

## **Modern Interpretation of Preconception Preparation For Women with Chronic Hypoplastic Endometritis**

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**Abstract:** In recent years, the interest of researchers in the specific nosology of pelvic inflammatory diseases (PID) - chronic endometritis - has increased significantly, which is explained by the presence of a whole set of problems related to etiopathogenesis, diagnostic criteria and characteristics. Approaches to the treatment of this pathology. The chronic inflammatory process in the endometrium is one of the main causes of menstrual disorders, miscarriage, infertility, failed IVF attempts, endometrial hyperplastic processes and sexual dysfunction. The need to continue to develop advanced methods of diagnosis and treatment of chronic endometritis is related to its medical and social importance, since the majority of patients with this pathology are women of active reproductive age [2, 4, 5, 7, 11, 13, 14].

**Key words:** Chronic endometritis, change of etiological structure with increasing importance of opportunistic and viral flora, mainly associative nature of pathogenic flora

Chronic endometritis is a clinical and morphological syndrome in which, as a result of continuous damage to the endometrium by an infectious agent, many secondary morphofunctional changes occur that disrupt the cyclic changes and receptivity of the mucous membrane of the uterine cavity.

The incidence of chronic endometritis, according to various authors, is widespread - from 0.2 to 66.3%, with an average of 14%. Apparently, such a wide range of the frequency of this pathology is explained by the results of examination of different groups of gynecological patients, as well as the use of different clinical and morphological criteria for diagnosis, which in some cases leads to overdiagnosis or, on the contrary, in the tissues underestimate the severity of changes. However, in recent years there has been a trend of increasing cases of chronic endometritis, which is clearly due to the spread of sexually transmitted infections, the widespread and often irrational use of intrauterine contraceptives, the increase in the number of abortions and various intrauterine drugs related to manipulations [4, 7, 11, 16, 18, 19].

Currently, the generally accepted point of view is that chronic inflammation occurs in the endometrium as a result of an imbalance between the hormonal and immune systems of the body, on the one hand, and pathogens - representatives of the microbiocenosis. Long-term and often asymptomatic persistence of infectious agents in the uterine mucosa leads to clear changes in its

structure, disrupts tissue proliferation and cyclic transformation, prevents normal implantation and placenta, forms an inadequate pathological response to the onset of pregnancy.

The characteristics of chronic endometritis in the current stage are as follows:

- lack of symptoms;
- change of etiological structure with increasing importance of opportunistic and viral flora;
- mainly associative nature of pathogenic flora (in at least 91-96% of cases);
- increasing resistance to traditional methods of treatment;
- disagreements in defining diagnostic criteria;
- inconsistency between clinical manifestations and examination data and morphological changes in the organ;
- the severity of consequences for the reproductive field in the form of synechia and sclerosis formation in the uterine cavity, menstrual disorders, conditions for the development of endometrial hyperplastic processes, pregnancy and infertility, IVF failures;
- decrease in the quality of life of women due to many clinical manifestations of the disease (menstrual disorders, chronic pelvic pain, dyspareunia, leucorrhoea, psychological problems, etc.);
- long treatment period and high costs.

The classification includes the division of chronic endometritis taking into account the etiological factor (according to C. Buckley, H. Fox, 2002):

- non-specific (against opportunistic microorganisms - *Escherichia coli*, streptococci, staphylococci, *Proteus*, fecal enterococci) against the background of bacterial vaginosis, intrauterine contraception, radiation therapy);
- specific (caused by chlamydia, gonococci, tubercle bacilli, mycoplasmas, viruses, fungi, protozoa, parasites).

It should be noted that in 30% of cases with histologically confirmed chronic endometritis, sterile cultures of the endometrium are detected, which indicates the important role of opportunistic flora in the development of the inflammatory process or the insufficient identification of the pathogen (especially in this case). viral invasion) [4, 7, 11, 14, 16, 18, 19]. In addition, the importance of the primary trigger gradually disappears, and secondary infection, immunological disturbances and dysfunction of the affected organ play a major role in the disease.

According to modern concepts, except for lactobacilli and bifidobacteria, almost all microbes present in the vagina can participate in the inflammatory process. Microecological disorders often serve as a mechanism for triggering the pathological process and then maintaining it.

In response to the introduction of a harmful factor, the mediator reaction at the site of inflammation, the activation of neutrophils and macrophages leads to a violation of blood microcirculation and rheological properties [3]. After these changes in the tissues, ischemia and hypoxia appear, reactive oxygen species and hydrogen peroxide are formed, which causes the process of lipid peroxidation and damage to cell membranes. In addition, inflammatory infiltrate cells intensively produce anti-inflammatory cytokines, growth factors and a number of other

biologically active substances. Continued local fibrinolytic activity under the influence of anti-inflammatory factors enhances angiogenesis in primary fibrinous adhesions, which increases morphological changes in uterine tissue and forms intrauterine synechiae [7]. Vascular endothelial growth factors, which affect angiogenesis, increase endothelial cell proliferation and vascular permeability, resulting in intermenstrual spotting and uterine bleeding. The possibility of development of pathological proliferation or atrophy against the background of chronic endometritis is determined by the imbalance between two multidirectional processes - proliferative activity and apoptosis of endometrial cells [16, 19].

In contrast to acute inflammation, chronic inflammation often loses its biological meaning, because in this case the ability of tissues to destroy and eliminate the damaging factor and complete regeneration significantly reduced or absent. The persistence of microorganisms belonging to the normal and opportunistic microflora of a person is due to their having antigens in common with tissue antigens of the body, therefore, autoimmune aggression plays an important role in the pathogenesis of chronic inflammation [21]. As a result of inducing autoimmune reactions with the help of cross-antigens and the development of secondary immunodeficiency, microorganisms, on the one hand, become insensitive to the effects of the host's immune system, and on the other hand, autoantibodies destroy not only damaged, but also healthy organ tissue [1]. Since the immune response of the mucosa is incomplete, the opportunistic flora in the uterine cavity can eventually become the leading microbial factor of the inflammatory process.

Clinical manifestations of chronic endometritis are not pathognomonic, but still to some extent reflect the depth of structural and functional changes in endometrial tissue. Various types of uterine bleeding are common - premenstrual, postmenstrual, intermenstrual. Complaints of painful pains in the lower abdomen, dysmenorrhea and dyspareunia are very frequent, and serous and serous-purulent fistulas are noted from the genital tract. Infertility (usually secondary) is diagnosed in 60.4% of cases, as well as unsuccessful attempts at IVF and embryo transfer in 37% [13]. It is noteworthy that 67% of patients with the development of anxiety-depressive disorders experience an increase in the level of personal anxiety [5].

#### Diagnosics

Diagnostic problems are related to the lack of a clear clinical picture of the disease, which include: it is not timely and fully examined and can lead to a late start of treatment, as well as to unreasonably prescribing several courses of antibacterial therapy.

Diagnosis of chronic endometritis is based on an integrated clinical approach using a number of anamnestic, instrumental and laboratory criteria.

Identification of possible pathogens involves the use of various informative methods, including: vaginal smear, femoflor, culture of discharge from the vagina and cervical canal, culture of the endometrium, culture of material from the removed intrauterine contraceptive device, specificity determination. detection of microorganisms in scrapings from the cervical canal using molecular methods, as well as antibodies to PID pathogens.

Sonographic criteria for chronic endometritis VN Demidov, filled regularly. Ultrasound examination is performed on days 5-7 and 22-24 of the menstrual cycle. The most common symptoms of the disease: changes in the ecostructure of the endometrium, expansion of the uterine cavity depending on the fluid content, diffuse focal and cystic changes in the subendometrial zone

of the myometrium, unevenness of the closing line and anterior asymmetry. and posterior walls of the uterus, thinning of M-echo, visualization of gas bubbles in the uterine cavity. Every second patient has several listed symptoms. The sensitivity of the method is 78%, the specificity is 82% [19].

Doppler measurements of uterine vessels are of particular importance during dynamic monitoring to evaluate the effectiveness of disease treatment. Violation of blood flow in uterine vessels, damage mainly at the level of basal and spiral arteries, as well as difficulties in seeing terminal arteries, indicate a significant violation of tissue perfusion against the background of a chronic inflammatory process. endometrium [19].

Hysteroscopy, based on macroscopic signs, can detect chronic endometritis in 35-60% of cases, so it is always necessary to perform a morphological examination of endometrial biopsy, which is the "gold standard" for the diagnosis of the disease [6]. In some cases, it is recommended to use an immunohistochemical method to determine the marker of plasma cells of the surface glycoprotein Syndecan-1 - CD138, which increases the accuracy of morphological examination of chronic inflammation in the endometrium by 25-30%. [16].

Assessment of hormonal status is necessary for adequate subsequent rehabilitation of patients and to decide the nature of hormonal therapy in the 2nd stage of treatment.

#### Treatment of chronic endometritis

It should be noted that incorrect therapeutic measures can cause the disease to become a hidden, permanent form, which greatly complicates further treatment.

At the first stage, it is believed that it is necessary to destroy the harmful agent or, in the case of viral invasion, to reduce its activity; for this, etiotropic drugs are used, taking into account the sensitivity of the isolated flora. as well as immunotropic agents.

There are different views on the necessity of antibiotic therapy for chronic endometritis, and the debate continues [4, 7, 10, 11, 14, 16-19]. We believe that in modern conditions, antibiotics should only be used when symptoms of the disease worsen, including. appear in response to physiotherapeutic procedures, and their appointment during remission is unreasonable, because it often leads to the development of dysbacteriosis, superinfection (autoinfection with opportunistic flora) and the exacerbation of the existing inflammatory process in the uterus.

Of course, the need to sanitize the endometrium is unquestionable, but traditional antibacterial therapy for chronic nonspecific endometritis turns out to be ineffective in most cases, taking into account the gradual change of priority pathogens, the development of resistance. antibiotics and their low concentration at the site of inflammation, as well as the selection of resistant strains of microorganisms. According to the WHO, 68 of the 115 main antibiotics currently developed are ineffective, and this trend is increasing. In recent years, the presence of several superinfections in which most modern antibiotics are ineffective or ineffective has been reported - Escherichia coli, staphylococci, Klebsiella and streptococci. Moreover, according to expert estimates, if antimicrobial drug resistance increases by only 15-17%, patient treatment costs will double [20].

It should be remembered that all chemotherapy drugs have significant side effects and organ toxicity to one degree or another. A significant part of the antibiotic is often inactivated by the liver and bypasses the source of inflammation and accumulates in fatty tissues. When carrying out

traditional therapy with parenteral forms of antibiotics, it is also possible to reduce the effectiveness of treatment due to a violation of the delivery of drugs to the designated place [4, 7]. According to VA. Lebedeva (2012), the main causes of complications of chronic inflammation are processes of hyperplasia of connective tissue, followed by sclerosis and hemodynamic disturbances in uterine tissue in the form of venous stagnation, which prevents the flow of drugs to the inflamed endometrium. All this leads to the ineffectiveness of treatment in one way or another, including in the long term (relapses, chronic, complications).

It can be seen that the rational limitation of pharmacotherapy, the introduction of methods and methods with multifaceted therapeutic effects, when the optimal clinical effect is achieved with a minimum drug load on the patient's body.

An important aspect of treatment is the normalization of vaginal microbiocenosis. For this purpose, antiseptics, antacids, eubiotics and probiotics have been proposed for local use.

The second stage of treatment of chronic endometritis should be aimed at restoring the morphofunctional potential of tissues and eliminating the consequences of secondary damage: correcting the consequences of metabolic diseases and acidosis, restoring hemodynamics and the activity of the endometrial receptor apparatus. helps to normalize the structure and function of the endometrium. For this purpose, various options of metabolic therapy (vitamins, antiplatelet agents, antihypoxants, enzymes, amino acids), physical factors, hormonal drugs (combined hormonal contraceptives, HRT) and spa treatment are used [4, 5, 14, 15, 19].

Physiobalneotherapy methods are determined differentially depending on the age of the patient, the duration of the disease, the functional state of the ovaries and the interest in childbearing.

For the treatment of chronic non-specific endometritis, we have recently used polyvalent bacteriophage and infrared laser intrauterine injection procedures, which allows us to carry out an antimicrobial effect by precisely targeting a wide range of possible pathogens of the inflammatory process. in the absence of a significant systemic effect in the uterine cavity, as well as to achieve an immunomodulatory effect, to improve hemodynamics in the pelvic organs and to stimulate the activity of receptors of the endometrium.

It is known that when two therapeutic factors are used simultaneously, their physiological and therapeutic effects can be mutually enhanced. At the same time, in a number of cases, the onset of new therapeutic effects was noted in clinical practice, which allows activation of general sanogenetic mechanisms and local reactions aimed at combating the pathological process.

When exposed to low-intensity laser radiation at the organ level, the sensitivity of receptors changes, interstitial edema and tissue tension decrease, blood flow rate normalizes, new collaterals are formed, and the duration of the inflammatory phase decreases. Improving microcirculation, improving tissue absorption of oxygen and stimulating cell proliferative activity activates reparative tissue regeneration. In addition, laser radiation has a bacteriostatic and/or bactericidal effect on some types of pathogenic flora, and also increases its sensitivity to antibacterial drugs [2, 15, 17].

The advantages of bacteriophages include their high sensitivity and specificity for homologous microorganisms. resistant to antibiotics. At the same time, bacteriophages do not destroy the normal microflora, do not have a toxic or inhibitory effect on the body's reactivity, and can be used simultaneously with other drugs. The activity of bacteriophages against pathogens of inflammatory

diseases is quite high - from 72 to 90%. Administration of bacteriophages for the treatment of infectious diseases induces specific and non-specific immune factors, which is particularly effective in the treatment of long-term diseases resulting from immunodeficiency [12].

The expediency of the combined use of laser and bacteriophage in the treatment of PID, including endometritis, empirically proven by us in pre-clinical experience. When bacteriophage preparations are irradiated with an infrared laser for 3 minutes at the frequencies most commonly used in therapy (80-1500 Hz). Under the influence of low-intensity laser radiation of the infrared spectrum, it was found that the lytic activity of phage particles does not decrease (Proteus strains) and against a number of clinically important, potentially pathogenic microorganisms (staphylococci, certain serovars). Escherichia coli and Pseudomonas aeruginosa strains) have a strong tendency to increase.

The course of treatment in our proposed method begins on the 5-7th day of the menstrual cycle, after the end of menstruation. Bacteriophages are injected into the uterine cavity three times a day. After emptying the bladder, the patient is placed on a gynecological chair. In aseptic conditions, 4-7 ml of liquid polyvalent piobacteriophage preparation is slowly injected into the uterine cavity through a thin flexible catheter using a syringe, depending on the size of the uterus and the patient's reaction to the injection. After that, a tampon moistened with bacteriophage is inserted into the posterior vaginal opening to prevent leakage of the drug and to implement its antimicrobial effect at the level of the vaginal mucosa. Then a laser therapy session is performed. For this, laser emitters of the infrared spectrum with a wavelength of 0.89  $\mu\text{m}$ , a pulse repetition rate of 80-1500 Hz, and a pulse power of 5 W (with mirror inserts). Laser therapy sessions are performed daily, the total duration of the treatment course is 7-10 days.

The method makes it possible to increase the effectiveness of treatment by improving microcirculation in the pelvic organs, normalizing the trophism of the inner lining of the uterus, eliminating swelling and infiltration of the endometrium, suppressing the growth of non-specific microflora, and optimizing local and general immune factors. , and reduce the frequency of possible systemic side effects.

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