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# ASSESSMENT OF THE RISK OF ENDOMETRIAL HYPERPLASIA IN THE PERIMENOPAUSAL PERIOD.

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**SUMMARY.** Endometrial hyperplasia is a gynecological disease characterized by the growth of the endometrium - the inner layer of the uterus, as a result of which its thickness and volume increase. According to statistics, a similar disease is diagnosed in 10-20% of patients. The disease develops in young women of childbearing age. With the onset of menopause, the risk of developing the disease increases several times. Normally, the functional layer of the endometrium increases in the first half of the cycle: the uterus is preparing for a possible pregnancy. If fertilization does not occur, then during menstruation, the functional layer is rejected and removed from the body. These cyclical changes are regulated by the correct ratio of female sex hormones. All processes depend on the correct ratio of female sex hormones. At the slightest hormonal failure, the maturation and rejection of the endometrium is disturbed, the cells actively divide, but are not removed in time, the inner layer of the uterus thickens, and excessive growth can occur both in separate areas and evenly. After a certain time, the endometrium is still rejected, and profuse bleeding occurs. In the absence of treatment, the process is constantly repeated. With endometrial hyperplasia, a variety of complications are possible, one of the serious ones is the malignancy of the process, developing into cancer. This article provides data related to this pathology.

**RELEVANCE.** Endometrial hyperplasia is most often observed in premenopausal women suffering from dysfunctional uterine bleeding that occurs after a delay in the next menstruation [1,4,10]. Bleeding can be prolonged with moderate or profuse blood loss, sometimes profuse (not stopping without the use of special measures in a hospital setting). To confirm the diagnosis of endometrial hyperplasia, the level of blood hormones is examined, an ultrasound examination of the small pelvis with a vaginal sensor is performed [2,3,7]. The main diagnostic method is a separate diagnostic curettage performed during hysteroscopy. Curettage is prescribed on the eve of menstruation or on the 1st day of

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bleeding. Part of the removed endometrial tissue is sent for histological examination to identify the form of the disease (glandular, glandular-fibrous or fibrous) and the presence of atypical (malignant) cells [5,6,8,9]. At present, the radioisotope study of the uterus is becoming increasingly important. With the help of this diagnostic study, it is possible to determine not only the presence of hyperplastic processes in the endometrium, but also the degree of their activity (to assess the risk of malignancy of the process).

**Purpose of the study.** To determine the main risk factors for endometrial hyperplastic processes in women in the perimenopausal period.

**Materials and research methods.** We examined 46 postmenopausal women. All patients complained of scanty spotting from the genital tract, 10 of them had leucorrhoea, 6 had pain. The combination of all three symptoms was present in 2 patients. The average age of the patients was 54.1 years, the average age of menarche was 14.9 years, i.e., it was higher than in the population, the average age of menopause was 49.5 years, the average duration of the postmenopausal period at the time of the examination was 5, 6 years old The average number of pregnancies was 3.2, and none of the patients had primary infertility. ThehistorydataisshowninFigure 1.

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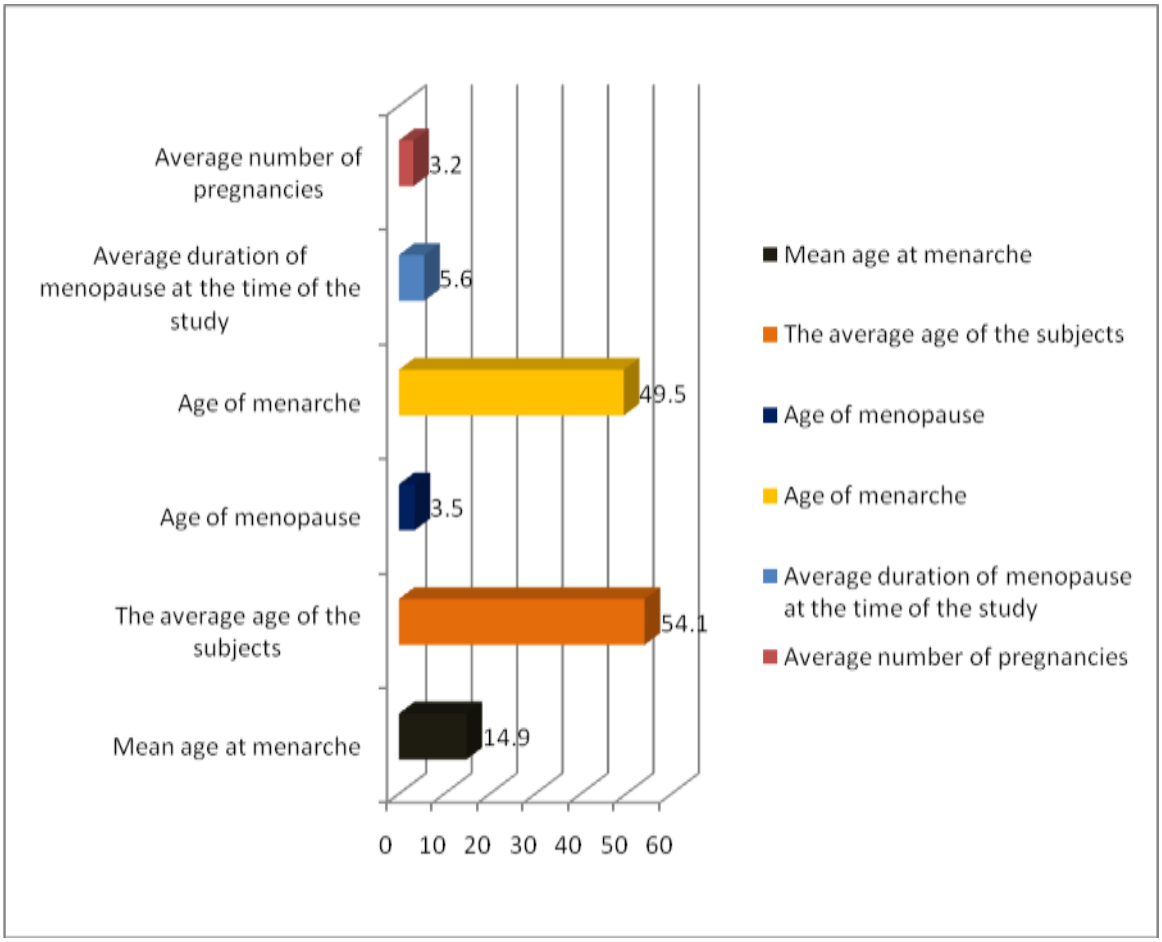
**Figure 1. Anamnestic data of the studied patients.**




None of the patients had a dramatic change in body weight during their lifetime. In the anamnesis of the examined patients, there were indications of inflammatory processes of the endometrium (in 8), endocervix (in 10), uterine appendages (in 6), vagina (in 6), numerous intrauterine manipulations, in particular artificial termination of pregnancy, diagnostic curettage, and in 4 patients - for the treatment of dysfunctional uterine bleeding. Recurrent symptoms were noted in 38 patients, 12 women were unsuccessfully treated in the past with 17-alpha-hydroxyprogesterone capronate for recurrent endometrial hyperplasia. Of the concomitant diseases, in addition to the "normal" age-related pathology, the most common was anemia of moderatese verity (26 women).

During the clinical examination, the patients did not reveal pronounced endocrine-metabolic disorders: in 24 women - 0 points in relation to the I pathogenetic variant of hyper plastic processes, in 22-1 points, of which 10 were due to obesity, which was of a

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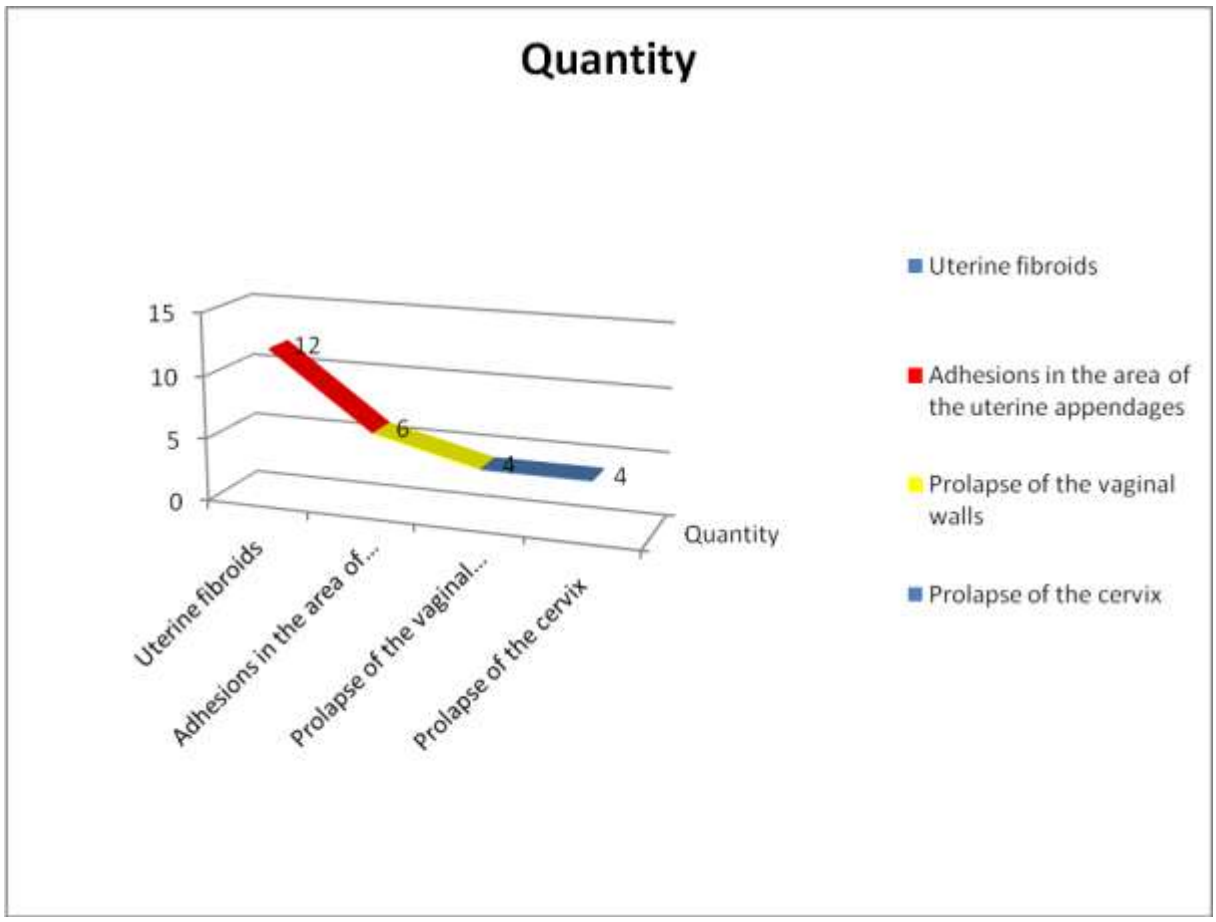
universal nature, in 12 - interstitial uterine myoma , the size of which did not exceed the size of the uterus at 7 weeks of pregnancy. Gynecological examination revealed uterine fibroids in 12 patients, adhesions in the uterine appendages in 6 patients, prolapse of the vaginal walls and cervix in 4 patients. All information is shown in Figure 2. See Figure 2 below.




In the rest of the patients, no pathology was detected during gynecological examination. The pupil symptom was absent in all patients. In 28 women, hyperemia and polyposis of the urethra were also noted. Cytological examination of vaginal smears revealed I-II reaction of the vaginal epithelium in all patients, however, cytological examination of aspirate and lavage from the uterine cavity revealed proliferation of the glandular epithelium in all 46 patients, of which 10 were pronounced. In addition, 10 out of 46 patients had individual signs of cellular atypia. In the contents of the uterine cavity in 16 patients, elements of inflammation (macrophages, histio cytes, cells in a state of lysis) were also determined; in 12 patients, structure less masses and elements of cellular decay.

During hysterography in 28 out of 46 patients, an x-ray picture was obtained, characteristic of a hyperplastic process in the endometrium - unevenness, serration of the contours of an unincreased, and sometimes slightly reduced, uterine cavity. Against this background, 8 patients had more pronounced filling defects. Hysteroscopy with separate diagnostic curettage was performed in 32 patients. When determining the indications for hysteroscopy, the results of previous diagnostic curettage and our studies were taken into account. With the help of hysteroscopy in 24 patients, a thin endometrium was revealed throughout, in 4 - small polyposis growths, in 4 - endometrial polyps against the background of atrophic mucosa. Given the absence of clinical and laboratory signs of hyperestrogenia, as well as the identified signs of the inflammatory process in 28 patients, we assumed that in the rest of the women, the cause of endometrial epithelium proliferation is a chronic inflammatory process of the endometrium. In this regard, all 46 patients underwent local and general treatment with drugs that have anti-inflammatory, reparative and anabolic effects. For local application in the form of intrauterine instillations, dimexide dimethyl sulfoxide, enzyme preparations (chymotrypsin, lidase, RNase, DNase), hydrocortisone were used. In the absence of contraindications, patients were prescribed prodigiosan intramuscularly. To stimulate anabolic processes in the endometrium, anabolic steroids or cyclic hormone replacement therapy were used in compliance with dosages corresponding to the level of hormones in the natural menstrual cycle.The course of treatment consisted of 8 intrauterine instillations, carried out every other day, injections of prodigiosan on the same days. Anabolic steroids or cyclic hormone therapy was continued up to 3 months. The clinical effect was evaluated 2 weeks and 3 months after the end of instillations. At the same time, control studies were performed: after 2 weeks, a cytological examination of aspirate from the uterine cavity, and after 3 months, a radioisotope and cytological examination. All patients received a positive clinical effect. During the first control cytological study, the following results were obtained: proliferation of the glandular epithelium was preserved in 16 patients, of which 1 had a pronounced hyperplastic process, individual signs of cellular atypia were found in 4, elements of inflammation in 15, structureless masses and elements of cellular decay in 11 patients .

Thus, during the first control study, a decrease in the proliferative and stability of the inflammatory components was noted, but the frequency of cytological signs of cellular decay increased. During the second control cytological examination, the following results were obtained: proliferation of the glandular epithelium was preserved in 4 patients, elements of inflammation were found in 6, structureless masses and elements of cellular decay were found in 4 patients. Cytological signs of a pronounced hyperplastic process were not found in any of the patients. In 32 patients, no pathological changes were noted during cytological examination of aspirate from the uterine cavity. The results obtained by us allowed us to suggest a possible variant of the pathogenesis of endometrial hyperplastic processes, which has not yet been discussed in the literature. In the postmenopausal period, a regular age-related atrophy of the external and internal genital organs occurs. Under these conditions, all or almost all of the biological barriers that prevent the penetration of infection into the internal genital organs are impaired or absent. As a result, some postmenopausal women, especially those with a burdened gynecological history, are likely to develop chronic endometritis and endocervicitis against the background of atrophic endometritis and endocervix.Further development of this process, apparently, can go in different ways: a destructive purulent inflammatory process, often with the development of pyometra, or a long-term productive inflammatory process with degenerative-proliferative changes, impaired repair and differentiation of cellular structures. It cannot be ruled out that the data obtained by us and other authors on the proliferative activity of the glandular epithelium in a significant proportion of postmenopausal patients with histologically established endometrial atrophy are explained precisely by degenerative-inflammatory changes. It is known that the long-term existence of actively proliferating cells, in this case, endometrial cells, regardless of the cause that caused the proliferation, facilitates the implementation of a hypothetical oncogenic factor. It is clear that therapy with drugs with progesterone-like action can be effective only if the proliferation is caused by hyperestrogenia. If proliferation is caused by an inflammatory process against the background of atrophy, progesin therapy, in our opinion, is not justified, since it exacerbates degenerative-catabolic processes in the endometrial epithelium.

Based on all of the above, we can assume the following stages in the development of hyperplastic processes in post menopause against the background of endometrial atrophy:

1) atrophy of the endometrium and endocervix

2) chronic atrophic endometritis and endocervicitis, in which elements of inflammation and some proliferation of the glandular epithelium are determined cytologically

3) pronounced proliferative changes with the formation of micropolyps;

hysteroscopy in these cases reveals atrophy and polypoid areas of the endometrium, cytological examination - a pronounced proliferation of glandular epithelium, hysterography - signs of a hyperplastic process, 4) polyps of the endometrium or endocervix.

Cytological diagnosis of a polyp or polypous hyperplasia against the background of endometrial atrophy is very difficult, since in these cases the same cytological picture is observed as in nonspecific endometritis. The proof of the validity of our proposed explanation of the pathogenesis of endometrial hyperplastic processes in post menopause is the high efficiency of our treatment.

**CONCLUSION.** Thus, in some postmenopausal women with bloody discharge, cytological, radiological and endoscopic signs of a hyperplastic process in the endometrium, apparently, are due to inflammatory and degenerative changes. Progesterone therapy is not indicated for such patients, as it exacerbates the degenerative-catabolic processes in the endometrium. Pathogenetically substantiated and effective is the use of drugs with anti-inflammatory and reparative-anabolic action. Effective treatment of hyperplastic processes of the endometrium, developing against the background of its atrophy, can be the prevention of cancer of the uterine body.

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