Background and precancerous diseases of female genital.

Malignant neoplasms of female genital organs

In benign tumors of the external genitals include fibroma, leiomyoma, lipoma (adipose tumor), myxoma (mucous tumor), hemangioma, lymphangioma, papilloma (papillary tumor), hydroadenoma.

Fibroma – this tumor is mainly localized inside the labia majora or in a thin submucous layer of vagina and it'is formed by cells of the connective tissue and collagen fibers.

Leiomyoma ***of the external genitals*** – a tumor that is formed from smooth muscle fibers or transverse, mainly in the tissues of the labia majora or vaginal wall.

Lipoma – a tumor that formed mature fatty tissue with connective tissue fibers in the pubic area and labia majora.

Lipoma

- Lipomas are benign, slow-growing, circumscribed tumors of fat cells arising from the subcutaneous tissue of the vulva
- The largest vulvar lipoma reported in the literature weighed 44 pounds.
- Lipomas are the second most frequent benign vulvar mesenchymal tumor. Because of the fat distribution of the vulva, most lipomas are discovered in the labia majora and are superficial in location.
- They are slow growing, and their malignant potential is extremely low.

- *Hemangioma*– a tumor that arises due to atelectasis vessels of the skin (as node) and mucous membranes of external genital organs.
- *Lymphangioma* – a benign tumor that develops from the lymphatic vessels of small nodules (blue color and soft consistency).
- *Papilloma* – epithelial tumor with papillary excrescence in the form of thin peduncle or wide area in the labia majora .
- *Hydroadenoma* – tumor, which is formed from elements of the sweat glands in younger women in the pubis and labia majora.

Papilloma

- Warty sessile growth arises most usually from labium major.

Hydradenoma

- The hidradenoma is a rare, small, benign vulvar tumor that originates from apocrine sweat glands of the inner surface of the labia majora and nearby perineum. Occasionally, they may originate from eccrine sweat glands.
- For unknown reasons, they are discovered exclusively in white women between the ages of 30 and 70, most commonly in the fourth decade of life. These tumors have not been reported prior to puberty. Hidradenomas may be cystic or solid. Approximately 50% of hidradenomas are less than 1 cm in diameter.
- These tumors have well-defined capsules
- Treatment - surgical

In precancerous diseases of external genitalia include leukoplakia, kraurosis and Bowen’s and Paget disease.

Vulvar leukoplakia developing mainly in the perimenopausal period (probably due to hormonal disorders and immune status), characterized by the proliferation of multi-layered epithelium and violation of its differentiation and maturation (para-and hyperkeratosis, acanthosis without express cellular and nuclear polymorphism, and no violations of the basal membrane) and shown dry white or yellowish plaques of different size with areas of sclerosis.

Treatment. Sedative therapy and also hormonal therapy (androgens? Sometimes with small doses of estrogens) are prescribed. Local treatment is performed by corticosteroid ointments. Good effect has magneto-laser therapy.

Leukoplakia

Leukoplakia signifies the presence of thickened elevated white patches in the skin of the vulva, often complicated by fissuring and ulceration. The patient complains of intense itching and the lesion may be precancerous.

The International Society for the Study of Vulval Disease has recently proposed the use of the term 'hyperplastic dystrophy' instead of leukoplakia.[1] It has also suggested that cases of hyperplastic dystrophy be classified into those without and those with atypia and maintained that only the latter may be precancerous. Undoubtedly this is a useful pathological classification which has a bearing on prognosis and treatment.

Vulvar kraurosis develops mostly in the perimenopausal period is characterized by papillary atrophy and mesh layers of skin, loss of elastic fibers and connective tissue and shown that skin and mucous membrane of the external genitals becomes atrophic, and fragile.

Treatment. Replacement therapy, psychotherapy, sleeping-draughts, sedative remedies are prescribed. But treatment is not always effective. From non-medicinous methods magneto-laser therapy have been also used.

Vulvar kraurosis

Bowen's and Paget disease

characterized by hyperkeratosis and acanthosis of the external genital organs, shows bright-red, eczema-like sharply limited spots with soft surface and infiltration of surrounding tissues. Treatment is surgical. Vulvectomy is recommended.

In ***benign (background) cervical diseases*** include such pathological processes in which the epithelium remains normoplaziya - ectopia of columnar epithelium, benign transformation zone (without atypia), cervicitis, subepithelial endometriosis, true erosion, polyps of mucous membrane.

IMPORTANT!!!

- **Congenital (physiological) ectopic cervix can continue till the age of 23.** These patients should receive medical supervision with regular cytologic investigations and do not need to undergo treatment.

AETIOLOGY OF CERVICAL DISEASES.

1.Heredity.

2.Mechanical and chemical effect on the cervix with:

- chemical and mechanical contraceptive agents;
- cervical injuries at childbirth;
- abortions and intrauterine procedures recorded in the medical history.

3. Changes in hormonal homeostasis:

- menstrual irregularities;
- early menarche;
- more than 3 pregnancies in the patient's medical history;
- absence of regular sexual life;
- early beginning of sexual life.

4. Infections:
   - herpetic infection;
   - Human Papilloma Virus;
   - cervical and vaginal inflammatory processes recorded in the patient's medical history;
   - multiple sexual partners;
   - frequent intercourse and chaotic sexual life;
   - trichomoniasis;
   - chlamidiosis;
   - mycoplasma and/or ureaplasma.
5. Change of the general condition with probable abnormalities of immune homeostasis:
   - work that entails use of chemical agents;
   - presence of chronic extragenital diseases.

HISTOLOGICAL CLASSIFICATION OF PATHOLOGIC PROCESSES IN THE CERVIX.

A. Benign pathologic processes.

I. Hyperplastic processes associated with hormonal abnormalities.

1. Ectopia (pseudoerosion).
2. Polyps.
3. Papillomas.
4. Simple leukoplakia.
5. Cervical endometriosis.

II. Pathologic processes associated with inflammatory genesis.

1.Genuine erosion.
2.Cervicitis.

III. Posttraumatic processes.

1.Ectropion.
2.Cicatrical deformities.

B. Pre-cancerous processes.

1. Cervical dysplasia:
   - mild;
   - moderate;
   - severe.
2. Leukoplakia with cellular atypia.
3. Erythroplakia.
4. Cervical adenomatosis.

B. Cervical carcinoma.

Ectopia of columnar epithelium (dishormonal, inflammatory, posttraumatic - ektropion) - move the cervical mucous membrane (columnar epithelium) of the vaginal part of the cervix.

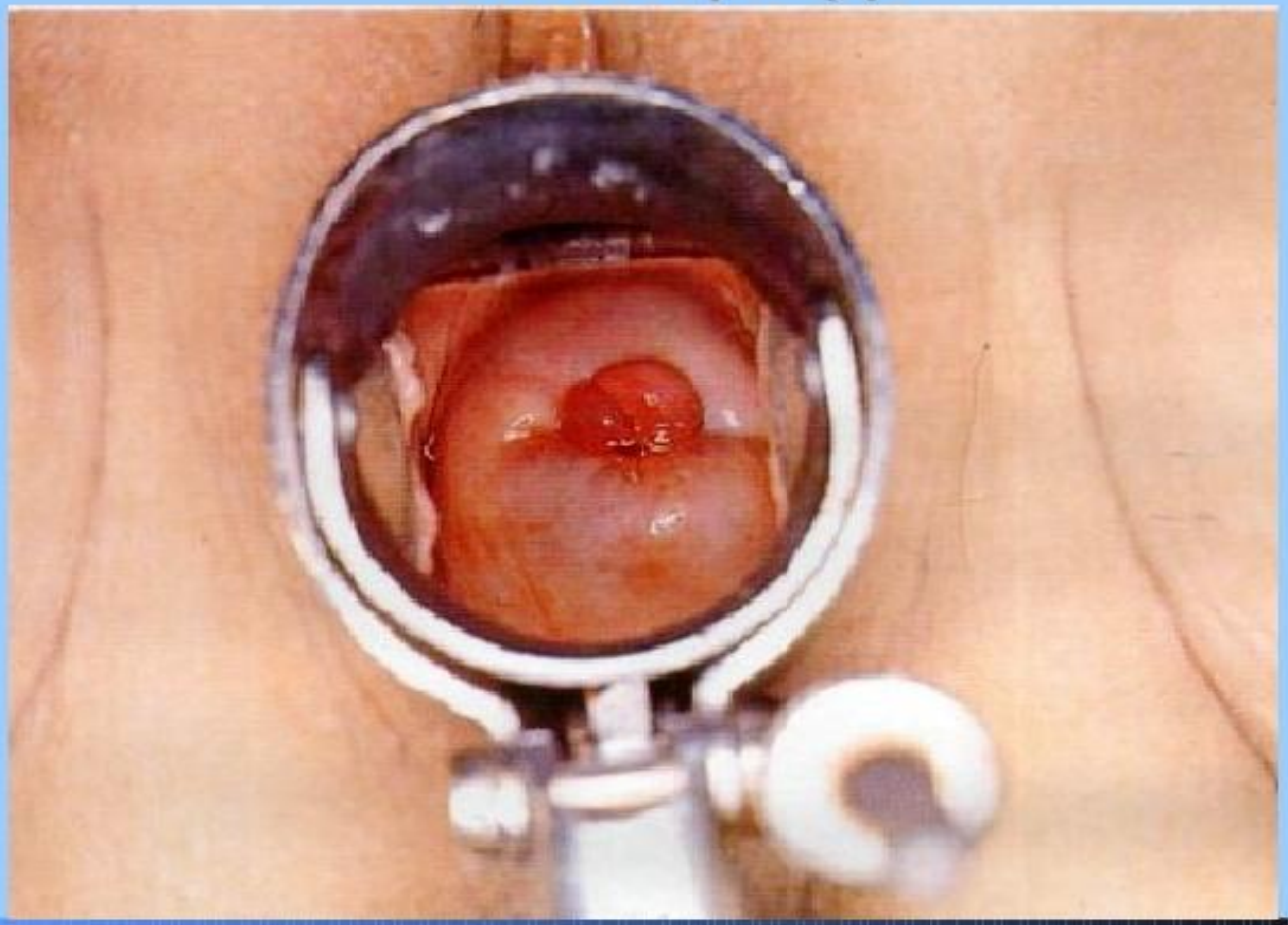
Cervicitis (endo-and exocervicitis) - inflammatory processes in the area of vaginal mucous membrane of the cervix and cervical canal of varying etiology.

Subepithelial endometriosis – posttraumatic (after treatment or examination) implantation of endometrial cells and their proliferation, depending on the phase of menstrual cycle, and shown from red to brown plaques on the exocervix surface.

True cervical erosion is a pathological process, which is a result of damage and following exfoliation of original squamous epithelium on cervical vaginal part if it undergoes harmful influences, especially mechanical traumatization or infection.

The polyps of mucous membrane of cervical canal are created from the mucous of the external os, middle or upper third part of endocervix. They can have a pedicle or wide base. Depending on the dominance in their structure of grandular or connective tissue grandular, grandular-fibrose and adenomatous polyps are distinguished.

Cervical polyp



Ectropion

Precancerous cervical deseases (dysplasia, CIN, cervical intraepithelial neoplasia) - **is the proliferation of cervical tissue with the phenomena of cell atypia.**

Thanks to colposcopic examination dysplasia were distinguished on simple leukoplakia, areas of dysplasia, papillary zone of dysplasia, precancer transformation zone, condylomas and precancerous polyps.

- *Simple leukoplakia* - during colposcopic examination shown in the form of white spots with a smooth or fine-grained relief.
- *Areas of dysplasia* – at colposcopic examination shown in the form of white monomorphic polygonal areas separated red borders.
- *Papillary zone of dysplasia* – at colposcopic examination shown as monomorphic red blotches on a background of white or pink spots.
- *Precancer transformation zone* – at popular colpocervicoscopy find as monomorphic white rims around ducts of gland.
- *Condylomas and precancerous polyps* — found mostly in the background long-term inflammatory process in the form of long or short papilla.

CLINICAL MANIFESTATIONS.

- Pathologic discharge.
- Contact bloody discharge.

DIAGNOSTIC METHODS OF INVESTIGATION.

- History taking.
- Speculum examination of the cervix.
- Shiller's test.
- Bacterioscopic and bacteriological investigation of cervical mucus and vaginal discharge.
- Cytologic investigation.
- Investigation to detect TORCH-infections (Chlamydia, mycoplasma, ureaplasma, herpetic infection, human Papilloma virus).

- Colposcopy.
- Cervical biopsy.
- Hormone blood level (estradiol, progesterone, follicle-stimulating hormone, luteinizing hormone).
- Investigation of local, humoral and cellular immunity (according to indications).

TREATMENT.

- **Treatment objective** is to eliminate the pathologic process of the cervix and those changes in the body that were conducive to the onset of this process.

Treatment principles:

- 1.To avoid recurrence of pathology.
- 2.To use organ-preserving treatment methods in women of reproductive age.

- Methods of treating p***recancerous cervical deseases***l are determined by the nature and degree of dysplasia and divided into:

1. Conservative

- Anti-inflammatory therapy - purposeful antibacterial, antimycotic, antiviral, antiseptic therapy intended to normalize biocenosis vagina.
- When papilloma viral infection using interferon drugs.
- Hormone therapy

2. Surgical

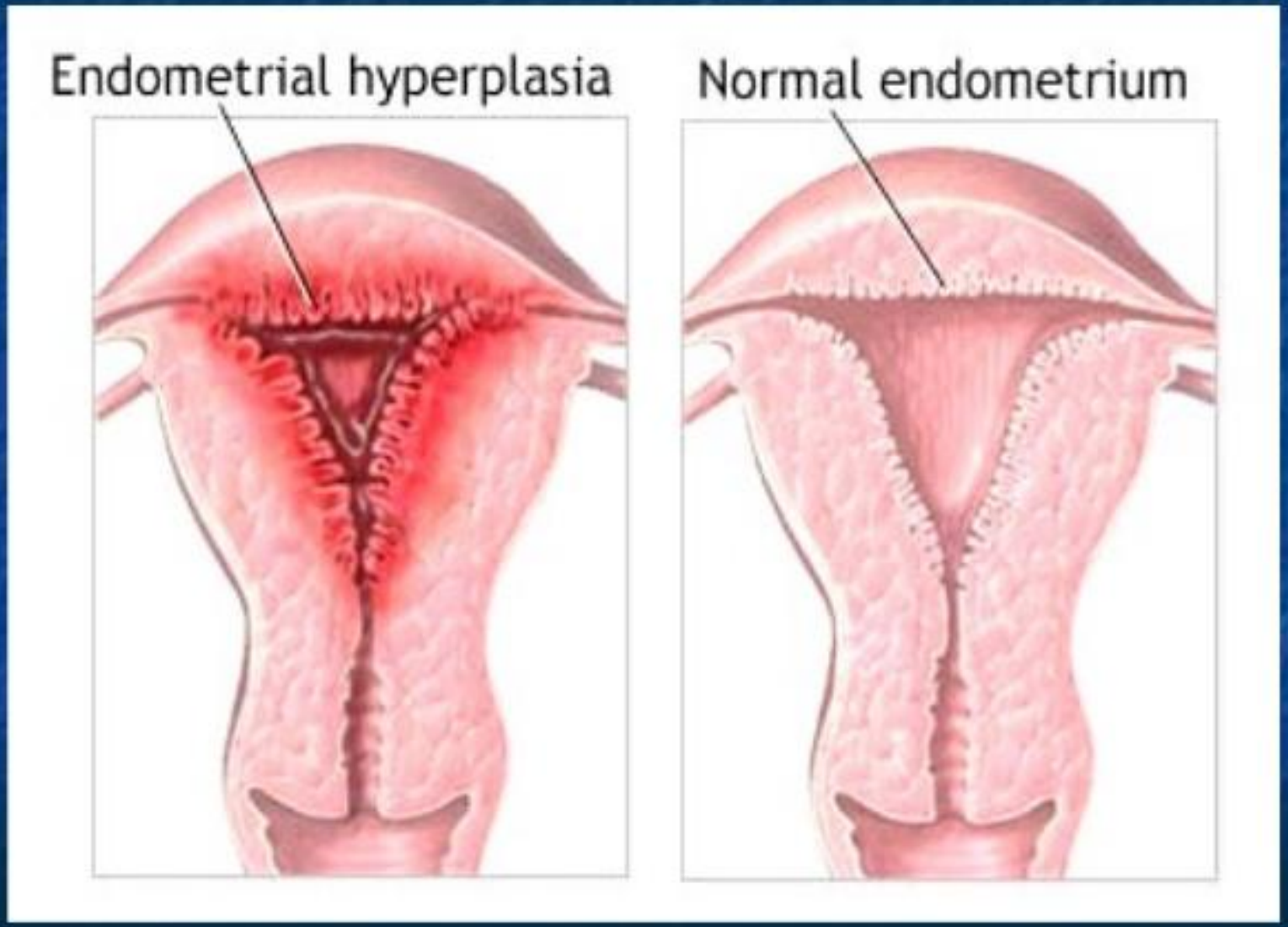
- Local destruction (chemical coagulation, diathermo-coagulation, cryodestruction, laser destruction, radio-wave method);
- Radical operative intervention (excision of cervical, cervical amputation, hysterectomy)

3. Combined

PREVENTION OF CERVICAL CARCINOMA.

- **Cervarix** – is a vaccine against certain types of human papillomavirus, cervical carcinoma and pre-cancerous conditions of the cervix.
- Cervarix is injected i.m. into deltoid muscle.
- The administration scheme is 3 doses every 0, 1 and 6 months.

Endometrial hyperplasia - benign pathology of mucous membrane of uterine and a pathological proliferation of endometrium glands, which characterized by progressing clinical and morphological manifestations from simple and complex hyperplasia to atypical precancerous states of endometrium and developing on a background of absolute or relative hyperestrogenia.


Endometrial hyperplasia
Normal endometrium

AETIOLOGY OF THE DISEASE

- Anovulatory infertility.
- Climacterical period.
- Persistence of follicle.
- Follicular cyst.
- Estrogen producing ovarian tumors.
- Obesity.
- Diabetes mellitus.
- Insulin resistance.
- Heredity.

Classification of endometrial hyperplasia (developed by International Society Pathologist-gynecologists and approved by WHO, 1994):

- **- simple endometrial hyperplasia without cellular atypia** - characterized as increasing the number of glandular and stromal elements, with a small superiority of the first. It is rarely transformed in a cancer (less than 2%), for example, glandular and glandular-cystic.
- - **complex endometrial hyperplasia without cellular atypia** - characteristic of the close location of glands with loss of stroma between them and increasing their structural complexity (more multirowed epithelium than in the case of simple hyperplasia);
- - **simple atypical endometrial hyperplasia** differs from simple and combined hyperplasia without cellular atypia by presence glands with atypical cells, which result in loss of polarity location and unusual configuration of nuclei (polymorphic);
- - **complex atypical endometrial hyperplasia** is characterized by a pronounced proliferation of epithelial glands component that is combined with tissue and cell atypiyeyu without invasion of basal membrane and nuclear polymorphism. It is considered an endometrium cancer in situ, a stroma is involved in pathological process, but invasive growth is not present. More than to 20% of cases it is transformed in an endometrium cancer.
- **adenocarcinoma.**

Clinical and morphological classification of endometrial hyperplasia [Y. Bohman, 1985]:

1. **Background processes:** glandular and glandular-cystic
   - **glandular hyperplasia,**
   - **glandular-cystic hyperplasia,**
2. **Endometrium polyps**
   - **glandular polyps,**
   - **glandular-fibrous polyps,**
   - **glandular-cystic polyps,**
   - **fibrous polyps.**
3. **Precancerous hyperplasia: atipical hyperplasia (adenomatosis).**
4. **Endometrial carcinoma.**

CLINICAL PRESENTATIONS.

- Menstrual irregularities (delay of menstruation during 2 -3 months).
- Metrorrhagia.
- Infertility.
- Nervous system abnormalities (depression, sleep disturbance, mood swings).
- Headache.
- General weakness, dizziness.
- Skin pallor.

DIAGNOSTICS

Main diagnostics objectives.

- Detection of hyperplasia and clinical interpretation of the results of histological examination performed on the endometrium.
- Determination of hormone dependency of the hyperplasia and evaluation of individual hormonal balance in the patient.

Investigation methods

- History of disease.
- Speculum examination.
- Bimanual examination.
- Cytological examination of the cervical matter.
- US.
- Hysteroscopy.
- Aspiration biopsy of endometrial tissue.
- Fractional diagnostic curettage of uterine cavity.
- Determination of blood hormone level: follicle-stimulating hormone, luteinizing hormone, estradiol, progesterone.
- Determination of thyroid gland functional activity.
- Administration of glucose tolerance test.

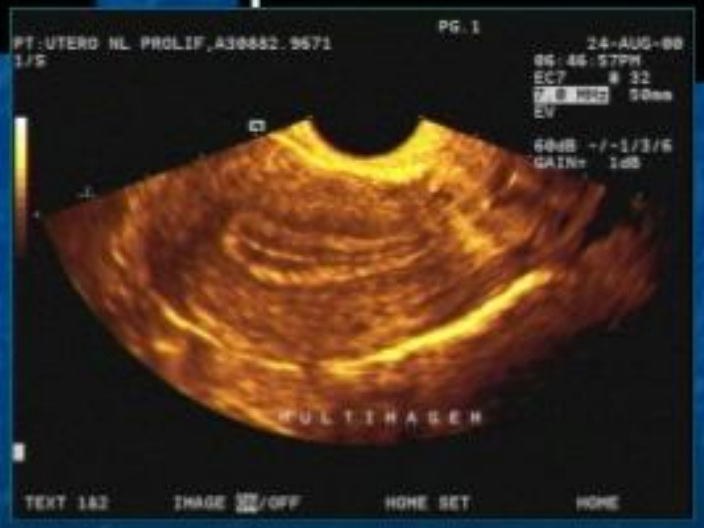
Ultrasonic data that serve as indication for histological examination of endometrial tissue:

- - thickness of endometrium exceeds 16mm;
- - EUR more than 0,33 (EUR stands for endometrial thickness – anterior posterior size of uterus ratio, this indicator allows the investigator to evaluate faster endometrium involution rate as compared to myometrium.

In postmenopausal women:
- thickness of endometrium exceeds 5mm;
- EUR more than 0,15.

- For monitoring of endometrial condition during hormonal therapy it is recommended to use hysteroscopy and aspiration biopsy.

УЛЬТРАЗВУКОВЕ



- Товщина ендометрію
- Проліферативна фаза
- Секреторна фаза

Гістероскопія дозволяє:

IMPORTANT!!!

- Only histological examination can confirm the diagnosis of endometrial hyperplasia.

TREATMENT STAGES

- **First stage –** extirpation of transformed endometrium in order to determine the type of endometrial pathology by means of morphological investigation and select the appropriate therapeutic approach.

- **Second stage** – hormonal therapy aimed at suppression of endometrial growth. The course of treatment is 6 months, histological reanalysis should be done after 6 months.

Gestagens:

- Norcolut, orgametril, utrogestan, dufaston to be taken from the 5th to the 25th day of the menstrual cycle during 6 menstrual cycles.
- 12,5% solution of 17- oxyprogesteron capronat to be administered i/m 500mg twice weekly.
- Depo-prover i.m. administration, 200-400mg once weekly.
- **GnRH agonists 3 – 6 injections:**
- - goserelin 3,6 mg s/c once per 28 days;
- - buserelin 3,75 i/m once per 28 days;
- - buserelin nasal spray 900mg once daily.

Third stage – optimization of hormonal status for prevention of hyperestrogemenia development.

In women of reproductive age:

- hormonal contraceptives containing gestagen with pronounced antiproliferative effect (Janine, Yarina, Jazz);
- local administration of gestagens (intrauterine system Myrena).

In perimenopausal women:

– menostasia with administration of GnRH agonists (3 months) combined with intake of gestagens during 6 months.

- **Fourth stage** – regular medical examinations during 5 years following effective hormonal therapy and 6 months following surgical treatment.

INDICATIONS FOR SURGICAL TREATMENT

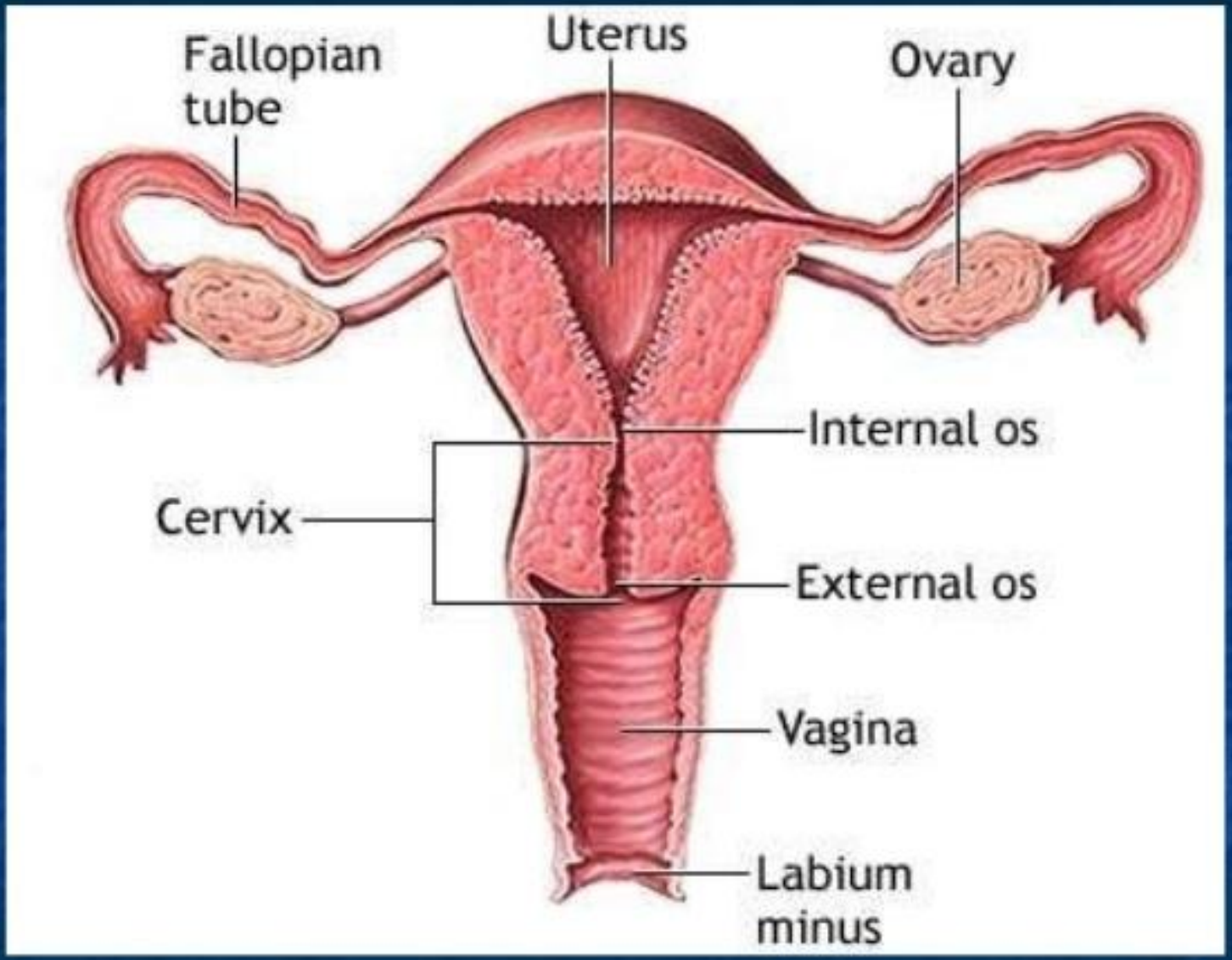
- **In reproductive age:**
- 1. Complex endometrial hyperplasia without atypia in cases when conservative therapy fails to demonstrate its effectiveness during 3 months.
- 2. Simple atypical or complex non-atypical hyperplasia in cases when therapy fails to demonstrate its effectiveness during 6 months.
- **In menopausal patients:**
- 1. Complex endometrial hyperplasia with atypia – in patients with confirmed diagnosis.
- 2. Simple atypical or complex non-atypical hyperplasia in cases when therapy fails to demonstrate its effectiveness during 3 months.

- **Types of surgical treatment:**

- Hysteroscopic resection or endometrial ablation;

- hysterectomy.

MALIGNANT NEOPLASMS OF FEMALE GENITAL ORGANS.


Fallopian tube
Uterus
Ovary
Internal os
Cervix
External os
Vagina
Labium minus

CANCER OF FEMALE REPRODUCTIVE ORGANS

Etiology

Cervix

- Human papillomavirus;
- - multiple sexual partners;
- - early beginning of sexual life;
- - high fertility;
- - poor sex hygiene;
- -immunodeficiency;
- - trichomoniasis;
- - chlamidiosis;
- - smoking.

Endometrium

- **Theories:**
- - sexual (late start and prolonged absence of sexual life);
- - reproductive (early menarche, late menopause, chronic anovulation, infertility, hysteromyoma, endometrial hyperplasia);
- pharmacological (administration of estrogens without progestins);
- - endocrinal pathology (obesity, diabetes mellitus, hyperlipidemia);
- - hereditary (cancerous diseases in the medical history of genetic relatives).

Ovary

- - Anamnestic record
- (family cancer);
- - Radiation;
- - Infertility;
- - Ovarian tumors and tumor-like growths;
- Metastases from mammary glands, lungs, gastrointestinal tract (Crukenberg's cancer), uterus.

Pathogenesis

Cervix

- Disorders of the cellular genetic apparatus involving cellular genes and virogenes, with invariable integration of the virogene into the cellular gene.

Endometrium

- Prolonged exposure of endometrium to estrogens in the environment of progesterone insufficiency.

Ovary

- Large amounts of estrogens and androgens induce hyperplasia and metaplasia of ovarian epithelium; the 'inclusion cysts' that develop after this penetrate the stroma of the ovary and cause malignant transformations;- Ovulation is a stress for ovarian tissue.

Clinical signs
Cervix

- - Leucorrhea (profuse white watery discharge);
- - Acyclic bloody discharge;
- - Contact bloody discharge (increased tissue fragility);
- - Pathologic leucorrhea (purulent);
- - Pain (when the process extends);
- - Impaired bladder and rectum function (in metastatic conditions).

Endometrium

- - Leucorrhea;
- - Acyclic uterine bleeding;
- - Pain;
- - Disturbance of urination and defecation.

Ovary

- - Acyclic bloody discharge;
- - Ascites;
- - Pain.

Diagnostics
Cervix

- - Medical history;
- - Speculum examination;
- - Shiller's test (treatment with Lugol's iodine solution);
- - Cytologic investigation of cervical matter;
- - Colposcopy;
- - Biopsy;
- - Hormone blood level;
- - Oncological marker level CA-125.

Endometrium

- - Medical history;
- - Speculum examination;
- - Bimanual examination (enlarged, softened uterus with deformed contours);
- - Cytological investigation of cervical matter;
- - Fractional diagnostic curettage;
- - Hysteroscopy;
- - US;
- - Hormone blood level;
- - Oncological marker level CA-125;
- - Computer-aided tomography;
- - Nuclear magnetic resonance;
- - Lymphography.

Ovary

- - Medical history;
- - Bimanual examination (enlarged, tuberous, painless ovaries);
- - Cytological investigation of cervical matter;- US;
- - Oncological marker level CA-125;
- - Hormone blood level;
- - Abdominal cavity puncture performed via posterior fornix, cytological investigation of extracted matter;
- - Computer-aided tomography (CAT);
- - Nuclear magnetic resonance (NMR);
- - Laparoscopy.

Treatment
Cervix

- - **Surgical**:
- a) preinvasive carcinoma (invasion depth under 3mm) – conization of cervix;
- 6) Wertheim's surgery (extensive panhysterectomy: extirpation of uterus, uterine appendages, parametrium, and local lymphatic nodes);
- **- Radiation therapy :** long-focus and intracavitary (applied at all stages);
- **- Chemotherapy** ineffective;
- **- Immunotherapy:**
- Leukocytic α-interferon, recombinant interferon, cycloferon, immunomodulators

Endometrium

- **- Surgical:**
- extensive panhysterectomy (Wertheim-Meigs surgery);
- **-Radiotherapy**
- Intracavitary and long-ficus;
- **- Hormonal therapy:**
- a) continuous administration of progestins;
- б) tamoxyphen (antiestrogen);
- **- Chemotherapy**
- Ineffective in cases when there are metastases in ovaries.

Ovary

- **Surgical:**
- extensive panhysterectomy (Wertheim-Meigs surgery);
- **- Chemotherapy:**
- cisplatin, carboplatin, cyclophosphan, doxorubicine;
- **- Hormonal therapy**
- continuous administration of progestins;
- tamoxyphen;
- **- Radiotherapy**
- ineffective.

Prevention
_Cervix

- - CERVARIX vaccination;
- - Early detection of cervical diseases;
- - Timely treatment

Endometrium

- - Early detection of endometrial and uterine diseases;
- - Timely treatment

Ovary

- Administration of oral contraceptives in women of reproductive age for the term of 1 year or longer;- Timely treatment of gynecological diseases.


Cervical Cancer