok-s-bezuspeshnymi-programmami-ekstrakorporalnogo-oplodotvoreniya-v-anamneze.html>
8. Pyrohova VI, Kozlovskiy IV. [Rehabilitation of reproductive function in women with chronic endometritis]. *Zdorove zhenshchiny*. 2015;2:94-96. Ukrainian. doi: <https://doi.org/10.15574/hw.2015.98.94>
9. Rudakova EB, Davydov PV, Davydov VV. [Intrauterine pathology in women who underwent the first attempt at in vitro fertilization and embryo transfer]. *Lechashchii vrach*. 2012;11:6-11. Russian. Available from: https://www.lvrach.ru/foreign_articles/
10. Alieva KU, Smolnikova VYu, Dyuzheva EV, Ipatova MV, Kalinina EA. [Modern approaches to the comprehensive assessment and preparation of the endometrium in patients with IVF]. *Ginekologiya*. 2012;14(3):16-18. Russian. Available from: <http://www.fesmu.ru/elib/Article.aspx?id=264017>
11. Tabolova VK. [The profile of local gene expression of growth factors and cytokines in the endometrium of the "implantation window" period in chronic

endometritis]. *Akusherstvo i ginekologiya*. 2014;12:74-78. Russian. Available from: <https://aig-journal.ru/articles/Profil-lokalnoi-ekspressii-genov-rostovyh-faktorov-i-citokinov-v-endometrii-perioda-implantacionnogo-okna-pri-hronicheskom-endometrite.html>

12. Titchenko YuP, Zarochentseva NV, Arshakyan AK, Men'shikova NS. [The use of ultrasound research methods in assessing the status of the endometrium in patients with chronic endometritis and miscarriage]. *Rossiyskiy vestnik akushera-ginekologa*. 2014;1:55-58. Russian. Available from: <https://www.mediasphera.ru/issues/rossijskij-vestnik-akushera-ginekologa/2014/1/031726-6122201419>

13. Burlev VA, Kuz'michev LN, Onishchenko AS, Piyasova NA, Shchetinina NS. [Influence of endometrial functional activity on IVF results and embryo transfer: molecular mechanisms of fertility regulation]. *Problemy reproduktsii*. 2010;16(2):41-52. Russian. Available from: <http://www.fesmu.ru/elib/Article.aspx?id=221027>

14. Lédée-Bataille N, Olivennes F, Kadoch J, Dubanchet S, Frydman N, Chaouat G, Frydman R. Detectable levels of interleukin-18 in uterine luminal secretions at oocyte retrieval predict failure of the embryo transfer. *Human Reproduction*. 2004;19(9):1968-73. doi: <https://doi.org/10.1093/humrep/deh356>

15. Jacqueline F Donoghue, C Jay McGavigan, Fiona L Lederman, Leonie M Cann, Lulu Fu, Eva Dimitriadis, Jane E Girling, Peter A W Rogers. Dilated Thin-Walled Blood and Lymphatic Vessels in Human Endometrium: A Potential Role for VEGF-D in Progesterone-Induced Break-Through Bleeding. *PLoS One*. 2012;7(2):e30916. doi: <https://doi.org/10.1371/journal.pone.0030916>

16. Maryam Eftekhari, Mozghan Sayadi, Farideh Arabjahan. Transvaginal perfusion of G-CSF for infertile women with thin endometrium in frozen ET program: A non-randomized clinical trial. *Iran Journal of Reproductive Medicine*. 2014;12(10):661-6. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4248151/>

СПИСОК ЛІТЕРАТУРИ

1. Борис Е. Н., Сусликова Л. В., Каминский В. В. Оптимизация подготовки морфофункциональной структуры эндометрия в программах вспомогательных репродуктивных технологий. *Репродукт. эндокринология*. 2015. № 1. С. 60-63. DOI: <https://doi.org/10.18370/2309-4117.2015.21.60-63>

2. Волкова Е. Ю., Корнеева И. Е., Силантьева Е. С. Роль маточной гемодинамики в оценке рецептивности эндометрия. *Пробл. репродукции*. 2012. № 2. С. 57-62. URL: <https://www.mediasphera.ru/issues/problemy-reproduktsii/2012/2/downloads/ru/031025-72172012213>

3. Демидов В.Н., Гус А.И. Патология полости матки и эндометрия. ВМК: практ. пособие. 2001. URL: http://med-vvolske.ru/docs/2018_04_06/-R8BsDQTR36K6saGAZHKK9iaFe.pdf

4. Клиническое значение морфофункционального состояния эндометрия при нарушениях репродуктивной функции / О. Ф. Серова и др. *Вопр. гинекологии, акушерства и перинатологии*. 2010. № 4. С. 43-48. URL: <https://aig-journal.ru/articles/Ocenka-receptivnosti-endometriya-u-pacientok-s-bezuspeshnymi-programmami-ekstrakorporalnogo-oplodotvoreniya-v-anamneze.html>

5. Коробко О. М. Роль комплексного дослідження порожнини матки у підвищенні ефективності лікування жіночого безпліддя після невдалих спроб допоміжних репродуктивних технологій. *Здоровье женщины*. 2011. № 9. С. 163-164. URL: <https://med-expert.com.ua/ua/publishing-activity-uk/zdorove-zhenshchiny-publishing-activity-uk/>

6. Коцабин Н. В., Макачук О. М. Роль морфофункционального стану ендометрію як провідного фактору успішної імплантації заплідненої яйцеклітини. *Архів клін. медицини*. 2014. № 2. С. 8-10. URL: https://issuu.com/glvisnyk.if.ua/docs/akm__2_2014

7. Оценка рецептивности эндометрия у пациенток с безуспешными программами экстракорпорального оплодотворения в анамнезе М. М. Ле-

виавшили и др. *Акушерство и гинекология*. 2012. №4. С. 65-69. URL: <https://aig-journal.ru/articles/Ocenka-receptivnosti-endometriya-u-pacientok-s-bezuspeshnymi-programmami-ekstrakorporalnogo-oplodotvoreniya-v-anamneze.html>

8. Пирогова В. И., Козловський І. В. Реабілітація репродуктивної функції у жінок з хронічним ендометритом. *Здоровье женщины*. 2015. №2. С. 94-96. DOI: <https://doi.org/10.15574/hw.2015.98.94>

9. Рудакова Е. Б., Давыдов П. В., Давыдов В. В. Внутриматочная патология у женщин, прошедших первую попытку экстракорпорального оплодотворения и переноса эмбрионов. *Лечащий врач*. 2012. № 11. С. 6- URL: https://www.lvrach.ru/foreign_articles/

10. Современные подходы к комплексной оценке и подготовке эндометрия у пациенток программы ЭКО / К. У. Алиева и др. *Гинекология*. 2012. Т. 14, № 3. С. 16-18. URL: <http://www.fesmu.ru/elib/Article.aspx?id=264017>

11. Таболова В. К. Профиль локальной экспрессии генов ростовых факторов и цитокинов в эндометрии периода «имплантационного окна» при хроническом эндометрите / *Акушерство и гинекология*. 2014. № 12. С. 74-78. URL: <https://aig-journal.ru/articles/Profil-lokalnoi-ekspressii-genov-rostovyh-faktorov-i-citokinov-v-endometrii-perioda-implantacionnogo-okna-pri-hronicheskom-endometrite.html>

12. Титченко Ю. П., Зароченцева Н. В., Аршакян А. К., Меньшикова Н. С. Применение ультразвуковых методов исследования в оценке состояния эндометрия у пациентов с хроническим эндометритом и невынашиванием беременности / *Рос. вест. акушера-гинеколога*. 2014. № 1. С. 55-58. URL: <https://www.mediasphera.ru/issues/rossijskij-vestnik-akushera-ginekologa/2014/1/031726-6122201419>

13. Функциональная активность эндометрия влияет на результаты ЭКО и перенос эмбрионов:

молекулярные механизмы регуляции фертильности / В. А. Бурлев и др. *Пробл. репродукции*. 2010. Т. 16, № 2. С. 41-52.

URL: <http://www.fesmu.ru/elib/Article.aspx?id=221027>

14. Detectable levels of interleukin-18 in uterine luminal secretions at oocyte retrieval predict failure of the embryo transfer / N. Lédée-Bataille et al. *Human Reproduction*. 2004. Vol. 19, No. 1. P. 1968-1973. DOI: <https://doi.org/10.1093/humrep/deh356>

15. Dilated Thin-Walled Blood and Lymphatic Vessels in Human Endometrium: A Potential Role for VEGF-

D in Progesterin-Induced Break-Through Bleeding / F. Jacqueline et al. *PLoS One*. 2012. Vol. 7, No. 2. e30916. DOI: <https://doi.org/10.1371/journal.pone.0030916>

16. Eftekhari Maryam, Sayadi Mozhgan, Arabjehani Farideh. Transvaginal perfusion of G-CSF for infertile women with thin endometrium in frozen ET program: A non-randomized clinical trial. *Iran Journal of Reproductive Medicine*. 2014. Vol. 12, No. 10. P. 661-666. URL: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4248151/>

The article was received
2020.09.14

