

## ЛЕКЦІЯ

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**Endometriosis**

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**I. Scientific-methodical ground of theme.** Endometriosis is one of the most common diseases of the reproductive system of women. It has medical aspect (disorders of functions of the genital organs, infertility), as well as social one (quality of life of women gets worse). The study of the main points of the pathogenesis, clinic, diagnosis and treatment of endometriosis allows to learn in practice the important methods of examinations in gynecology, to improve skills of evaluation of clinical situations, to perform necessity medical care based on the principles of evidence-based medicine. An important component of lecture is study management of diseases, that promotes early diagnosis of pathology and effective treatment of it.

**II. Educational aims of lecture.** Lecture covers the theories of development of endometriosis, peculiarities of clinical course, principles of diagnosis and treatment.

**III. The purposes of development of the person.** Young specialists need to identify the disease at early stages, that will allow to save the reproductive function of woman.

**IV. Plan of the lecture**

1. What is genital endometriosis.
2. Classification of endometriosis.
3. Theories of development of endometriosis.
4. Clinical manifestations.
5. Diagnosis of endometriosis.
6. Treatment of endometriosis.
7. Literature.

**1. Genital endometriosis** is a benign hormonal dependent disease based on heterotopia of endometrium on the background of disorders of hypothalamic-pituitary-ovarian system, immune disbalance in the presence of a genetic propensity.

Endometriosis takes the third place after pelvic inflammatory diseases and uterine myoma. Endometriosis is a condition of women of reproductive age, but can occur in girls with established menstrual function and women in post-menopause, receiving replacement hormonal treatment. It has a prevalence rate of 20-50% in infertile women and as high as 80% in women with chronic pelvic pain.

**2. Classification.***I. Genital endometriosis.*

## 1. Internal endometriosis.

1.1. Endometriosis of body of uterus (I, II, III stages (adenomyosis) depending on the depth of the defeat of the myometrium):

- glandular, cystic, fibrosis forms;
- focal, nodal, diffuse forms.

## 1.2. Endometriosis of cervical canal.

## 1.3. Endometriosis of intramural part of uterine tubes.

## 2. External endometriosis.

## 2.1. Peritoneal endometriosis:

- endometriosis of ovaries (infiltrative, tumoral forms);
- endometriosis of uterine tubes;
- endometriosis of pelvic peritoneum (red, black and white forms).

## 2.2. Extraperitoneal endometriosis:

- endometriosis of vaginal part of cervix;
- endometriosis of vagina, vulva;
- retrocervical endometriosis;

- endometriosis of uterine ligaments;

- endometriosis of parametrial, paravesical, paracolpal fat (with or without growth into urine bladder, rectum).

## 3. External-internal endometriosis.

4. Combined forms of genital endometriosis (genital endometriosis and other genital or extragenital pathology).

*II. Extragenital endometriosis* - endometriosis of gastrointestinal tract, urinary organs, skin, umbilicus, postoperative wound, lungs, pleura.

**3. Theories of development of endometriosis.** Etiology is unknown, but there are many theories of development of endometriosis. The most common and well studied theories are:

1. Embryonal and dysontogenetic theory. Endometriosis develops from offset plots of embryonic tissue, of which in the process of embryogenesis genital organs of the woman are formed, and, in particular, the endometrium is located in unusual place.

2. Theory of endometrial origin. Endometriosis develops from the elements of the endometrium, which grow into the wall of the uterus, ovaries, fallopian tubes. Disbalance of sexual hormones and surgical procedures (abortions, diagnostic curettage, manual examination of the uterus after delivery, caesarean section, enucleation of myomatous nodes) promote growing in of endometrium. Surgical trauma of the endometrium may cause penetration of the elements of the mucous membrane of the uterus in blood, lymph and spread them to other organs and tissues.

3. Transformation of coelomic epithelium. Endometriosis develops as a result of metaplasia of embryonic peritoneum or coelomic epithelium.

4. Retrograde menstruation and implantation theory. Fragments of the mucous membrane of the uterus desquamate from uterus during menstruation. They are transported through fallopian tubes as a result of reflux and fall into the abdominal cavity and are implanted in various organs and tissues.

5. Hormonal theory. Endometriosis develops as a result of disbalance of sexual hormones caused by disorders of the central regulation of the hypothalamic-pituitary-ovarian relations

6. Immunological theory. Antigens, produced by degrading endometrial proteins, have been identified, they stimulate an immune response characterized by peritoneal irritation and fibrosis. There appears to be evidence of decreased cellular immunity to endometrial tissue in sufferers.

7. Lymphatic and vascular spread. Vascular and lymphatic embolization to distant sites outside the peritoneum is probable and endometriotic tissue has been found within lymph channels, lymph nodes and pelvic veins.

8. Genetic and familial aspects. There are racial differences and a higher incidence of endometriosis is encountered in the first-degree relatives of patients. Monozygotic twins are markedly concordant for endometriosis.

*Risk factors:*

- in anamnesis – pathological labor, gynecological operations (abortions, cesarean section, uterine curettage, electrocoagulation, cryosurgery and electroexcision of cervix);
- hormonal disorders;
- long use of intrauterine contraceptives;

- family endometriosis (in mother, sisters);
- decrease of immunological tolerance.

*The macroscopic picture of endometriosis.* Endometriosis may have the form of nodes, infiltrations without clear contours or cystic formations, full of hemorrhagic or thick brown liquid. Endometriosis is characterized by the following features:

- the absence of connective capsule around it;
- the ability to infiltrative growth in surrounding organs and tissues with the destruction of them. This can be explained by enzymatic activity of endometriosis, the ability to provide the lipolytic enzymes;
- the ability of endometriosis for metastasis.

**4. Clinical manifestations.** There is a wide variation - some women are asymptomatic yet have a severe degree of endometriosis on laparoscopy, others have only one or two localized deposits and experience considerable pain. Main clinical symptoms are:

- dark brown discharges from the genital tract before the beginning and to the end of menstruation during 3-5 days, which can be explained by emptying of endometrial cavities into uterus;

- disorders of the menstrual cycle like hyperpolymenorrhea, this symptom is more pronounced by diffuse form of adenomyosis;

- pain is a classic symptom of endometriosis. It appears before and during menstruation (cyclic pain), and is more pronounced at the nodal form of adenomyosis (chronic pain). Endometriosis should be considered in a patient presenting with significant dysmenorrhea (secondary dysmenorrhea). Deep dyspareunia may be due to scarring of the uterosacral ligaments, nodularity of the rectovaginal septum, cul-de-sac obliteration, and/or uterine retroversion. All of these may also lead to chronic backache. These symptoms are exaggerated during menses;

- infertility. Luteal phase deficiency and luteinized unruptured follicles syndrome occur with increased frequency.

- anemia.

Endometrioid heterotopias of perineum and vagina have a view of blue round or irregularly shaped lesions - "eyes". Before menstruation size of these lesions is increasing, and during menstruation dark blood is allocated from them.

Foci of endometriosis in the vaginal part of cervix have small size (up to 5 mm in diameter), reddish color of the background of pale-pink mucous membrane of the cervix. Before menstruation they become blue-purple color, increase and bleed.

The endometrioid cyst of ovary can be unilateral or bilateral, has various sizes. Typical signs are adhesions to surrounding tissues, dense capsule, hemorrhagic content that has the color of chocolate ("chocolate" cysts), chronic pain, growing on before or during menstruation, with irradiation to the back, sacrum and rectum.

By retrocervical endometriosis heterotopias are developed on the back surface of the cervix and isthmical part of the uterus, as well as at the level of attachment of the sacro-uterine ligaments. Dense, small fixed nodes, sharply painful on palpation, which are increased before menstruation are determined behind cervix by gynecological examination. The basic symptom is pain, which increase before and during menstruation and irradiate in vagina, sacrum, rectum.

#### 5. Diagnosis.

1. Complains:

- pain - algodysmenorrhea, pain in low abdomen, dyspareunia;

- infertility (primary, secondary);

- hemorrhagic syndrome - poor blood discharges some days before or after menses, metrorrhagia, hyperpolymenorrhea, disorders of menstrual cycle;

- prolonged uneffective treatment of chronic adnexitis, metritis;

- psychoneurological disorders;

- disorders of function of surrounding organs (dysuria, pain defecation).

2. Bimanual examination, vaginal and rectal examinations (size and shape of the uterus are changed - before menstruation sizes of uterus are increased (up to about 8-9 weeks of pregnancy), after the end of menstruation reduced by 2-3 weeks (up to 6-7 weeks). The uterus becomes ball form.

3. Ultrasound examination (classic chocolate cyst of the ovary). The typical appearance is that a cyst containing low-level homogenous internal echoes consistent with old blood.

4. Magnetic resonance imaging (MRI), computer tomography. MRI is helpful in detecting rectal involvement and has been shown to accurately detect rectovaginal endometriosis and cul-de-sac obliteration in more than 90% of cases when sonographic gel was inserted in the vagina and rectum;

5. Hysteroscopy, hysterosalpingography, colposcopy, rectoromanoscopy, cystoscopy.

6. Laparoscopy. Laparoscopy is considered the primary diagnostic modality for endometriosis. Evidence of endometriosis was found during laparoscopy in 20-50% of asymptomatic women. The classic lesions of the disease are blue-black or have powder-burned appearance. However, the lesions can be red, white or nonpigmented. Peritoneal defects and adhesions are also indicative. Bear in mind that microscopic evidence of endometriosis may be found in normal-appearing peritoneum.

7. The final stage of diagnosis is histological investigation of biopsy material and removed tissues.

Differential diagnosis - myoma, chronic adnexitis, genital tumors, hyperlastic processes of endometrium, ectopic pregnancy, nephroptosis, appendicitis, paraproctitis, proctitis, colitis, adhesive ileus obstruction.

#### 6. Treatment depends on:

• age;

• localization and spread of disease;

• stage of symptoms and duration of disease;

• presence of fertility and necessity of recovery of reproductive system;

• presence of other gynecological diseases;

• effectiveness of previous treatment;

• diseases of other organs and systems.

#### 1. Hormonal therapy

- Estrogen-gestagenic drugs (combined oral contraceptives).

Monophase drugs (Regulon, Logest, Marvelon, Diane-35) are used for 1 tablet daily constantly from the 1<sup>st</sup> till the 21<sup>st</sup> day of menstrual cycle, two- and three-phase drugs (Tri-Regol, Tricvilar) - from the 5<sup>th</sup> till the 25<sup>th</sup> day of menstrual cycle. Duration of treatment is 6-12 months. Combined oral contraceptives suppress the secretion of gonadotropic emissions, inhibit the synthesis of steroids in the ovaries and proliferative processes in endometrium. Cyclic processes in endometrium and endometrioid heterotopias are blocked. Regressive changes which lead to sclerosis and obliteration of endometrioid foci are developed after long-term use of such therapy.

- Gestagens - progesterone, utrogestan, dufaston (10 mg 1-3 times a day orally from the 5<sup>th</sup> till the 25<sup>th</sup> day of menstrual cycle or from the 14<sup>th</sup> - till the 26<sup>th</sup> day of menses for 6-9 months); medroxyprogesterone acetate (Depo-provera) - 50 mg 1 time a week or 100 mg once in two weeks intramuscularly for a period of 6 months; 17-oxyprogesterone capronat 12,5% - 1 ml once a week on the 7<sup>th</sup>, 14<sup>th</sup>, 21<sup>st</sup> day of menses for 3-6 months,

norethisteron (Norcolut, Primolut NOR) 5-10 mg per day from the 5<sup>th</sup> till the 25<sup>th</sup> day of menstrual cycle or from the 14<sup>th</sup> till the 26<sup>th</sup> day of menses during 6-9 months.

- Antigonadotropins – danazol, danol, danogen. They block the ovulatory release of gonadotropins and receptors of estradiol, progesterone and androgens in the ovaries. Danazol is used in dose 800 mg per day for 6-8 months.

- Agonists of gonadotropin releasing hormones (GnRH) – triptoreline (Diphereline, Decapeptyl), goserelin (Zoladex), Buserelin. Agonists of GnRH block the receptors in the gonadotropic zones of anterior part of the pituitary gland and inhibit the secretion of gonadotropins. So, the secretion of sex hormones in the ovaries decreases. Drugs of prolonged action (deposited form) are: Zoladex – 3.8 mg subcutaneous injection in the abdominal wall once in 28 days; Decapeptyl-Depo 3.75 mg intramuscularly once in 28 days, Buserelin - endonasal spray, daily dose of 900 mg for an irrigation of the nasal mucous membrane (for 2 pressings 3 times a day). Duration of treatment is 3-6 months.

- Antiestrogens – Tamoxifen (20-40 mg daily for 6-9 months), Toremifene (10-20 mg 2-3 times a day for 6-9 months).

2. Nonspecific anti-inflammatory therapy:

- Nonsteroidal anti-inflammatory therapy – Diclofenac natrii, Indometacin, Mesulid;

- Contrycal.

3. Medicaments that influence on central nervous system – sedatives, psychotherapy, tranquilizers.

4. Systemic enzymotherapy.

5. Immunomodulators, antioxidants, vitamins.

6. Hepatoprotectors.

7. Physiotherapy.

8. Treatment of other extragenital diseases.

9. Diet.

Indications for surgery:

- internal endometriosis and hyperplastic processes of ovaries or precancer diseases of endometrium;

- adenomyosis (diffuse or node form) with hyperplasia of endometrium;

- endometrioid cysts of ovaries (more than 5 cm);

- ineffectiveness of treatment during 6 months;

- diseases of other organs and systems and disturbance of their function;

- purulent diseases of appendages of uterus;

- adhesive process of ampular part of tubes combined with endometriosis which is the main reason of infertility;

- umbilical endometriosis;

- endometriosis of postoperative scar;

- endometriosis combined with abnormalities of female genitalia;

- presence of somatic pathology that can be treated by hormones.

Operations. By adenomyosis subtotal hysterectomy without appendages with excision of a mucous membrane of the cervical canal is performed. Cryo- and laser therapy, radiosurgery are recommended in patients with endometriosis of cervix. Endometrioid ovarian cysts can be removed by laparotomy or laparoscopy. Total hysterectomy is recommended by combined adenomyosis, retrocervical endometriosis and the defeat of the cervix. Use of hormonal therapy after surgery for at least 3-6 months is recommended for the effectiveness of surgical treatment for relapse prevention.

### Literature

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