RESPUBLIC OF UZBEKISTAN

MINISTRY OF HIGHER EDUCATION, SCIENCE AND INNOVATIONS

MINISTRY OF HEALTH OF THE REPUBLIC OF UZBEKISTAN

TASHKENT STATE MEDICAL UNIVERSITY

DILOBAR VALIJANOVNA GULAMMAXMUDOVA

UMIDA MASHARIFOVNA YUSUPOVA

Field of study: **Healthcare**

TEXTBOOK

"FUNDAMENTALS OF EARLY DETECTION AND PREVENTION OF GYNECOLOGICAL DISEASES IN WOMEN"

in the subject: "Obstetrics" and "Gynecology"

for educational areas

"Medical Case" - 5510100

"Professional Education" - 5511100 ("Medical Work")

Tashkent - 2025

Authors:

Yusupova U.M. – PhD, Tashkent State Medical University
Associate Professor of the Department of Obstetrics and Gynecology, Reproductive Medicine

Gulammakhmudova D.V. – PhD, Tashkent State Medical University
Assistant of the Department of Obstetrics and Gynecology, Reproductive Medicine

Reviewers:

Muminova Z.A. – Doctor of Medical Sciences, Tashkent State Medical University
Professor of the Department of Obstetrics and Gynecology, Reproductive Medicine

Negmatshaeva X.N.- Candidate of Medical Sciences, Andijan State Medical Institute
Associate Professor of the Department of Obstetrics and Gynecology

The textbook is prepared based on the standard curriculum of the subject "Obstetrics and Gynecology," the current curriculum, and the requirements of the qualification description for the specialty 5511100. The manual is intended for bachelors of the Faculty of "General Medicine," studying the subject "Obstetrics and Gynecology," and is used in the process of forming professional competencies.

This textbook was reviewed by a monothematic commission and recommended for approval by the Center for the Development of Medical Education of the Ministry of Health of the Republic of Uzbekistan._____**2025, protocol№**.

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Protocol №. ____2025

LIST OF ABBREVIATIONS

ACTH - adrenocorticotropic hormone
AMC - abnormal uterine haemorrhages
VNS - autonomic nervous system
GnRH - gonadotropic releasing hormone
COCs - combined oral contraceptives
DHEA-S - dehydroepiandrosterone sulfate
RHTH - hormone replacement therapy
CT - computed tomography
LH - luteinizing hormone
XS - menstrual cycle
MRI - magnetic resonance imaging
LFE - lutein phase deficiency
NSAIDs - nonsteroidal anti-inflammatory drugs
PTS - polycystic ovary syndrome
TSH - thyrotropic hormone
T3 - triiodothyronine
T4 - thyroxine
FSH - follicle-stimulating hormone
CNS - central nervous system
17-ONP - 17-hydroxyprogesterone
WHO - World Health Organization (WHO)
ICD-10 - International Statistical Classification of Diseases, Problems Related to Health. Tenth revised edition
TUOC - tumour-like formations of ovaries
TU - ovarian tumours
Ultrasound examination

ENTRANCE

Maintaining and improving maternal and child health is one of the most important state tasks in the Republic of Uzbekistan. Morbidity and mortality rates among women and children reflect not only the quality of medical care provided to women and children, but also the overall state of the country's healthcare system and are of socio-political significance.

In this regard, within the framework of the Concept for the Development of the Healthcare System of the Republic of Uzbekistan (2019-2025), in order to further improve the medical care provided to women of reproductive age, pregnant women and children, the Resolution of the President of the Republic of Uzbekistan dated November 8, 2019 No. PP-4513 was adopted. This resolution is called "On Improving the Quality and Further Expanding the Coverage of Medical Care Provided to Women of Reproductive Age, Pregnant Women, and Children."

Improving the quality of medical care as a means of preserving and strengthening public health is of particular importance.

As a result of studying the topic "Aspects of Modern Gynecology," the student should know:

• etiology, pathogenesis and preventive measures of the most common diseases, modern classification of diseases;

• organization of obstetric and gynecological care for the population, methods of diagnosis, management and treatment of gynecological diseases;

• maintenance of standard accounting and reporting medical documentation.

Student must know:

• determination of the volume of additional examination in accordance with the prognosis of the disease, clarification of the diagnosis and obtaining a reliable result;

• selection of the type of patient care depending on each clinical situation (ambulance, hospitalization);

• formation of indications for the chosen treatment method, justification of pharmacotherapy, determination of the route, regimen, and dosage of drugs, assessment of the effectiveness and safety of treatment, taking into account etiological and pathogenetic factors;

• use of primary and secondary prevention methods (based on evidence-based medicine);

• assessment of social factors affecting the patient's health;

• diagnosis - synthesis of information about the patient, identification of pathology and its causes;

• providing first aid in emergency situations.

Student must master:

• basic diagnostic and therapeutic measures for providing first aid in emergency and life-threatening situations;

• proper maintenance of medical documentation;

• general clinical examination methods;

• interpretation of the results of laboratory and instrumental diagnostic methods;

• advanced diagnostic algorithm

TOPIC 1: MENSTRUAL CYCLE AND ITS REGULATION

The reproductive system (RS) is one of the most important functional systems of the human body, the main task of which is to ensure the continuity of the biological species. The optimal functional activity of RS is usually formed in the age range of 16-18 years. It is during this period that the body is ready for pregnancy, fetal development, and breastfeeding after birth.

The peculiarity of the functions of the reproductive system is that they gradually weaken over time: around 45 years of age, generative, and at 50 years of age, menstrual activity begins to fade, and subsequently, hormonal activity gradually decreases.

RS has a five-level structure: 1) extrahypothalamic (cranial cortex), 2) hypothalamus, 3) pituitary gland, 4) ovaries, 5) target organs and tissues (Fig. 1). This system operates on a hierarchical principle, that is, the lower level is subordinate to the higher level. The basis of the mechanism for managing RS functions is the principle of negative feedback, which exists between different levels (Fig. 1). For example, with a decrease in the level of peripheral hormones, in particular estradiol, the production of gonadotropin releasing hormone (GRL) by the hypothalamus and gonadotropic hormones by the pituitary gland increases.

There is another peculiarity of regulation in the female body, which is explained by the mechanism of positive feedback. As a result of a significant increase in the concentration of estradiol in the preovulatory follicle, the activity of the hypothalamus and pituitary gland increases, and the production of gonadotropins increases. As a result, the secretion of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) reaches its peak during the ovulatory period.

Female RS activity is characterized by cyclicity. The totality of these processes is expressed in modern scientific literature by the concept of the "menstrual cycle."

The menstrual cycle is cyclical changes occurring in the hypothalamic-pituitary-ovarian system, as well as morphofunctional changes occurring in the reproductive organs (uterus, fallopian tubes, mammary glands, vagina) under their influence.

The final stage of each menstrual cycle is menstrual bleeding (menstruation). The first day of menstruation is considered the start date of the new cycle. The first menstrual phenomenon observed in girls is called menarche. The average age of menarche is usually 12-14 years.

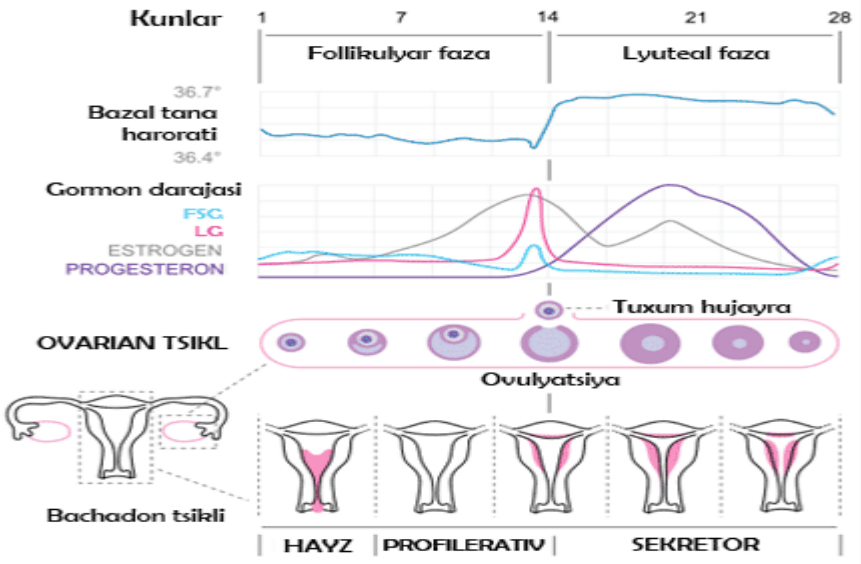

Figure 1. Management of the female reproductive system:

The duration of the menstrual cycle is determined by the time from the first day of one menstruation to the first day of the next and lasts from 24 to 38 days under normal conditions. In

adolescent girls, the duration of the cycle during the first 1.5-2 years after menarche can be relatively variable - from 24 to 38 days. Such a cycle is called a norm-setting cycle. A special type of norm-setting cycle is the ideal cycle, the duration of which is 28 days.
If the cycle is shorter than 24 days, this condition is called anteponation (anteponing cycle), and conversely, if it is longer than 38 days, it is called postponation (postponing cycle).
The duration of normal menstruation averages 3-8 days (normally 3-7 days), and the volume of blood loss averages 50-80 ml (normally up to 80 ml).
Ovarian and uterine cycles
The menstrual cycle is conventionally divided into ovarian and uterine cycles.
- The ovarian cycle represents the cyclical processes occurring in the ovaries under the influence of gonadotropic and releasing hormones. These processes consist of two phases:
1. Follicular (folliculin) phase - maturation of the follicle and egg cell, followed by rupture of the follicle and release of the egg cell (ovulation).
2. Luteal phase - associated with the formation of the corpus luteum.
- The uterine cycle is characterized by cyclical processes in the endometrium. Sequential in the endometrium:
regeneration,
proliferation,
secretory activity,
desquamation of the functional layer (menstruation) occurs.
Biological significance
The biological significance of changes in the ovaries and endometrium lies in ensuring the maturation of the egg, its fertilization, and the implantation of the zygote into the uterus. If fertilization does not occur, the functional layer of the endometrium is rejected, resulting in bloody discharge from the genital tract. After this, the reproductive system restarts its cyclical processes.
Regulation of menstrual cycle
Level I regulators of the menstrual cycle are the cerebral cortex, in particular, the limbic system and amygdaloid nuclei. The cerebral cortex regulates the activity of the hypothalamic-pituitary system through neurotransmitters. They transmit nerve impulses to the neurosecretory nuclei of the hypothalamus. Neuropeptides (dopamine, noradrenaline, serotonin, kiss-peptin, opioid peptide family), as well as the epiphyseal hormone melatonin, play an important role in this process.
Factors such as stress, climate change, or work rhythm (for example, night shifts) negatively affect the ovulation process. This is mainly due to changes in the synthesis and consumption of neurotransmitters and melatonin.
The central nervous system has many receptors that are sensitive to estradiol and other steroid hormones. This shows that they play an important role not only in feedback mechanisms, but also in neurotransmitter exchange processes.
Level II regulator - hypothalamus
The second-level regulator of the reproductive system is the hypothalamus, which, as the central link of the nervous and endocrine systems, coordinates the activity of all internal organs and maintains the homeostasis of the body. The hypothalamus controls the activity of the pituitary gland, as well as the gonads (ovaries), thyroid gland, and adrenal glands (Fig. 1).
There are two types of neurosecretory cells in the hypothalamus that provide the hypothalamic-pituitary interconnection:
1. Neuroendocrine neurons - producing oxytocin and vasopressin (antidiuretic hormone), which enter the posterior pituitary gland.
2) Hypophysiotropic neurons - cells that produce hypothalamic neuropeptides (releasing factors), biologically active amines. They reach the adenohypophysis through the hypothalamic-pituitary portal system.

The site of synthesis of gonadotropin release hormone (GnRH) is the arcuate nuclei of the mediobasal hypothalamus. A specific releasing hormone for LH has been identified, synthesized, and described, which is called luliberin. However, the isolation and synthesis of FSH-specific folliliberin remains impossible to this day. For this reason, hypothalamic gonadotropin-liberins are collectively called GnRH, since they stimulate the secretion of both LH and FSH from the anterior pituitary gland.

GnRH secretion is genetically programmed and is carried out on the basis of a pulsating rhythm - approximately every 60-90 minutes (circhoral, i.e., hourly rhythm). Today, the permissive (initiating) role of GnRG in the activation of the reproductive system has been proven. Pulsating secretion of GnRH is formed during puberty and indicates the maturation of the neurosecretory structures of the hypothalamus. Syrhoral secretion of GnRH activates the hypothalamic-pituitary-ovarian system. Under the influence of GnRH, LH and FSH are released from the adenohypophysis.

GnRH secretion is modulated by the feedback mechanism of neuropeptides of extrahypothalamic structures, as well as sex hormones.

The peak increase in estradiol in the preovulatory period increases the synthesis and secretion of GnRH, which increases the release of gonadotropins, and as a result, ovulation occurs. Progesterone, on the other hand, has two effects on the production of gonadotropins: both inhibitory and stimulatory, that is, it acts on the basis of the principle of feedback at the hypothalamic and pituitary levels.

Dopaminergic structures play a leading role in the regulation of prolactin secretion. Dopamine inhibits prolactin secretion, while thyroliberin stimulates it. Dopamine antagonists enhance prolactin secretion.

Hypothalamic neurosecretions affect the body in several ways:

• Paraphyseal pathway - passes through blood vessels to the sinuses of the dura mater, and from there to the general blood flow.

• Transpituitary tract - passes through the portal vein system to the adenohypophysis. The peculiarity of the portal system is that blood flow in it can move in two directions (both to the hypothalamus and the pituitary gland). This is of great importance in the implementation of feedback mechanisms.

Reaction of ovarian sex hormones on the pituitary gland is carried out mainly through the vertebral arteries.

Thus, the cyclic secretion of GnRH triggers the hypothalamic-pituitary-ovarian system, but its function is not autonomous, but is modulated by central nervous system neuropeptides and ovarian steroids based on feedback mechanisms.

III degree - anterior pituitary gland (adenohypophysis)

Three types of cells are distinguished in the adenohypophysis:

1. Chromophobe cells perform a reserve function.
2. Acidophilic cells.
3. Basophilic cells.

The following hormones are synthesized in the adenohypophysis:

Gonadotropic hormones: follicle-stimulating hormone (FSH, follitropin), luteinizing hormone (LH, luteotropin).

Prolactin (Prl).

• Other tropic hormones: thyrotropin (TTH), somatotropin (STH), adrenocorticotropin (ACTH), melanotropin (MSH), lipotropin (LPG).

LH and FSH are glycoproteins by chemical nature, while prolactin is a polypeptide.

Factors controlling the secretion of LH and FSH (Fig. 1):

1. GnRH - enters the adenohypophysis through the portal system and stimulates the secretion of gonadotropins.
2. Ovarian sex hormones (estradiol, progesterone) - have a negative or positive effect based on the principle of feedback.

3. Inhibin A and B are synthesized in the ovaries. In particular, inhibin B, together with estradiol, inhibits FSH secretion in the second half of the follicular phase (after the selection of the dominant follicle). As the number of follicles decreases with age...
The biological role of FSH:
• growth of follicles in the ovary, proliferation of follicular granulosa cells;
• synthesis of aromatic enzymes that convert androgens into estrogens (production of estradiol);
• Synthesis of LH receptors in follicular granulosa cells (preparation for ovulation);
• Stimulate the secretion of growth factors (GF) in the form of activin, inhibin, and insulin, which play an important role in folliculogenesis and the synthesis of sex steroids.

Biological role of LH:
• In conjunction with the FSH, it causes ovulation;
• Ensures the synthesis of estradiol in the dominant follicle;
• Activates the synthesis of androgens in follicular theca cells;
• ensures luteinization of granulosa cells and the formation of the corpus luteum after ovulation;
• Regulates the synthesis of progesterone and other steroids in lutein cells of the corpus luteum.
Prolactin (Prl) is a polypeptide synthesized by adenohypophysis cells (lactotrophs), which controls lactation, stimulates the development of the mammary gland ducts, supports corpus luteum activity, and progesterone synthesis. In addition, it has various biological effects: it reduces the mineral density of bone tissue, increases the activity of pancreatic cells, causes insulin resistance (diabetic effect), participates in metabolism, nutritional behavior, sleep and wakefulness cycles, libido, and other processes.
Level IV of the reproductive system - Ovarium. The main structural unit of the ovary is the follicle, which contains the oocyte (egg cell). In the gonads, the growth and maturation of follicles, ovulation, the formation of the corpus luteum, and the synthesis of sex steroids occur. The process of folliculogenesis in the ovary is continuous - from the antenatal period to postmenopause. At birth, a girl's ovary contains approximately 2 million primordial follicles.
Most of them undergo atretic changes during life (atresia - regression), and only a very small part develops fully, passing from the primordial stage to the mature follicle and forming the corpus luteum after ovulation. By menarche, 200-450 thousand primordial follicles are stored in the ovaries of a girl (this is called the ovarian reserve). Only 400-500 of them can ovulate during a woman's lifetime, while the rest suffer from atresia (approx.
In the process of follicular atresia, apoptosis - programmed cell death - plays an important role. As a result of this biological process, complete breakdown of the cell occurs under the influence of its lysosomal apparatus. During each menstrual cycle, usually only one follicle grows and one oocyte develops inside it. Multiple pregnancies can occur if multiple follicles mature.
Growth factors (factors) play an important role in the mechanisms of auto- and paracrine regulation of the reproductive system not only at the ovarian level, but also at the entire system level.
Growth factors are biologically active substances that stimulate or inhibit cell differentiation, transmit hormonal signals, and are synthesized and function in non-specific cells of various tissues of the organism.
The autocrine effect occurs when the growth factor (GF) directly affects the cells that synthesize it.
The paracrine effect manifests itself in the effect on neighboring cells.
Intracrine effect - O'O acts as a messenger (signal transmitter) inside the cell.
The endocrine effect affects distant cells through blood flow.
Growth factors (GF) that play a key role in the physiology of the reproductive system:
• Insulin-like growth factors (GFR-I and GFR-II): synthesized in granulosa cells and other tissues. It stimulates the synthesis of androgens in the teka cells of the ovary, the aromatization of androgens into estrogens, the proliferation of granulosa cells, and the formation of LH receptors. Their synthesis is regulated by insulin.

• Epidermal growth factor (EGF): the strongest stimulator of cell proliferation, detected in granulosa cells, endometrial stroma, mammary glands, and other tissues. Estrogen-dependent tissues (endometrium, mammary gland) can exhibit an oncogenic effect.
• Vascular endothelial growth factor (VEGF): plays an important role in angiogenesis in growing follicles, as well as in the myometrium and endometrium. Increases the mitogenic activity of endothelial cells, increases the permeability of the vascular wall. The severity of COPD is high in endometriosis, uterine fibroids, ovarian and breast tumors, and PCOS (polycystic ovary syndrome).
• Transforming growth factors (TOF-α and TOF-β): stimulate cell proliferation, participate in follicle growth and maturation, granulose in cell proliferation. Exhibits mitogenic and oncogenic effects; their expression increases in endometrial and ovarian cancer.
Proteins belonging to the TOO-β family: inhibins, activin, folliclestatin, and the anti-Müller hormone (AMH).
• Inhibins (A and B): are formed in granulosa cells and other tissues. They inhibit FSH synthesis similarly to estradiol (through a negative feedback mechanism). The formation of inhibin B is enhanced in the middle of the follicular phase, parallel to the increase in estradiol concentration after the selection of the dominant follicle, and when it reaches its maximum, it inhibits FSH release.
• Activin: detected in granulosa cells of the follicle and gonadotrophic cells of the pituitary gland. It stimulates FSH synthesis, the proliferation of granulosa cells, the aromatization of androgens into estrogens; inhibits the synthesis of androgens in theca cells; prevents spontaneous (pre-ovulatory) luteinization of the preovulatory follicle; stimulates the production of progesterone in the corpus luteum.
• Follistatin: FSH-blocking protein, secreted by the anterior pituitary gland and granulosa cells; Inhibits FSH excretion.
• Anti-Müller hormone (AMH): belongs to the TOO-β family and is produced in granulosa cells of preantral and small antral follicles in women. It plays an important role in the mechanisms of follicle recruitment and selection. AMG is a quantitative indicator of the ovarian reserve and is used in clinical practice to assess the ovarian reserve and predict the response to ovulation stimulation. It is also used as a marker for granulosa cell ovarian tumors, as AMG levels are significantly elevated in these cases. AMG is not regulated by gonadotropins, does not enter the classic negative feedback loop (unlike FSH, estradiol, inhibin B), is not dependent on the cycle phase, and acts as a paracrine factor in the regulation of the reproductive system.
Folliculogenesis (follicle development in the ovaries).
In the female ovaries, follicles are at different stages of maturation. Folliculogenesis begins from the 12th week of antenatal development; the majority of follicles undergo atresia. The factors that initiate the growth of the primordial follicle have not been fully determined.
Primordial follicles are characterized by a single layer of flat pregranulosa cells, small immature oocyte (not completed by the second meiotic division); theca (membrane) cells are absent.
Stages of follicle growth:
1) First stage - from primordial follicles to preantral follicles - hormone-independent growth (FSG-independent).
This process lasts approximately 3-4 months, until follicles with a diameter of 1-4 mm are formed. In the primary preantral follicles, there is a single layer of granulosa cells, the oocyte begins to enlarge, and theca appears.
Secondary preantral follicles are characterized by 2-8 layers of granulosa cells and a fully formed layer of theca cells (Fig. 2).
At this stage, IGF-I plays an important role in folliculogenesis. The process of follicle growth (emergence from rest) occurs constantly and depends on the woman's age. For example, at 24-25 years of age, growth begins in about 50 follicles, at 34-35 years - in 17-25, and at 44-45 years - only in 3-8 follicles. After 36 years of age, atresia and apoptosis processes in the primordial follicles intensify.

In addition, the number of growing follicles depends on the ovarian reserve and sharply decreases in cases of ovarian resection.

2) The second stage - the growth of preantral follicles to the antral follicle stage.

This lasts about 70 days and occurs with the participation of a minimal concentration of FSH - this is the stage of hormone-dependent follicle growth. IGF-I and AMH also play an important role at this stage.

In the center of the antral follicles is a fluid-filled cavity, the diameter of which at the beginning of the menstrual cycle is 3-4 mm (determined by ultrasound on any day of the menstrual cycle). They have a tendency to grow rapidly in the initial period of the follicular phase (Fig. 2-3).

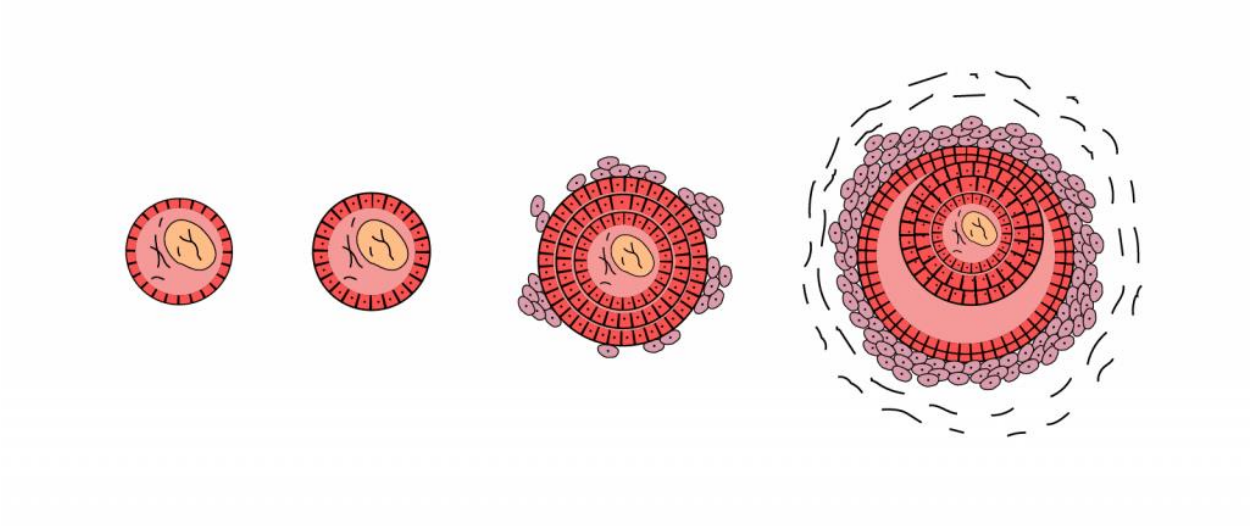

Figure 2. Stages of follicle maturation.

3) The third stage is the selection of the dominant follicle and its maturation.

This stage lasts about 20 days and is entirely dependent on FSH.

On days 25-26 of the previous cycle, under the influence of an increase in FSH concentration, the antral follicles begin to actively grow. On the 2nd-5th day of the menstrual cycle, their diameter reaches 5-6 mm. One dominant follicle separates from these follicles. It grows to a diameter of 18-20 mm and undergoes ovulation under the influence of the LH peak.

A preovulatory mature follicle has the following characteristics:

• there are multilayered granulosa cells,

• has a large cavity filled with follicular fluid,

• located under the ovary capsule,

• the oocyte is covered with a shiny membrane (zona pellucida) and is located at one end of the follicle, on the ovarian cartilage (cumulus oophorus) (Fig. 3).

At this stage, the following factors are actively involved in follicle maturation:

• EGF and TGF-α - affect the proliferation of granulosa cells;

• IGF-I - enhances the effect of FSH on granulosa cells;

• VEGF plays an important role in the blood supply of the dominant follicle and ovary stroma.

Figure 3. Follicles of the ovary at different stages of maturation.
Preovulatory mature follicle.

This, the total duration of folliculogenesis from the beginning of the growth of primordial follicles to the ovulation of the mature follicle is approximately 200 days. The follicular phase of the menstrual cycle corresponds only to the final stage of formation of the dominant follicle and ovulation.

Since the processes of folliculogenesis occur continuously, follicles at different stages of maturation in the ovaries can be detected on any day of the menstrual cycle (echographically) (Fig. 3).

The ovarian cycle consists of two phases: follicular and luteal.

The follicular phase begins on the first day of the next menstrual cycle. In an ideal menstrual cycle, this phase lasts approximately 2 weeks. It is characterized by the growth and maturation of the dominant follicle, culminating in its ovulation on days 13-14.

Then the luteal phase begins. It lasts from days 14-15 to 28, and the processes of formation, development, and regression of the corpus luteum occur. If the cycle is forward or backward, the duration of the follicular phase may differ from the ideal cycle.

Follicular phase (first stage of ovarian cycle)

Gonadotropin-dependent follicle growth begins at the end of the previous menstrual cycle. Due to corpus luteum regression, FSH secretion by the pituitary gland increases in response to a decrease in the levels of progesterone, estradiol, and inhibit B (based on the mechanism of negative feedback).

Under the influence of FSH, the antral follicles continue to grow. On the 4th-5th day of the menstrual cycle, their diameter reaches 4-5 mm. During this period, FSH:

• proliferation and differentiation of granulosa cells,
• synthesis of LH receptors in them,
• activation of aromathases and
• stimulates the synthesis of estrogens and inhibitors.

LH stimulates the synthesis of androgens, which are mainly the ancestral substance of estradiol, in the early stages of the follicular phase.

FSH levels reach their maximum values on days 5-6 of the cycle and then decrease (due to an increase in the concentration of estradiol and inhibit B, synthesized in the granulosa cells of the growing antral follicles). Subsequently, together with LH, it ascends to the ovulatory peak on days 13-14 (Fig. 4).

The selection of the dominant follicle is carried out on days 5-7 of the cycle, from among the antral follicles with a diameter of 5-10 mm. The dominant follicle has the following advantages:

• larger diameter,
• more granulosa cells,

• High number of FSH receptors.
Due to this, it continues to grow despite a decrease in FSH levels and can continue to synthesize estradiol.
From the second half of the follicular phase, the growth of the dominant follicle depends not only on the influence of FSH, but also on the influence of LH. An increase in the concentration of estradiol and growth factors - IGF and VEGF - plays an important role in the rapid growth of the leading follicle. During ovulation, the diameter of the dominant follicle reaches 18-21 mm (Fig. 3).
In the remaining antral follicles, a decrease in FSH levels in blood serum initiates atresia (apoptosis) processes. It is noted that high levels of androgens synthesized in immature follicles also play an important role in the mechanisms of atresia (Fig. 2-3).
Ovulation - the rupture of a mature follicle and the emergence of an egg cell from it.
The ovulation process occurs as a result of the maximum level of estradiol in the preovulatory follicle (Fig. 4), which stimulates the ovulatory release of LH and FSH by the pituitary gland through a positive feedback mechanism. Ovulation occurs 10-12 hours after the LH peak or 24-36 hours after the estradiol peak (Fig. 4).
The process of rupture of the follicle's basement membrane occurs under the influence of various enzymes and biologically active substances: collagenase in granulosa cells, prostaglandins, oxytocin, relaxin, as well as proteolytic enzymes such as plasmin and histamine produced by luteinized cells. Under the influence of the LH peak, progesterone, synthesized in the luteinized cells of the preovulatory follicle, plays an important role in the activation of proteolytic enzymes, thereby causing rupture of the follicle's basement membrane.
Ovulation is accompanied by bleeding due to the rupture of capillaries surrounding the teka cells around the follicle.

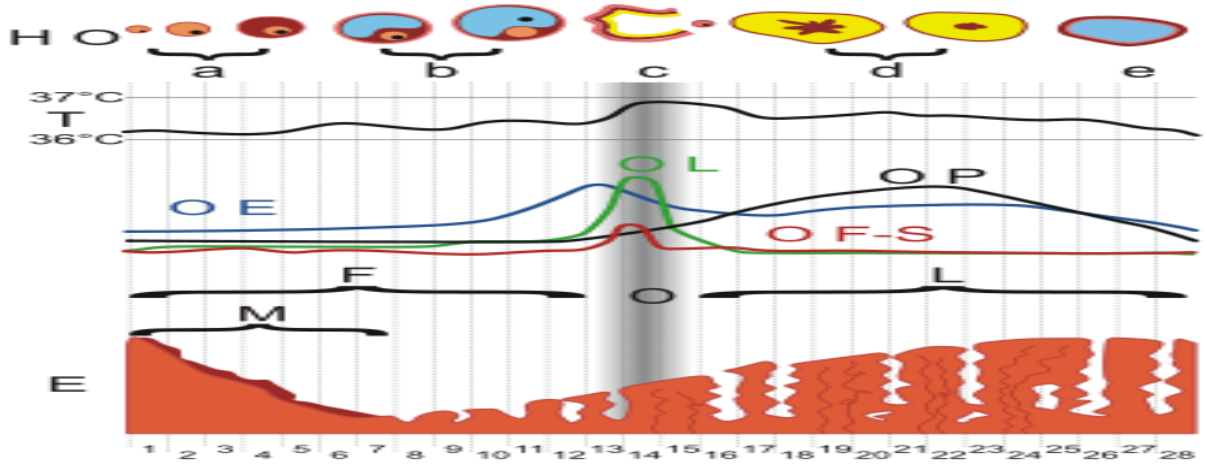

Figure 4. Ovarium-menstrual cycle
Lutein phase of ovarian cycle
After ovulation, new capillaries quickly grow into the cavity of the ovulated follicle, granulosa cells become more luteinized, turning into a corpus luteum that secretes progesterone (this process occurs under the influence of LH). Luteinization of granulosa cells is morphologically manifested by an increase in their size and the formation of lipid inclusions.
The corpus luteum is a temporary hormonally active structure that functions for 14 days, regardless of the total duration of the menstrual cycle. A full-fledged corpus luteum develops only in the phase when a sufficient number of granulosa cells rich in LH receptors are formed in the preovulatory follicle.
The following stages are distinguished in the development of the corpus luteum:
• **Proliferation** - active luteinization of granulosa cells under the influence of LH;

• **Vascularization** - the growth of capillaries into the corpus luteum;
• **Development** (growth) - occurs on days 21-22 of the cycle; the morphological formation of the corpus luteum is completed, the concentration of sex steroids increases (see Fig. 4). The combined effect of progesterone and estradiol ensures pre-implantation (secretory) transformation of the endometrium and prepares it for implantation;
• **Regression** - decreased activity of the corpus luteum, which is associated with a decrease in LH receptors. High concentrations of estradiol and prolactin (PRL) at the end of the menstrual cycle also have a luteolytic effect; as a result of corpus luteum regression, the level of progesterone decreases (see Fig. 4), which causes desquamation of the endometrium in the uterus, and the cycle resumes.
If fertilization and implantation of the fetal egg occur (days 21-22 of the cycle), the developing human begins to produce chorionic gonadotropin (CHG), which stimulates the continued development of the corpus luteum. In this case, the corpus luteum of pregnancy is formed, which continues to produce progesterone at high concentrations, which is necessary for the preservation of pregnancy.
The corpus luteum of pregnancy persists for 8-10 weeks, then regresses, and the hormonal support of pregnancy is taken over by the already formed placenta by the end of the 1st trimester.
Hormonal function of ovaries

Cyclical processes occurring in the ovaries are characterized not only by morphological changes in the follicle and corpus luteum, but also by steroidogenesis - the synthesis of sex hormones, which is closely related to them.

According to the currently accepted theory, there is a bicellular theory of steroid biosynthesis in the ovaries: LH stimulates the synthesis of androgens in theca cells, while FSH activates the synthesis of aromathase enzymes in granulosa cells, which convert androgens into estrogens.

In the ovaries, steroid-producing structures are granulosa cells, theca cells, and, to a certain extent, stromal cells.

• Teka-cells are the main source of androgens;
• Granulosa cells are the main source of estrogens;

Progesterone is also synthesized in theca cells, but in the highest degree it is produced in the lutein cells of the corpus luteum (cells of luteinized granulosis).

The common substrate of all steroids, including hormones synthesized in the adrenal glands and testes, is cholesterol (see Fig. 5).

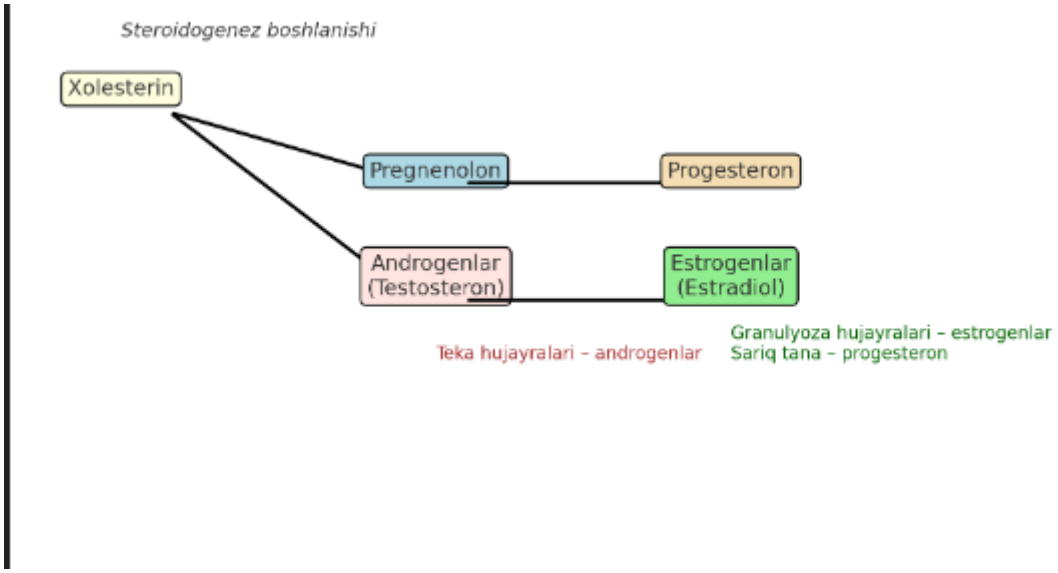

Figure 5. Biosynthesis of sex steroids (simplified scheme).
Extragonadal synthesis of sex hormones.
The synthesis of sex hormones occurs not only in the gonads, but also outside them. It is known that adipose tissue contains the P450 aromathase enzyme system, which participates in the conversion of androgens into estrogens. This process can also be triggered by various mitogenic growth factors (FR) or directly by estradiol itself.
In addition, biologically active testosterone (dihydrotestosterone) is also synthesized outside the gonads - in peripheral target tissues, such as hair follicles and sebaceous glands, under the influence of the enzyme 5-α-reductase. About 96% of all sex steroids are bound to proteins, in particular, to sex steroid binding globulin (GSPG) and albumins, the synthesis of which is carried out by the liver.
The biological effect of hormones manifests itself through free fractions that are not bound to proteins. Their level varies in various pathological conditions, in particular, insulin resistance, liver diseases, etc.
Estrogens.
The main fractions of estrogens are: estrone (E1), estradiol (E2), estriol (E3). The most biologically active estrogen is estradiol. Estriol, on the other hand, is a peripheral metabolite of estrone and estradiol and is not an independent secretory product of the ovaries. In 1965, the fourth estrogen - estetrol (E4) - was described and has a weak estrogenic effect, which has not yet been sufficiently studied.
Biological effects of estrogens:
1. On reproductive target organs:
• Proliferation of the endometrium and myometrium, growth of the epithelium of the vagina and cervix;
• Cervical canal mucus secretion;
Growth of the mammary gland ducts.
2. In non-reproductive target tissues:
• Proliferation in the urethra and bladder mucosa;
• development of the musculoskeletal system, increased bone mineralization (due to the synthesis of osteoblasts);
• Decreased secretion of sebaceous glands;
• Increased synthesis and maturation of collagen in the skin;
• Reduction of hirsutism (antiandrogenic effect through a decrease in GSPH clearance);
• Antiatherogenic effect (reduces atherogenic fractions of lipids);
• Fatty tissue distribution and female skeletal formation, female voice timbre;
• Improvement of the functions of the central nervous system (cognitive and others);
• Protective (antiatherosclerotic) effect on the vascular endothelium;
• Increased coagulation properties, tendency to thrombosis (due to increased synthesis of coagulation factors in the liver);
• Increasing libido levels.
The biological effect of estrogens on various organs and tissues depends on the number of specific receptors and their sensitivity. Two types of estradiol receptors have been identified:
• ER-α - nuclear receptors, has a proliferative effect;
• ER-β - membrane receptors, have an antiproliferative effect.
Gestagens, mainly progesterone, play a key role in controlling the ovarian-menstrual cycle and maintaining pregnancy. Their functions are systematized as follows:
Biological effects of progesterone:
1. Reproductive system:
• Activates proteolytic enzymes in the preovulatory follicle → disrupts the basement membrane and ensures complete ovulation.
• Causes secretory transformation of the endometrium, preparing it for implantation.
• Ensures decidual transformation of the endometrium during pregnancy.

• Reduces T-killer cell expression through Progesterone-Induced Pregnancy Factor (PIGF) → protects the embryo from rejection by the immune system.
• Has a muscle relaxation effect (especially in the myometrium), prevents premature contractions.
2. Mammary glands:
• Stimulates the proliferation of alveolar epithelium → prepares for lactation.
3. General systemic impacts:
• affects the thermoregulatory center of the hypothalamus → is explained by an increase in basal temperature after ovulation.
• Has an antimineralocorticoid effect (mild diuretic effect).
• Has an antiestrogenic effect on the endometrium and mammary gland, preventing hyperplasia and tumor development.

- Receptor exposure:
- • Progesterone receptors (PR) type A - predominate in the epithelium of the endometrium and mammary glands → have an antiproliferative effect.
- Therefore, progesterone analogs are used in the treatment of endometrial and breast hyperplastic processes.
- • PR type B - predominates in the myometrium → has a proliferative effect.
- o This plays an important role in the development of uterine fibroids.
- o In modern treatment methods, selective PR B receptor blocking modulators are effectively used in the treatment of myoma.

Androgens.
The main androgenic fractions are the strong androgen - testosterone, its weak anterior form - androstendione, as well as dehydroepiandrostendione (DGEA) and its sulfate (DGEA-S). The most biologically active androgen is dehydrotestosterone, which is synthesized by the enzyme 5-α-reductase of testosterone in peripheral tissues (hair follicles, sebaceous glands).
The main sites of androgen synthesis in a woman's body:
• ovaries,
• adrenal glands,
• adipose tissue,
• skin and its appendages (hair, sebaceous and sweat glands).
Biological effects of androgens:
• atrophy of the endometrium and myometrium;
• atrophic changes in the glandular tissue of the mammary glands;
• stimulation of atresia in ovarian follicles;
• suppression of the secretion of pituitary gonadotropins;
• enhance the synthesis of osteoblasts, accelerate the ossification of epiphyseal growth zones;
• anabolic effect (protein synthesis, increase in muscle mass);
• Increase the growth of thick (straight) hair in androgen-dependent and independent zones;
• increase the secretion of sebaceous glands;
• rough voice;
• retention of liquids and electrolytes;
• control of sexual behavior (libido).
Level I of regulation of reproductive function is the sections of the internal and external reproductive system (uterus, fallopian tubes, vaginal mucosa), as well as the mammary glands, sensitive to changes in the level of sex steroids. The most pronounced cyclical changes occur in the endometrium and constitute the uterine cycle.
Uterine cycle
Cyclical changes in the endometrium relate to its functional outer layer (consisting of compact epithelial cells) and intermediate layer. They fall out during menstruation. The basal layer does not shed during menstruation and ensures the restoration of desquamated layers.

Cyclical changes in the functional layer occur in three consecutive stages, corresponding to the ovarian cycle: the proliferation stage, the secretion stage, and the desquamation (menstruation) stage.

Desquamation phase

Menstruation observed at the end of each cycle is associated with the shedding of the functional layer. The onset of menstruation is the first day of the cycle.

Menstruation lasts an average of 3-5 days. Endometrial hypoxia increases due to the regression of the corpus luteum and a sharp decrease in the level of sex steroids. The onset of menstruation is facilitated by prolonged spasm of the arteries, blood stasis, and the formation of thrombi. Increased endothelial permeability, brittleness of the vessel walls, numerous small hemorrhages, and leukocyte infiltration also exacerbate hypoxia. Proteolytic enzymes secreted by leukocytes accelerate tissue dissolution.

Subsequently, the vessels dilate paretically, and blood flow increases. Due to this, pressure in the microcirculatory system increases, the walls weaken and crack, and necrotic parts of the functional layer actively shed. By the end of the 1st day, 2/3 of the functional layer is deposited, usually on the 3rd day.

Menstrual discharge contains blood and cervical mucus, which are rich in leukocytes. Menstrual blood practically does not clot, is rich in calcium ions, has little fibrinogen, and no prothrombin. On average, 50-70 ml of blood is lost during one menstruation.

After the destruction of the necrotic layer of the endometrium, the stage of regeneration begins. At this stage, epithelialization occurs due to the cells of the basal layer. These processes are controlled by estrogens and help stop bleeding. Some authors distinguish regeneration as a separate stage of the uterine cycle.

Proliferation phase

After the end of menstruation, starting from the 3-5th day, the thickness of the functional layer increases under the influence of estrogens. In this case, all elements of the basal layer (glands, stroma, blood vessels) grow actively. The glands are initially straight or slightly curved, while the spiral arteries are less curved.

In the late period of proliferation (11-14 days), the glands bend more and become screw-shaped, and the spiral arteries reach the surface of the endometrium. By this time, the thickness of the functional layer reaches 7-8 mm.

Secretion phase

It begins after ovulation (days 13-14) and lasts for 14 days. This period is associated with the activity of the corpus luteum. Under the influence of progesterone and estradiol, endometrial glands begin to produce secretions (glycosaminoglycans, glycoproteins, glycogen).

• Early secretion phase (15-18 days): glands bend and their lumens expand. Estrogen levels decrease for a short time, and superficial hemorrhages are observed.

• Medium secretion phase (days 19-23): progesterone reaches its maximum level. The thickness of the endometrium is 9-12 mm. It is clearly divided into 2 layers: deep (spongiosis) and upper (compact). During this period, the most favorable conditions for implantation ("implantation window") are formed.

Late secretion phase (24-27 days): endometrial trophism is disrupted, degenerative changes intensify. The glands bend and take on a star-shaped shape, and dilation and hemorrhages are observed in the vessels. This condition is called anatomical menstruation and occurs 1 day before menstruation.

Changes in cervical and vaginal mucosa

Cervix: in the follicular phase, under the influence of estrogen, the canal dilates, mucus increases, reaches its maximum during ovulation ("fern symptom").

• In the lutein phase, the channel narrows under the influence of progesterone, the mucus thickens and does not stretch.

In the vaginal epithelium: under the influence of estrogens, proliferation increases, the number of cells increases, the KP index is high (60-80%). In the lutein phase, under the influence of progesterone, apoptosis and cell shedding increase, the KP index is low (20-25%).

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Table 1.

Functional diagnostic tests.

Test nomi	Follikulyar faza (estrogen ta'siri)	Ovulyatsiya davri	Lutein faza (progesteron ta'siri)
"Zrachok" simptomi (tashqi bachadon og'zi ochilishi)	+ (tashqi og'iz ochiladi)	Maksimal ochilish (diametri keng)	– (og'iz yopiladi)
Servikal shilliq "paparotnik" simptomi (kristallanish)	+ (mavjud)	Maksimal kristallanish (aniq "paparotnik")	– (yo'qoladi, shilliq quyuqlashadi)
Shilliqning cho'zilish simptomi	4–6 sm	Maksimal 8–10 sm	0–2 sm (yo'qoladi)
Bazal tana harorati (BTT)	< 37 °C	Tushish / "ovulyator cho'qqisi"	> 37 °C (2-jadval o'rtacha +0,4–0,6 °C)
Kariopiknotik indeks (KPI)	Yuqori (60–80%)	Eng yuqori	Past (20–25%)

Morphological changes are also observed in the mammary glands during the menstrual cycle as a result of hormonal influence. Under the influence of estrogens, in the first half of the cycle, the epithelium of the milk ducts of the mammary glands undergoes active proliferation, their length and branching increase. In the second half of the cycle, under the predominant influence of progesterone, the number and activity of secretory epithelial cells increase in the alveolar (acinus) parts. Thus, the alternating effects of estrogen and progesterone play an important role in preparing the mammary glands for pregnancy and lactation.

Questions.

1. What is the concept of a menstrual cycle, and what is its average duration?
2. What are the main phases of the menstrual cycle?
3. In which phase does ovulation occur, and what is its physiological significance?
4. How many days does menstruation (bleeding accompanied by the separation of the endometrial layer) usually last?
5. What is the role of the estrogen hormone in the menstrual cycle?
6. What are the main functions of the hormone progesterone?
7. In which organ does the egg develop and undergo maturation?
8. What morphological and functional changes occur in the endometrium during the menstrual cycle?
9. What are the specific differences between the follicular phase and luteal phase?
10. What changes are observed in the level of luteinizing hormone (LUH) during ovulation?

Situational problem.

1. Condition: The last menstruation in a 22-year-old woman was 35 days ago. Currently, there is pain in the lower abdomen, the basal body temperature has risen to 37.2°C.
Question: Which phase of the cycle is characterized by these features?
2. Situation: A 17-year-old girl had no menstruation for 2 months. She is not pregnant. Body weight decreased sharply, and physical exercises intensified.
Question: What is the most likely cause of amenorrhea?
3. Condition: A 28-year-old woman experiences chest pain, mood changes, and swelling 14 days before menstruation.

Question: Which phase do these signs correspond to?
4. Situation: A 32-year-old woman complains of severe abdominal pain and heavy bleeding on the first day of menstruation.
Question: Which hormonal imbalance can cause this condition?
5. Situation: A 20-year-old girl's menstrual cycle lasts 21 days, and menstrual bleeding lasts 7 days. Hemoglobin levels are low.
Question: What pathology does this condition increase in risk?
6. Condition: In a 29-year-old woman, menstrual bleeding is minimal, but the cycle is regular (28 days). Ovulation is not observed.
Question: What is this cycle called?
7. Condition: On the 12th day of menstruation in a 25-year-old woman, clear, stretchy discharge from the cervix is observed.
Question: What does this symbol indicate?
8. Condition: A 35-year-old woman experiences back pain, swelling, and irritability before menstruation.
Question: What syndrome explains this condition?
9. Condition: In an 18-year-old girl, the cycles have been irregular for 2 years since the onset of the menstrual cycle - from 30 to 60 days.
Question: What could be the physiological cause of such changes at this age?
10. Condition: A 27-year-old woman had a high progesterone level on the 16th day of menstruation.
Question: Which phase of the cycle does this result correspond to?

Tests.
1. What is the average duration of the menstrual cycle?
A) 14 days
B) 21 days
C) 28 days
D) 35 days
2. In which phase of the menstrual cycle does ovulation occur?
A) Follicular phase
B) Lutein (yellow body) phase
C) Ovulatory phase
D) Menstrual phase
3. Which hormone increases sharply during ovulation?
A) FSH
B) LH
C) Progesterone
D) Prolactin
4. Where is progesterone mainly formed?
A) Pituitary gland
B) In the corpus luteum
C) In the adrenal cortex
D) Endometrial
5. How many days does menstrual bleeding usually last?
A) 1-2 days
B) 3-7 days
C) 8-10 days
D) more than 10 days
6. What is the main function of estrogens?
A) Preparation of the endometrium for secretion

B) Stimulation of follicle maturation and proliferation
C) Reduction of hormone secretion after ovulation
D) Increasing body temperature
7. In which phase does basal body temperature rise?
A) Follicular
B) Ovulator
C) Lutein
D) Menstrual
8. On what day of the cycle (in the 28-day cycle) does ovulation usually occur?
A) Day 7
B) 10th day
C) Day 14
D) 21st day
9. What is the effect of progesterone on the uterus?
A) Leads to endometrial proliferation
B) Prepares the endometrium for secretion
C) Stimulates ovulation
D) The follicle begins to grow.
10. What is the average duration of the lutein phase?
A) 7 days
B) 10 days
C) 14 days
D) 21 days

TOPIC 2: MENSTRUAL CYCLE DISORDERS. AMENORRHEA

Amenorrhea **(code N91.0-N91.2 according to ICD-10)** is an absence of menstruation for 6 months or more.

Amenorrhea is not an independent disease, but a symptom of various degrees of reproductive system pathology, neuroendocrine disorders, and benign and malignant tumor processes.

The frequency of amenorrhea is approximately 1.8-3.5% among women of reproductive age and 3.5-5% among female students. Amenorrhea accounts for 10-15% of menstrual and generative dysfunction. Primary amenorrhea is significantly less common than secondary and accounts for approximately 10% of amenorrhea.

Classification. Depending on the degree of disorders in the regulation of menstrual function, different forms of amenorrhea are distinguished (Fig. 1).

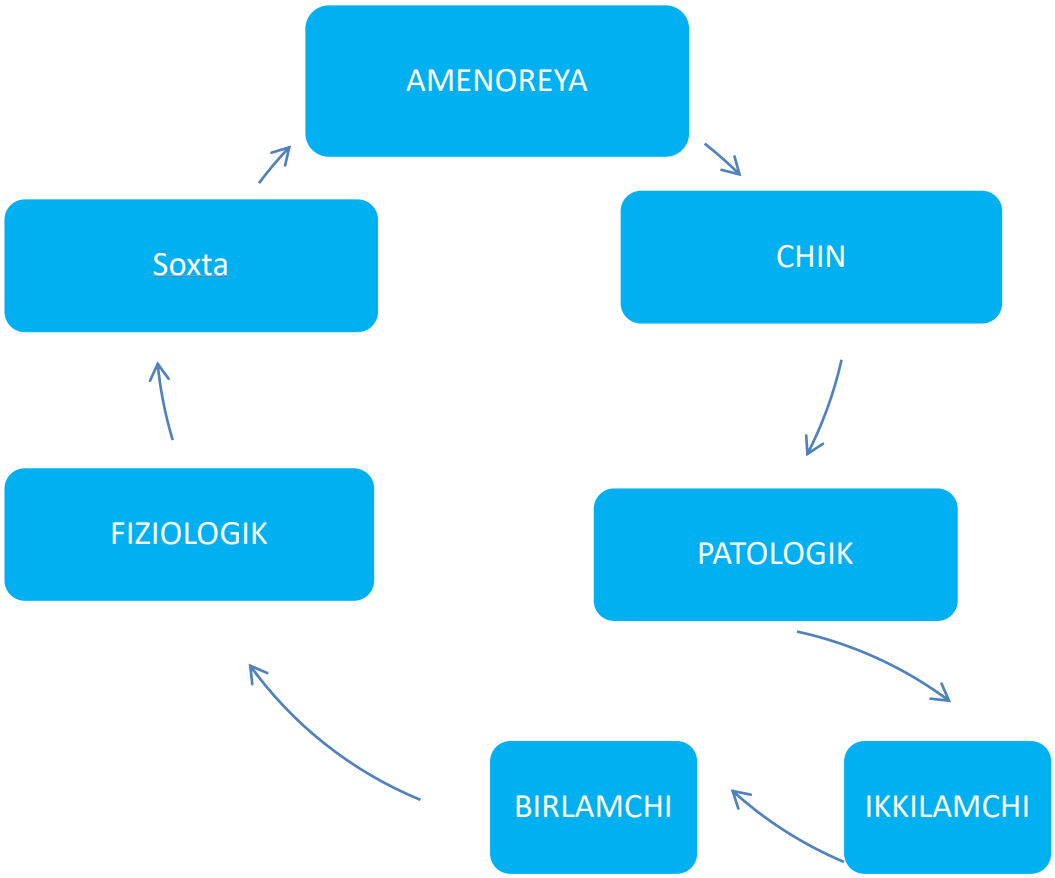


Figure 1 - Classification of amenorrhea

Amenorrhea can be false (fals) and true (verum). False amenorrhea is a condition in which cyclic processes in the hypothalamus-pituitary-ovaries-uterine (HPO) system occur normally, but no menstrual bleeding occurs. The main causes of false amenorrhea include atresia of the hymen, vagina, or cervical canal, as well as developmental defects of the genital organs. Menstrual blood accumulates in the vagina, forming hematokolpos; in the uterus - hematometra; in the fallopian tubes - hematosalpinx. Sometimes menstrual blood enters the abdominal cavity through the fallopian tubes, mimicking the "acute abdomen" clinic. Treatment of false amenorrhea is performed surgically: incision of the hymen, expansion of the vagina and cervical canal.

True amenorrhea is a condition in which there are no cyclical changes in the HPO system, clinically manifested by absence of menstruation. True amenorrhea can be physiological or pathological.

Physiological amenorrhea is observed in:

• in girls before puberty;
• during pregnancy;
• during lactation;
• in the postmenopausal period.

Pathological amenorrhea is divided into primary and secondary:

• Primary amenorrhea - the first absence of menstruation after the age of 16.
• Secondary amenorrhea - absence of menstruation lasting 6 months or longer in previously menstruated women.

Etiologically, true pathological amenorrhea can be associated with impaired gonadal function (gonadal) or extragonadal causes.

PRIMARY TRUE PATHOLOGICAL AMENORRHEA OCCURRING AS A RESULT OF GONAD DISORDER

The main causes of primary true pathological amenorrhea caused by impaired gonadal function are:

1. Gonadal dysgenesis.
2. Testicular feminization syndrome (Morris syndrome, pseudo-male hermaphroditism).
3. Primary ovarian hypofunction ("resistant" ovarian syndrome).

Gonadal dysgenesis is a congenital pathology in which the ovaries lack functionally active hormone-producing tissue due to chromosomal abnormalities.

Forms of gonadal dysgenesis:

• Typical form (Shereshevsky-Turner syndrome) - karyotype 45XO;
• Hidden form - the karyotype has a mosaic nature, 45XO/46XX;
• Mixed form - the mosaic karyotype necessarily contains the Y chromosome or part of it (the most common karyotype is 45XO/46XY);

Pure form (Sweyer syndrome) - karyotype 46XX or 46XY.

For ovarian development, there must be two sex X chromosomes, i.e., the female karyotype - 46XX. During meiosis of germ cells, chromosome set anomalies can occur. When such sex cells unite and enter the fertilized egg, a pathological set of chromosomes appears. As a result, the ovaries develop morphofunctionally and cannot produce sex steroids. Estrogen deficiency increases excess gonadotropin synthesis, therefore this amenorrhea is considered hypergonadotropic.

The clinical picture is characterized by primary amenorrhea and variability of symptoms. Such patients may typically have short stature, chest, kidney, ureter, and cardiovascular system developmental anomalies. Gynecological examination reveals immaturity of secondary sexual characteristics, hypoplasia of internal and external genitalia, atrophy of the vulva and vaginal mucosa.

Diagnosis is primarily based on the clinical presentation specific to each form of dysgenesis. When determining the level of the hormone in blood plasma, a sharp increase in gonadotropins (LH, FSH) is observed, and the level of estradiol is low. A hormonal test with progestogen gives a negative result, which confirms estrogen deficiency; a test with estrogen and progestogen is positive, excluding the possibility of amenorrhea in the uterine form.

Genetic examination includes the determination of sex chromatin in oral swabs and the determination of the karyotype, in which the absence of sex chromatin and the corresponding karyotype are determined.

On ultrasound examination of the turtle cavity, the ovaries are in the form of connective tissue with a length of 1-1.5 cm and a width of 0.3-0.5 cm, characterized by the absence of follicles; the endometrium is linear, the uterus is reduced in size.

Treatment depends on the presence of the Y chromosome. If present, endoscopic surgical removal is necessary before the age of 20, as there is a high risk of malignancy of the gonads. If the Y chromosome is absent in the karyotype or the gonads have been surgically removed, hormone replacement therapy is administered until natural menopause.

This therapy focuses on:

• Body feminization, development of sexual hair, breasts, and uterus;
• suppression of gonadotropin levels;
• Cyclical changes in the endometrium and the development of a menstrual reaction;
• Prevention of conditions related to estrogen deficiency (osteoporosis, metabolic disorders, cardiovascular diseases);
• Social adaptation;
• Improving the quality of life.

Restoration of generative function is possible with the help of assisted reproductive technologies using donor eggs.

Testicular feminization syndrome (Morris syndrome, pseudo-male hermaphroditism). In such patients, the karyotype is 46XY. The presence of the Y chromosome determines the formation of an egg from an indifferent gonad, but due to the lack of the enzyme 5α-reductase due to a genetic defect, the hormonal secretion of these eggs is incomplete. This enzyme converts testosterone into a more active dihydrotestosterone. As a result, the process of spermatogenesis and differentiation of the external genitalia of the male type does not occur.
There are complete and incomplete forms of Morris syndrome.

Full form: Patients have a female-like phenotype with well-developed mammary glands. The external genitalia are female-type, but the vagina is incomplete (blind), the uterus and ovaries are absent. The eggs can be located in the abdominal cavity, inguinal canals, or inside the large lips.
• Incomplete form: External genitalia are similar to the male type; the labia majora merge, the clitoris enlarges, the urogenital sinus is preserved. The uterus, ovaries, and fallopian tubes are absent; the eggs are usually located in the abdominal cavity.
Diagnostics: In the diagnosis of Morris syndrome, bimanual vaginal examination, hormonal and ultrasound examinations, determination of the karyotype, and laparoscopy are important.
Such patients may have a history of surgical interventions for congenital inguinal hernias, which is rare in women. Due to the high risk of malignancy, the surgical removal of underdeveloped ovaries is mandatory. Subsequently, hormone replacement therapy is administered.
If necessary, correction of the external genitalia and vaginal plastic surgery are performed.
. Primary ovarian hypofunction (resistant ovarian syndrome).
In this form of amenorrhea, chromosomal pathology is absent, but a decrease in the follicular apparatus of the ovaries is observed. Damage to the follicular apparatus can lead to ovarian hypoplasia as a result of pathological processes during pregnancy or inflammatory or tumor processes in childhood, which causes a decrease in ovarian sensitivity to gonadotropins ("resistant" ovaries).
Clinical presentation: In "resistant" ovarian syndrome, in addition to amenorrhea or hypomenstrual syndrome, there is immaturity of secondary sexual characteristics, hypoplasia of external and internal genitalia.
Laboratory tests: Blood levels of FSH and LH increase sharply, while estrogen levels decrease. Diagnosis includes bimanual vaginal examination, ultrasound (US), and gonadal biopsy with laparoscopy. In these examinations, a decrease in the size of the uterus and ovaries is revealed; histological analysis reveals the presence of primordial and preantral follicles in an ovarian biopsy.
Treatment: Patients with "resistant" ovarian syndrome receive cyclic hormone replacement therapy, which produces a menstrual-like response. At the same time, such women have impaired reproductive function.

PRIMARY TRUE PATHOLOGICAL AMENORRHEA CAUSED BY EXTRAGONADIC CAUSES.

This group includes amenorrhea caused by the following reasons:
1. Classical congenital adrenal cortex dysfunction.
2. Hypothyroidism.
3. Damage to the central nervous system and hypothalamic-pituitary region.
4. Endometrial disorders.

Congenital adrenal cortex dysfunction, classic form (false female hermaphroditism). It develops as a result of congenital deficiency of the enzyme C21-hydroxylase, which reduces cortisol production and increases excess ACTH secretion. As a result, bilateral congenital hypoplasia of the adrenal cortex occurs, and the synthesis of androgens increases. **Karyotype 46XX.**

Clinical signs: virilization is observed in the external genitalia (enlargement of the clitoris, fusion of the labia majora and minora, preservation of the urogenital sinus), but the uterus and ovaries are properly developed.

Diagnostics: based on clinical and laboratory studies, determination of karyotype, measurement of androgen levels before and after the dexamethasone test, ultrasound (UZ) examination.

Treatment: glucocorticosteroid preparations (dexamethasone) are used; in cases of severe virilization - plastic surgery on the genital organs is performed.

Hypothyroidism. This occurs as a result of hereditary defects in the biosynthesis of thyroid hormones in the thyroid gland, infectious-inflammatory processes or autoimmune diseases, as well as insufficient intake of iodine into the body. Under conditions of thyroid hormone deficiency, the growth of thyroid cells increases, which produce more TSH; the function of pituitary LH-producing cells is suppressed, the FSH/LH ratio increases, and the level of prolactin also increases.

Clinical signs: immaturity of the genitals and secondary sexual characteristics, disorders in the growth and development of bone tissue.

Diagnosis is based on blood tests to determine the levels of TSH, thyroxine, triiodothyronine, and sex hormones. Taking thyroid medications restores the menstrual cycle.

Damage to the hypothalamic-pituitary region can be organic (traumatic, toxic, infectious, tumor) or neuro-psychic.

Amenorrhea often occurs in cases of schizophrenia, manic-depressive psychosis. Cerebral forms of primary true pathological amenorrhea include neural anorexia and psychogenic amenorrhea.

Neural anorexia amenorrhea: usually observed as a result of a tendency to lose weight and rapid weight loss of 15% or more, since adipose tissue is the source of extragonadal estrogen synthesis.

With a weight loss of 46 kg, the pituitary gland's ability to respond to the administration of gonadoliberins is sharply reduced or completely lost.

Clinical presentation: decrease in body weight by 15-25% of the age-appropriate norm, sharp decrease or absence of appetite, moderate hypoplasia of the mammary glands and genitals.

Diagnostics: low gonadotropin levels on hormonal tests, decreased uterine volume despite normal ovaries on ultrasound.

Treatment: normalization of diet, enzyme preparations, vitamins B, C, E, valerian infusion are prescribed. Psychotherapy is administered.

Psychogenic amenorrhea occurs as a result of emotional-psychological trauma, mental or physical overload. Excessive release of ACTH, endorphins, and neurotransmitters under stress reduces or blocks the production and release of gonadoliberins, resulting in a decrease in gonadotropins.

Clinical signs: in addition to amenorrhea, astheno-neurotic, astheno-depressive, or astheno-hypochondriac syndromes are observed.

Treatment: conducted jointly with a psychoneurologist; antidepressants, neuroleptics, vitamins B, A, E are prescribed, work and rest regimen are normalized, stress is eliminated.

Injuries to the organic central nervous system may be accompanied by primary amenorrhea:

Chronic meningoencephalitis, arachnoiditis.

• Hypothalamic injuries or tumors, which can manifest as adiposogenital dystrophy (Pehrkranz-Babinski-Frelich syndrome), hereditary diencephalic-retinal degeneration (Lorenz-Moon-Barde-Bidle syndrome). In these diseases, obesity and skeletal developmental defects are observed. Patients with Lorenz-Moon-Barde-Bidle syndrome have mental excess (oligophrenia).

Gipofiz shikastlanishi natijasida yuzaga keladigan birlamchi amenoreya gipofizar nanizm (pangipopituitarizm) va gipofizar kaheksiya (Simmon kasalligi) bilan kechadi.

Primary amenorrhea in uterine form occurs as a result of developmental anomalies of the uterus, including in Rokitansky-Küstner-Mayer-Hauser syndrome, where the uterus and vagina are composed of thin connective tissue. This amenorrhea can also develop under the influence of endometrial damaging factors (endometrial disorders resulting from tuberculosis) or decreased sensitivity of endometrial receptors to sex hormones.

SECONDARY TRUE PATHOLOGICAL AMENORRHEA

Unlike primary amenorrhea, secondary amenorrhea is more common and accounts for up to 75% of the structure of all forms of amenorrhea. This is a common symptom associated with polycystic ovary syndrome, metabolic syndrome, adrenal and thyroid dysfunction.

Depending on the degree of damage to the hypothalamic-pituitary-ovarian-uterine system, secondary amenorrhea is divided into the following forms:
1. Hypothalamic form.
2. Pituitary form.
3. Ovarian shape.
4. Uterine amenorrhea.

Hypothalamic secondary true pathological amenorrhea, like the primary form, can develop as a result of organic and functional damage to the central nervous system.

This group includes the following cases:
• Psychogenic amenorrhea
• Nerve anorexia
• "Physical pregnancy"

False pregnancy: occurs in women who really want to have children or, conversely, do not want to get pregnant. Amenorrhea occurs, the mammary glands swell, and body weight increases (due to fat accumulation). Pathogenesis is associated with increased secretion of luotropin and prolactin, which suppresses the production of follitropin, and as a result, anovulation and amenorrhea develop.

Treatment: psychotherapy and sedatives are prescribed. The menstrual cycle usually recovers spontaneously within 1-3 months.

Also:
• Neuropsychiatric amenorrhea
• Amenorrhea with galactorrhea

o Del Castillo - Forbes - Albright syndrome: amenorrhea in non-pregnant women due to psychological trauma or a tumor in the hypothalamic-pituitary region.
o Chiari-Frommel syndrome: amenorrhea and galactorrhea occurring in the puerperium.

In both cases, the hypothalamus reduces the production of prolactostatin, which suppresses prolactin secretion. In the presence of pituitary tumors, prolonged hyperprolactinemia suppresses follitropin secretion, which disrupts the secretory function of the ovaries and leads to amenorrhea.

Secondary true pathological pituitary amenorrhea.

This group includes secondary amenorrhea caused by organic damage to the adenohypophysis, for example, necrotic changes develop as a result of a tumor or circulatory disorder. These conditions are manifested in the following diseases:

Shihan syndrome (postpartum hypopituitarism): the disease develops as a result of necrosis of the anterior pituitary lobe, which is caused by massive blood loss (800 ml and more) or spasm of arterial vessels against the background of bacterial shock during childbirth or abortion.

Clinical manifestations: manifested by varying degrees of endocrine gland hypofunction (thyroid, adrenal, and sex glands). These symptoms include amenorrhea, agalactia, headache, dizziness, anorexia, breast atrophy, hair loss, and others.

Simmons syndrome: develops as a result of infectious damage, trauma, circulatory disorders, or pituitary tumors of the adenohypophysis. In such patients, amenorrhea, cachexia, atrophy of the genitals, hypothyroidism, and hypocorticism are observed.
Itsenko-Cushing's disease: The development of the disease is caused by basophilic adenoma of the pituitary gland, in which pronounced signs of hypercorticism, excessive production of corticotropin, and a sharp decrease in gonadotropins are observed.
Patients clinically:
• Uneven obesity in the upper body, thin arms and legs;
• Red-brown stripes on the skin of the abdomen, thighs, and chest (steria);
• The shape of the moon's face (lunar face) is red-brown;
• Excessive hair growth on the face, body, and limbs;
• Arterial hypertension
Hyperprolactinemia. As a result of increased prolactin synthesis in the hypothalamus, the production and release of GnRH decreases, and as a result, the levels of LH and FSH also decrease. In the ovaries, prolactin slows down gonadotropin-dependent steroid synthesis, reduces ovarian sensitivity to exogenous gonadotropins, and decreases the secretion of progesterone by the corpus luteum.
Pathological hyperprolactinemia develops as a result of anatomical or functional disorders of the hypothalamic-pituitary complex.
Anatomical causes:
• Pituitary tumors (craniopharyngioma, glioma, granuloma)
• Hormone-active tumors (prolactinoma, prolactin and ACTH-secreting mixed adenomas)
• Pituitary cortex injury or surgery, traumatic brain injury, radiation exposure
Functional causes:
• Stress, neuroinfections (meningitis, encephalitis)
• Various endocrine diseases (hypothyroidism, Cushing's disease, Nelson's syndrome, acromegaly)
Less common reasons:
• Kidney failure
• Ectopic prolactin production (bronchogenesis carcinoma, hypernephroma)
• Thoracic surgery or injuries
• Iatrogenic causes (drugs):
o Drugs affecting dopamine secretion and metabolism: phenothiazines, haloperidol, metoclopramide, domperidone, pimozid, sulpiride
o Medications that reduce dopamine reserves in the central nervous system: reserpine, monoamine oxidase inhibitors, opioids
o Serotonin system stimulating drugs: amphetamines, hallucinogens

Clinical presentation:
• Menstrual cycle disorders, often in the form of secondary amenorrhea
• Indirect or direct infertility
Galactorrhea: the release of milk in the form of several drops or streams is observed in 67% of women with hyperprolactinemia, the degree of which is not associated with prolactin.
• About half of the patients experience headaches (often migraine-type), dizziness, and an acute transient increase in arterial pressure.
Acromegaly and gigantism. The disease develops as a result of acidophilic adenoma of the pituitary gland, in which the synthesis of somatotropic hormone increases and gonadotropins are suppressed. Patients manifest with amenorrhea against the background of gigantism or acromegaly. If the disease develops before puberty - gigantism, after puberty - acromegaly develops.
Diagnostics: anamnesis, clinical signs, physical examination, hormonal tests, X-ray examination of the Turkish chair, computed tomography.

Treatment: surgical removal upon detection of a tumor. Primary importance in treatment was given to hormone replacement therapy and specific etiological (etotropic) therapy.

Secondary true pathological amenorrhea in ovarian form. The following forms are distinguished:

1. *Early ovarian insufficiency (syndrome of premature ovarian termination, "early menopause").* The disease is characterized by the cessation of menstruation in women aged 35-37 years. Studies show that in the antenatal and postnatal periods, various negative factors (radiation, chemicals, teratogenic drugs, influenza, measles, mumps viruses) can damage the ovaries, replace them with connective tissue, and lead to the apoptosis of hormone-active cells in the follicles. As a result, the hormonal function of the ovaries abruptly stops, and the synthesis of gonadoliberin and gonadotropins increases through the mechanism of negative feedback. Therefore, this form of amenorrhea is considered hyper-gonadotropic.

2. *Ovarian termination syndrome can develop after subtotal ovarian resection,* especially in the presence of cystadenoma, in particular endometrioid cysts.

Clinical presentation: characterized by vegetative-vascular signs typical of the postmenopausal period - fever, sweating, fatigue, headache, etc., accompanied by decreased work capacity. Menarche and menstrual function are initially normal and do not deteriorate for a long time. The disease usually begins with amenorrhea, rarely preceded by an oligomenorrhea period. Obesity is not typical in such women. Against the background of amenorrhea, atrophic processes develop in the mammary glands and genitals

3.*Hormone tests:* the level of gonadotropins, in particular FSH, increases significantly, the level of estradiol sharply decreases.

Transvaginal ultrasound: ovaries are reduced, follicles are absent, uterus is smaller than normal, endometrium is linear.

Treatment: aimed at preventing and treating conditions associated with estrogen deficiency (vegetative-vascular disorders, urogenital problems, osteoporosis, and cardiovascular diseases). For this purpose, hormone replacement therapy (HART) with natural estrogens is carried out up to the age of natural menopause.

Polycystic ovary syndrome (Stein-Leventhal syndrome).

The disease is characterized by menstrual cycle disorders, chronic anovulation, hyperandrogenism, enlargement of the ovaries and features of their morphological structure: bilateral enlargement of the ovaries by 2-6 times, hypoplasia of stromal and theca cells, multiple cystic-atretic follicles with a diameter of 5-8 mm, thickening of the ovarian capsule.

Clinical signs: menstrual cycle disorders, primary infertility, excessive hair growth, acne. Menarche usually begins at the age of 12-13. In most women (70%), the menstrual cycle is disrupted by the oligomenorrhea type starting from menarche; in less frequent cases (7-9%), abnormal uterine bleeding is observed. Secondary amenorrhea (up to 30%) occurs in untreated women over 30 years of age, often accompanied by obesity; in women with normal body weight, it begins during menarche and does not depend on the duration of anovulation.

Diagnosis: Based on the criteria of the 2004 Rotterdam Consensus:

• Oligomenorrhea and/or anovulation

• Hyperandrogenism (clinical and/or biochemical signs)

• Ultrasound signs of polycystic ovaries: ovarian volume >8 cm3, hyperechogenic enlargement of the stroma, number of antral follicles up to 10 mm in diameter ≥10, increased blood flow in the stroma and extensive vascular network through Doppler.

If two of these three signs are present, and other causes of TPS are excluded, TPS is diagnosed.

Hormone test: in most patients, the level of LH, testosterone, DHEA-S, 17-OPP increases; The LH/FSH ratio is >2.5; sometimes the level of prolactin increases.

Treatment:

• Normalization of body weight and metabolic disorders

• Restoration of ovulatory cycles

• Reproductive function restoration

• Elimination of endometrial hypoplastic processes
• Clinical signs of hyperandrogenism - hirsutism, elimination of acne.

Resistant ovarian syndrome.

Its development is associated with genetic defects in the receptor apparatus of the follicles. There is also data indicating the autoimmune nature of the pathology - antibodies that block FSH receptors in the ovaries have been identified. Intra-ovarian factors play a significant role in regulating FSH binding with follicular receptors.

Clinical presentation:

• Secondary amenorrhea up to 35 years of age
• Infectious and autoimmune diseases are more common among patients.
• The onset of the disease is associated with severe viral infections or stressful situations.
• No other complaints except absence of menstruation
• Menarche occurs on time, the menstrual cycle gradually transitions to the oligomenorrhea type, amenorrhea develops until the age of 35.
• Pregnancy is rare

Specific diagnostic features:

• Absence of vegetative-vascular disorders (heating, sweating) characteristic of ovarian termination syndrome and early menopause
• Female body type, body mass index 20-24 kg/m2
• Secondary sexual characteristics are normally developed
• Gynecological examination: hypoestrogenic signs such as hyperemia and thinning of the vulvar and vaginal mucosa.

Hormone test:

• High LH and FSH levels
• Low estradiol levels
• Prolactin level within normal range

Ultrasound (UZT) scan:

• The ovaries are of normal size, with numerous follicles 5-6 mm in diameter.
• Uterus of normal size, endometrium thin

Treatment:

• Replacement hormone therapy (e.g., Femoston 1/5)
• Purpose: prevention of estrogen deficiency, normalization of the menstrual cycle, suppression of gonadotropin levels

Amenorrhea associated with androgen-producing ovarian tumors.

When this tumor (androblastoma) develops, a large amount of testosterone is synthesized, which blocks the gonadotropic function of the pituitary gland.

Clinical presentation: initially a period of defemination, followed by the development of signs of virilization.

Diagnostics: clinical signs, gynecological and ultrasound examinations, detection of ovarian tumors, laparoscopy and biopsy.

Treatment: only surgical.

Amenorrhea due to ionizing radiation or surgical removal of the ovaries (post-castration syndrome).

Cause: removal of functional ovaries or significant ovarian dysfunction as a result of ionizing radiation, resulting in acute hypoestroneia.

Clinical presentation: signs of climacteric syndrome - vegetative-vascular, neuropsychiatric, and metabolic-endocrine disorders.

Diagnosis: usually detected without difficulty.

Treatment: Replacement hormone therapy (SHRT) is prescribed.

Secondary true pathological amenorrhea in uterine form.

This Uterine form of secondary true pathological amenorrhea may be caused by:

1. Tuberculous endometritis - damage to the endometrium caused by tuberculosis.
2. Mechanical injury of the endometrium - removal of the basal layer with hard intrauterine scraping.
3. Damage to the endometrium from chemical, thermal, or cryodestructive - as a result of the use of chemical solutions, high temperature, or cold.
4. Asherman syndrome (intrauterine synechiae) - develops as a result of frequent and severe intrauterine scratches or endometritis; accounts for approximately 3% of the causes of secondary amenorrhea. A characteristic sign is the cessation of menstrual bleeding after surgical intervention.

Hormone levels: This type of amenorrhea is called normogonadotropic because sex and gonadotropin hormones are within normal limits.

Diagnosis:

• Transvaginal ultrasound (UZT) can be used to suspect internal synechiae.
• Gestagen and estrogen-gestagen tests give a negative result.

The typical appearance of internal synechiae is determined by hysteroscopy and hysterosalpingography.

The infectious genesis of Asherman syndrome is determined by:

• Anamnestic data on the presence of a chronic inflammatory process.

Microbiological examination through endometrial biopsy and immunohistochemical studies.

Treatment:

• Surgically performed: incision of adhesions using histerorectoscopy.
• After the operation, an intrauterine spiral is inserted into the uterine cavity to prevent recurrence.
• Hormone therapy with natural sex steroids (Femoston 2/10, Cyclo-Proginova) is recommended for 3-6 months after surgery.

In the presence of endometritis, a course of antibacterial therapy is prescribed depending on the sensitivity of microorganisms.

• Medications that improve blood circulation and metabolism in the endometrium are used: pentoxifylline, diosmin, distriptase, Wobenzym.

Combined oral contraceptives (COCs) are not recommended, as they inhibit endometrial proliferation and exacerbate atrophic processes.

Surgical removal of the uterus. When diagnosing secondary amenorrhea in uterine form, the patient's somatic and sexual developmental characteristics, history of tuberculous or gonorrheal endometritis, diagnostic scrapes, miscarriage, and medical abortions are taken into account. Hormones in the blood are usually within the normal range. Hysteroscopy and endometrial biopsy are important diagnostic tools.

Treatment: Depending on the cause.

DIAGNOSIS OF MENSTRUAL FUNCTION IN AMENORRHEA BASED ON THE LEVEL AND NATURE OF DAMAGE TO THE MANAGEMENT SYSTEM.

Anamnestic and physical examination data are important in the diagnosis of amenorrhea, which help determine how hormonal secretion disorders affected the process of puberty and the development of secondary sexual characteristics.

History: presence of mental disorders, eating habits, physical activity and lifestyle, influence of environmental conditions, family history (genetic anomalies, cases of growth and developmental disorders).

Physical examination: morphometric parameters and constitutional features, distribution and density of the subcutaneous fat layer, distribution and growth rate of body hair, development of

mammary glands and their secretory activity. Signs of increased androgen secretion (hyperandrogenism) are also detected.

Hirsutism is an increase in male-type hair growth, assessed on the Ferriman-Gallwey scale in different areas of the body (a hirsutism score of 8 or higher is considered pathological).

Virilisation (masculinization) is the development of secondary male sexual characteristics, which includes hirsutism, lowering of the voice, development of certain muscle groups, enlargement of the clitoris, etc. At the same time, the woman's secondary sexual characteristics decrease (defeminization), such as breast shrinkage and vaginal atrophy.

A special gynecological examination is performed: examination of the external genitalia, speculum examination, and bimanual abdominal-vaginal or abdominal-rectal examination. The results of the clinical and anamnestic stage determine the spectrum of additional instrumental and laboratory studies.

Ultrasound examination of the pelvic organs, thyroid gland, and mammary glands is performed; if necessary, the adrenal glands are also examined. To exclude pituitary tumors, contrast CT or MRI of the pituitary gland is performed in women with normal thyroid function in cases of hyperprolactinemia. Histological examination with hysteroscopy, hysterosalpingography, laparoscopy and brain MRI if necessary High frequency of genetic anomalies and hereditary diseases, especially in cases of primary amenorrhea, requires genetic examination, including karyotyping and genetic counseling. After the exclusion of a tumor or congenital pathology of the reproductive system, hormonal studies and functional tests are conducted to assess its functional state.

FSH, LH, prolactin, TSH, T3, T4, progesterone, DHEA-C, 17-OPK, testosterone, cortisol, and ACTH levels are determined. Functional hormonal tests help in differential diagnosis and are designed to stimulate or suppress the activity of individual endocrine glands. If necessary, additional specialists are involved in the examination of patients: ophthalmologist (examination of the fundus, peripheral and color vision areas), therapist, endocrinologist, neurologist, psychiatrist, and psychologist.

AMENORRHEA TREATMENT

Treatment of patients with amenorrhea is complex and depends on the form of amenorrhea. The main goal of treatment is to identify and eliminate the disease that caused amenorrhea. In patients with obesity (body mass index >30 kg/m2) to reduce excess weight, a low-calorie diet is used for 3-4 months, which includes dosed physical exercise and taking orlistat at a dose of 120 mg before each meal. In women with impaired glucose tolerance, metformin (500 mg, 3 times a day) is considered appropriate during treatment. In patients with ovarian amenorrhea, cyclic vitamin therapy with cyclic estrogen-progestogen preparations (Femoston 1/10, Femoston 2/10, Cyclo-Proginova) is used to eliminate functional disorders. Clomifen citrate (Klostilbegit), gonadotropins, choriogon for ovulation stimulation in patients with chronic anovulation. If ovulation does not occur within 3-4 cycles, it is assessed as resistance to clomiphene, and a different method of ovulation stimulation is chosen.

Currently, research is being conducted with aromase inhibitors (letrosol) to stimulate ovulation. It is recommended to take them at a dose of 2.5-5 mg per day on days 5-9 of the menstrual cycle.

If anovulation occurs against a background of low FSH and LH levels and there is no result from indirect stimulation, gonadotropins are used. Gonadotropin drugs mainly include FSH (Puregon) or FSH and LH in equal amounts (Menopur, Menogon) and are recommended to be administered intramuscularly at 75-150 IU daily for 7-12 days. When the diameter of the dominant follicle according to ultrasonography reaches 18-22 mm, the hormone choriogonadotropin (6500-10000 IU, Ovitrelle, Pregnyl) is used for ovulation. After the use of COCs, ovulation becomes possible due to the rebound effect that occurs after its cessation.

To support the lutein phase after ovulation stimulation, progestogens are prescribed in the second phase of the cycle: didrogesterone 10-20 mg/day orally or microsinated progesterone 200-400 mg/day vaginally between 16-25 days.

In patients with first-degree gonadal amenorrhea, previous ovarian syndrome, and pituitary insufficiency, as in menopausal syndrome, O'BGT with estrogen-progestogen preparations (cyclic preparations: Cyclo-Proginova, Femoston 2/10) is performed.

Hyperprolactinemia is well corrected with bromocriptine or Dostinex - at a dose of 0.5 mg, 1-1.25 tablets 2 times a week.

In the presence of thyroid pathology, depending on its type, thyroxine (levothyroxine sodium, 25-150 mcg/day), radioactive iodine, or antithyroid drugs (thiamazole, 15-60 mg/day) are used.

Glucocorticoid preparations (dexamethasone) are used to correct the hormonal function of the adrenal cortex.

Psychotherapy is effective in cases of amenorrhea caused by false pregnancy, nervous anorexia, and stress. In severe cases, hospitalization is indicated.

Surgical treatment is associated with anomalies in the development of the genital tract:

• In the presence of hymen atresia in girls, perform a cross-shaped incision.
• Removal of a transverse vaginal septum.
• In cases of vaginal aplasia, an artificial vagina is created (colpopoiesis).

In patients with gonadal dysgenesis and Y-chromosome, the gonads are removed, as they have a high risk of malignancy.

Central nervous system tumors (including macroprolactinomas) are treated with surgery, radiation therapy, or a combination thereof. Pituitary microadenomas are usually medically controlled, and surgical intervention is rarely required.

Questions.

1. Define primary and secondary amenorrhea.
2. Which physiological conditions are accompanied by amenorrhea?
3. Name the three main causes of primary amenorrhea.
4. Why is pregnancy the most common cause of secondary amenorrhea?
5. Which laboratory tests should be prescribed first during amenorrhea?
6. What is the role of hyperprolactinemia in the development of amenorrhea?
7. What is the mechanism of amenorrhea in Asherman syndrome?
8. How can hypothalamic amenorrhea be differentiated from ovarian insufficiency using a hormonal profile?
9. Why does primary amenorrhea occur in Turner syndrome?
10. What is the clinical significance of the diagnosis and treatment of amenorrhea for a woman's reproductive health?

Situational tasks.

Task 1

A 15-year-old girl comes to the doctor: complains of absence of menstruation. Secondary sexual characteristics are developed: chest and hair growth are age-appropriate. Upon examination - vagina is shortened, uterus is not detected. Ultrasound: uterus absent, ovaries normal.

Question: What is the most likely diagnosis?

Task 2

A 27-year-old woman complains of a 6-month absence of menstruation. Previously, the cycle was regular. Pregnancy test negative. Analyses: FSH and LH are normal, prolactin is sharply elevated. MRI: microadenoma of the pituitary gland.

Question: What is the mechanism of amenorrhea and the main treatment method?

Task 3

A 32-year-old woman experiences a lack of lactation and menstruation after difficult childbirth and significant blood loss. Complaints: fatigue, weight loss, hair loss.

Question: What syndrome does the patient have and which organ is affected?

Task 4

29-year-old woman: irregular menstruation, infertility. Examination: obesity, hirsutism. Ultrasound: ovaries enlarged, numerous small follicles. Laboratory: LH↑, FSH normal, testosterone↑.
Question: What is the most likely syndrome and its pathogenesis?

Task 5

35-year-old woman: menstruation does not recur after diagnostic lubrication. Ultrasound: endometrium thinned, uterine cavity closed or with compartments.
Question: What is the most likely diagnosis and how to confirm it?

Test.

1. What is amenorrhea?
a) absence of menstruation in a woman of reproductive age for more than 6 months
b) Painful menstruation
c) Shortening of the menstrual cycle
d) Severe menstrual bleeding

2. When is primary amenorrhea detected?
a) Absence of menstruation in girls over 13 years of age in the absence of secondary sexual characteristics
b) Absence of menstruation in a girl over 15 years of age with the presence of secondary sexual characteristics
c) absence of menstruation for more than 6 months in a woman with a previously regular menstrual cycle
d) All of the above

3. What is secondary amenorrhea?
a) Absence of menstruation from birth
b) absence of menstruation for more than 6 months in a woman with a previous normal cycle
c) Bleeding between cycles
d) Preservation of menstruation with disruption of ovulation

4. The most common cause of secondary amenorrhea is:
a) Pregnancy
b) Turner syndrome
c) Pituitary tumor
d) Hypothyroidism

5. Which hormone is tested first in cases of amenorrhea in a woman of reproductive age?
a) Progesterone
b) Choriogonadotropin (CHG)
c) Prolactin
d) Estradiol
6. Polycystic Ovarian Syndrome (POSO) is characterized by:
a) Primary amenorrhea
b) Secondary amenorrhea or oligomenorrhea
c) Hyperaprolactinemia
d) Atrophy of the ovaries

7. The cause of amenorrhea in hyperaprolactinemia:
a) Estrogen deficiency
b) Decreased secretion of gonadotropins (LH and FSH)
c) Decreased progesterone levels

d) Decreased sensitivity of the endometrium

8. The following can cause hypothalamic amenorrhea:
a) Chronic stress, anorexia, excessive physical activity
b) ovarian insufficiency
c) Endometrial hypoplasia
d) Congenital pathology of the uterus

9. What type does Asherman syndrome (intrauterine synechiae) belong to?
a) Ovarian
b) uterus
c) hypothalamus
d) Pituitary gland

10. Amenorrhea in Turner syndrome (45,X0):
a) Secondary
b) Primary
c) False
d) True

TOPIC 3: DIAGNOSIS AND TACTICS OF ABNORMAL UTERINE BLEEDING.

Abnormal uterine bleeding is bleeding, duration, volume and/or frequency of bleeding loss.
Acute AUB is an episode of bleeding that requires immediate intervention to prevent massive blood loss.
Chronic AUB - excessive bleeding, recurring for more than 3 months in terms of duration, volume, and/or frequency.
Definition:
Anomalous uterine bleeding (AUB) is any deviation from the normal state of the menstrual cycle in which there is a change in the regularity and frequency of menstruation, the duration of bleeding, or the amount of blood lost.
AUB refers to bleeding from the uterine body and cervix, but does not include bleeding from the vagina and vulva.
The duration of a normal menstrual cycle is usually 24-38 days, and the duration of menstruation is up to 8 days. However, when diagnosing AUB, it is important to consider the natural variability and range of the menstrual cycle in each woman.
Abnormal uterine bleeding (AUB) is a condition in which bleeding is excessive in relation to:
• duration - more than 8 days and/or
• blood loss volume - more than 80 ml and/or
• frequency - if the cycle is less than 24 days.
* Major menstrual bleeding (MMSB) is characterised by menstrual bleeding of more than 80 ml.
Iron metabolism disorders usually begin to be felt against the background of blood loss of more than 60 ml per month.
The clinician may suspect that the volume of blood loss exceeded 80 ml due to a combination of three signs:
- decrease in serum hemoglobin/hematocrit, ferritin levels,
- formation of blood clots,
- the need to frequently change hygiene products throughout the day.
The menstrual rate is a very subjective indicator and should only be used for research purposes; in practice, excessive blood loss should be based on the patient's perception.
According to NICE (2007, 2016 and 2018), taking into account the difficulties in assessing monthly blood loss, the choice of tactics is determined not by the result of blood loss

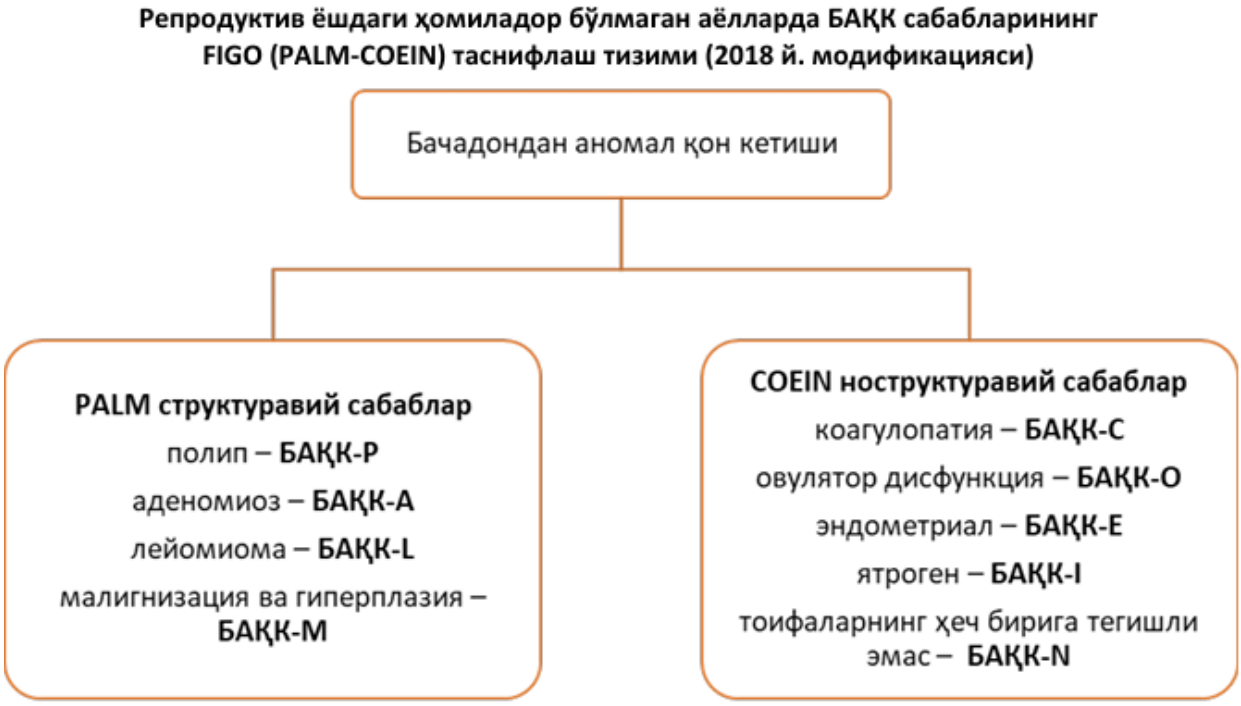
measurement, but by the patient's self-esteem (distress, impaired work capacity, sexual activity, and overall quality of life).
Excessive menstrual bleeding is excessive menstrual blood loss that negatively affects a woman's physical, social, emotional, and/or material well-being and quality of life.

Нормал ва аномал қон кетишларининг мезонлари (FIGO, 2018 й.)		
Ҳайз кўриш давринг тоифаси	**Хусусияти**	
	Нормал	**Аномал**
Такрорийлиги	нормал (24-38 кунгача)	▪ ҳайз даври ёки қон кетишлар кузатилмаслиги = аменорея ▪ тез-тез (<24 кун) ▪ камдан-кам (>38 кун)
Мунтазамлиги	мунтазам (ҳайз давринг ўзгарувчанлиги <7-9 кунни ташкил қилади) *эслатма*: 18-25 ёшгача ≤9 кун; 26-41 ёшда ≤7 кун; 42-45 ёшда ≤9 кун	▪ номунтазам (ҳайз давринг ўзгарувчанлиги ≥10 кунни ташкил қилади)
Қон кетишининг давомийлиги	нормал ≤8 кун	▪ узоқ давом этади >8 кун
Қон кетишининг миқдори	нормал	▪ ажраладиган қон кўп келиши ▪ ажраладиган қон кам бўлиши
	NICE бўйича кўп қон кетишининг таърифи: ҳаддан ташқари кўп менструал қон кетиши – бу аёлнинг ҳаёт сифатига салбий таъсир кўрсатувчи қон кетишидир	
Менструаларо қон кетиши	кузатилмайди	▪ тасодифий, номунтазам ▪ циклик (ҳайз давринг бошланиши, ўртаси ёки тугашида)

ХКТ-10 бўйича кодланиши

N92	**Жуда кўп, тез-тез ва номунтазам ҳайзлар**
N92.0	Мунтазам циклда жуда кўп ва тез-тез хайз кўриш (меноррагия, полименорея)
N92.1	Номунтазам циклда жуда кўп ва тез-тез хайз кўриш (менструаларо даврда номунтазам қон кетишлар, ҳайзлар ўртасида номунтазам, қисқарган интерваллар, менометроррагия, метроррагия)
N92.2	Пубертат даврда кўп хайз кўриш (ҳайз кўриш давринг бошланишида кўп қон кетиши, пубертат меноррагия,пубертат қон кетишлар)
N92.3	Овулятор қон кетишлар (мунтазам менструал қон кетишлар)
N92.4	Менопаузадан олдинги даврда жуда кўп қон кетишлар (меноррагия ёки метроррагия: климактерик, менопаузада, климактерик олдинги, менопаузадан олдинги)
N93	**Бачадондан бошқа аномал қон кетишлар**
N93.8	Бачадон ва қиндан бошқа аниқланган аномал қон кетишлар (дисфункционал ёки функционал бачадон ёки қиндан қон кетишлар)
N93.9	Бачадон ва қиндан аниқланмаган аномал қон кетиши
N95.0	**Менопаузадан кейинги қон кетишлар**

In 2011, the FIGO expert group proposed the PALM-COEIN classification, which divides AMC into two main groups - those associated with organic pathology and those not associated with organic pathology.
First group (PALM) - disorders detected using visual diagnostic methods:
• Polyp (Polyp)
• Adenomyosis
• Leiomyoma
• Malignancy and Hyperplasia
The second group (COEIN) - inorganic disorders:
• Coagulopathy
• Ovulatory dysfunction
• Endometrial functional disorders (Endometrial)
• Iatrogenic changes
• Not yet classified disorders



ETIOLOGY AND PATHOGENESIS

AUB is the most common form of genital bleeding, but not the only one. For a complete and accurate diagnosis of this pathology, it is necessary to know the main pathological conditions that may be accompanied by bleeding from the genital tract.
Causes of genital bleeding are classified as follows:
Genital bleeding may be associated with:
- diseases of the vulva: benign (cysts, condylomas, angiokeratomas, papular rashes, etc.) and malignant tumors;
- diseases of the vagina: benign (cyst of the Gardner canal, polyp, vaginal adenosis) and malignant tumors;
infectious lesions (vaginitis, bacterial vaginosis);
- cervical diseases: benign (polyp, ectopion of the cylindrical epithelium, endometriosis) and malignant processes; infectious lesions (cervicitis);

- diseases of the uterine body: benign (uterine fibroids, endometrial polyps, endometrial hyperplasia, adenomyosis), malignant (adenocarcinoma, sarcoma) tumors; infectious lesions (endometritis); disorders of folliculogenesis (anovulation) processes;
- diseases of the uterine appendages: inflammatory diseases of the uterine appendages, upper part, rupture of an ovarian cyst, cancer of the fallopian tube, cancer of the ovary;
- extragenital diseases: urinary tract infections, colitis, hemorrhoids, bladder cancer;
- systemic pathology: diseases of the blood system (Wilbrand-Jurgens disease, thrombocytopenia, platelet dysfunction, acute leukemia, leakage factor deficiency); liver diseases, renal failure, congenital adrenal cortical dysfunction, Cushing's syndrome and disease; diseases of the nervous system, hyperprolactinemia; stress and physical overload; smoking; lesions of the vulva in red squamous lichen, Behçet's disease, vesicle, Crohn's disease; hormonally active tumors of the ovaries and adrenal glands;
- traumatic injury to the genitals (including due to violent acts of a sexual nature), injury to a foreign body, pelvic bone;
- associated with iatrogenic factors: bleeding from the biopsy and destruction zone of the cervix after resection, electrical, thermal or cryodestructive destruction of the endometrium;
- medications associated with the consumption of: cytostatics, anticoagulants, psychotropic drugs, female sex hormones of any age, tamoxyfen, antibiotics (epidermal toxic necrosis and the development of Stephen-Johnson syndrome), glucocorticoids;
- unclassified (other) diseases: developmental anomalies and vascular tumors of the genitals.

According to the above-mentioned classification system, developed by FIGO experts in 2011, the main causes of uterine abnormalities are considered in terms of the presence or absence of organic uterine pathology.

Depending on the patient's age (pubertate, reproductive, premenopausal, menopausal periods), the frequency of occurrence of various diseases in the structure of CAA causes varies.

Abnormal uterine haemorrhage associated with organic pathology

Polyp (AUB-P)

Endometrial polyps and cervical canal polyps are epithelial formations that can contain various structural components: vascular, glandular, fibromuscular, and connective tissues.

Most often, polyps are asymptomatic. This is mainly qualitative formation.

The classification system does not provide for clarification of the number of polyps, their size, and localization.

Category R1 means that the polyp has been detected using any examination method (ultrasound, hysteroscopy, confirmed or not confirmed by histopathology).

Polyp category R0 has not been identified.

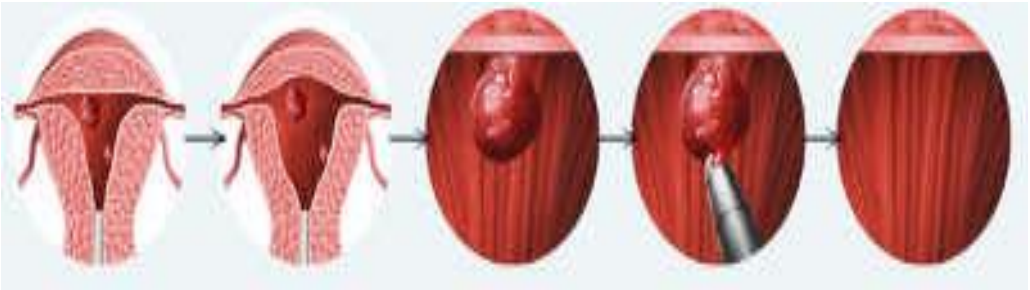


Figure 1. Endometrial polyp

Adenomyosis (AUB-A)

The diagnosis of adenomyosis (internal endometriosis, uterine body endometriosis) is currently made based on ultrasound examination data, in extremely complex cases using magnetic resonance imaging. When performing an ultrasound examination, precise diagnostic criteria are

used (presence of endometrioid heterotopias in the myometrium, hypertrophy of the myometrium, diffuse and nodular
(multi-stage) form).
The diagnosis of adenomyosis using MRI also implies clear criteria. Detection of adenomyosis - category A1, absence - A0.

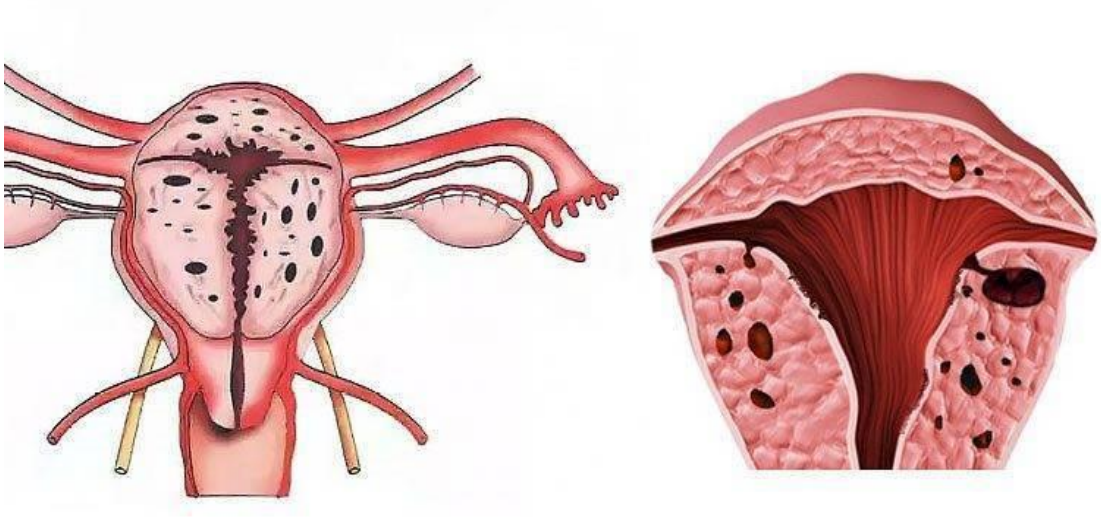


Figure 2. Uterine adenomyosis

Leiomyoma (AUB-L)
The presented basic classification system of PALM reflects only the presence of leiomyoma, category L1. The specific features of the location, number, and size of the nodes are not important. The absence of leiomyoma is designated as L0.
In medical practice, a number of classifications are used, which determine the localization of myomatous nodes, distinguish subclasses, and allow for the determination of treatment tactics.
According to the classification, the 2011 FIGO distinguishes uterine cavity-deforming leiomyoma (submucosus [submucosal [SM]) from its other forms (others [O]). Among all myoma localizations, it is submucosal that is most often accompanied by ABA.

Figure 3. Uterine myoma (leiomyoma)

Miomaning joylashishiga qarab kasallikning quyidagi turlarini ajratish mumkin:

Mioma turi	O'sma joylashuvi
Subseroz mioma	Mioma bachadonni boshqa kichik tos a'zolaridan ajratib turuvchi seroz qobiq ostida, bachadonning tashqi tomonida joylashgan bo'ladi.
Interstitsial (mushak ichi) mioma	O'sma bachadon mushak qavatining o'rtasida joylashgan.
Submukoz (shilliq osti) mioma	Neoplazma bachadonning shilliq yuzasi ostida joylashgan bo'lib, uning bo'shlig'iga chiqib turadi.
Intraligmentar (boylamlararo) mioma	O'sma bachadon tanasi tashqarisidan chiqib, maxsus anatomik tuzilmalar — ayol jinsiy organlarni kichik tosda ushlab turuvchi boylamlar orasiga kirib boradi.
Bachadon bo'yni miomasi	Bachadon silliq mushak to'qimalarining tashqi qavati va biriktiruvchi to'qima tolalarida shakllanadi.

Menstrual bleeding in the uterine mucosa can be several times greater than the normal daily volume. As a result of these processes, secondary iron deficiency anemia develops.
Uterine bleeding with submucosal location of myoma is associated with a number of factors:
1) disruption of the architecture of vessels supplying blood to submucosal myomatous nodes; in these vessels, complete or partial loss of the adventitial membrane occurs, which, on the one hand, increases their permeability, and on the other hand, reduces their contractile activity when the integrity of the vessels is disrupted;
2) decreased uterine tone;
3) an increase in the area of the menstrual surface.

Malignization and hyperplasia (MAG-M)
Atypical hyperplasia and endometrial cancer are relatively rare, but very important in the structure of causes of abnormal uterine bleeding in girls and women of reproductive age. When a precancerous endometrial hyperplasia or malignant process is previously detected in women complaining of abnormal uterine bleeding (AUB), special classifications developed by WHO (WHO) and FIGO, designed to categorize hyperplasia and endometrial cancer, are used for diagnosis.

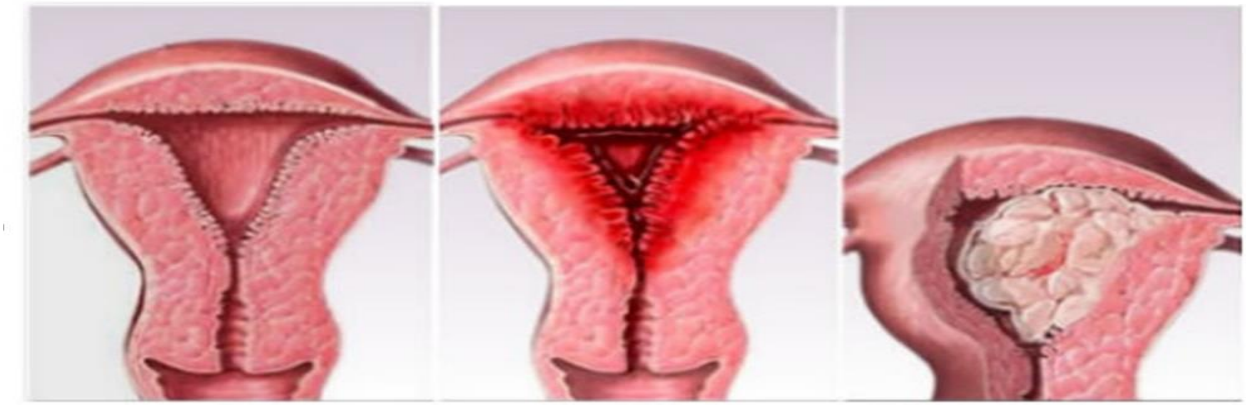


Figure 4. Endometrial hyperplasia.

Uterine haemorrhage not associated with organic uterine pathology

Coagulopathy (AUB-C)

Disorders of the blood coagulation system play an important role in the etiology of excessive menstruation in women of different age groups.

The most frequent cause of excess menstruation occurring within two years after the onset of menstruation or after it is various hemostatic disorders, which account for about half of the observations.

Many researchers emphasize the validity of conducting screening measures to identify disorders of the blood coagulation system in the development of ACS in women.

Among systemic diseases with impaired blood clotting, the most common are:

• von Willebrand-Jurgens disease (13%), thrombocytopenia and platelet dysfunction (18%), coagulation factor deficiency (12%);

• serious liver diseases; • chronic renal failure.

- If abnormal uterine bleeding occurs as a result of anticoagulant therapy for various diseases, then this BAQK is rightfully considered iatrogenic. At the same time, the group of experts classified such women as having coagulopathy (CC-C).
- Ovulatory dysfunction (AUB-O)
- Ovulatory dysfunction is one of the most common causes of excessive menstruation in girls - women in puberty, women of late reproductive age, and women in the premenopausal period.
- The following disorders lead to ovulatory dysfunction:
- Central nervous system disorders: hypergalactinemia, neuro-psychic stress, dietary disorders (overweight, anorexia), sharp weight loss, extreme sports training;
- Endocrinopathies: polycystic ovary syndrome, hypothyroidism, Cushing's syndrome, a tumor with congenital hormonal disorders (adrenal gland or ovary);
- taking medications: sex steroids (COCs, progestogens), corticosteroids; drugs affecting the metabolism of neurotransmitters, for example, phenothiazines and tricyclic antidepressants affecting the dopamine system; cytostatic drugs;
- Other causes: chronic kidney and liver diseases, multiple organ failure.

Endometrial category (AUB-E)

Endometrial causes of BAQK (endometrial dysfunction) are considered as the main disruption in the local regulation of the mechanisms of "hemostasis" in the endometrium.

The results of scientific research show that at the local level, excessive production of vasoconstrictors occurs, for example, endothelin-1 and prostaglandin F2α, and/or rapid breakdown of blood clots formed in the endometrium during menstruation under the influence of an excess plasminogen activator. At the same time, at the local level, the production of vasodilators (prostaglandin E2 and prostacyclin) increases.

Currently, there are no generally accepted tests for assessing these disorders in clinical practice. Therefore, AUB-E category still remains an exceptional diagnosis and is presumed in women after excluding other objectively detectable disorders.

Iatrogenic category (IACD-I)

The iatrogenic category includes various interventions that cause or contribute to BAQQ:

• Pharmacological agents: hormonal preparations (often), some antibiotics, anticonvulsants;

• Intrauterine instruments.

The mechanism of AUB development occurs through direct influence on the endometrium, influence on blood clotting processes, or systemic influence on ovulation mechanisms. Systemic administration of sex steroids (estrogens, progesterones, and androgens) in one or a combination leads to a change in steroidogenesis in the ovaries (this effect occurs by blocking the

hypothalamus and/or pituitary gland or by directly affecting the ovaries) and, as a result, affects the endometrium.

Many irregular or abnormal uterine bleeding is associated with the misuse of steroid hormones. For example, irregular use of hormonal drugs leads to a decrease in the blocking effect on FSH, which can lead to the restoration of follicle maturation and abnormal bleeding due to estrogen production and endometrial proliferation.

A decrease in estrogen and progesterone levels in the bloodstream can be caused by the use of anticonvulsants and antibiotics (e.g., rifampicin and griseofulvin).

Unclassified BAQK (BAQK-N)

The category "Non-classified Abnormal Uterine Bleeding (NBAB) " means that currently, standard research methods do not allow for the classification of BAB into the above-mentioned categories.

In the future, when new data are obtained as a result of special biochemical or molecular genetic studies, additional categories of CKD may be identified, and methods of their pathogenetic therapy may be proposed.

This category also includes conditions associated with vascular pathologies and other unspecified mechanisms.

DIAGNOSIS

БАҚКни ташхислаш алгоритми

Анамнезни йиғиш:

- менархе ва менопауза бошланиши ёши;
- ҳайз кўриш даври ва қон кетиши хусусиятлари;
- қон кетишининг ифодаланганлиги (жуда кўп, кўпмас, қон лаҳталари билан);
- тос соҳасидаги оғриқлар (оғриқнинг даражаси, оғриқ қолдирувчи дори-воситалари ёрдам бериши/бермаслиги) ва/ёки бачадон бўшлиғи аномалиялари, аденомиоз ёки миома мавжудлигини кўрсатиши мумкин бўлган “сиқилиш” симптомлари;
- даволаш усулларига таъсир қилиши мумкин бўлган бошқа омиллар (масалан, ёндош касалликлар ёки аввалги даволаниш);
- жарроҳлик аралашувлар;
- дори-воситаларни қабул қилиш;
- гемостазнинг эҳтимол бузилишларининг симптомлари ва белгилари;
- ҳаёт сифатига таъсир кўрсатиши.

Физикал текширув:

- умумий кўрик ва физикал текширув;
- тос соҳасини текшириш:
  - жинсий аъзоларнинг ташқи кўриги;

– кўзгуларда текшириш, Папаниколау бўйича суртма олиш (зарур бўлганда);
– бимануал қин орқали текшириш.

Лаборатор текширувлар:

- қон гуруҳи ва резус-омили;
- ҳомиладорликни аниқловчи тест (сийдик ёки қонда);
- тромбоцитлар сонини текшириш билан қоннинг умумий клиник таҳлили (гемоглобин, гематокрит);
- коагулограмманинг бирламчи тахминий текшируви (ФҚТВ, ПТВ, фибриноген);
- ТТГ (кўрсатмаларга кўра);
- Chlamydia trachomatis (кўрсатмаларга кўра).

Мумкин бўлган визуал диагностик текширувлар (кўрсатмаларга кўра):

- бачадон бўшлиғига физиологик эритмани юбориш билан соногистерография;
- трансвагинал УТТ;
- МРТ;
- гистероскопия.

Тўқималардан намуна олиш мумкин бўлган усуллари (зарур бўлганда):

- эндометрий офис биопсияси;
- нишонли гистероскопия;
- ДвК.

History

It is recommended to collect a gynecological and reproductive history and conduct a standard physical examination for all patients with CKD.
The anamnesis should include the following questions: the nature of menstruation, the volume of blood loss, concomitant symptoms (pain, dysmenorrhea, etc.), family history of BAQK.
In up to 20% of women of all ages with CKD, the main cause is disorders of the blood coagulation system. Therefore, it is necessary to identify hemostasis disorders in all patients with CKD through preliminary screening.
To detect hemostasis disorders in excess menstruation, screening should be conducted based on the presence of one or more of the following signs:
1. Excessive menstruation with menarche;
2. One of the following types of bleeding: postpartum, during surgery, or related to dental intervention;
3. Two or more of the following symptoms: hematomas 1-2 times a month, nosebleeds 1-2 times a month, frequent bleeding gums, family history of bleeding.
Congenital coagulopathies are observed in up to 50% of adolescents with BAQK/BKMQK and in 10-20% of women. In 70% of cases, von Willebrand disease is detected, less often there is insufficiency of coagulation factors XI, VII, VIII or carriage of Hemophilia A or B.
It is recommended to obtain information about medication intake from a patient with AUB.
Drugs that can cause AUB:
• Preparations of sex hormones: estrogens, progestogens, including drugs that affect their synthesis or are used as analogs;
• Nonsteroidal anti-inflammatory drugs (NSAID): can cause ovulatory dysfunction;
• drugs that affect dopamine metabolism, including phenothiazines and tricyclic antidepressants;
• Anticoagulants taken orally (for example, apiksaban, rivaroksaban) and low molecular weight heparins have a greater effect on menstrual volume;
• Indirect-acting anticoagulants (varfarin and others);

• Biologically active additives: ginkgo, ginseng, preparations contained in pustyrnik.
The benefit for clinicians is that it is important to indicate that bleeding is caused by ovulatory or anovulatory causes when choosing further examinations and treatment tactics.
It is important to distinguish anovulatory ABA from ovulatory ABA, as they can lead to the development of endometrial hypoplasia:
Ovulatory AUB: These women typically experience severe cyclical (every 24-38 days) menstrual bleeding over several consecutive cycles, with no intermenstrual or postcoital bleeding. They may have dysmenorrhea and other premenstrual symptoms.
Anovulatory AUB: Irregular (asic), unpredictable, prolonged and/or massive bleeding-inducing episodes often occur after menstrual delay and are accompanied by episodes of amenorrhea. Bu holatlar ko‘pincha endometriy gipoplaziya va endometriy saraton uchun xarakterlidir. Tartibsiz qon ketishlar bo‘lgan ayollarning 25–50% da poliplar yoki submukoz miomalar mavjud bo‘ladi.
Physical inspection
Physical examination of patients with acute ABA should assess acute signs of blood loss (hypovolemia and anemia) and exclude other sources of bleeding unrelated to the uterus.
When examining patients with BAQK, the following concomitant signs should be considered:
• excess weight;
• Symptoms of TSPSA (e.g., hirsutism and acne);
• signs of thyroid disease and dysfunction (for example, thyroid nodules);
• sign of insulin resistance (for example, black acanthosis around the neck);
• signs indicating disorders of the blood coagulation system: petechiae, crusts, pallor of the skin, or swelling of the joints (at the same time, the absence of these signs does not exclude dysfunction of the hemostasis system).

Recommended laboratory tests for patients with AMC

БАҚК билан касалланган аёлларда ўтказилиши тавсия этилган лаборатор диагностик текширувлар	
Лаборатор баҳолаш	**Специфик лаборатор текширувлар**
Бирламчи лаборатор текширувлар	– қон гуруҳи ва резус-омили – ҳомиладорликни аниқловчи тест – тромбоцитлар сонини текшириш билан қоннинг умумий таҳлили (гемоглобин, гематокрит)
Гемостаз тизимининг бирламчи лаборатор текширувлари	– фаоллаштирилган қисман тромбопластин вақти – протромбин вақт – фибриноген
Виллебранд касаллигида бирламчи текширувлар	– фон Виллебранд омили антигенининг концентрацияси – плазмада фон Виллебранд омилининг фаоллиги – тромбоцитлар агрегацияси (ристоцетин) – VIII-фон Виллебранд омилининг боғловчи фаоллиги
Бошқа лаборатор текширувлар	– тиреотроп гормони – қонда зардоб темирининг миқдори, темирни боғлашнинг умумий қобилияти, ферритин миқдори (зарур бўлганда) – жигар функцияларини баҳолаш – инфекцияланиш хавфи юқори ва яллиғланиш белгилари мавжуд бўлган аёлларда Chlamydia trachomatisra текшириш

MEDICATION THERAPY.

Treatment of acute AUB
Preliminary assessment of patients admitted with acute ABA should include the rapid detection of signs of hypovolemia and hemodynamic instability.
If the patient is hemodynamically unstable or shows signs of hypovolemia, it is necessary to quickly introduce fluids through one or two veins through large-diameter catheters, and also prepare for blood transfusions (as indicated).
After the patient's condition stabilizes, the next step is to identify the most probable cause of acute AUB and choose the most appropriate and effective treatment strategy for stopping bleeding.
There are two main purposes for the treatment of acute AUB:
1. stop the current episode of severe bleeding;
2. reduction of blood loss in subsequent menstrual cycles.
In patients with AUB, the use of tranhexamic acid is recommended as the first-line hormone-free therapy, which is effective in reducing blood loss.
Tranhexamic acid (cyclocapron) is a synthetic derivative of the amino acid lysine, which has an anti-fibrinolitic effect due to the reversible blockade of plasminogen.
The drug does not affect blood clotting parameters. The use of tranexamic acid (cyclocapron) in 4 doses every 6 hours (4 g/day) during the day blocks local fibrinolytic processes in the endometrium and reduces blood loss by 30-55%.
It is recommended to use nonsteroidal anti-inflammatory drugs as normal therapy to reduce the volume of blood loss in patients with BAQK.
- ibuprofen 600-1200 mg/day,
- Naproxen from 250-500 to 1100 mg per day,
- mefenamic acid 1500 mg/day,
- nimesulid 200 mg/day.
In patients with AUB and anemia or latent iron deficiency, the use of iron therapy is recommended. In the absence of organic pathology of the pelvic organs, hormonal hemostasis is recommended as a method for stopping acute PMA.
Hormonal hemostasis is the first line of drug therapy to stop acute AUB without known or suspected blood clotting disorders.
For hormonal hemostasis in acute AUB, single-phase COCs containing at least 6-8 mcg of ethinyl estradiol in 1 tablet at equal intervals (every 6-8 hours) are used, with a subsequent stepwise reduction of the dose to 1 IU/day. Duration of therapy - 21 days from the start of treatment. After the cessation of AMC, it was recommended to continue taking COCs according to the contraceptive regimen for the next few months. Potential contraindications and warnings for the use of COCs according to the FDA: smoking over 35 years of age, arterial hypertension, venous thromboembolic complications, including pulmonary embolism in the anamnesis or present, cerebrovascular disease, ischemic heart disease, migraine with aura, breast cancer in the past or present, severe liver diseases in the stage of decompensation, diabetes with vascular complications, cardiac valve pathology with complications, extensive surgical interventions with prolonged immobilization.

Scheme for hormonal hemostasis (control of acute AUB)

Bosqich	Preparat va doza	Davomiyligi	Maqsad / Ta’sir
1	Monofazli kombinatsiyalangan KOK, etilinestardiol ≥30 mkg, 1 tabletka har 6–8 soatda	Qonash to‘xtaguncha (kunlik jami 3–4 tabletka)	O‘tkir qonashni tezkor to‘xtatish

Bosqich	Preparat va doza	Davomiyligi	Maqsad / Ta’sir
2	Dozani asta-sekin kamaytirib, 1 tabletka/kun	21 kun	Endometriy proliferatsiyasini nazorat qilish, keyingi sikllarda qon yo‘qotishni kamaytirish
3	KOKni kontratseptiv sxema bo‘yicha davom ettirish	Bir necha oy	AMKning takrorlanishining oldini olish

Treatment of chronic AMK

Combined oral contraceptives (COCs)
o Recommended for the purpose of reducing blood loss in patients with AUB who require contraception.
Taking 1 tablet of monophasic COCs according to a contraceptive regimen for 21 days reduces menstrual bleeding by 40-50%.
2. Progestagens
o As an alternative to COCs, it is used in the treatment of chronic ABA.
21-day (cyclic) or 28-day (continuous) dosage regimens are equivalent in effect to COKs.
Used preparations: didrogesterone, microzinated progesterone, medroxyprogesterone acetate, norethisterone, progesterone 1% or 2.5%, hydroxyprogesterone capronate 12.5%.
o The use of progesterone in the lutein phase is less effective in reducing menstrual bleeding volume and is not used in the treatment of AUB.
1. Danazole
o A synthetic steroid with moderate androgenic properties.
o Suppresses ovarian steroidogenesis and strongly affects endometrial tissue, reducing menstrual bleeding by 80%.
o Recommended dose: 100-200 mg/day, for 3 months.
2. Levonorgestrel-containing intrauterine system (LNG-IV/IV-LNG)
o Recommended as first-line drug therapy to reduce blood loss in patients with AUB who are not planning pregnancy.
Indications: no identified pathology, myoma <3 cm (non-deforming uterine cavity), suspected or diagnosed adenomyosis.
The LNG-IUD is T-shaped and constantly secretes levonorgestrel (20 mg/24 hours) into the uterine cavity.
o Efficiency up to 90% and long-term use.
o In the opposite case, it is recommended to wait at least 6 cycles to assess benefits and effectiveness.
The system needs to be changed regularly: Mirena - every 5 years, Liletta - every 6 years.
2. Gonadotropin-releasing hormone (Gn-RH) agonists
o Other medications are used in patients with ineffective or associated pathology (myoma, endometriosis, etc.).
o Effectively reduces menstrual blood loss, reverses steroidogenesis, and leads to endometrial atrophy.
o Reduces dysmenorrhea and pelvic pain associated with endometriosis.
Patients who have been taking Gn-RH agonists for more than 6 months are recommended restorative therapy with menopausal hormone therapy drugs, if it has not started earlier.

Surgical treatment

Surgical methods include:
1. Dilation and curettage - expansion of the uterine cavity and cleansing of the inner layer.
2. Myomectomy - removal of the myoma; methods: hysteroscopic, laparoscopic, laparotomic, or vaginal.
3. Endometrial ablation - reduction of bleeding by removing the inner layer of the uterus.

4. Embolization of uterine arteries - control of bleeding by reducing blood supply.
5. Hysterectomy - complete removal of the uterus; this is the final method in the treatment of CKD and is used in patients in whom other surgical methods are ineffective.

Questions:

1. Identify abnormal uterine bleeding.
2. What are the main causes of AUB in adolescents?
3. What is the essence of the PALM-COEIN classification in CBC?
4. What organic causes can cause AUB?
5. Which functional (inorganic) causes often form the basis of AUB?
6. What diagnostic methods are used when examining a patient with AUB?
7. What are the main principles of treating acute AUB in women of reproductive age?
8. How does the clinical picture of AUB differ in women of reproductive age and in postmenopause?
9. What complications can chronic abnormal uterine bleeding cause?
10. What are the indications for surgical treatment of AUB?

Situational tasks:

1. A 15-year-old girl complained of menstruation lasting more than 10 days. Six months have passed since menarche. On examination - signs of anemia.
Determine the main cause of the bleeding and the doctor's tactics.

2. A 28-year-old woman complains of irregular intermenstrual bleeding accompanied by pain in the lower extremities. Ultrasound revealed a formation in the uterine cavity.
What disease can be suspected and what diagnosis should be made?

3. Patient 35 years old. After 2 years of childbirth, she has a large and prolonged period. Ultrasound: enlarged uterus, multiple nodes.
Which diagnosis is unlikely? What is the treatment method?

4. A 46-year-old woman with obesity and diabetes complains of uterine bleeding. An ultrasound examination revealed thickening of the endometrium.
What checks are necessary to eliminate the dangerous process?

5. A 22-year-old patient came with complaints of sudden massive bleeding from the genital tract. Menstruation is usually irregular.
What is first aid?

6. A 39-year-old woman complains of intermenstrual bleeding. A gynecological examination revealed contact bleeding after sexual intercourse.
Which diseases should be eliminated first?

7. A 13-year-old girl complained of recurring bleeding after menarche. Comorbidities - nosebleeds, bleeding gums.
What should be suspected and what tests should be prescribed?

8. A 50-year-old woman complained of bleeding from the genital tract in postmenopause.
What is the main reason for the examination and the subsequent tactics?

9. A 32-year-old patient has IUDs and complains of intermenstrual bleeding.
What is the cause of diagnosis and what methods can be used?
10. A 22-year-old patient came with complaints of sudden massive bleeding from the genital tract. Menstruation is usually irregular.

What is first aid?

11. A 39-year-old woman complains of intermenstrual bleeding. A gynecological examination revealed contact bleeding after sexual intercourse.

Which diseases should be eliminated first?

12. A 13-year-old girl complained of recurring bleeding after menarche. Comorbidities - nosebleeds, bleeding gums.

What should be suspected and what tests should be prescribed?

13. A 50-year-old woman complained of bleeding from the genital tract in postmenopause.

What is the main reason for the examination and the subsequent tactics?

14. A 32-year-old patient has IUDs and complains of intermenstrual bleeding.

What is the cause of diagnosis and what methods can be used?

15. A 42-year-old woman suffers from hypertension. Complains of prolonged and frequent menstruation, decreased work capacity. In the tests - iron deficiency anemia.
In this case, which method of treating ABA is preferable?

Test.

1. A 15-year-old girl applied with a menstrual cycle lasting more than 10 days. The menarche occurred 6 months ago. Which AUB category is most likely?
a) Coagulopathy (CA-C)
b) Ovulatory dysfunction
c) Endometrial
d) Iatrogenic
2. Bleeding between menstruations in a 28-year-old woman, ultrasound: uterine formations. Which diagnosis is most likely?
a) Submucosal myoma
b) polycystic syndrome
c) Coagulopathy
d) Endometrial dysfunction
3. Frequent and prolonged menstruation in a 35-year-old woman, ultrasound: enlarged uterus with multiple nodes. What is the most likely cause of AUB?
a) Myomas
b) Ovulatory dysfunction
c) Coagulopathy
d) Endometrial dysfunction
4. 46-year-old woman with obesity and diabetes mellitus, frequent hyperemia, ultrasound: thickened endometrium. Which inspection is the main one?
a) Endometrial biopsy
b) Testing for TSH and prolactin levels
c) von Willebrand factor test
d) Ultrasonography
5. 22-year-old woman with sudden severe bleeding, menstruation is usually vague. What is first aid?
a) Intravenous fluids, blood transfusion
b) Starting KOK
c) Endometrial biopsy
d) IV implantation

6. 39-year-old woman, intermenstrual bleeding, contact bleeding. Which pathology is excluded first?
a) Cervical polyps
b) Ovulatory dysfunction
c) Coagulopathy
d) Endometrial dysfunction
7.13-year-old girl, repeated severe bleeding after menstruation, bleeding from the nose and gums. Which check is needed?
a) Coagulogram and von Willebrand test
b) Endometrial biopsy
c) Ultrasonography
d) COC therapy
8. 50-year-old woman, postmenopause, vaginal bleeding. What is the most likely reason?
a) Malignancy of the endometrium or cervix
b) Coagulopathy
c) Myoma
d) polycystic syndrome
9. A 32-year-old woman with IUD, bleeding between menstruations. What diagnostic methods may be needed?
a) Transvaginal ultrasound and hysteroscopy
b) Endometrial biopsy
c) Gn-RH agonists
d) Danazole therapy
10.42-year-old woman, hypertension, multiple and prolonged menstruation, iron deficiency anemia. Which treatment is best suited?
a) Drug therapy: tranexamic acid, NSAIDs, iron
b) Hysterectomy first of all
c) Gn-RH agonists
d) Immediate installation of the BIV-LNG

TOPIC 4: OBSTETRIC BLEEDING IN THE FIRST HALF OF PREGNANCY.

Obstetric haemorrhage
Obstetric bleeding is one of the most dangerous complications of pregnancy and childbirth. Obstetric bleeding is one of the leading causes of maternal mortality worldwide.
The main condition for successful treatment of blood loss is a unified methodological approach and cooperation of various specialists: obstetrician-gynecologists, anesthesiologist-reanimatologists, and transfusiologists. Obstetric bleeding is considered a preventable condition, but in developing countries, it remains one of the most common causes of obstetric complications.
Classification of bleeding by time
All obstetric bleeding is classified according to the time of occurrence:
- According to the World Health Organization (WHO):
1. Bleeding during pregnancy (midwifery and non-midwifery)
2. Birth and postpartum hemorrhages (early and late postpartum hemorrhages)
- By local classification:
1. Bleeding in the first half of pregnancy
2. Bleeding in the second half of pregnancy
Causes of pregnancy-related haemorrhage
- Spontaneous abortion (incipient, ongoing, incomplete abortion)
- Bleeding after medical abortion
- Abortion of pregnancy (at any time, most often at an early stage)

• Ectopic pregnancy
• HYDATIDIFORM MOLE

Etiology.

The leading factor in the etiology of spontaneous termination of pregnancy is chromosomal pathology, the frequency of which reaches 82-88%.

The most common chromosomal pathologies in spontaneous premature miscarriage are autosomal trisomy (52%), monosomy X (19%), polyploidy (22%). Other forms are noted in 7% of cases.

In 80% of cases, death occurs first, followed by egg expulsion.

Among the etiological factors, metroendometritis of various etiologies occupies the second place, causing inflammatory changes in the uterine mucosa and hindering the normal implantation and development of the fetal egg. Chronic endometritis, most often of autoimmune genesis, was noted in 25% of healthy women who terminated pregnancy by induced abortion, in 63.3% of women who had a normal abortion, and in 100% of women who had it.

Other causes of sporadic premature miscarriage include anatomical, endocrine, infectious, and immunological factors, which are more likely to cause habitual miscarriage. The causes of sporadic spontaneous abortion are very diverse and not always clearly defined. These include social factors such as harmful habits, harmful production factors, disorganization of family life, heavy physical labor, stressful situations, etc., as well as medical factors: genetic disorders in the parental karyotype, endocrine disorders, defects in uterine development, pre-abortion infectious diseases, etc.

Risk factors. It is one of the main risk factors for young healthy women. According to the data obtained as a result of analyzing the results of 1 million pregnancies, the risk of spontaneous abortion in women aged 20 to 30 is 9-17%, at 35 - 20%, at 40 - 40%, at 45 - 80%.

Parity. Women with two or more pregnancies have a higher risk of pregnancy compared to nulliparous women, and this risk is age-independent.

History of spontaneous abortions. The presence of previous spontaneous abortions increases the risk of miscarriage. In women with a history of one spontaneous abortion, the risk is 18-20%, the risk after two abortions is 30%, and the risk after three abortions is 43%. For comparison: the risk of spontaneous abortion in women with a successful previous pregnancy is 5%.

Smoking. Smoking more than 10 cigarettes a day increases the risk of spontaneous abortion in the first trimester of pregnancy. These data are especially important when analyzing miscarriages in women with a normal chromosomal set.

Spontaneous abortion and use of nonsteroidal anti-inflammatory drugs.Risk factor: taking nonsteroidal anti-inflammatory drugs in the pre-pregnancy period. Inhibition of prostaglandin synthesis → implantation failure.

Statistics:

o When using NSAIDs: 25% spontaneous abortion

o In women who did not use NSAIDs: 15%

Fever (hyperthermia). An increase in body temperature above 37.7 C automatically leads to an increase in premature abortion.

Injuries, including invasive methods of prenatal diagnostics (choriocentesis, amniocentesis, cordocentesis) - the risk is 3-5%.

Caffeine intake. When consuming more than 100 mg of caffeine (4-5 cups of coffee) per day, the risk of premature miscarriage increases significantly, and this trend applies to a fetus with a normal karyotype.

Teratogenic effects - infectious agents, toxic substances, medications with a teratogenic effect - are a risk factor for spontaneous abortion.

Folic acid deficiency. If the concentration of folic acid in blood serum is less than 2.1 ng/ml (4.9 nmol/l), the risk of spontaneous abortion increases significantly from 6 to 12 weeks of pregnancy, which is associated with a higher frequency of fetal anomalous karyotype formation.

Hormonal disorders and thrombophilic conditions usually appear as the main cause of recurrent (typical) abortions rather than spontaneous abortions. In this case, insufficient lutein phase is the main etiological factor.

ECU. According to numerous publications, 12-25% of pregnancies end in spontaneous abortion. In the clinic, patients mainly complain of bleeding from the genital tract, pain in the lower abdomen or lower back when menstruation is delayed.

Classification

By timing of abortions: early - up to 16 weeks, late - up to 22 weeks. Stages of abortion development depending on clinical symptoms: threatened miscarriage, onset, abortion in the process, incomplete, complete (fetal underdevelopment) and habitual abortion (Figure 1).

Figure. 1. Stages of abortion:

a - threatened abortion; b - initiated abortion; c - ongoing abortion; d - cervical abortion; e - incomplete abortion; f - complete abortion

Bleeding in spontaneous abortion mainly occurs in three stages: Initiated abortion, ongoing abortion, incomplete abortion.

The risk of miscarriage manifests with the following signs: Increased uterine contractile activity. There are pulling pains in the lower abdomen and lower back area. Tone of the uterus is increased, the cervix is not contracted, the internal cervix is closed. The body of the uterus corresponds to the gestational age. No bloody discharge. Ultrasonography reveals the fetal heartbeat. Pregnancy can be preserved.

Incipient abortion. In an initiated abortion, against the background of increased uterine contractions, the fetal egg partially separates from its wall, and bloody discharge appears. The pain intensifies, often in the form of contractions. Bloody discharge comes from the vagina. Due to the separation of the fetal ovary in a small area, the uterine size corresponds to the gestational age. The cervix is preserved, the canal is closed or slightly open. The patient needs to be hospitalized and the pregnancy can be preserved.

In a threatened abortion, the fetal ovary is completely separated from the uterus, and regular contractions of the myometrium are detected. The uterine volume is smaller than the gestational age.

In later stages, the fluid surrounding the fetus may leak. The internal and external larynxes are open. The fetal ovarian element is located in the cervical canal or vagina.
Bloody discharge of varying intensity, often in large quantities. Pregnancy cannot be preserved. Hospitalization is recommended, uterine curettage is performed to stop bleeding.
Incomplete abortion. Characterized by remnants of elements of the cervical ovary. Incomplete uterine contractions and incomplete closure of the uterine cavity lead to continued bleeding, in some cases leading to significant blood loss and hypovolemic shock. Most often, incomplete abortion occurs after 12 weeks, especially in cases where the abortion begins with dehydration. Upon bimanual examination, the uterus is smaller than the gestational age, and there is a large amount of bloody discharge from the cervical canal. Ultrasonography reveals remnants of the fetal ovary in the uterine cavity, and remnants of placental tissue in the second trimester. Hospitalization and uterine curettage are recommended.Qonli ajralmalar turli intensivlikda, ko‘pincha ko‘p miqdorda.Homiladorlikni saqlab bo‘lmaydi. Shifoxonaga yotqizish tavsiya etiladi, qon ketishni to‘xtatish uchun bachadonni kuretaj qilish amalga oshiriladi

Complete abortion.

If the gestational age is less than 14-16 weeks, it is advisable to perform ultrasound examination (USG) and, if necessary, curettage of the uterine walls, since there may be remnants of the fetal ovary and decidual tissue in the uterine cavity. Antibiotic therapy, anemia treatment as indicated, and administration of antirhesus immunoglobulin to women with Rh-negative blood are recommended. Since oxytocin can have an antidiuretic effect, the administration of high doses of oxytocin is discontinued after uterine emptying and stopping bleeding. During and after the operation, isotonic sodium chloride solution with oxytocin (30 IU/1000 ml solution) is administered intravenously at a rate of 20 ml/hour (the uterus is less sensitive to oxytocin in the early stages). If necessary, treatment of post-hemorrhagic anemia and antibiotic therapy are continued. Women with Rh-negative blood are administered antirhesus immunoglobulin. It is advisable to monitor the condition of the uterus using ultrasound.
An infected abortion is a condition characterized by fever, chills, weakness, pain in the lower abdomen, and bloody or sometimes bloody purulent discharge from the genital tract. Physical examination reveals tachycardia, tachypnea, and muscle defenses of the anterior abdominal wall. Upon bimanual examination, the uterus is painful, soft in consistency, and the cervical canal is dilated.
Treatment includes bed rest, sedatives, and antispasmodics. With the onset of abortion, antifibrinolytic agents and progestogens (didrogesterone, vaginal micronized progesterone) are additionally prescribed, and corticosteroids are used for hyperandrogenism. After 20 weeks, when there is a risk of miscarriage, non-drug physiotherapeutic treatment methods are used: needle insertion, electroanalgesia, endonasal galvanization.
Hormonal therapy includes natural micronized progesterone 200-300 mg/day or didrogesterone 10 mg twice a day, vitamin E 400 IU/day.
Drotaverine is prescribed intramuscularly 4 mg (2 ml) 2-3 times a day with pronounced pain, then 3 to 6 tablets per day (40 mg in 1 tablet).
Methylxanthines - pentoxifylline (7 mg/kg body weight per day). Papaverine suppositories 20-40 mg per day are administered rectally twice.
The administration of agents that affect hemostasis (Vikasol, Tranhexamic acid, Aminocaproic acid, and other drugs) to pregnant women with bloody discharge is unjustified and has not shown clinical effectiveness, since bleeding during abortion occurs due to the separation of the chorion (early placenta), not disruption of coagulation. On the contrary, the doctor's task is to prevent blood loss, so that it does not lead to a disruption of hemostasis.
Surgical treatment: Used in pregnant women with isthmocervical insufficiency.

Ectopic pregnancy

Ectopic pregnancy is one of the causes of bleeding in the first half of pregnancy. Ectopic pregnancy is a pregnancy in which the fertilized egg is implanted outside the uterine cavity and develops. Therefore, in practice it is often called Gravitas extra uterina or ectopic pregnancy. The frequency of pregnancy varies from 4 to 12.6%. Infertility occurs in 70-80% of cases after tubal pregnancy.

Classification. According to the location of the egg cell

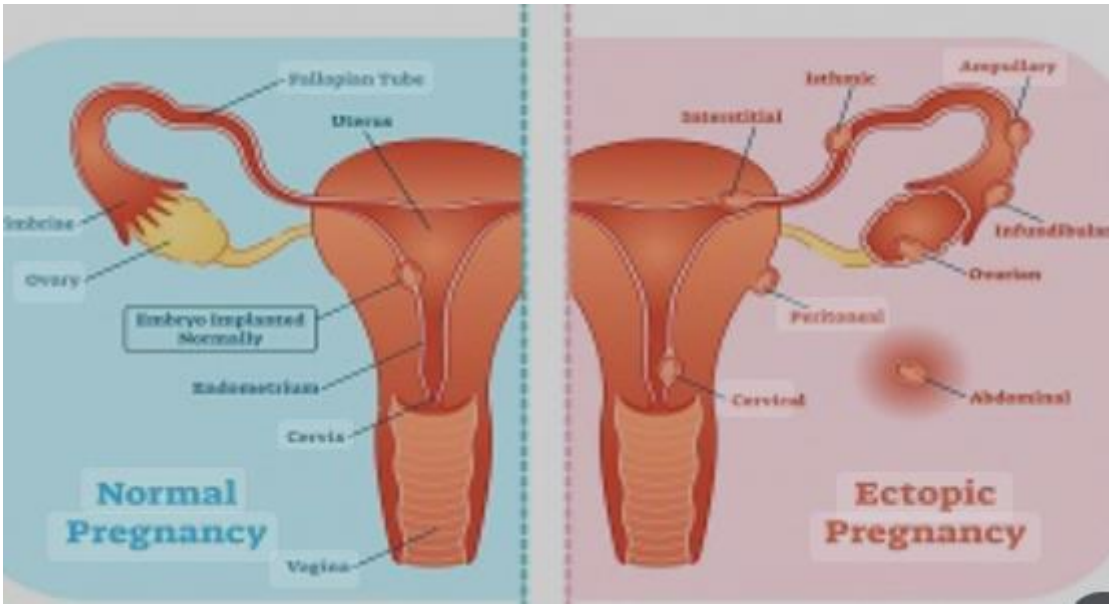


Figure 2. Location of ectopic pregnancy:

The most common type in practice is uterine tubal pregnancy (99%).

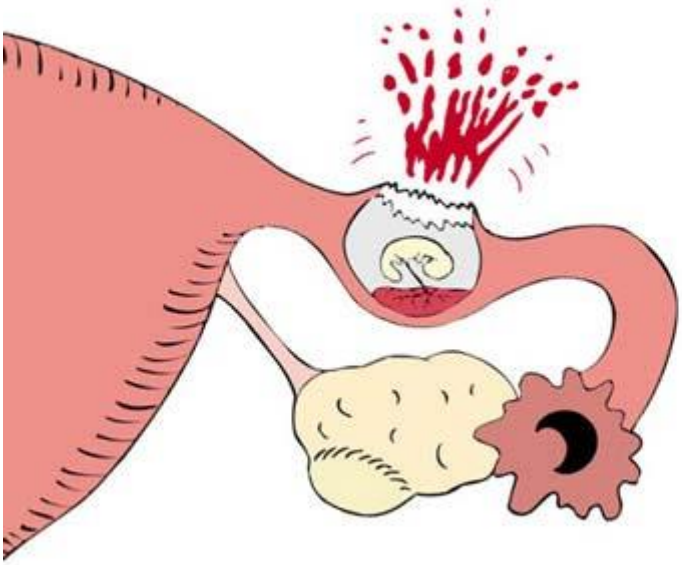


Figure 3. Fallopian tube pregnancy:

Based on the location of the fetus, the following are distinguished:

a) pregnancy of the ampullary part;
b) pregnancy of the isthmic portion;
c) Interstitial pregnancy.

A typical site for fetal implantation is the ampullary part of the tube (80%), followed by the isthmic part (17%), and less often the interstitial part (1-3%).

In some cases, multiple pregnancy, bilateral tubal pregnancy, or a combination of tubal and uterine pregnancy may occur.

Inflammatory changes in the tube (folds, synechiae, atresia, cicatricial changes, etc.);

Infantilism of the internal genitalia (thin, curved tubes, narrowed lumen);

Tumors compressing the fallopian tubes (myoma, ovarian cysts).

In addition, factors contributing to the occurrence of ectopic pregnancy are: smoking, alcoholism, drugs, hormonal preparations (long-term treatment), IUDs, endometriosis, prolonged postpartum lactation, operations on the fallopian tubes.

Based on the clinical course, tubal pregnancy occurs in three forms: progressive, "tubal abortion," and rupture of the fallopian tube. Bleeding occurs only in tubal abortion and rupture of the fallopian tube.

Clinical presentation of progressive tubal pregnancy.

Progressive tubal pregnancy often proceeds like a normal uterine pregnancy. The woman complains of nausea, vomiting, and delayed menstruation. His general condition is satisfactory. A speculum examination reveals cyanosis of the mucous membranes of the labia, vagina, and cervix. A bilateral examination reveals a slight enlargement of the uterus. In the area of the fallopian tube where the fetus is located, a retort-shaped or whistling (vereteno) formation of dough-like density is palpable.

It is necessary to differentiate progressive ectopic pregnancy with dysfunctional uterine bleeding, early uterine pregnancy, hydrosalpinx, and retention cysts.

Laboratory tests (accelerated ESR, leukocytosis, glucosuria, CHG - chorionic gonadotropin) are important in diagnosing the disease, as well as ultrasound scanning, laparoscopy, diagnostic scraping of the uterus.

Treatment of progressive ectopic pregnancy is carried out only surgically in a gynecological hospital. Some authors recommend conservative methods for treating progressive ectopic pregnancy.

The following are used for treatment: methotrexate, vinblastin, prostaglandins E2 and F2a, antiprogesterone drug RU-486, trichosanthin. These drugs are used under ultrasound control.

Clinical presentation of tubal abortion.

During a tubal abortion, the patient complains of severe (rare or constant) pain in the lower abdomen, bloody discharge from the genitals, and delayed menstruation. The fetal egg separates from the fallopian tube, resulting in bleeding into the abdominal cavity and severe pain. Part of the blood passes from the fallopian tube into the uterus and beyond, causing blood-mixed discharge from the genital tract.

In the next stage, the patient develops a clinical picture of hemorrhagic shock, the severity of which depends on the amount of blood loss.

Diagnosis. The diagnosis is made based on the patient's medical history (complaints of severe pain, delayed menstruation, and bloody discharge), as well as clinical signs. A gynecological examination is important for diagnosis. Microscopic examination reveals small amounts of bloody discharge from the cervix. On examination with both hands, the posterior fornix of the vagina is prominent, painful, the body of the uterus is slightly enlarged, as well as softness and pain in the affected tubes.

A picture of hypochromic anemia is observed in blood tests. Widely used methods for confirming the diagnosis: ultrasound, laparoscopy, puncture of the posterior vaginal fornix, etc.

In differential diagnosis, the disease is distinguished by: spontaneous abortion, exacerbation of chronic salpingooforitis, ovarian apoplexy, acute appendicitis, and food poisoning.

Clinical presentation of uterine tube rupture.

The disease begins unexpectedly with sharp ("stabbing") pain in the lower abdomen. After a rupture of the fallopian tube, severe bleeding occurs, and signs of hemorrhagic shock gradually develop.

The patient experiences weakness, dizziness, and tinnitus. Upon examination, pallor, rapid breathing, tachycardia (pulse up to 100 beats per minute), and decreased arterial pressure are observed. The abdomen is slightly swollen, palpation reveals Shchotkin-Blumberg sign, phrenicus symptom, and other symptoms. . A rupture of the fallopian tube is not difficult to detect, as it is usually accompanied by clinical signs of hemorrhagic shock: dizziness, loss of consciousness, pallor of the skin, cold sweating, cooling of the skin, decreased arterial pressure and pulse, etc.

Palpation of the abdomen reveals local pain in the pelvic region, a Shchetkin-Blumberg sign, and percussion reveals a decrease in voice in the lower parts.

Women often complain of abdominal pain, which can spread to the rectum, subcostal area, stomach area, and other areas.

Vaginal examination reveals protrusion of the posterior fornix and sharp pain during examination (banka symptom or "Douglas cavity cry"), the uterus is enlarged, sharp pain is felt at the site of tube rupture.

Blood tests show decreased hemoglobin and erythrocyte levels, and accelerated ESR. For confirmation of the diagnosis, the following are widely used: ultrasound examination, puncture of the posterior fornix of the vagina and, as a result, blood with a dark clot.

An emergency surgical operation awaits the patient in the gynecological hospital.

Rehabilitation of patients after ectopic pregnancy - restoration of menstrual and reproductive function.

Cervical and cervico-isthmus pregnancy

Cervical and isthmus-cervical pregnancy is a rare complication of pregnancy and belongs to the variant of distal ectopic pregnancy.

In true cervical pregnancy, the fetal egg develops only in the cervical canal. In isthmus-cervical pregnancy, the space where the fetus is located includes the cervix and the isthmus (cervical) area.

The localization of cervical and isthmus-cervical pregnancy accounts for 0.3-0.4% of all cases of ectopic pregnancy. The frequency of this pathology ranges from 1 case out of 12,500 pregnancies to 1 case out of 95,000 pregnancies (Fig. 4).

Figure 4. Cervical pregnancy

Cervical and isthmus-cervical pregnancy poses a serious threat not only to health but also to the patient's life. The most dangerous complication of this pathology is maternal mortality, the main cause of which is bleeding (in 75-85% of cases), less often an infection.

The etiology of cervical pregnancy is associated with the following factors:

1. Implantation of the fetal egg into the uterine body is impossible or difficult, which is associated with insufficient development of the endometrium or insufficient maturation of the trophoblast;
2. The presence of factors contributing to the sliding of the blastocyst into the cervical canal.

Such conditions usually arise in the following women: those who have had previous deliveries and complications of the postpartum period, who have had multiple abortions, who have undergone surgery on the uterus, who have uterine fibroids, who have isthmocervical insufficiency.

During cervical pregnancy, first the trophoblast, then the chorionic papillae of the fetal egg are implanted into the cervix or isthmus, penetrating the mucous membrane and muscle layer.

The destruction of muscle elements and vessels leads to bleeding and disruption of pregnancy development. In some cases, the cervical wall can be completely destroyed, and the chorionic papillae can penetrate the parametrium or vagina. Due to the lack of protective mechanisms characteristic of the decidual layer of the uterine body, the cervical wall is destroyed very quickly under the influence of the developing fetal egg.

Cervical pregnancy is observed only in the early stages of pregnancy - up to 8 weeks. In the isthmus-cervical localization, the pregnancy can last longer: up to 16-20-24 weeks. In extremely rare cases, pathological distal ectopic pregnancy can reach the end of pregnancy.

Clinical picture.

Clinical manifestations largely depend on the gestational age and the degree of implantation of the fetal egg.

The main sign of cervical pregnancy is bleeding from the genital tract after the delay of the next period without pain. Bleeding can be moderate, profuse, or very severe. In many women, small, mixed-blood discharge is observed periodically before the onset of bleeding. In some pregnant women, such discharge appears only at early stages, after which the pregnancy can proceed without pathological signs for a certain period.

Diagnosis of cervical pregnancy presents significant difficulties in the early stages. The diagnosis of isthmus-cervical pregnancy is relatively easy to establish from 8-12 weeks of gestation.

In typical cases, these are pregnant women who have experienced childbirth and abortions, who are admitted to the hospital with various degrees of bleeding. The patient's general condition corresponds to the volume of blood loss.

Examination with a mirror reveals an eccentric position of the external opening, and in some patients, a network of dilated venous vessels is visible in the vaginal part of the cervix.

On a bilateral examination, the cervix has a soft consistency, is enlarged in the form of a sphere, on which a smaller, denser uterine body is located in the form of a "cap." Behind the external opening, the fetal egg, tightly bound to the cervical wall, is palpated. Attempts to isolate it with a finger or instrument are accompanied by increased bleeding.

In recent years, ultrasound examination has been very helpful in the timely diagnosis of cervical and isthmus-cervical pregnancy. Ultrasound allows for the detection of a sausage-like dilation of the cervix, which is larger than the body of the uterus. In some women, not only the fetal egg is visible in the dilated cervical canal, but also the heart activity of the embryo is recorded.

In extremely rare cases of isthmus-cervical pregnancy, the correct diagnosis is made after the birth of the child. Obstruction of the placenta or its parts requires instrumental or (rarely) finger access to the uterus, in which the attentive physician determines that the lower segment of the cervix is elongated and thinned, and the body of the uterus is intact.

Treatment. Treatment of patients with cervical and isthmus-cervical pregnancy is carried out only surgically. As soon as the diagnosis is made, it is necessary to undergo surgery. Any, even

the slightest, delay of the doctor creates a risk of death from profuse bleeding. Selective surgery is considered uterine extirpation.

Hydatidiform mole

Hydatidiform mole is one of the causes of bleeding in the first half of pregnancy. Hydatidiform mole is an extremely rare disease, with 1 case per 15,000 births. Hydatidiform mole is more common during pregnancy and less commonly after abortion or childbirth.

In the uterus, the chorionic villi degenerate, forming vesicles filled with clear fluid, appearing like a bunch of white grapes.

Chorionic villi are characterized by the following changes: proliferation of syncytial and cytotrophoblasts, edema, mucus formation, and loss of stromal vessels.

In a complete Hydatidiform mole, such changes encompass the entire embryonic egg, and the embryonic elements are completely absent.

Partially in the eyeball, trophoblastic changes are focal.

The etiology of Hydatidiform mole has not been sufficiently studied to date.

The disease has endocrine, viral, immunological, and genetic characteristics.

Clinically, three types of elbugoz are distinguished:

• full Hydatidiform mole,

• partially Hydatidiform mole

• destructive Hydatidiform mole .

The complete Hydatidiform mole originates entirely from the paternal genome, often being diploid and containing the 46XX karyotype, in 5% of cases it may have the 46XY genome. The common caruncle lacks embryonic elements. It is characterized by diffuse edema of the villi, with varying degrees of trophoblast proliferation (from mild to severe).

After complete evacuation of the abomasum, tumor transformation is observed in 20% of cases and persistent trophoblastic tumor (PTO) develops.

Partial elbo'g'oz is quite rare. It appears more often in the late stages of pregnancy and includes both maternal and paternal genetic material. The 69XXX karyotype is most common, and the 69XXY karyotype is less common. Fetal elements are necessarily present in the partial epiglottis. In contrast to the usual Hydatidiform mole, focal proliferation of the trophoblast is less pronounced. The frequency of malignancy of the partial scrotum is 4-7.5%.

The most common form is persistent trophoblastic disease, which develops after Hydatidiform mole and is characterized by the preservation of the proliferative activity of trophoblast elements, which is accompanied by an elevated or increasing level of beta-chorionic gonadotropin.

In this case, it is not always possible to identify individual clinical signs of the disease (in the uterus, vaginal cavity, lungs, etc.).

Morphologically, persistent trophoblastic disease can be represented by:

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Morphologically, persistent trophoblastic disease can be represented by:

• common Hydatidiform mole,

• choriocarcinoma,

• epitheliocytic trophoblastic tumor,

• trophoblastic tumor of the placental site.

The patterns of pathogenesis are characteristic of all types of trophoblastic disease, including anthrax. These include: a single histogenesis arising from the trophoblast, a tendency to metastasize, the ability to transition from one species to another, common biological characteristics, i.e., a pronounced ability to produce hormones (chorionic gonadotropin, chorionic somatomammotropin, chorionic thyrotropin).

Figure 5. Hydatidiform mole

Clinical presentation. The main clinical symptoms of complete uterine rupture include: vaginal bleeding (more than 90%), mismatch of uterine size with gestational age: uterine size exceeding gestational age (more than 50% of TPE cases), relatively short-term - partial uterine rupture (partial TPE), bilateral tecalutinous cysts 8 cm and larger (20-40%).

In women of childbearing age, the first symptoms of the disease can be various menstrual cycle disorders: from amenorrhea to hypermenorrhea and hypomenorrhea.

Symptoms of pregnancy can also be observed: nausea, dizziness, and taste disturbances.

Other manifestations of the disease include: abdominal enlargement, independent detection of the tumor in the vagina, palpation of the tumor in the pelvic region through the anterior abdominal wall.

Symptoms such as coughing and hemoptysis are also common. In widespread forms of the disease, headaches, dizziness, visual impairment, and fainting episodes may be observed.

In women in the perimenopausal period, as well as in patients who have previously undergone hysterectomy, tumor foci (in the lungs, liver, and other parenchymal organs) can be accidentally detected, which often leads diagnostic research in the wrong direction.

The clinical picture of Elbo'g'oz does not give clear signs in the early stages. Most women experience delayed menstruation, which confirms pregnancy. If the woman does not want pregnancy and wants to terminate it, ultrasound or direct abortion reveals changes characteristic of the abdomen.

This condition is confirmed histologically. The first clinical symptom of erysipelas is bloody discharge, which the woman considers a risk of pregnancy termination. Approximately 35% of women experience early signs of toxicosis (nausea, salivation, vomiting). In some patients, early signs of toxicosis are combined with signs of late gestosis (edema, hypertension, and proteinuria).

In most women, bimanual examination reveals a discrepancy between uterine size and the estimated gestational age. Often, the uterine volume is greater than the gestational age according to the medical history. Bilateral luteal cysts of the ovaries are detected in almost half of the cases.

Based on the patient's complaints and gynecological examination, it is possible to suspect the development of erysipelas.

For confirmation of the diagnosis, an ultrasound examination is used (the uterus is enlarged, the embryo is absent, small, homogeneous cystic tissue is present in the uterine cavity). Focal edema

of the embryonic (with signs of developmental delay) and chorionic villi can be detected in an incomplete cyst.
Invasive erysipelas manifests as defects in the contours of the uterine cavity walls. Ultrasound examination clearly reveals luteal cysts of the ovaries.
All patients undergo mandatory blood serum CHG (chorionic gonadotropin) testing.
The final diagnosis of anthrax is made after a histological examination of the surgical material.
Anthrax can cause hematogenous metastases to the lungs. This complication occurs more often in an invasive form, and less often in a complete Hydatidiform mole . Therefore, radiography of the lungs is recommended for all women diagnosed with erysipelas.
The most serious complication of erysipelas is its transformation into a malignant form of trophoblastic disease - choriocarcinoma.
High risk criteria for malignant neoplasms include: uterine size greater than the gestational age, serum HCG level of 105 IU/ml or higher, luteal cyst diameter of 6 cm or more, woman's age of 40 or older.
The main method of treating anthrax is its evacuation using vacuum aspiration. The operation consists of: dilating the cervical canal and subsequent vacuum aspiration of the contents of the uterus, conducting a control revision of the uterus after vacuum aspiration. During the operation, oxytocin or prostaglandins are administered continuously in drops.
During the observation period, contraception is recommended to the woman.
Laparotomy (opening of the abdominal cavity) and hysterectomy are performed in cases of uterine perforation or bleeding that is not subject to conservative therapy, as well as in cases that pose a threat to the woman's life.
If the luteal cyst ruptures, surgical treatment (resection) is performed with the condition of preserving the ovary, and the patient's cyst is removed by vacuum aspiration.
After treatment, the patient should be under medical supervision for one year.
Weekly blood serum HCG monitoring is conducted. The level of HCG should decrease after 3-4 weeks, and then the examination is carried out monthly.
Some women are recommended chemotherapy after the removal of the cyst. Indications for chemotherapy are: persistent elevated HCG levels (above 20,000 IU/ml) after 4-6 weeks of observation, the presence of lung metastases, and suspected choriocarcinoma.
The drug of choice for chemotherapy is dactinomycin, the single dose is 0.5 mg, the course dose is 2.5 mg. The number of courses is determined individually.

Questions:
1. Name the most common causes of bleeding in the first half of pregnancy.
2. What clinical signs are characteristic of threatened abortion?
3. How does an incomplete abortion differ from a complete one?
4. What complications can arise during ectopic pregnancy?
5. Describe the clinical picture of a tubal abortion.
6. What ultrasound signs are characteristic of Elbo'g'oz?
7. What is meant by non-growing (stopped, "frozen") pregnancy, and how can it be diagnosed?
8. Which laboratory diagnostic methods help differentiate normal pregnancy from pathological conditions (e.g., elbo'g'oz)?
9. What is the management tactics for a patient at risk of miscarriage?
10. What are the indications for emergency hospitalization for bleeding in the first half of pregnancy?

Situational questions
1. The woman is 25 years old, menstruation is delayed by 6 weeks, there are pulling pains in the lower abdomen and a small amount of bloody discharge. Upon examination: cervix is closed, the uterus corresponds to the gestational age.
Your approximate diagnosis and tactics?

2. Pregnancy is 8 weeks, with bloody discharge and pain in the lower abdomen. Upon examination: uterus premature, cervical canal partially open, fetal egg partially in uterine cavity.
What type of abortion is possible?
3. The woman is 30 years old, has a delayed menstruation of 7 weeks, complains of slight bloody discharge and dizziness. Ultrasound: fetus in uterus without heartbeat, size smaller than term.
Your diagnosis and management tactics?
4. Patient 28 years old, 6-week delay, sudden abdominal pain, weakness, decreased blood pressure, pallor. Upon examination: rapid pulse, abdominal pain, protrusion of the posterior vaginal fornix.
What complications can be considered and what measures should be taken?
5. Pregnancy 12 weeks, bloody discharge "in the form of blisters," the uterus is significantly longer than expected. UZI - a "snowstorm" scene.
Which diagnosis is most likely?
6. Woman 22 years old, 9 weeks pregnant, pain in the lower abdomen, slight bloody discharge. Upon examination: the uterus is not enlarged, the HCG test is positive, the fetal egg is not visible in the uterine cavity on ultrasound.
Which illness should be suspected?
7. Gestational age 10 weeks, bloody discharge with thick clots, complete expulsion of the fetal egg. Examination: uterus contracted, no bleeding.
What diagnosis?
8. Woman 27 years old, 6 weeks of delayed menstruation, pain in the lower abdomen and bloody discharge. Ultrasound: the uterine cavity is empty, a heterogeneous tumor in the area of the fallopian tube.
Which diagnosis is most likely?
9. Pregnancy is 11 weeks, pain in the lower abdomen and moderate bloody discharge. Upon examination: cervix is open, the fetal egg partially protrudes into the cervix.
Your diagnosis and treatment tactics?
10. The woman is 29 years old, with bloody discharge and pain in the lower abdomen at 7 weeks. Ultrasound - fetal size does not correspond to the term, no heartbeat.
Your diagnosis and management tactics?

Test.

1. The main clinical sign of a malignant abortion is:
    a) Contractile pains and cervical dilation
    b) Small amount of bloody discharge, closed neck
    c) Complete miscarriage of the fetal egg
    d) Fever and chills
2. Characteristic of incomplete abortion:
    a) Cervix closed, pregnancy preserved
    b) Embryonic egg is fully developed, uterus is empty
    c) Fragments of the fetal egg remain in the uterus, bleeding continues.
    d) No bleeding
3. The most informative diagnostic method in case of suspected abortion is:
    a) pelvic ultrasound
    b) Hysteroscopy
    c) MRI
    d) Radiography
4. The most common location of ectopic pregnancy is:
    a) Ovarian
    b) Abdominal
    c) Fallopian tube
    d) Cervix uteri

5. Symptoms of tubal abortion:
a) Acute pain, collapse, no discharge
b) severe pain, insignificant bloody discharge, pain in the lower abdomen
c) Fever and chills
d) No complaints at all
6. In which case is Kulenkampf's symptom (protrusion of the posterior vaginal fornix, sharp pain) observed:
a) Dangerous abortion
b) Ectopic pregnancy with intra-abdominal bleeding
c) anthrax
d) Cervical polyp
7. The most characteristic feature of Elbuguz is:
a) No bleeding
b) Heavy bleeding with blisters
c) Acute pain and collapse
d) Contractile pain, without discharge
8. The most common complication of Elbo'g'oz is:
a) Metastasis to the lungs
b) Heart failure
c) Thrombophlebitis
d) Jaundice
9. Ultrasound image of hydatidiform mole:
a) "Snowstorm" appearance (fetus is not visible, multiple vesicular structures)
b) A live fetus with a beating heart
c) Tumor with smooth contours
d) Fluid in the abdominal cavity (ascites)
10. What is the level of human chorionic gonadotropin (hCG) in hydatidiform mole?
a) Low or normal
b) Significantly higher than in normal pregnancy
c) Does not change

TOPIC 5: INFLAMMATORY DISEASES OF THE FEMALE GENITAL ORGANS

Among all gynecological diseases, inflammatory diseases of the female genital organs (IHD) occupy the first place in the number of cases when women seek outpatient and inpatient care.

According to the literature, 65-70% of girls and women who applied to the polyclinic are patients suffering from inflammatory diseases of the genitals; their proportion among gynecological patients requiring inpatient treatment is 20-30%.

The significance of inflammatory diseases of the female genital organs is determined not only by their abundance, but also by their leading role in persistent disorders of reproductive function. It has been established that it is inflammatory diseases that cause infertility, mainly tubal obstruction, which cannot be treated conservatively or surgically.

Inflammatory diseases of the female genital organs also have social significance, since their recurrent and prolonged nature causes persistent loss of working capacity in many women.

According to medical examinations and referrals, the most common diseases in girls in childhood are vulvitis and vulvovaginitis (60-70%), and in women of reproductive age, endocervicitis (47-52%) and combined inflammatory processes of the genitals (27-35%) are more common.

The prevalence of inflammatory diseases of the genitals in childhood is explained by the topographic and morphological features of the growing organism, as well as hypoestrogenism, which makes the mucous membrane susceptible to infection.

The incidence of vulvovaginitis in patients aged 3 to 7 years is associated with insufficient hygienic skills of girls, a high frequency of extragenital pathology, and the inappropriate use of antiseptics and antibiotics.

Half of the vaginal microbiocenosis disorders are asymptomatic, therefore they remain uncorrected. Recently, many researchers have been inclined to believe that the biotopes of human open spaces are interconnected, however, the mechanisms of cooperative interaction between microorganisms and the host, the factors ensuring the colonization resistance of mucosal biotopes, have not yet been fully clarified.

Simultaneous study of the microecological characteristics of the microbiota of the mucous membrane of various biotopes (respiratory tract, urogenital, and intestinal) during inflammatory diseases accompanied by sexually transmitted infections in women of reproductive age is relevant and allows predicting the pathological process. The microbiocenosis of the genital tract in adolescent girls and women of reproductive age is a complex system that includes microorganisms belonging to almost all groups and performs important, specific functions. Normally, the main part of microorganisms in the female genital tract is lactobacilli.

Dederlein Lactobacilli (Lactobacillus spp.) is a common group that includes about 135 species of bacteria from the Lactobacillaceae family, which can live in the vagina of females. Each species of lactobacilli usually performs several important functions, but in general, they are divided into three groups:

− Lactobacilli producing hydrogen peroxide (acidophilus, crispatus, gasseri, johnsonii, vaginalis) and they perform the function of natural antiseptics;

− lactic acid-producing lactobacteria.

They form an acidic environment in the urogenital organs;

− only lactobacilli that attach to other bacteria or to the vaginal mucosa, and they block receptors, preventing the consolidation of pathogenic microorganisms.

This group of vaginal bacteria got its name in honor of German obstetrician-gynecologist Albert Dederlein (1860-1941). She described them in 1887 and correctly defined their role in the female vagina.

Lactobacilli are gram-positive bacteria that are anaerobes, do not form spores, and divide by simple mitosis. The basis of the activity of this system is the interaction between the macroorganism and the microflora of the microbiocenosis, which serves to maintain balance in the urogenital tract and prevent pathological processes.

The physiological state of the vaginal microflora is maintained by the vaginal wall immune system, which is influenced by infectious-inflammatory diseases of the pelvic organs, the urinary system, gastrointestinal tract (GIT), antibiotic therapy, intestinal dysbacteriosis, and other factors.

When the concentration of lactobacilli decreases, the balance of the remaining microflora is disrupted: the population of other microorganisms (both specific to this biotope and from other biotopes) increases more than 1000 times (108-1013 CFU/ml of vaginal secretion), and the natural protective function of the vagina decreases.

Under such conditions, under the influence of additional factors, there is a risk of upward infection and the possibility of inflammatory diseases of the uterus and its appendages.

Saprophytic microorganisms (fungi, lactic acid bacteria) and opportunistic pathogenic microflora (Escherichia coli, Proteus, streptococci, staphylococci, etc.) easily enter the vagina when intestinal dysbacteriosis is pronounced.

In modern studies, conditionally pathogenic microflora, in particular obligate, non-spore-forming anaerobic microorganisms (Bacteroides, Fusobacterium, Eubacterium, Peptostreptococcus, etc.), are considered the main etiological factor of the inflammatory process of the genital tract.

Physiological barriers play an important role in the prevention of inflammatory diseases of the female genital tract.

They include:

- closed genital opening, separating the vagina from the external environment;

- the cells of the stratified squamous epithelium of the vagina are rich in glycogen and are necessary for the life of lactobacilli.
As a result of the breakdown of glucose into lactic acid, the vaginal environment becomes acidic, which prevents the development of pathogenic and conditionally pathogenic microflora entering the vagina.
The amount of glycogen in the vaginal epithelium depends on the production of estrogen hormones by the ovaries. Their insufficient production often occurs in cases of ovarian hypofunction associated with gynecological and extragenital diseases, a decrease in the amount of glycogen in epithelial cells, which, in turn, negatively affects the vital activity of lactobacilli.
− Mucus of the cervix and cervical canal: the passage of microbes through the cervical canal is limited by its relatively narrowness and the muscle constriction located in the area of the internal cervix. The role of the cervix as the main physiological barrier depends on the mucous secretion filling the cavity of the cervical canal, in the glands of which (as well as in the fallopian and fallopian tubes) IgA immunoglobulins with bactericidal properties have been identified.
Mucus begins to fill the cervical canal in the first phase of the menstrual cycle; its maximum amount is determined during ovulation (therefore, the " pupillary sign" is positive in the middle of the menstrual cycle).
If estrogen is not produced in sufficient quantities, cervical mucus is also not produced in sufficient quantities, which negatively affects the barrier function of the cervix.
− Periodic desquamation of the functional layer of the endometrium during menstruation;
- Fallopian tube secretion.
However, these physiological mechanisms are often insufficient for effective control of pathogenic microorganisms.
Therefore, during upward and downward infection, the fallopian tubes are affected first, which often leads to the development of significant cicatricial processes and persistent tubal infertility.
The eggshell is protected from infectious agents by a dense protein coating. Usually, infection spreads to the ovaries when the fallopian tubes are damaged: from their ampullary ends, it flows to the ovaries located next to the secretion containing pathological microbes.
The risk of egg yolk infection is highest during ovulation and in the early stages of corpus luteum development, as an anatomically significant defect in the protein coating appears on their surface. Ovid tissue is relatively resistant to pathogenic microbes.
The mechanisms of protection of the internal genitalia described above exist only under physiological conditions. In pathological conditions, the functions of this barrier are disrupted, which facilitates the spread and development of infection.

CLASSIFICATION OF INFLAMMATORY DISEASES OF THE FEMALE GENITAL ORGANS

Depending on the location of the pathological process, the following are distinguished:
1. Inflammatory diseases of the lower genital tract:
- vulvitis;
− bartholinite;
- vaginitis;
- endoservicitis - inflammation of the mucous membrane covered with cylindrical epithelium, passing into the cervical canal;
- cervicitis;
- exocrvicitis (inflammation of the vaginal part of the cervix, covered with stratified squamous epithelium).
Inflammatory diseases of the upper genital tract:
− endo (myo) metritis;
− metritis;
- myometritis;

- pyrometer;
− uterine abscess;
- salpingooforitis;
- abscess: fallopian tube, ovary, tuboovarian;
- Pyosalpinx;
- Tuboovarian inflammatory disease;
- pelvioperitonitis;
− parametrite.
The boundary between the upper and lower sections of the genital tract is the internal cervix.
Depending on the clinical course, inflammatory processes are divided into:
− sharp;
− subacute;
− chronic (unidentified duration of the disease or duration of more than 2 months) - in the stage of remission or exacerbation.
By etiological factor:
− nonspecific;
- specific.
ICD-10 codes:
- N76 Other inflammatory diseases of the vagina and vulva;
− N76.0 Acute vaginitis (vulvovaginitis);
− N76.1 Subacute and chronic vaginitis, vulvovaginitis;
− N76.2 Acute vulvitis;
− N76.3 Subacute and chronic vulvitis;
− N76.4 Abscess of the vulva (furuncle);
− N76.5 Vaginal ulceration;
- N76.6 Wound of the vulva;
− N76.8 Other specified inflammatory diseases of the vagina and vulva;
− N77.0 Vulvar ulceration in infectious and parasitic diseases, herpesvirus infection (A60.0) or tuberculosis (A18.1);
- N77.1 Vaginitis, vulvovaginitis, vulvitis in infectious and parasitic diseases: candidiasis (B37.3), herpesvirus infection (A60.0), ascariasis (B80);
− B37 Candidiasis
• B37.3 Candidiasis of vulva and vagina
• B37.4 Candidiasis of other urogenital localizations;
− A18.0 Tuberculosis of the genitals;
− A51.0 Primary genital syphilis;
− A54.0 Gonococcal infection of the lower genitourinary tract (without abscesses in the periurethral or accessory glands);
− A54.1 Gonococcal infection of the lower genitourinary tract (with an abscess in the periurethral and accessory glands);
− A56.0 Chlamydial infections of the lower genitourinary tract;
- A59.0 Urogenital trichomoniasis;
− A59.0 Urogenital trichomoniasis, vaginal discharge, prostatitis caused by Trichomonas vaginalis;
− A59.8 Trichomoniasis of another localization;
− A59.9 Trichomoniasis unspecified;
− A60.0 Herpetic infections of the genital and urogenital tract;
− A63.0 Anogenital (venereal) scrotum;
- A64 - sexually transmitted diseases, unspecified;
− B80.0 - vulvovaginitis during helminth invasion;
- N70 Salpingitis and oophoritis (including tubal abscess, tuboovarian, ovarian abscess, pyosalpinx, salpingo-oophoritis, tuboovarian inflammatory disease);

- N77.8 Injury and inflammation of the vulva and vagina in diseases classified in other sections;
- N71 Inflammatory diseases of the uterus (except cervix) (including uterine abscess, metritis, myometritis, pyometritis, endo (myo) metritis);
- N72 Inflammatory diseases of the cervix (except for cervical erosion and ectropion without cervicitis);
- N73 Inflammatory diseases of other pelvic organs in women;
− N74 Inflammatory diseases of the pelvic organs in women with diseases classified in other sections.

INFLAMMATORY DISEASES OF THE LOWER GENITAL SECTION

Features of the course and treatment tactics of inflammatory diseases in women

Vulvovaginal candidiasis (candidiasis vulvovaginitis, candidiasis of the vulva and vagina). The main clinical signs are itching, burning in the genitals, or vaginal discharge.

Epidemiology

The majority of women of reproductive age (75%) experience uncomplicated (acute) candidiasis once, in 40-45% of women the disease repeats more than 2 times, and in 10-20% of cases, candidiasis is complicated, often recurring. In patients with endocrinopathies, the frequency reaches 30%, in pregnant women - 30-35%, and in AIDS patients - up to 40%.

Etiology

Candidiasis is an infectious-inflammatory process involving Candida spp. fungi.

Types of Candida causing vulvovaginal candidiasis:

1. Candida albicans (up to 90% of cases);
2. Candida non-albicans (C. glabrata, C. tropicalis, C. krusei, C. parapsilosis, less often - C. lipolytica, C. norvegensis, C. rugosa, C. zeylanoides, C. famata).

They are common in recurrent candidiasis, patients with diabetes mellitus, AIDS, and postmenopausal women (8-20%).

Candida spp. are opportunistic pathogens, facultative anaerobes, tropism to tissues rich in glycogen (vaginal mucosa).

Transmission routes:

− endogenous distribution;
- through sexual intercourse;
- congenital candidiasis - transmission to the fetus through the placenta or vertically (diagnosed from the first hours of life to 6 days);
− exogenous infection of newborns (from the mother's hands, from maternity hospital staff, or from environmental objects).

Risk factors for developing vulvovaginal candidiasis:

Endogenous factors:

− disorders of local immunity, resistance deficiency associated with the innate properties of the vaginal epithelial cells;
- endocrine diseases (decompensated and subcompensated diabetes mellitus, obesity, thyroid pathologies, etc.);
− background gynecological diseases.

Exogenous factors:

- medications: broad-spectrum antibiotics (systemic or topical use), glucocorticoids, cytostatics, immunosuppressants, radiation therapy;
− microclimate with high temperature and humidity;
− use of tight clothing, underwear made of synthetic fabric, hygienic pads;
− long-term use of intrauterine products (especially copper-containing), vaginal diaphragms, rinsing with antiseptics;
− use of spermicides.

Classification of vulvovaginal candidiasis:
- acute vulvovaginal candidiasis;
- recurrent (chronic) vulvovaginal candidiasis (with exacerbations of at least 4 times over 12 months).

According to the classification proposed by D. Eschenbach and currently used in the recommendations of the USA (CDC, 2015) and other countries, vulvovaginal candidiasis is divided into:

− Uncomplicated (simple) candidiasis is a newly diagnosed or sporadic (less than 4 times a year) candidiasis of the vulva and vagina, with mild vaginitis in a woman, in the absence of risk factors (such as diabetes mellitus, decreased immunity through treatment with cytostatics or glucocorticoids) and caused by C. albicans.

− Complicated candidiasis is a condition caused by non-albicans fungi in women without weakened immunity, or occurring in women with diabetes mellitus, decreased immunity (e.g., AIDS), weight loss, or receiving immunosuppressive therapy (e.g., corticosteroids).

Criteria for complicated vulvovaginal candidiasis:
- pronounced objective symptoms (erythema, edema, ulcers and cracks on the skin of the mucous membrane and perianal area);
- episodes of candidiasis more than 4 times a year (recurrent form);
− the causative agent of the infection is C. non-albicans;
− risk factors associated with a decrease in immunity (diabetes mellitus, treatment with cytostatics, glucocorticoids).

Clinical picture.

Complaints:
- itching, burning in the vulva and vagina area;
- pain in the vagina;
− cottage cheese secretions;
- dyspareunia (pain during sexual intercourse);
− dysuria (pain or difficulty urinating).

Objective features:
- swelling, hyperemia of the mucous membrane;
− the presence of whitish coatings, easily removable by tampon;
- cracks in the skin and mucous membrane of the vulva, posterior commissure, and perianal area in severe candidiasis;
− in recurrent candidiasis, dryness, atrophy, lichenification, and small white discharge from the vagina can be observed in the affected area.

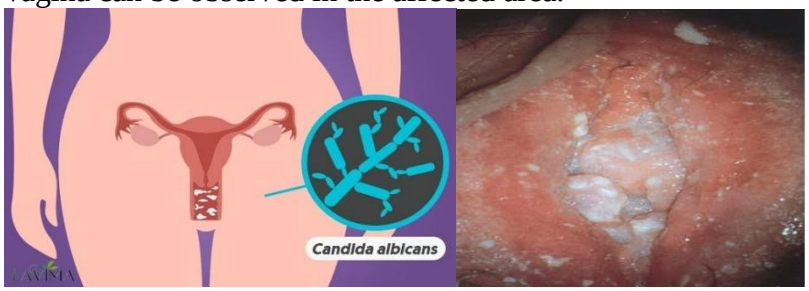

Figure 1. Candidosis of female genital organs

Diagnostics

Confirmation of the diagnosis should be based on the combination of clinical symptoms and laboratory test results, i.e., it is necessary to identify the causative agent of the infectious process.

Laboratory methods:
- Microscopy of Gram stained smears (identification of yeast-like budding cells, pseudomycetes);

− cultural research (planting material on a selective nutrient medium) - to identify the causative agent (C. albicans or non-albicans) at the species level and determine treatment tactics in the case of a recurrent course or ineffectiveness of antimycotic treatment;
− molecular-biological methods - aimed at identifying DNA and/or RNA fragments specific to Candida spp.

Nonspecific vaginitis

Nonspecific (aerobic, simple) vaginitis is an inflammatory disease of the vaginal mucosa resulting from the activation of opportunistic aerobic microorganisms and their effect on epithelial cells.

Epidemiology

The frequency of vaginitis is within 5-25%.

Etiology and pathogenesis

The disease is polymicrobial in nature, with a predominance of aerobic microflora:
• negative gram family Enterobacteriaceae (mainly Escherichia coli),
• Gram-negative cocci - Group B streptococci (Streptococcus agalactiae),
• enterococci,
• Staphylococcus aureus.

Transmission routes: Not classified as sexually transmitted infections; associated with a large number of sexual partners, their frequent exchange, various sexual relations (oral, anal).

Risk factors associated with the development of vaginitis:

- sexual characteristics (multiple and frequent sexual partners); past genital infections; frequent vaginal lavage (spinting, shower); frequent use of vaginal tampons; iatrogenic factors: antibiotic therapy, intrauterine contraceptives, vaginal rings and pessaries, use of spermicides.

Clinical picture

Complaints:
• large amounts of purulent discharge with a putrid odor and signs of atrophy of the vaginal epithelium;
• discomfort in the introitus and vagina;
• dyspareunia;
• burning, itching;
• irritation and pain in the vulvar area.

Objective features:
• a large amount of purulent discharge with an unpleasant odor, yellowish or light gray, completely covering the walls of the vagina;
• hyperemia and edema of the vaginal walls;
• Ph of vaginal fluid - deviated towards alkaline (>6 to 7.5);
• amin test - negative;
• unpleasant odor with a putrid smell;
• vulvar abscess (Staphylococcus aureus) - the appearance of nodules and pustules in hair follicles;
• development of furuncle (carbuncle) - occurs with central necrosis in infection of hair follicles (Staphylococcus aureus).

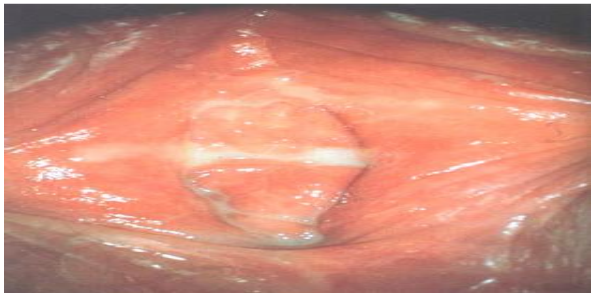

Figure 2. nonspecific vaginitis

Acute nonspecific (aerobic) vulvovaginitis, due to streptococcus group A
Nonspecific vaginitis has an extremely negative impact on women's reproductive health. The presence of vaginitis increases the following risks:
HIV and other sexually transmitted infections;
- historectomy and some other gynecological operations, infectious complications after abortion;
−neoplasms of the cervix;
- development of endometritis, salpingooforitis, parametritis after invasive manipulations and surgical interventions (histrosalpingography, endometrial biopsy, introduction of intrauterine contraceptives, scraping of the uterine cavity walls, historectomy, cesarean section);
- spontaneous abortion, intrauterine amniotic infection, premature rupture of membranes, premature birth, birth of children with low birth weight, endometritis and sepsis after cesarean section.
Diagnosis of vaginitis. Examination of a native smear of vaginal fluid using a phase-contrast microscope. An important criterion is the presence of more than 10 leukocytes per 1 epithelial cell in the field of view. It is characteristic to detect toxic leukocytes (granulocytes) and parabasal epithelial cells in smears.
Cultural diagnostics. Vaginal discharge is collected from the posterior fornix and delivered to the laboratory within 1 hour. In the laboratory, inoculation is carried out on various selective media. In most women, aerobic bacteria (S. agalactiae, S. aureus, E. coli) grow. This method helps in choosing treatment tactics, as it allows determining sensitivity to antibiotics.
Molecular diagnostics. It is actively developing and correlates well with microscopy results in severe and moderate forms of vaginitis. All women with laboratory-confirmed diagnosis and symptoms of aerobic vaginitis require treatment.
If there are no symptoms in men who are sexual partners of women with aerobic vaginitis, they are not treated. The main choice in the treatment of aerobic vaginitis is a wide range of antibiotics, which: are effective against most bacteria of intestinal origin; have a bactericidal effect; have a weak or no effect on the normal vaginal microbiota. The complex treatment may include drugs that affect the anaerobic and aerobic microbiota, as well as vaginal and rectal microflora.
The preferred form of treatment is the use of vaginal preparations.
Intravaginal treatment options:
• neomycin + nystatin + polymyxin B;
• neomycin + nystatin + ternidazole + prednisolone;
• combination of clindamycin and steroids (hydrocortisone 300-500 mg);
Clindamycin 2% cream (intravaginal).
Systemic treatment options:
• kanamycin;
• Fluoroquinolones.
During pregnancy and lactation:
• Treatment for aerobic vaginitis is recommended for all pregnant women with symptoms.
• Screening and treatment of the male sexual partner (s) (if they do not have symptoms) are not required.

INFLAMMATORY DISEASES OF THE UPPER GENITAL TRACT.

Transmission routes
1. In UCID (inflammatory diseases of the upper genital tract), the ascending active route of infection can be carried out through the following mechanisms:
- Gonococci and chlamydia often attach to the surface of motile spermatozoa or trichomonads;
- pathogens can actively pass through the cervical canal into the uterine cavity, fallopian tubes, and abdominal cavity.
Transmission routes
Ascending passive transport is likely due to the contractile activity of the uterus and fallopian tubes and under the influence of negative pressure generated during diaphragmatic movements.
1. Hematogenous (descending) route - bacteria spread from the primary extragenital focus to the fallopian tubes and ovaries (mostly characteristic of genital tuberculosis).
2. Lymphogenic route - usually occurs as a result of endometrial damage (as a result of gynecological manipulations) and/or prolonged presence of intrauterine contraception (IUT) in the uterine cavity.
3. Contact pathway - inflammation spreads through direct contact with an inflamed organ in the abdominal cavity, particularly in appendicitis (appendicular-genital syndrome), cystitis, and colitis.

Classification

According to the duration of inflammatory processes, they are divided into acute and chronic.
In clinical practice, acute, subacute, and chronic forms of the course are distinguished. Acute inflammation is understood as a disease that has occurred for the first time and has clear clinical signs.
According to the nature of the crossing, the following are distinguished:
- catarrhal;
− purulent:
• purulent endometritis;
• pyosalpinx;
• Piovar;
• ovarian abscess;
• purulent tuboovarian structure;
• pelvioperitonitis.
According to the classification of V. I. Krasnopol'skiy (2002), the forms of IUCN are:
− Uncomplicated forms: salpingitis, ooforitis, salpingooforitis.
Complicated forms: pyosalpinx, ovarian abscess (piovar), purulent tuboovarian formation.
Severe purulent-septic diseases: panmetritis, parametritis, interintestinal and subdiaphragmatic abscesses, genital fistulas, purulent-infiltrative omentitis, diffuse peritonitis, sepsis.
Clinical presentation
1. Acute inflammation of the pelvic organs:
− high body temperature;
- pain in the lower abdomen;
− nausea and vomiting are possible;
− disorders of general condition;
- severe intoxication;
− changes in blood tests (leukocytosis, increased ESR, appearance of C-reactive protein).
2. Subacute inflammation - a primary process with milder symptoms than acute inflammation of the internal genitalia:
− subfebrile body temperature;
− absence of pronounced intoxication;
− mild pain reaction;
− low leukocytosis and moderately elevated ESR in the blood test.

This process usually proceeds slowly. The distinction between acute and subacute inflammation is conditional, as inflammatory symptoms are often assessed subjectively.
Chronic UTI (inflammatory diseases of the upper genital tract) can occur in two forms: as a consequence of acute inflammation that occurs after incomplete treatment; less often - develop immediately in a primary chronic form.
Chronic CKD is usually wave-like, with periods of exacerbation and remission alternating. It is necessary to distinguish between primary and secondary salpingitis.
Primary salpingitis develops as a result of the spread of infection from the lower parts of the genital tract upwards, from the cervix (cervical) or perianal flora to the fallopian tubes. Diagnostic or therapeutic procedures can also play an important role in this.
Secondary salpingitis - an inflammatory process develops due to the transmission of infection from neighboring organs, for example, when the appendix is inflamed (in appendicitis).

Diagnostics

Anamnesis. When studying the anamnesis, the presence of sexual intercourse, the absence of barrier methods, frequent changes in sexual partners, the appearance of symptoms of the disease after sexual intercourse, intrauterine manipulations, abortion, childbirth, prolonged uterine bleeding, etc., are taken into account; chronic foci of infection are also identified: external genital (vulvovaginitis) and external non-genital (appendicitis, cholecystitis, perigepatitis, tonsillitis, etc.).
Complaints. The patient is bothered by pain in the lower abdomen, weakness, malaise, fever, and pathological discharge from the genital tract. Dysuric phenomena and diarrhea may be observed. With the formation of purulent tuboovarian formations and pelvic abscesses, pain can spread to the rectum, the affected limb, accompanied by abdominal distension and diarrhea.
Main clinical manifestations. In prepubertal girls with primary pelvioperitonitis, symptoms appear suddenly without the prodromal period: sudden abdominal pain, fever up to 39-40°C, diarrhea, vomiting.

Physical examination:

Palpation of the abdomen reveals pain, mainly in the lower part.
With the development of pelvioperitonitis, the sign of peritoneal irritation (irritability symptom) in the lower abdomen is positive.
Bimanual rectovaginal or rectoscopic examination:
o in sexually inactive patients - rectal-abdominal;
in sexually active patients - vaginal-abdominal examination.
Pain and slight growth are detected in the area of the uterine appendages.
When a tuboovarian inflammatory tumor develops, a large-sized structure may be detected in the area of the appendages. In the presence of pelvic ganglioneuritis, there is pain at the exit of the pelvic nerves, but there are no anatomical changes in the internal genitalia. In endometritis, the uterus is painful

In sexually active patients:

• Mirror examination - signs of cervicitis or vaginitis: redness (hyperemia) of the vaginal part, cervix and external cervical canal, vaginal walls, cervical canal discharge, and pathological vaginal discharge.
Laboratory and instrumental studies

Laboratory studies:

• Clinical blood analysis - leukocytosis, a change in the leukocyte formula, an increase in ESR, the appearance of C-reactive protein.
Microscopic and microbiological examination - the study of secretions from the genital tract and urinary tract, determination of antibiotic sensitivity.
• Molecular-biological methods - detection of gonococcal, chlamydial, ureaplasma, mycoplasma infections using polymerase chain reaction (PCR).
Instrumental studies:

Ultrasound examination of the pelvic organs (UST) - transabdominal, transrectal, or transvaginal: In endometritis, the boundaries of the endometrium and myometrium are indistinct;
o Echogenicity of the myometrium changes, the uterine cavity dilates, hypoechoic contents and fine-grained suspension (pus), BIC, embryonic elements may be detected; in salpingitis - thickened and dilated fallopian tubes, fluid inside; in oophoritis - enlarged ovary, hypoechoic structure, tuboovarian formations; in some cases, fluid is detected in the pelvic cavity. Sensitivity: 32-42%, specificity: 58-97%.
o Hysteroscopy - in the presence of a pathological substrate in the uterine cavity, against the background of antibiotic treatment:hyperemia and edema of the uterine mucosa;necrotic remnants of the mucosa;embryonic elements;remnants of placental tissue;foreign bodies (ligature, BIC).
Laparoscopy is the most informative in the diagnosis of salpingo-oophoritis: Edema and hyperemia of the fallopian tubes; Condition of the fimbrial section; Presence and nature of tubal discharge; Accumulation of exudate in the rectouterine depth; In primary pelvioperitonitis - hyperemia or attenuation of the pelvic peritoneum, edema and hyperemia of the fimbrial section (the "red wreath" sign), small amounts of viscous fluid of various characteristics.

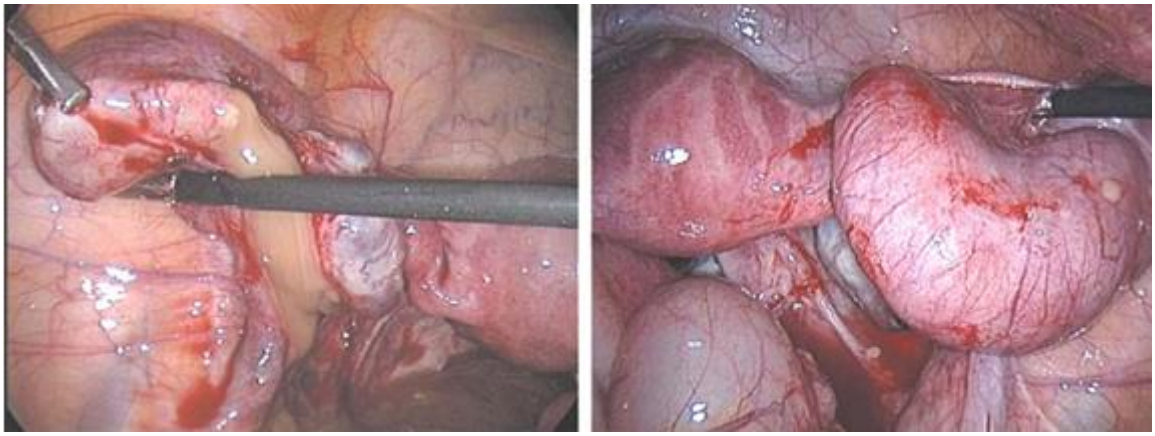

Figure 3. Pyosalpinx

Treatment.

Indications for inpatient treatment for the disease:
1. Body temperature above 38°C.
2. Signs of severe intoxication.
3. Complex forms (presence of an inflammatory conglomerate - a tuboovarian formation).
4. Pregnancy.
5. Presence of intrauterine contraception (IUT).
6. Uncertain or suspicious diagnosis, with signs of peritoneal irritation.
7. Intolerance to oral medications.
8. Absence of positive dynamics within 48 hours against the background of ongoing treatment.

Non-medicinal treatment.

In acute salpingo-oophoritis, physiotherapy is used only in combination with antibacterial, detoxifying, and other medications. Treatment can be initiated immediately after diagnosis.
 Contraindications for physiotherapy use are general (typical for physiotherapy) and conditions characteristic of genital organ pathology.
In acute salpingitis, oophoritis: low-frequency magnetotherapy; treatment with a permanent magnetic field.
In subacute inflammation: SMCH-therapy (with desimeter waves); magnetotherapy and laser therapy; laser therapy; drug electrophoresis with pulse currents.
During stable remission: ultrasound therapy; low-frequency electrostatic field therapy; laser therapy; nonspecific electrotherapy; drug electrophoresis with pulse currents.
☞ The optimal time to start physiotherapy is 5-7 days of the menstrual cycle.

Plasmapheresis. In chronic inflammatory processes, especially in combination with chronic extragenital inflammatory diseases, plasmapheresis is pathogenetically justified.

• In this procedure, not only toxic substances, antigens, antibodies, immune complexes, and immunocompetent cells are removed, but also their detoxification and immune systems are unblocked.

• The maximum effect of plasmapheresis is observed immediately after the cessation of menstruation, during the first phase of the cycle.

- Drug treatment.

I. Acute Inflammatory Diseases of the Upper Genital Tract

Antibacterial drugs or their combinations are selected taking into account the type of pathogen and its sensitivity to antimicrobial agents.

In mild forms, the main therapy consists of: antibacterial drugs, nitroimidazole derivatives, antihistamines, and NSAIDs.

1. CHD of chlamydial and mycoplasma etiology (occurs in sexually active patients).

Preferred antibiotics - agents that accumulate inside the cell and block protein synthesis: Tetracyclines: doxycycline monohydrate, tetracycline; Macrolides: azithromycin, jozamycin, clarithromycin, midekamycin, oleandomycin, roxithromycin, spiramycin, erythromycin; Fluoroquinolones: lomefloxacin, norfloxacin, ofloxacin, pefloxacin, ciprofloxacin, sparfloxacin.Modern antibiotics for acute, uncomplicated chlamydial or mycoplasma salpingooforitis: azithromycin;doxycycline monohydrate.

2. Gonococcal CKD.

• Used: "protected" semi-synthetic penicillins (antibiotic + β-lactamase-degrading substance), since 80% of gonococcal strains are resistant to penicillin.

• Also effective: III-IV generation cephalosporins (ceftriaxone, cefotaxime, etc.), fluoroquinolones.

In acute, uncomplicated gonococcal salpingooforitis: ceftriaxone; amoxicillin + clavulanic acid; cefotaxime; fluoroquinolones (lomefloxacin, norfloxacin, ofloxacin, pefloxacin, ciprofloxacin, sparfloxacin); spectinomycin.

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3. In the absence of a pathogen

(in the acute stage of this process, if laboratory testing is not possible)

 A combination of several broad-spectrum antibiotics is used for 7-10 days.

Possible combinations:

• amoxicillin + clavulanic acid and doxycycline;
• doxycycline and metronidazole;
• Fluoroquinolone and lincosamide;
• Fluoroquinolone and metronidazole;
• macrolide and metronidazole.

4. In severe cases

(in the presence of pelvioperitonitis, sepsis, purulent formations in girls):

• III-IV generation cephalosporin + doxycycline;
• ticarcillin + clavulanic acid (or piperacillin + tazobactam) and doxycycline (or macrolide);
• Fluoroquinolone and metronidazole (or lincosamide). Carbapenem and doxycycline (or macrolide);
- gentamicin and lincosamide.

If necessary, antibiotic therapy with therapeutic-diagnostic laparoscopy can be started 30 minutes before or during anesthesia, or immediately after surgical treatment. In severe cases, parenteral administration of medications is preferred.

Antimycotic therapy.
In chronic vulvovaginal candidiasis, long-term antibiotic treatment, and the development of candidiasis of the mucous membranes and skin, the use of antifungal drugs is indicated. The most commonly used antimycotics are:
• fluconazole (for children under 12 years old and weighing less than 50 kg at a dose of 3-12 mg/kg, for children over 12 years old and weighing more than 50 kg at a single dose of 150 mg on the 2nd and last day of antibiotic intake);
• Itrakonazole (100 mg for children over 14 years old or 5 mg/kg for children weighing less than 50 kg, 2 times a day, for 3 days, starting 5 days before the end of antibiotics);
• natamycin (100 mg 24 times a day during the period of antibiotic administration).
Treatment by efferent methods.
Antibacterial therapy can be combined with plasmapheresis (small plasma exfusion). After the completion of antibacterial therapy, a sequential course of plasmapheresis is allowed.
Anti-inflammatory therapy
The use of prostaglandin synthesis blockers is indicated: nimesulid (for children older than 12 years at a dose of 1.5 mg/kg of body weight, but not exceeding 100 mg, 2 times a day; maximum daily dose - 5 mg/kg).
- or diclofenac (for children aged 6-15 years, only in tablets coated with an intestine-soluble coating, at a dose of 0.5-2 mg/kg of body weight, 2-3 times; Adolescents older than 16 years can be prescribed 50 mg orally or rectally in the form of suppositories 2 times a day for 7 days).
Other nonsteroidal anti-inflammatory drugs can also be used. In patients with liver, kidney, and cholelithiasis, diclofenac is prescribed orally with caution, while indomethacin is not recommended for patients with liver, kidney, and erosive-ulcerative cholelithiasis.
Desensitization therapy
Among antihistamines, clemastin, ciphenadine, chloropyramine, loratadine, and ketotifen are recommended.
Restoration of intestinal biocenosis
To normalize intestinal microflora (especially in the post-antibiotic period), probiotics, prebiotics, and combined preparations can be used.
Immunomodulatory therapy
For the correction of immune disorders, interferons are used in combination in rectal or intravaginal form for 10 days daily (human recombinant alpha-2, alpha-2b interferon).

Chronic inflammatory diseases of the pelvic organs.

In the course of chronic salpingooforitis, the phases of exacerbation and remission are distinguished.
In the acute phase, the disease can proceed in two variants:
In the first case, the true inflammation intensifies, i.e., ESR increases, pain predominates in the appendages, leukocytosis, hyperthermia, and an exudative process is observed in the uterine appendages.
• In the second, more common case, clinical signs and acute phase changes in blood formula are not pronounced, general condition worsens, mood becomes unstable, neurotic reactions, symptoms of neuralgia of the pelvic nerves are observed.
In the exacerbation of salpingo-oophoritis according to the second variant, antibacterial drugs are used rarely, only in cases of exacerbation of inflammatory symptoms. In complex therapy, physical factors, enzyme preparations, and nonsteroidal anti-inflammatory drugs are used.
Indications for surgical treatment of pelvic inflammatory diseases:

- If conservative therapy is ineffective within 12-24 hours for acute salpingitis and salpingooforitis;

- When plevioperitonitis has a poor response to treatment for 2-4 hours or more (in plevioperitonitis with gonorrhea, the condition often improves after 2-3 hours of antibacterial treatment and the need for surgery disappears);
- Pain and/or signs not detected during clinical examination of the pelvic organs;
- In the formation of complicated forms of CKD (hydrosalpinx, pyosalpinx, tuboovarian purulent tumors, etc.).

The scope of the operation depends on the form of the disease, the degree of destructive changes, the patient's age and condition. The most common surgical operations are:
- Revision of the abdominal organs (determination of the condition of the appendix, exclusion of interintestinal and subphrenic abscesses, assessment of the prevalence and severity of the pelvic inflammatory process);
- Cutting and removal of adhesions in the female genital organs;
- Oophoriectomy;
- Salpingooforectomy;
- Salpingiectomy;
- Salpingotomy, drainage of the fallopian tubes;
− Separation of intrauterine adhesions;
- Cutting of joints, opening and uncoupling of seroseles;
- Opening and drainage of phlegmon (abscess);
− Removal of granulation;
- Drainage of an abscess in the female genital organs;
− Extirpation of the uterus, including with appendages;
− Resection of the ovary;
- Abdominal sanitation.

Questions:

1. What are the main causes of inflammatory diseases of the pelvic organs?
2. What is the most common route of infection transmission in inflammatory diseases of the pelvic organs?
3. What are the main clinical symptoms characteristic of acute salpingooforitis?
4. What laboratory diagnostic methods are used when pelvic inflammatory diseases are suspected?
5. Which instrumental examination is considered the "gold standard" in the diagnosis of PID?
6. What risk factors contribute to the development of pelvic inflammatory diseases?
7. What complications can arise if CICD is not treated in a timely manner?
8. What is the treatment tactics for a patient with a tuboovarian abscess?
9. How does the clinical course of acute and chronic pelvic inflammation differ?
10. What are the preventive measures that reduce the risk of developing pelvic inflammatory diseases?

Situational problems:

1.The patient is 23 years old, complains of pain in the lower abdomen, body temperature 38.2°C, and purulent discharge from the genital tract. History - unprotected sexual intercourse a week ago.
Task: Which preliminary diagnosis can be made and what examinations should be prescribed?
2. A 29-year-old woman reported acute pain in the right iliac region, a body temperature of 39°C, and nausea. Examination reveals pain and muscle tension in the right iliac region.
Task: In which cases is differential diagnosis necessary?
3. The patient is 34 years old, two weeks after the insertion of the IUD (spiral), fever, chills, and pain in the lower abdomen appeared.
Task: Which complications should be suspected and what measures should be taken?

4. 21-year-old girl complains of pain and discharge during sexual intercourse. In the anamnesis - frequent change of sexual partners.

Task: What tests should be conducted, and which pathogens are most likely?

5. 27-year-old woman was hospitalized with persistent lower abdominal pain, subfebrile temperature, and menstrual cycle disorders. History - acute adnexitis.

Task: Which diagnosis is most probable and which examination is most informative?

6.The patient was 36 years old with severe pain, high fever, and signs of intoxication. Ultrasound result - tuboovarian abscess.

Task: Which treatment method should be chosen?

7. A woman at the age of 25 was diagnosed with infertility a year after acute salpingitis.

Task: What does the development of infertility depend on, and what tests are used to determine reproductive function?

8. The patient, 31 years old, complains of pain in the lower abdomen and irregular menstruation. Ultrasound - hydrosalpinx.

Task: What treatment tactics should be chosen to preserve reproductive function?

9.The girl is 22 years old, and pain and discharge continue even after the antibiotic course.

Task: Which complications arising from chronic CKID should be excluded?

10. A 40-year-old woman complains of chronic lower abdominal pain, decreased work capacity, and a depressive state. In the anamnesis - repeated episodes of adnexitis.

Task: What are the features of treating chronic inflammatory diseases of the pelvic organs, and what does rehabilitation include?

Test.

• The most common pathogens in inflammatory diseases of the pelvic organs are:
a) Chlamydia trachomatis
b) Neisseria gonorrhoeae
c) Escherichia coli
d) All of the above
• The main route of infection spread in CHD is:
a) Hematogenic
b) ascending from the lower genitalia
c) Contact path
d) Lymphogenic
• The most characteristic sign of acute salpingooforitis is:
a) uterine bleeding
b) Acute pain in the lower abdomen, fever, discharge
c) Absence of pain
d) Appearance of skin rashes

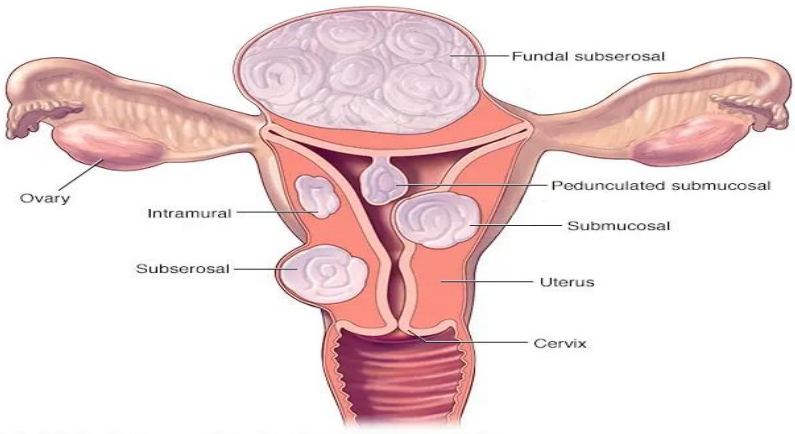
 Examination, which is considered the "gold standard" in the diagnosis of IOP:
a) pelvic ultrasound
b) Laparoscopy
c) Complete blood count
d) Bacterioscopy
 The most frequent complication leading to infertility after CKID:
a) Uterine fibroids
b) Formation of adhesions and obstruction of the fallopian tubes
c) Disorders of the menstrual cycle
d) Hormonal background disorders
 Which of the following conditions requires emergency surgical care?
a) Chronic adnexitis
b) Tuboovarian abscess
c) Mild endometritis
d) Non-inflammatory salpingitis
 Which method of contraception can increase the risk of developing PPROM?
a) Intrauterine spiral (IVS)
b) Oral contraceptives
c) Protective equipment (preservatives)
d) Calendar method
 The most frequently increased laboratory indicator in acute pelvic inflammation is:
a) Blood leukocytes
b) Platelets
c) Hemoglobin
d) Glucose
 The most informative method for diagnosing tubal-peritoneal infertility after CKID is:
a) Hysterosalpingography
b) pelvic ultrasound
c) General urinalysis
d) Cytology from smear
 Measures included in the prevention of HIV/AIDS:
a) Treatment of AIDS and other sexually transmitted diseases in partnership
b) Use of barrier contraception
c) Limit the number of sexual partners
d) All of the above

TOPIC 6: UTERINE MYOMAS, ENDOMETRYOSIS. DIAGNOSIS AND TREATMENT.

Uterine fibroids are benign tumors of the uterus, occupying one of the leading places in the structure of diseases of the female reproductive system. Today, one in every 4-5 women in the world suffers from myoma, and one in every 5 women with myoma is considered infertile.
As a modern trend, there is an increase in the incidence of myoma in reproductive age, the pathology is "rejuvenating," i.e., it occurs at the age of 19-30. Despite the wide range of methods for treating uterine fibroids, in most cases, radical surgical treatment measures are necessary.
Uterine myoma (leiomyoma, fibroma, fibromioma) is a hormone-dependent benign monoclonal tumour that develops from muscle and connective tissue elements.
The frequency of uterine fibroids accounts for 25-30% of all gynecological diseases. After 30 years, the risk of developing uterine fibroids increases to 76-80%. Surgical treatment is required in 50-70% of patients, and the proportion of hysterectomy is 81-92%.

ETIOLOGY, PATHOGENESIS
CLASSIFICATION OF UTERINE MYOMAS.

Depending on the localization, myomatous nodules can be located in the body of the uterus (in 95% of cases) and cervix (in 5% of cases).
Three growth variants of uterine myoma nodes are distinguished in relation to the myometrium:

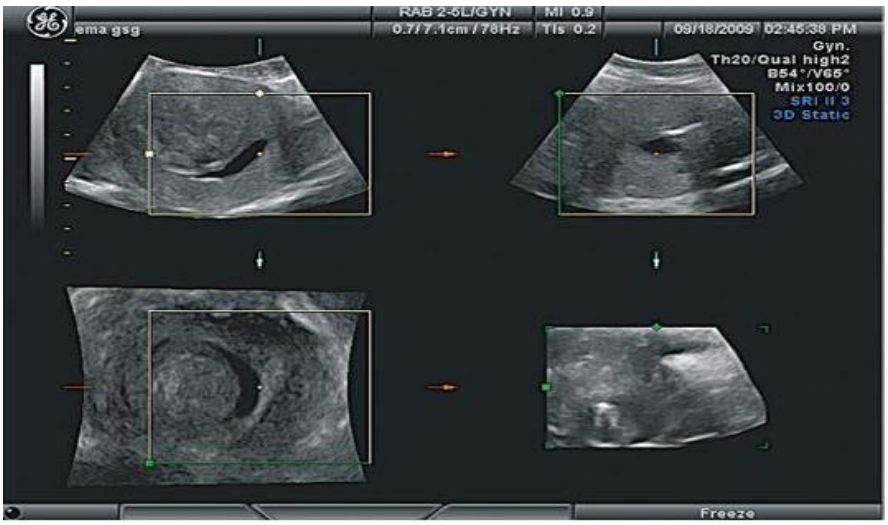


Subperitoneal (subserosal) myoma - the growth of the myoma occurs towards the abdominal cavity.
Intermuscular (interstitial myoma, intramural) - the tumor is located in the thickness of the uterine wall.
Submucosal (submucosal myoma) - myoma growth occurs towards the lumen. Submucosal fibroids are mainly located in the muscular layer. Myoma is a specific form of submucosal nodes - birth tumors, in which the growth of a node in the uterine cavity occurs in the direction of the internal pharynx. By histological structure, the following tumors are distinguished:
Uterine fibroids are tumors that develop primarily from muscle tissue. Uterine fibroma is a tumor that grows from connective tissue. Fibradenomyoma is a tumor originating mainly from glandular tissue.
Topographic classification: submucosal nodes
0 type - a fully localized myomatous node in the uterine cavity;
Type I - less than 50% of the size of the myomatous node is located intermuscularly, most of which is located in the uterine cavity;
Type II - more than 50% of the size of the myomatous node is located intermuscularly, with a smaller part in the uterine cavity;
subserous nodules
Type 0 - myomatous nodule with a pedicle, located completely in the abdominal cavity;
Type I - less than 50% of the volume of the myomatous node is located intermuscularly, most of which is located in the abdominal cavity;
Type II - more than 50% of the volume of the myomatous node is located intermuscularly, a smaller part of it is located in the abdominal cavity.
Depending on the functional state of the muscle elements, according to the morphogenetic type, the following are distinguished:
Simple myoma - benign hyperplasia of muscles, without mitoses.
The proliferating myoma cells of the tumor retain their normal structure, but their number per unit area is higher compared to simple uterine fibroids, and the number of mitoses does not exceed 25%.

Raisarcoma is a multifocal tumor with atypical phenomena of proliferation of myogenic elements, the number of mitoses reaches 75%.
By size, the following are distinguished:
Small node (up to 2 cm)
Median node (2-6cm)
Large node (greater than 6 cm)
giant node (uterus over 20 weeks of pregnancy)
Features of blood supply to myomatous nodes.
Myomatous nodules are insufficiently supplied with blood vessels, the main part of which passes through a connective tissue capsule. Intramural nodes have a pronounced vascular pedicle, submucosal nodes do not have a vascular pedicle, and subserous nodes are poorly supplied with vessels.

CLINICS, DIAGNOSIS.

Uterine fibroids may have no clinical manifestations, be minimal, or have acute clinical signs and reduce the patient's quality of life.
The main symptoms of the pathology are:
Pain. Characteristic localization of pain - lower abdomen. The cause of pain is the stretching of the peritoneal node, compression of the pelvic nerve plexuses, rapid tumor growth, impaired blood supply to the tumor, and contractile pain during menstruation in submucosal fibroids.
Bleeding. Large, prolonged menstruation (menorrhagia) is characteristic, which is associated with an increase in the menstrual surface and a decrease in the contractile activity of the uterus. Acyclic uterine bleeding (metrorrhagia) can occur, caused by pathological changes in the endometrium.
Impairment of the function of adjacent organs. When the tumor is large and located anteriorly, the urinary tract is compressed, and urination is impaired. Posterior cervical nodes complicate the act of defecation.
COMPLICATIONS OF UTERINE MYOMAS:
- bleeding;
- twist of the nodal pedicle;
- disruption of node supply;
nodular necrosis,
- infection
DIAGNOSIS OF UTERINE MYOMASIS: Diagnosis of uterine myomas is based on a comprehensive examination of patients:
- Patient complaints;
- General and gynecological history;
- Gynecological examination. Includes determining the size of the uterus, myomatous nodes, and the location of the nodes.
- Laboratory research methods.
Instrumental methods: The method of ultrasound examination using abdominal and transvaginal sensors remains the leading method of examining myomas. The informativeness of ultrasound examination in the diagnosis of uterine fibroids reaches 93-96%. With the advent of 3D ultrasound, topical diagnostics of nodules entered a qualitatively new stage. Computer remodeling allows assessing the condition of the uterine cavity in multiple nodes, the degree of its deformation with submucosal fibroids, and the presence of changes in the structure of the endometrium. Improved visualization of interstitial and interstitial-subserosal nodes.



MEDICATIONAL TREATMENT OF UTERINE MYOMAS

The choice of treatment method for uterine fibroids depends on the size of the tumor, the location of the nodes, clinical signs, the patient's age, and her reproductive plans.

Organ-preserving treatment methods: combined use of conservative organ-preserving surgery, medicinal and surgical methods.

Drug therapy is aimed at slowing down the growth of myomatous nodes, involution of the myoma, elimination of myoma symptoms, as well as reducing the size of the uterus and nodes during preoperative preparation.

Medications used in the medicinal treatment of uterine fibroids:

Progestogens: Norkolut, Dufaston, Utrojestan, etc. according to the scheme from 16 to 25 or from 5 to 25 days from 6 months to 2 years. In patients in the peri-menopausal period - in a continuous mode for 6 months with subsequent introduction into menopause.

The specific mechanism of action is associated with the action of drugs on receptors for gestagens, estrogens, androgens, minerals, and glucocorticoids.

When menstrual function is impaired in patients with myoma, progestogens ensure the transition of the endometrium from the proliferative stage to the secretory stage. The local progestogenic effect is exerted by the intrauterine system (Miren).

Combined oral contraceptives - COCs (monophasic): Yarina, Janine, Femoden, etc. (Prevention of uterine myoma growth + contraception). The drugs affect different levels of the hypothalamus-pituitary-ovarian-uterine system. The production of releasing hormones by the hypothalamus, which suppress the gonadotropic function of the pituitary gland, is inhibited, which slows down the growth of myomatous nodes. In cases of increased sensitivity of tumor receptors to drug components, both the progestogen and estrogen components of COCs can contribute to the development of myomas.

Antigonadotropins: danal (danazole, danogen, danoval), gestrinone (nemestran).

Affects the size of the myoma, shrinks to 55%, however, after discontinuation of the drug, signs of uterine myoma dilation and disruption of its nutrition may be observed. The use of drugs of this group in patients in the perimenopausal period is preferable, since therapy leads to a persistent decrease in steroidogenesis and the onset of menopause. Gonadoliberin-releasing hormone (aGnRH) agonists: buserelin, zoladex, diferelin, etc.

This group of drugs increases the synthesis of FSH and LH. Subsequently, sensitization arising on the principle of feedback contributes to a decrease in the synthesis of gonadotropins. The positive effect of treatment was noted both during its implementation and for some time after treatment. Before myomectomy, it can be used to reduce the size of the uterus and nodes (up to

76%) and to reduce blood loss (up to 35-40%). Against the background of therapy, expulsion of submucosal nodes may be observed.

Antigestogens - modulators of progesterone receptors (MPR), substances that have the ability to competitively bind to progesterone receptors of myoma tissue, which excludes the effect of endogenous progesterone.

The drugs reduce endometrial cell proliferation; reduce the number of estrogen and progestogen receptors in myoma; have a weak antiandrogenic effect.

Mifepristone is a derivative of norethisterone. Continuous regimen 50 mg/day for 3-6 months.

Ulipristal acetate (Esmiya) is a second-generation selective modulator of progesterone receptors. It has a steroid structure and has a specific effect on progesterone receptors. Used for the preoperative treatment of moderate and severe uterine fibroids in women of reproductive age over 18 years. After discontinuation of treatment, the growth of myomatous nodes is not restored, since the Ulipristal acetate molecule stimulates apoptosis in myoma cells.

SURGICAL TREATMENT OF UTERINE MYOMAS

Surgical treatment of uterine fibroids: radical, organ-preserving.

ENDOMETRYOSIS

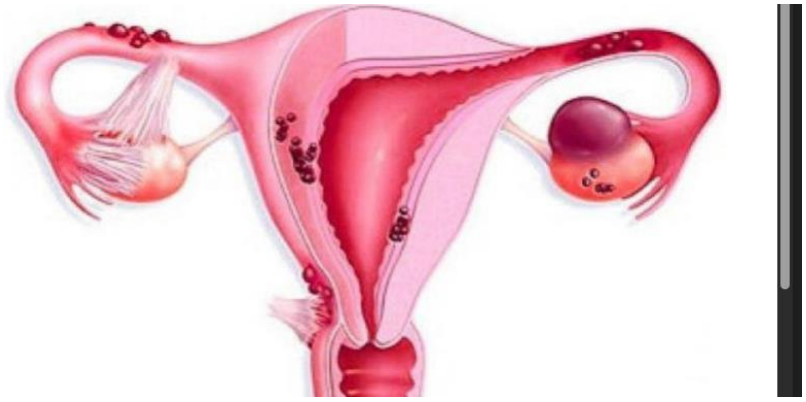
Endometriosis is a multifactorial, dishormonal, immune-dependent, genetically determined disorder characterised by the presence and growth of ectopic endometrium with signs of cellular activity. Endometriosis is a tumor-like process characterized by infiltrative growth. Endometriosis is a chronic, benign, estrogen-dependent inflammatory disease.

Endometriosis is traditionally divided into:

- sexual
- extragenital

Genital, in turn, includes:

- internal or adenomyosis (endometriosis of the uterine body)
- external (endometriosis of the cervix, vagina, perineum, retroperitoneal region, ovaries, fallopian tubes, peritoneum, rectal-uterine fossa, etc.).



Adenomyosis is a benign pathological process in which the inner layer of the uterus (endometrium) invades the uterus. The disease is not an independent phenomenon; it belongs to the internal form of endometriosis.

Endometrioid cysts are massive, benign structures filled with hemorrhagic contents, resulting from the growth of endometrioid tissue on the surface of the ovary.

Retrocervical endometriosis - the posterior location of the endometrioid focus can grow towards the cervix, rectum.
ICD-10 codes:
uterine endometriosis N80.0
N80.1 ovarian endometriosis
Endometriosis of fallopian tubes N80.2
N80.3 pelvic peritoneal endometriosis
Endometriosis of rectovaginal septum and vagina
N80.5 intestinal endometriosis
Cutaneous scar endometriosis N80.6
N80.8 other endometriosis
N80.9 unspecified endometriosis

Etiology and pathogenesis

Despite the fact that endometriosis is a multifactorial disease and has been studied for a long time, the etiology of this pathological process is still unclear.
Many theories of the pathogenesis of endometriosis have been proposed:
1**. Implantation** (J. A. Sampson's theory of retrograde menstruation, 1921) is the most common method. During menstruation, endometrial lobules enter the abdominal cavity through the fallopian tubes, adhere to the mucous membrane of the peritoneum, and transform into endometrioid foci. Estrogens play an important role in this process. Evidence in favor of retrograde menstruation suggests that girls with obstruction of the genital tract have an increased incidence of endometriosis, which prevents menstruation from flowing through the vagina and, as a result, increases tubular reflux. However, although up to 90% of women have retrograde menstruation, most do not develop endometriosis, which indicates the presence of additional factors.
2. Metaplastic. Such a mechanism may be the differentiation of the coelomic epithelium in the endometrioid glands. It is assumed that the cause of the development of endometriosis in girls before the onset of menarche is Müller's remnants - cells of paramezone-nephric origin located in the pelvis and stimulated by estrogen production after the maturation of the hypothalamic-pituitary-ovarian axis. Deep peritoneal disease without superficial implantation indicates this process and may explain the advanced stages observed in very young patients.
3. Theory of immune imbalance. In patients with endometriosis, a decrease in phagocytic receptivity (the primary response to a foreign body) by activated unbound macrophages is noted, which can be an ineffective mechanism for cleansing menstrual discharge. Also, a high frequency of autoimmune diseases was noted in patients with surgically confirmed endometriosis.
4.Vascular and lymphatic spread: presumed in the presence of pulmonary endometriosis.
5**. The theory of oxidative stress.** Various types of inflammation and high levels of angiogenic mediators are always detected in the abdominal fluid of patients with endometriosis. Oxidative stress products contribute to the inflammatory response due to the formation of free radicals and low levels of protective antioxidants.
6. Genetic predisposition to the disease was revealed in studies involving brothers and sisters.
Despite its ability for infiltrative growth, tendency to recurrence, and tendency to invasion, endometriosis belongs to the category of benign proliferative diseases.

Epidemiology

Epidemiological factors were assessed mainly in women with pelvic pain and infertility. According to general estimates, the prevalence of the disease in treated women is 1-7% due to gynecological operations, including ligation of the fallopian tubes.
The study evaluated pathological samples taken from patients during vaginal hysterectomy due to chronic pelvic pain, the prevalence of endometriosis was 8.3%.

High rates are observed in groups of patients undergoing laparoscopy due to pelvic pain (12-70%) or infertility (9-50%), especially in the adolescent population with chronic pain and drug resistance. Such a large range of indicators can be explained by the diversity of the research method: diagnostic criteria, not previously used in recent studies, have been introduced.
During the epidemiological assessment, the working group of the ENDO study obtained operative results and MRI-based prevalence indicators. These results indicate that the prevalence of endometriosis can be higher than previously established values and is closely related to infertility.

Endometriosis is usually observed in women of reproductive age, but the age at the time of diagnosis differs significantly. Unlike previous paradigms, even girls suffering from chronic pelvic pain before the onset of menstruation should be examined for endometriosis, since the disease has been recorded even in this group of young patients. In addition, endometriosis can be observed in menopausal women. The severity of the symptoms increases with age, and the frequency, according to the data, reaches its peak at 40 years of age.
It is assumed that the prevalence of the disease is more common among women of the European race, as well as among women with a low body mass index.
Due to the fact that endometriosis can be asymptomatic, it is difficult to assess its prevalence.

Classification.

Several systems for classifying endometriosis have been proposed. It should be taken into account that currently none of them are considered the gold standard.
1. Revised scale of the American Society of Reproductive Medicine.
The classification of endometriosis is usually based on visual assessment during laparoscopy. The overall indicator corresponds to one of 4 stages (from I to IV or from minimal to severe) and is based on the following parameters:

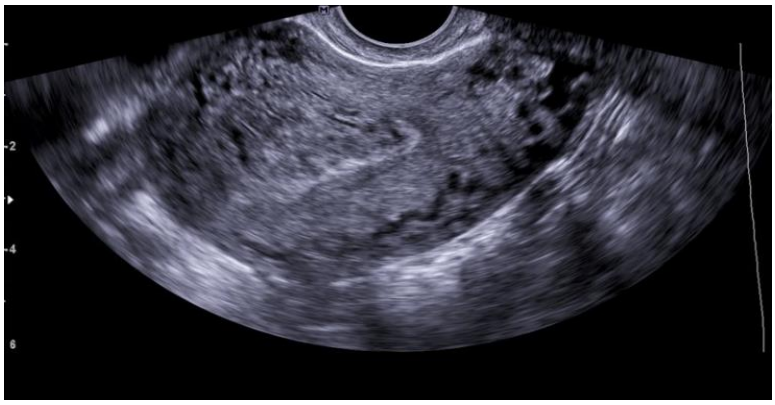
Classification of endometrioid ovarian cysts (edited by L.V. Adamyan, V.I. Kulakov):
Stage I - finely dotted endometrioid formations on the surface of the ovaries, without the formation of cystic cavities in the peritoneum of the rectum and uterine cavity;
Stage II - endometrioid cyst of one ovary, not larger than 5-6 cm, with small endometrioid inclusions in the peritoneum of the pelvis. A slight adhesive process in the area of the uterine appendages without intestinal involvement;
Stage III - endometrioid cysts of both ovaries (a cyst larger than 5-6 cm in diameter and a small endometrioid cyst of the other). Endometrioid heterotopies of small size in the parietal

peritoneum of the pelvis. A adhesive process characterized by partial involvement of the intestine in the area of the uterine appendages;
Stage IV - large (more than 6 cm) bilateral endometrioid ovarian cysts, the pathological process spreads to neighboring organs: the urinary bladder, rectum, and sigmoid colon.
Classification of adenomyosis (edited by L.V. Adamyan, V.I. Kulakov):
The clinical classification of adenomyosis provides for four stages of the spread of the pathological process:
Stage I - the heterotopy of adenomyosis is localized only in the submucosa;
Stage II - the pathological process spreads to the muscle layer;
Stage III - the pathological process occupies the entire thickness of the myometrium, reaching the serous layer of the uterus;
Stage IV - an extrauterine parietal process is added to the pathological process.
peritoneum and adjacent organs
Clinical presentation
The most important clinical manifestations of endometriosis are:
• pelvic pain (dysmenorrhea, dyspareunia, dysuria, dyschesia, and chronic pelvic pain)
• infertility
• menstrual cycle disorders
• abnormal uterine bleeding
• presence of tumor-like formations (endometrioid cysts) in the pelvis.
Rare symptoms:
• painful rectal bleeding or blood in the urine (hematuria)
• pain in the shoulder joint
• periodic lung problems (pneumothorax).
• cyclic cough, chest pain, or bloody cough (bloody spitting)
• cyclic cicatricial edema and pain.
While none of the symptoms or indicators are sufficient for a separate diagnosis, a clinical suspicion of endometriosis is generally sufficient for a preliminary diagnosis.
Endometriosis should be suspected in the presence of the following symptoms, including
Young women under the age of 17:
• chronic pelvic pain.
• dysmenorrhea, which negatively affects the quality of life and daily activities.
• pain that occurs during and/or after sexual intercourse - dyspareunia.
• gastrointestinal symptoms associated with menstruation - intestinal pain, constipation or diarrhea, tenesmus.
• urinary system symptoms associated with menstruation, such as pain during urination, appearance of blood in the urine.

DIAGNOSIS, COMPLAINTS, ANAMNESIS.

When identifying complaints and collecting anamnesis, it is necessary to pay attention to the following factors:
• frequent menstruation, premenstrual, postmenstrual, postcoital bleeding;
• dysmenorrhea and/or dyspareunia, symptoms of which do not disappear or are weakly suppressed by the use of combined oral contraceptives (COCs) and NSAIDs;
• presence of endometriosis in the patient's mother or sister;
• regular ovulation, conduction of the fallopian tubes and
normal spermogram in a partner;
• diarrhea, constipation, nausea, pain during defecation, intestinal spasms, bloating;
• presence of allergy to herb flowering, allergic rhinitis, and hypersensitivity to food products;
• depression, anxiety, chronic fatigue syndrome;
• presence of migraine;
• frequent, forced urination.

Physical examination.
A standard physical examination is being conducted. A gynecological examination is mandatory.
All patients with suspected endometriosis were recommended visual examination of the external genitalia, examination of the cervix in a mirror, bimanual vaginal and rectovaginal examination.
During a gynecological examination, pay attention to the following changes that may be observed in endometriosis:
lateral displacement of cervix
• immobile and sharply displaced uterus
• volumetric derivatives of excesses
• contraction and tension of the vaginal fornices.
• pronounced stenosis of the cervix.
• presence of nodules in the uterosacral region, thickening, tension and/or formation of the sacrouterine ligament.
• presence of a small bumpy formation in the rectovaginal area.
• pain and limited mobility of the intestinal mucosa (during rectovaginal examination).
Transvaginal ultrasound of the pelvic organs was recommended as a primary instrumental diagnosis in patients with suspected endometriosis.
Transvaginal ultrasound is an informative method, the sensitivity of which in the diagnosis of endometriosis is on average 91%, for deep infiltrative forms - 79%, and satisfies the criteria in cases of damage to the sacrouterine ligaments, rectovaginal septum, vaginal wall, Douglas' cavity, and the rectosigmoid part of the intestine.
Transvaginal ultrasound examination allows for the detection of ovarian endometriosis (echo signals are identical, low-grade) or deep pelvic endometriosis with uterosacral ligaments (hypoechoic linear thickening) or endometriosis with the rectovaginal septum.
If transvaginal ultrasound is difficult to perform, then transabdominal and/or transrectal ultrasound can be performed.



MRI of the pelvis should be considered as a research method for assessing the degree of deep infiltrative endometriosis involving the intestine, bladder, or ureter.
Laparoscopy is considered the "gold standard" in the diagnosis of endometriosis. The method provides direct visualization with confirmation of the presence of endometriosis glands or stroma outside the uterine cavity through a biopsy.

Treatment
Endometriosis should be considered as a chronic disease, which requires a lifelong treatment plan for maximizing the use of medications.
Drug treatment.

To prevent repeated surgical interventions. An interdisciplinary approach should be applied, since the list of differential diagnoses is large, and often no intervention provides effective long-term treatment.
For the elimination of pain syndrome in patients with endometriosis, the use of nonsteroidal anti-inflammatory drugs is recommended.
NSAIDs can be prescribed independently or in combination with another method (for example, hormonal therapy) for a period of up to 3 months in the absence of contraindications.
The following preparations may be offered as a selection:
• ibuprofen: orally 400 mg every 4-6 hours, naproxen: orally 250-500 mg 2 times a day, no more than 1250 mg/day;
• nimesulide: up to 200 mg per day;
• selecoxib: 200 mg once a day orally;
Hormonal therapy.
In patients with endometriosis, monotherapy with progestogens is recommended in a continuous mode, as well as in a cyclical mode in patients planning pregnancy. Gestagens can be used as first-line therapy, as well as to prevent recurrence after surgical treatment.
Progestagens can be used in various forms: oral (diyenogest), injected (MPA), and levonorgestrel-containing IUDs.
In patients with diffuse and infiltrative forms of endometriosis, the prescription of gonadotropin-releasing hormone agonists is recommended upon diagnosis or after surgical treatment
The use of AGn-RH causes a profound hypoestrogenic condition, requiring the prescription of "add-back" therapy for relief after more than 6 months of use.
symptoms of menopause and, first of all, for the prevention of osteoporosis.
Due to the high frequency of side effects in patients with endometriosis, danazole is recommended in limited doses.
Danazole (synthetic androgen) previously had both subjective and objective benefits, but currently its use is limited by adverse effects (hepatotoxic, androgenic, anabolic, hypoestrogenic).
In order to determine the prevalence of the disease and remove the lesions, surgical treatment using the laparoscopic method was recommended in patients with genital endometriosis (if conditions are available and there are no contraindications).
For complete removal of the pathological process, morphological confirmation of the diagnosis, and reduction in the frequency of relapses, enucleation is recommended (if possible) using a laparoscopic approach after emptying the wall of the endometrioid cyst and cleaning the cavity.

Questions:
1. What are the main risk factors for uterine fibroids and their development?
2. What are the clinical manifestations of uterine fibroids in women of reproductive age?
3. Which diagnostic methods are most informative in uterine fibroids?
4. List the main complications of uterine fibroids.
5. In what cases is surgical treatment of uterine fibroids indicated?
6. What is endometriosis and how does it differ from adenomyosis?
7. What are the typical complaints of patients with endometriosis?
8. What visual and laboratory diagnostic methods are used in endometriosis?
9. Why is endometriosis dangerous if left untreated?
10. What are the main directions of drug and surgical treatment of endometriosis?

Situational problem:
1. A 42-year-old woman complains of frequent menstruation and pain in the lower abdomen. On examination, the uterus is enlarged up to 10 weeks of pregnancy, dense in consistency.
What is your presumptive diagnosis?
• What kinds of verification do you assign for verification?

• Treatment tactics?
2. A 35-year-old patient complains of infertility and chronic pelvic pain. Ultrasound examination reveals foci of hypoechoic structures in the ovaries and a normal-sized uterus.
• What disease can be suspected?
• What diagnostic methods can be used?
Possible treatment options?
3. The woman is 45 years old, the uterine fibroids are located 8 cm subserosely. No complaints.
Does the patient need treatment?
What factors influence the choice of tactics?
4. A young woman, 28 years old, complains of increasingly painful menstruation over the past 2 years. In laparoscopy - foci of endometriosis in the peritoneum.
• Management tactics?
How is treatment related to her reproductive plans?
5. Patient 38 years old, uterine fibroids are located 6 cm submucosally. Complains of bleeding and anemia.
• Which operations
6. Woman 33 years old, chronic pelvic pain, dyspareunia. On MRI - endometriosis of the rectovaginal septum.
• What are your next steps?
• What specialists should be involved in the treatment?
7. The patient is 47 years old, the uterine myoma is rapidly increasing. Complains of pain and pressure in the lower abdomen.
• What complications should be avoided?
• What kind of inspection is required?
• Treatment tactics?
8. The girl is 25 years old, infertility is 2 years. In laparoscopy - foci of ovarian endometriosis (endometriosis).
• How does endometriosis affect fertility?
• What treatment is indicated if you want to get pregnant?
9. The woman is 40 years old, has multiple uterine fibroids, nodules up to 3 cm in size, complains of frequent menstruation and weakness.
What methods of conservative treatment can be used?
• What is the role of hormonal therapy?
10. A 29-year-old patient with severe pain syndrome during menstruation. On ultrasound - adenomyosis.
• How does adenomyosis differ from endometriosis?
What are the possible treatment options for women planning pregnancy?

Tests:
1. The most common symptom of uterine fibroids is:
A) Amenorrhea
B) Heavy menstrual bleeding
C) leukemia.
D) Insomnia.
2. Which method is considered the "gold standard" in the diagnosis of endometriosis?
A) ultrasound examination of the pelvic organs
B) Laparoscopy
C) Hysteroscopy
D) Hysterosalpingography
3. The main risk factor for uterine myoma growth is:
A) Increased estrogen levels
B) Hypoandrogenism

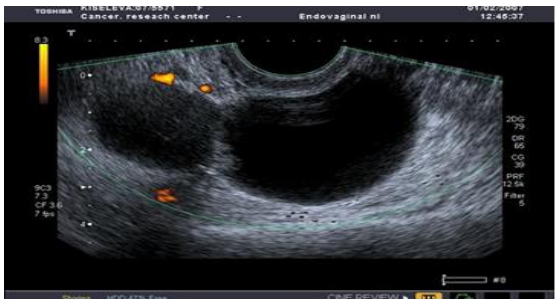
C) Menopause
D) Infection.
4. Which disease is characterized by the symptom of "chocolate cysts" of the ovaries?
A) Uterine fibroids
B) Endometriosis
C) Polycystic ovary disease
D) Adnexitis
5. Which type of uterine fibroids is the most common cause of uterine bleeding?
A) Subserosal
B) Intraligamentary
C) Submucosal
D) Intramural
6. The most common complications of endometriosis in women of reproductive age are:
A) Infertility
B) Menopause
C) Uterine bleeding
D) Myoma
7. Which method of treating multiple myomas in a woman who is not planning pregnancy is considered the most radical?
A) Myomectomy
B) Hysterectomy
C) Hormonal therapy
D) Embolization of uterine arteries
8. Which hormonal drug is most often prescribed for endometriosis?
A) Estrogens
B) Gestagens
C) Androgens
D) Corticosteroids.
9. What condition causes the regression of uterine fibroids?
A) Pregnancy
B) Adolescence
C) Menopause
D) Stress
10. The classic symptom of endometriosis is:
A) Secondary amenorrhea
B) Progressive dysmenorrhea
C) Galactorea
D) Asymptomatic course

TOPIC 7: BENIGN TUMORS OF THE OVARIAN. OVARIAN CYSTS AND CYSTOMAS.

Benign ovarian tumors (BOM) are a group of pathological accessory formations of ovarian tissue resulting from impaired processes of cell proliferation and differentiation.
Benign ovarian tumors are an acute problem in gynecology, as they often develop in women of childbearing age and lead to a decrease in reproductive potential.
Among all ovarian tumors, benign tumors account for about 80%, however, most of them are prone to malignancy. Timely detection and removal of ovarian tumors is very relevant from the point of view of the prevention of ovarian cancer.
The question of the etiology of benign ovarian tumors remains debatable. Various theories consider the following as etiological aspects:
hormonal,

• viral,
• the genetic nature of ovarian tumors.
The development of benign tumors in the ovaries is preceded by a state of hyperestrogenism with subsequent focal hyperplasia and cell proliferation. Embryonic changes play an important role in the development of germinogenic structures and sex cord tumors. One of the causes of tumor development is a disruption of the complex mechanism of neuroendocrine regulation. The development of ovarian tumors largely depends on increased FSH secretion by the pituitary gland.
The mechanism of tumor formation can be schematically described as follows:
- primary weakening of ovarian function and decrease in the level of ovarian estrogens;
- compensatory increase in the level of pituitary gonadotropins, primarily FSH.
Under conditions of prolonged increase in FSH secretion, diffuse hyperplasia appears in the ovaries, followed by focal hyperplasia and proliferation of cellular elements, which can culminate in tumor formation.
Recently, the issue of the hereditary form of ovarian cancer has been widely discussed. Naturally, these forms are significantly less common than sporadic forms. According to world literature, only 5-10% of patients suffer from hereditary forms. The expression of genetic engineering achievements made it possible to identify a number of oncogenes associated with familial forms of ovarian and breast cancer.
These include BRCA-1 and BRCA-2 oncogenes. In carriers of this gene, the incidence of ovarian cancer can reach 70% by the age of 60. It is no coincidence that a number of authors, taking into account the high probability of developing this oncological pathology, propose prophylactic tumor removal in women of this group after the end of reproductive age.
Risk factors for the development of ovarian tumors:
• Early or late menarche, the onset of late (after 50 years) menopause, menstrual cycle disorders.
• Decreased reproductive function, infertility, and miscarriage are also associated with the risk of developing ovarian tumors.
Chronic inflammatory diseases of the uterine appendages can form a premorbid background of the tumor process.
In the etiology and pathogenesis of ovarian tumors, genetic factors, neurohumoral and endocrine disorders are of great importance.
Risk groups.
1. Women with chronic inflammatory diseases of the pelvis.
2. Women suffering from hormonal disorders - menstrual cycle disorders, hormonal infertility.
3. Women who underwent surgery on the ovaries in the anamnesis - cystectomy, etc.
4. Aggravated heredity - ovarian and endometrial tumors in close relatives.
5. Women with breast cancer.
6. Women with pathological pregnancy.
Benign ovarian tumors are often associated with hereditary endocrinopathies - diabetes mellitus, thyroid diseases, HPV, and herpesvirus type II.
The frequency of ovarian tumors is 13.3%, with a significant portion of the identified pathology attributed to tumor-like processes (TPO) - 58.8%, true tumors - 39.1%. Regarding the structure of individual hystotypes of benign ovarian tumors (BTN),
In first place are epithelial tumors (76%), among which: serous - 69.9%, mucinous - 14.8%, endometrioid - 11.8%;
In second place are tumors of the stroma of the genital tract - 14.9%, among them - granulosa cells - 28.2%, thecomas, fibromas - 6.4%.
The majority of patients with MTT (69.1%) were in the age group from 31 to 60 years, with ovarian cancer most often occurring in postmenopause.
Terms:

• A cyst is a pathological cavity filled with a certain substance, caused by the retention or excessive secretion of fluid - this is a tumor-like process (TPO). Cysts are divided into 5 main types:
- retention,
- ramolision (from softening),
-persistant organs (atretik follicle; corpus luteum cyst),
- parasitic - traumatic.
Cystomas - true tumors of the ovaries.
Histological classification of ovarian tumors (WHO, Geneva, 1977):
1) Epithelial tumors:
a) serous (cystadenoma and papillary cystadenoma, superficial papilloma, adenofibroma and cystadenofibroma);
b) mucinous (cystadenoma, adenofibroma and cystadenofibroma);
c) endometrioid (adenofibroma and cystadenofibroma, adenoma and cystadenoma);
d) light cell or mesonephroid (adenofibroma);
d) Brenner tumors (benign);
e) mixed epithelial tumors (benign)
2) Tumors of the stroma of the genital tract: thecoma, fibroma.
3) Hermogenic tumors: dermoid cysts, ovarian stroma.
4) Tumor-like processes:
a) follicular cysts;
b) cysts of the corpus luteum;
c) endometrioid cysts;
d) simple cysts;
d) inflammatory processes;
e) paraovarian cysts.
When compiling this classification, called histological classification, the microscopic characteristics of tumors are used. Creating such a classification, reflecting the level of modern knowledge, is a progressive step.
Clinical presentation: Early stages are usually asymptomatic.
The average observation period for an ovary tumor specialist is 1.8-0.2 years. No specific signs are observed in ovarian tumors. Complaints are not specific. Symptoms of the disease depend on the size and location of the tumor. The most frequent complaints were pain in the lower abdomen (31.2%), as well as in the lower back, sometimes in the groin area. Often they have a dull, painful character. Acute pain occurs only when the tumor pedicle is twisted and bleeding occurs when the tumor capsule ruptures. Pain is not associated with menstruation. They arise as a result of irritation of the serous membranes, spasm of smooth muscles, and circulatory disorders.
The second most common complaint is menstrual irregularity. Benign ovarian tumors are identified taking into account medical history and instrumental examinations. During gynecological examination, the presence of the tumor, its location, size, consistency, mobility, sensitivity, surface character, and relationship with pelvic organs are determined.
Conducting a rectovaginal examination allows for the exclusion of tumor invasion into adjacent organs. Difficulties in the timely diagnosis of ovarian tumors associated with the absence of clinically expressed precancerous conditions are complicated by their unclear pathogenesis.
In recent years, ultrasound examination (USI) has become increasingly widespread, the high informativeness of which, the absence of contraindications, ensures the priority of this method. In recent years, preference has been given to transvaginal echography. Color Doppler mapping plays a certain role in the differential diagnosis of benign and malignant tumors, since malignant tumors are characterized by well-vascularized malignant tumors, atypical venous blood flow, and low blood resistance.The presence or absence of blood flow in the ovarian arteries in the postmenopausal period, according to SDK data, is of great importance in choosing the doctor's tactics.



In benign ovarian tumors, diagnostic laparoscopy has 100% diagnostic accuracy and often becomes therapeutic.
MRI is especially important in detecting tumor involvement in organs near the tumor.
Treatment: Treatment goals for benign ovarian tumors and tumor-like formations depend on age, reproductive status, and tumor histotype.
In reproductive age, it is necessary to strive to preserve ovarian tissue during surgery and prevent PCOS.
• The main task in perimenopause is radical treatment, which allows preventing recurrence and maintaining a high quality of life.
It should be borne in mind that currently the choice of management tactics is determined by the quality of life, including sexual considerations, since for complete social rehabilitation of the patient, it is necessary to quickly return patients to normal activities.
Surgical tactics for benign ovarian tumors are determined by the woman's age, reproductive status, and the histotype of the neoplasm.
From the point of view of evidence-based medicine, anti-inflammatory, hormonal, and enzyme therapy of ovarian tumors does not significantly change the objective results of treatment. Treatment of benign ovarian tumors is carried out only surgically.

Questions:
1. What are the main types of benign ovarian tumors?
2. What are the most common complaints of patients with benign ovarian tumors?
3. What ultrasound markers help differentiate benign ovarian tumors from malignant ones?
4. How does serous cystadenoma differ from mucinous cystadenoma?
5. What is a dermoid cyst, and at what age is it most common?
6. What complications can occur in benign ovarian tumors?
7. What is the essence of Maig's syndrome, and with which ovarian tumor is it associated?
8. Which treatment method is considered the primary treatment for benign ovarian tumors?
9. In what cases is observation rather than surgery indicated for ovarian cysts?
10. Why do benign ovarian tumors require dynamic monitoring even after removal?

Situational problem:

1. The patient, 26 years old, complained of pulling pain in the lower right side of the abdomen. On ultrasound - a single-chamber anechogenic formation with a thin capsule measuring 5 cm.
Question: Which disease is most likely and what is the management strategy?

2. Random ultrasound examination of a 52-year-old woman in the postmenopausal period revealed the formation of the left ovary 6 cm wide, with a smooth contour, without blood flow. No complaints.
Question: What is the probability of a benign process and the doctor's subsequent actions?

3. A 32-year-old patient complains of abdominal enlargement, swelling, and shortness of breath. Upon examination - ascites, right-sided hydrothorax, pelvic formation.
Question: What syndrome does the patient have and which ovarian tumor can cause it?

4. In a 20-year-old girl, the formation of an ovary containing elements of fatty tissue and bone structures was revealed.
Question: Which diagnosis is more likely?

5. A 30-year-old patient presented with acute pain in the lower abdomen, nausea, and weakness. On ultrasound examination - on the pedicle of the ovarian cyst, signs of impaired blood flow.
Question: Which one is more complex?

A 6.45-year-old woman complains of irregular menstruation and a feeling of heaviness in the lower abdomen. Ultrasound examination reveals a septate multi-chamber cystic tumor, with no signs of malignancy.
Question: Which benign tumor can be considered and what treatment is prescribed?
7. In a 34-year-old patient, during a planned examination, the formation of an ovary of 4 cm was revealed, no complaints. The doctor recommends observation in dynamics.
Question: In what cases can benign ovarian tumors be observed?

8. Patient 28 years old, pregnancy 10 weeks. On ultrasound, the right ovary is 6 cm long, single-chambered, thin-walled.
Question: What is the management tactic in this situation?

9. A 38-year-old woman complaining of pain in the lower abdomen. On ultrasound - ovarian tumor, dense, with hypoechoic inclusions. In laparoscopy - a fibrous formation.
Question: Which type of benign tumor is more likely?

A woman at the age of 10.40 had a cyst removed during laparoscopy for a benign ovarian tumor. After 2 years, a benign tumor of a new ovary appeared.
Question: What is the management tactic in this situation?

Tests:

1. Which group of benign ovarian tumors is included?
a) Endometrioid cyst
b) Serous cystoma
c) Dermoid cyst
d) All of the above
2. Which is the most common benign ovarian tumor?
a) Serous cystoma
b) Mucous cystoma
c) Dermoid cyst
d) Brenner tumor
3. From which cells does a dermoid cyst develop?
a) Mesothelial cells
b) from germinative (embryonic) cells
c) Stromal cells
d) from epithelial cells
7. Brenner o‘smasi qaysi to‘qimadan rivojlanadi?
a) Epitelial hujayralardan
b) Germinativ hujayralardan
c) Stromal hujayralardan
d) Mushak to‘qimasidan
4. What are the most characteristic signs of benign ovarian tumors?

a) Slow growth
b) In most cases, asymptomatic
c) Low risk of malignancy
d) All of the above
5. What is the most common complication in benign ovarian tumors?
a) Torsion (leg rotation)
b) Inflammation
c) Rupture
d) All of the above
6. What is the main characteristic of a mucous cystoma?
a) Contains a liquid suspended substance
b) contains a liquid resembling a mucous substance
c) Occurs mainly bilaterally
d) Malignization is common.
8. What signs are most often detected during ultrasound examination of benign ovarian tumors?
a) Smooth capsule
b) Single-chamber
c) Being filled with a homogeneous liquid
d) All of the above
9. What are the clinical characteristics of a dermoid cyst?
a) May contain hair, fat, and teeth
b) Occurs mainly in women of reproductive age
c) Malignization is very rare.
d) All of the above
10. What is the main treatment method for benign ovarian tumors?
a) Antibiotic therapy
b) Physiotherapy
c) Surgical removal
d) Hormone therapy

TOPIC 8: INDEVELOPMENT AND INCORRECT LOCATION OF WOMEN'S GENITAL ORGANS. GENITAL ANOMALIES IN GIRLS, ADOLESCENTS, AND YOUNG WOMEN. KÜSTNER-ROKITANSKY SYNDROME.

Developmental defects (synonym developmental anomalies) - a collective term denoting deviations from the normal structure of the organism as a result of intrauterine or postnatal (less often) developmental disorders.
Congenital malformations are also called congenital defects, congenital disorders, or congenital deformities. Congenital malformations can be defined as structural or functional deviations from the norm (e.g., metabolic disorders) that manifest during intrauterine development and can be detected before birth, at birth, or in later life stages.

TERMS

Aplasia (from the negative suffix "a" and the Greek word "plasis" - formation) is a developmental defect, the congenital absence of a part of the body or organ.
Agenesis - (from the Greek a - neg. part and genesis - origin, formation), absence of development (syn. aplasia), a term used to denote an ugliness consisting of the congenital absence of a particular organ, part of it, or part of the body.
Atresia (from the Greek a - particle and tresis - hole) - the complete absence of a cavity or natural opening in an organ with a tubular structure (for example, in the aorta, esophagus, etc.).
Hypoplasia - cessation of the development of an organ, part of it, or the whole organism as a result of the cessation of cell proliferation;

Hyperplasia - (from Greek hyper - excessive and rlasso - I create, I create), excessive cell regeneration (R. Virchow). The process of hyperplasia, i.e., numerical hypertrophy (see. Hypertrophy) is the proliferation of cells.
Malformation - a morphological defect of an organ, part of an organ, or a large part of the body resulting from a disruption of the developmental process due to genetic aberrations.

INTERNATIONAL CLASSIFICATION OF DISEASES, X REVIEW
52.0 Congenital absence of vagina
Q52.1 Vaginal duplication. Barrier-separated vagina
Exception: vaginal duplication with body and cervical duplication (Q51.1)
Q52.2 Congenital rectovaginal fistula
Exception: Cloaca (Q43.7)
Q52.3 Female hymen completely covering the vaginal opening
Q52.4 Other congenital abnormalities of vagina
Vaginal malformation BDU Cyst: Nuck canal, congenital vagina, embryonic
Q52.5 Lip fusion
Q52.6 Congenital anomaly of clitoris
Q52.7 Other congenital anomalies of vulva
Congenital: absence, cyst of vulva, anomaly
Q52.8 Other specified congenital anomalies of female genital organs
Q52.9 Congenital anomaly of female genital organs, unspecified.

CLASSIFICATION

Currently, there are many classifications of vaginal and uterine developmental defects, based on differences in the embryogenesis of the internal genitalia, the results of radiological examination, and the identification of individual clinical and anatomical forms.
Classification of uterine and vaginal developmental defects.(L.V. Adamyan, A.Z. Khashukova)
Class I vaginal aplasia
1. Complete aplasia of the vagina and uterus:
a) rudiment of the uterus in the form of two muscle rolls;
b) uterine rudiment in the form of a single muscle shaft (right, left, center);
c) absence of muscle rolls.
2. Complete vaginal aplasia and functioning rudimentary uterus:
a) a functioning rudimentary uterus in the form of one or two muscle rolls;
b) a rudimentary uterus working with cervical aplasia;
c) a rudimentary uterus working with cervical canal aplasia;
In all variants, hemato- and pyometra, chronic endometritis and perimetritis, hemato- and pyosalpinx are possible.
3. Vaginary aplasia in a functioning uterus:
a) aplasia of the upper third;
b) aplasia of the middle third;
c) aplasia of the lower third.
Grade II. Unicornuate uterus
1. One-horned uterus with rudimentary horns, adjacent to the main horn cavity.
2. The rudimentary branch is closed.
In both cases, the endometrium can be active or inactive.
3. Hollow rudimentary branch.
4. Absence of a rudimentary branch.
Class III uterine and vaginal duplication
1. Doubling of uterus and vagina without disruption of menstrual blood flow

2. Doubling of uterus and vagina with partially aplastic vagina
3. Doubling of uterus and vagina in one nonfunctioning uterus
Grade IV. Bilateral uterus
Incomplete form
2. Full form
3. Saddle shape
5th grade. Intrauterine septum
1. Complete intrauterine septum - to the internal pharynx
2. Incomplete intrauterine septum
Grade VI. Developmental defects of fallopian tubes and ovaries
1. Unilateral aplasia of uterine appendages
2. Tubular aplasia (one or both)
3. Availability of additional pipes
4. Ovarian aplasia
5. Hypoplasia of the ovaries
6. Presence of accessory ovaries
Grade VII. Rare forms of genital defects
1. Defects of urogenital development: extrophy of the bladder.
2. Intestinal-genital developmental defects: congenital rectovestibular fistula with vaginal and uterine aplasia; congenital rectovestibular fistula with a unicornuate uterus and a functioning rudimentary horn.

Classification by E.A. Bogdanova and G.N. Alimbayeva

Class I - hymen atresia (variants of hymen structure);
Class II - complete or incomplete aplasia of vagina and uterus:
- complete aplasia of the uterus and vagina (Rokitansky-Custer-Meyer-Hauser syndrome);
- complete aplasia of the vagina and cervix in a working uterus;
- complete vaginal aplasia in a functioning uterus;
- partial aplasia of the vagina up to the middle or upper third in a working uterus;

Class III - defects associated with incomplete or incomplete union of paired embryonic genitalia:
- complete duplication of the uterus and vagina;
- doubling of the uterine body and cervix in the presence of one vagina;
- duplication of the uterine body in the presence of one cervix and one vagina (saddle-shaped uterus, two-horned uterus, uterus with a complete or incomplete internal septum, a rudimentary working closed-horned uterus);

Class IV - defects associated with duplication and aplasia of paired embryonic genitalia:
- uterine and vaginal duplication with partial aplasia of one vagina

CAUSES AND FACTORS OF RISK

Approximately 50 percent of all developmental defects cannot be attributed to any specific cause, but some causes or risk factors are known.

Socio-economic factors.

Despite the fact that low income can be an indirect determinant. Developmental deficiencies are more pronounced in families and countries with insufficient resources. It is estimated that approximately 94% of severe developmental disabilities are observed in middle and low-income countries, where women often do not have sufficient and sufficiently good food and may be exposed to any agent or factor. For example, infections or alcohol that trigger or exacerbate abnormalities in prenatal development.

In addition, being a mature mother increases the risk of chromosomal abnormalities, including Down syndrome, while being a young mother increases the risk of some congenital defects.

Genetic factors

Consanguinity

In some ethnic groups, such as Ashkenazi Jews and Finns, a relatively high prevalence of rare genetic mutations is observed, which leads to an increased risk of developmental defects.

Infections

The presence of infections such as syphilis or measles in mothers is a common cause of congenital malformations in low and middle-income countries.

Maternal nutrition

Conditions such as iodine and folic acid salt deficiencies, obesity, or diabetes mellitus are associated with some developmental defects. For example, folic acid deficiency increases the risk of being born with a neural tube defect. In addition, excessive consumption of vitamin A can affect the normal development of the embryo or fetus.

Environmental factors

The effects of certain pesticides and other chemicals, as well as certain medications, alcohol, tobacco, psychoactive substances, or radioactive radiation on the mother's body during pregnancy can increase the risk of developing congenital malformations in the fetus or newborn. Working or living near or in the immediate vicinity of landfills, metallurgical plants, or mines can also be a risk factor, especially when the mother's body is exposed to other environmental hazards or is malnourished.

PATHOGENESIS

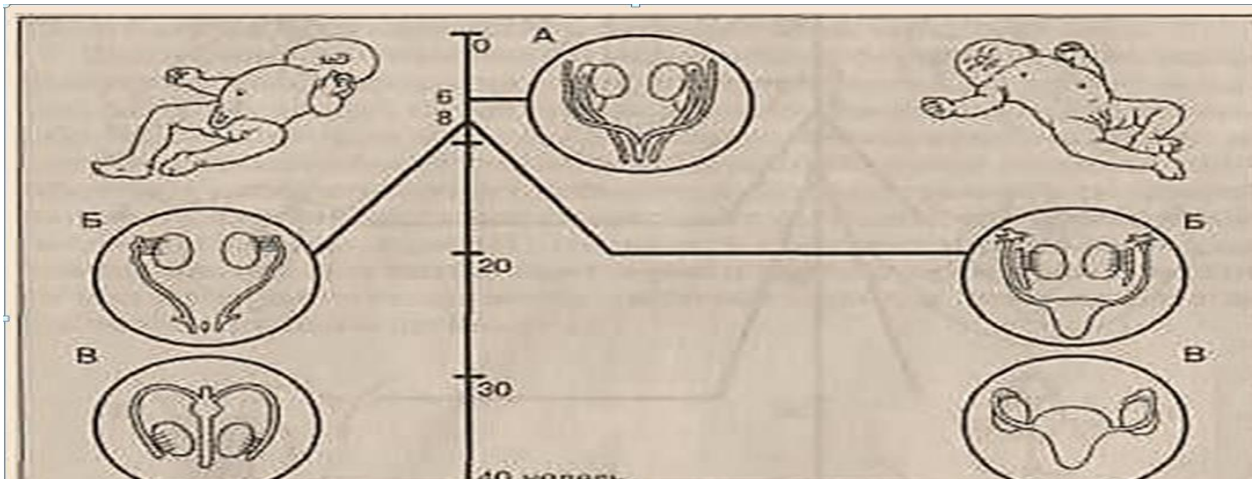
The formation of gonads is determined by the sex chromosome (X or Y). Female genitalia are formed from paired Müllerian ducts, while male genitalia are formed from Wolffian ducts. There is an opinion that the development of the female type of internal and external genitalia is associated with a genetic loss of tissue response to androgens. The underdevelopment or lack of estrogen receptors in the cells of the Müllerian ducts can inhibit their formation, leading to changes such as uterine aplasia.

Müller's ducts are formed as a result of the penetration of coelomic epithelium into the lateral surface of the mesonephros. Slowing of the proliferation of the epithelium covering the genital margins by the coelom, from which the Müllerian ducts are formed, leads to disruption of their further development. The Müllerian and Wolffian ducts are formed at 5-6 weeks of embryonic development, and at 20 weeks, the uterus and vagina are formed. Table 1.

From the 4th month of embryonic life, the formation of the external genitalia begins. In both sexes, they are formed by the genital tubercle, the cleft of the cloaca, and two pairs of folds surrounding the cleft, inner (genital folds) and outer (genital coils) folds. The developmental site of the external genitalia is the ventral part of the caudal part of the abdominal wall, which lies in the area of the cloaca. In this area, a conical (cloacal) tubercle appears and divides into two at the sixth week. Its elongated, conical, or even cylindrical, protruding part is called the phallus, or genital tubercle.

The distal part of the genital fissure expands into the vestibule of the vagina, where the female urethra and vagina open. The genitalia turn into the labia majora, in which a large amount of adipose tissue accumulates, and they cover the labia minora.

1. Jadval



Stages of development of male and female sex.

The formation of the genitourinary system can be divided into 3 stages:
Stage I (2-3 weeks of pregnancy) - the primary intestinal tube divides into the upper part of the allantois and the lower part of the cloaca, the coelom is formed.
Stage II (4-5 weeks) - the cloaca is divided into two sections - the urogenital sinus and rectum. Müller belts are formed, which undergo sewerage.
Stage III (8-12 weeks) - separation of the urogenital sinus. Fusion of the Müllerian ducts and formation of the bicornuate body of the uterus.
Consequently, the most severe defects develop in the early stages of embryonic development. In stage I of female genital development, under the influence of unfavorable factors, defects in the development of the cloaca are formed. Uterine and vaginal aplasia is caused by factors affecting the 6th week of pregnancy.
Doubling of the uterus and vagina is formed from the 7th to the 9th week of pregnancy. When the formation of the internal genitalia is disrupted, the uterus takes on a saddle-shaped shape at 16-18 weeks.

CLINIC. DIAGNOSIS AND TREATMENT.

The only symptom that occurs with menstruation in defects without disruption of menstrual blood flow may be dysmenorrhea. Developmental defects of the uterus in reproductive age are a common cause of infertility or inability to conceive.

APPLASIA OF UTERUS AND VINA

Complete form (Mayer-Rokitskiy-Kyustner-Hauser syndrome).
No manifestations occur until sexual maturation begins. The main complaint of girls at the age of 15-16 is the absence of menstruation - amenorrhea I.
Examination of the external genitalia reveals the absence of an access to the vagina (Fig. 1) or (if there is a hole in the hymen) a shallow depression behind the hymen. In some patients, the vagina can be short (2-4 cm).

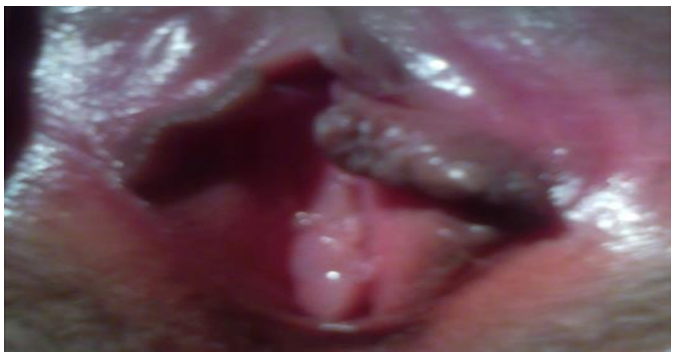


Figure 1. Fusion of clitoris and urethra in vagina

On a rectoabdominal examination, a dense ligament can be palpated in the uterine projection. The uterus is not detected on ultrasound (Fig. 2).

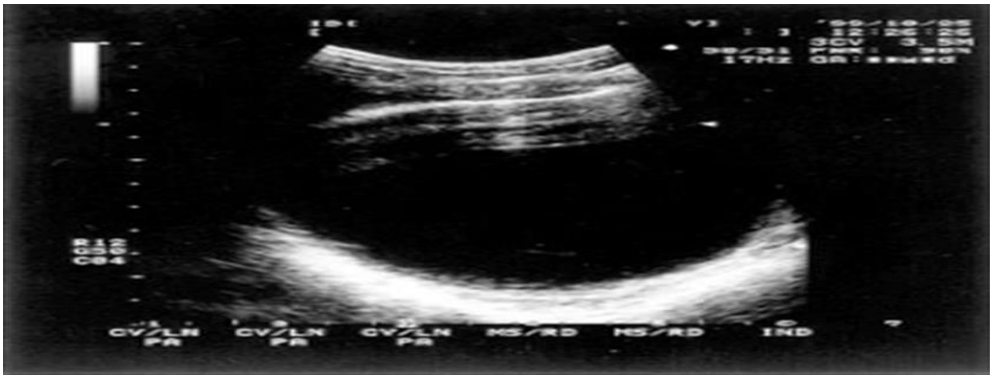


Figure 1. The uterus was not detected on ultrasound.

The goal of the treatment is the patient's sexual rehabilitation, that is, the creation of the vagina. The treatment method is selected individually, depending on the patient's pelvic structure, the topography of the pelvic organs, the timing of the onset of regular sexual activity, the possibility of independent bougienage of the new vagina, as well as taking into account the patient's capabilities and preferences.

Methods of creating a new vagina:

• non-operative - colpoelongation;

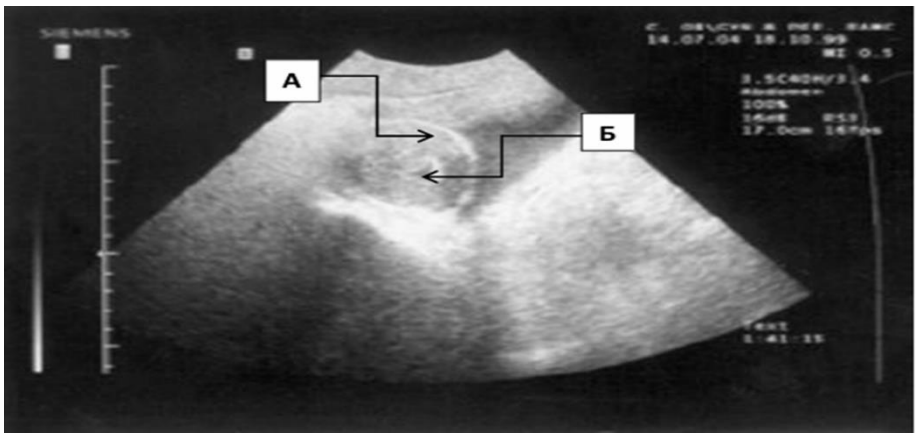
• operative - colpopoiesis from the mucous membrane and skin of the peritoneum, intestinal lobes, vulva, synthetic materials.

In recent years, Professor Mats Brennström has developed and successfully applied in clinical practice a method of uterine transplantation that allows women without a uterus to become pregnant and give birth. In 2014, for the first time in Sweden, delivery was successful in women whose uterus was transplanted from their mothers.

CERVICAL APPLASIA IN FUNCTIONING UTERUS

During puberty, a girl experiences attacks of severe, unbearable pain in the lower abdomen, which recur once a month and do not stop even with the use of antispasmodics and analgesics. Often they are accompanied by symptoms of peritoneal irritation, nausea, and vomiting due to menstrual blood flowing through the tubes into the abdominal cavity.

A gynecological examination reveals the absence of the entire vagina or its upper part. A spherical, dense, mobile, painful formation is detected in the pelvis. Ultrasound examination can reveal the absence of the cervix during menstruation, hematometra (blood accumulation in the uterine cavity) (Fig. 3, hematosalpinx (blood accumulation in the fallopian tubes), hemoperitoneum (free blood in the pelvic cavity).



1. *Figure 1. Echogram of uterine aplasia. Hematometer.*
   a. Uterine body b. Uterine body dilation.

PARTIAL VINAL APLASIA IN FUNCTIONING UTERUS

Vaginal aplasia is more common than other defects of the female genital organs. This is because it originates from two buds: the caudal part of the Müllerian ducts and the urogenital sinus. Aplasia of the upper third of the vagina During puberty, the girl experiences pain attacks in the lower abdomen every month, which intensify over time. Upon examination with mirrors, the vagina is short, no longer than 7-8 cm long, and ends blindly. Rectoabdominal examination reveals a slightly enlarged and painful pear-shaped uterus in the pelvic cavity.
Ultrasound examination reveals blood accumulation in the upper part of the vagina, sometimes hematometra and hematosalpinx (Fig. 5).

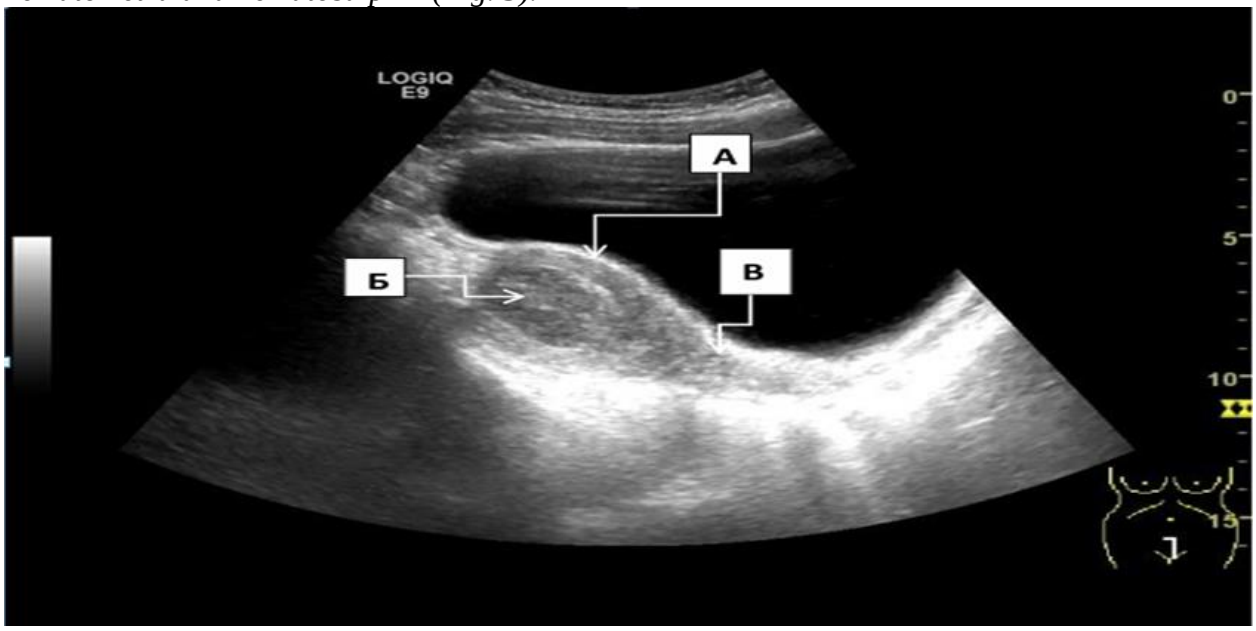


Fig. 5. Aplasia of the upper part of the vagina.
a. body of the uterus.
b. blood in uterine cavity
c. cervix

Middle third vaginal aplasia

When the patient reaches the age of menstruation, they begin to be bothered by pulling, swelling pains in the lower abdomen, frequent urination may occur.
When examining the vagina in mirrors, its length does not exceed 2-3 cm and ends blind. Rectoabdominal examination reveals an elongated, immobile elastic formation in the projection

of the upper part of the vagina. The uterus cannot be palpated separately. Ultrasound reveals hematocolpos, sometimes hematometra, and hematosalpinx.

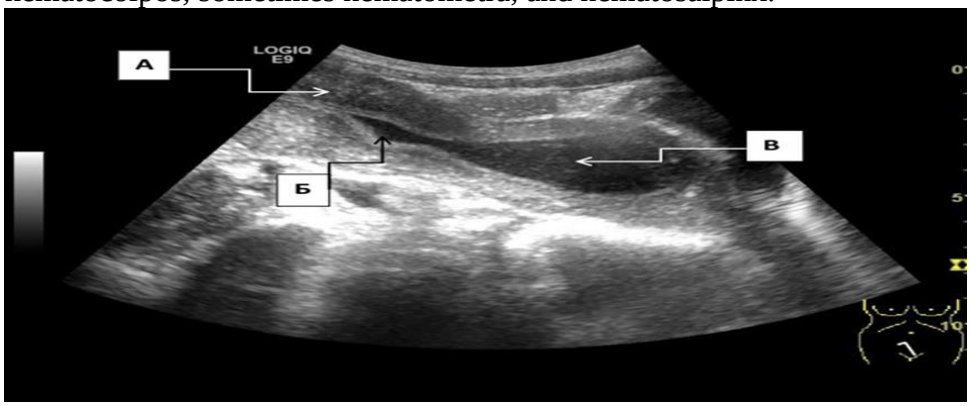
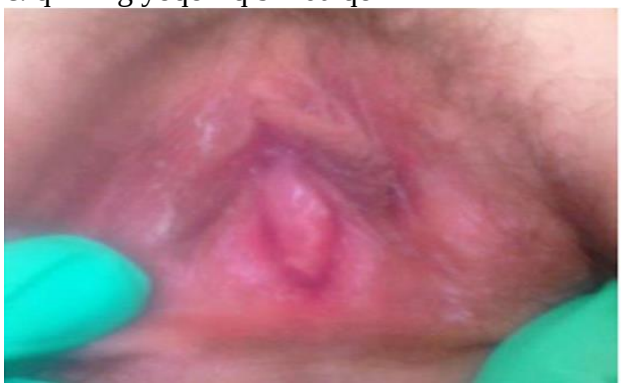


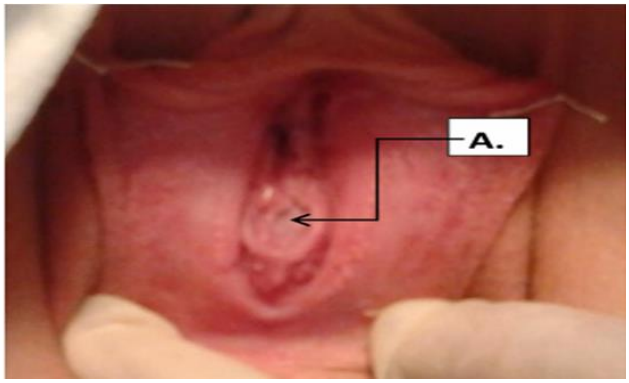
Fig. 5. Middle vaginal aplasia.
a. body of the uterus.
b. cervix
c. blood in the upper part of the vagina

Aplasia of lower vagina

As the patient reaches the age of menstruation, she begins to be bothered by monthly pain in the lower abdomen, which gradually intensifies, and delayed urination and defecation may be added. Examination of the external genitalia reveals the absence of a vagina (Fig. 7, 8). Rectoabdominal examination reveals an elongated, immobile, dense-elastic formation in the vaginal projection, which can have enormous dimensions and be palpable through the anterior abdominal wall.5.rasm. qinning o'rta qismi aplaziyasi.
a. bachadon tanasi.
b. bachadon bo'yni
c. qinning yoqori qismida qon

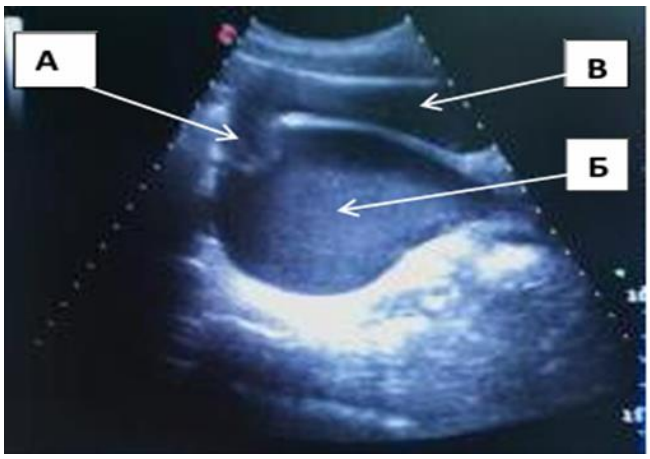


1. Rasm.qin aplaziyasi.



7.rasm. qinni pastki qismi aplaziyasi

On ultrasound examination, blood accumulation in the vagina (hematokolpos) is clearly visible (Figures 9, 10). Treatment is operative with preliminary colpoelongation to stretch the vaginal vestibule tissues and ensure their maximum mobility during plastic surgery.



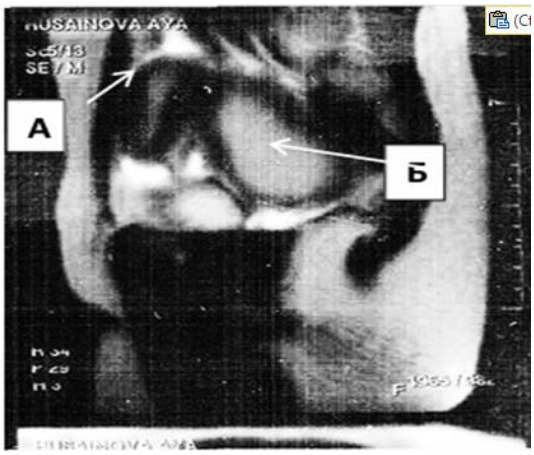


Figure 8. aplasia of the lower part of the vagina Figure 9. MRI. hematometry and a. cervical hematocolpos
blood in the vagina
c. bladder

COMBINATION OF UTERINE AND VEGETABLE DUPLICATION AND APLASIA

Diagnosing these defects is difficult because girls menstruate on time, and the menstrual cycle is usually not disrupted. Doubling with unilateral complete aplasia of the uterus, cervix and vagina.
Shortly after menstruation, patients experience pain in the lower abdomen during menstruation, which intensifies with each subsequent menstruation. It does not disappear even after taking analgesics and antispasmodics.
During a gynecological examination, it is very difficult to detect this pathology.
Only ultrasound examination reveals two uteruses, sometimes a hematometer and hematosalpinx on one side (Fig. 10).

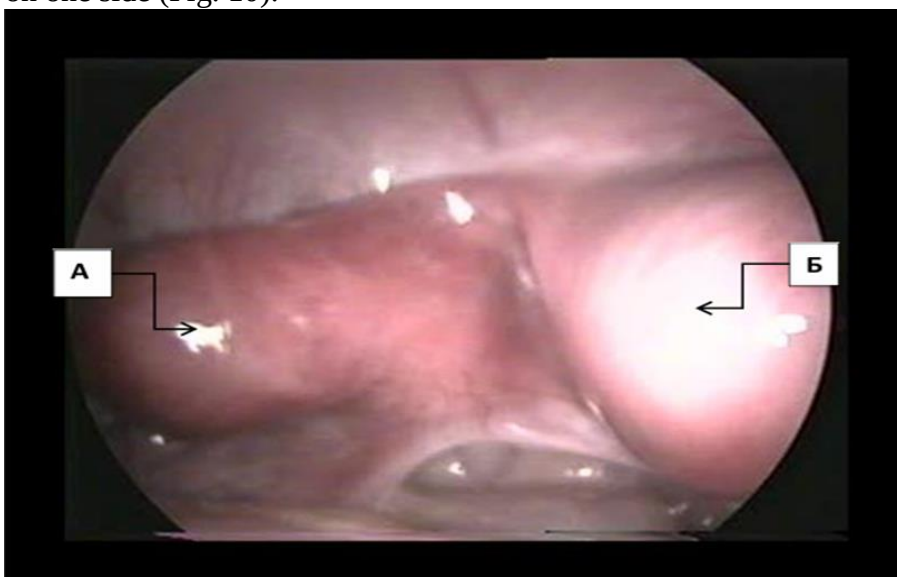
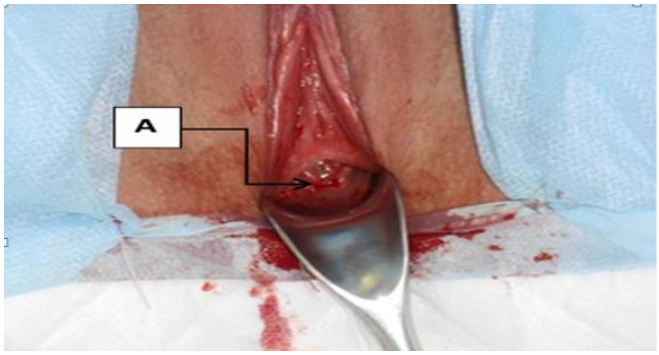


Figure 10. Laparoscopy. Hematometer.

Doubling of uterus and vagina with partial aplasia of one vagina.

In patients, months after menstruation, the period is painful, and with each subsequent menstruation, the pain intensifies.
During the gynecological examination, the external genitalia were unchanged. The vagina is deep, the cervix is examined. The protrusion or drooping of one of the vaginal walls is determined (Fig. 11, 12).



1 1. Fig. Complete duplication of the uterus and vagina *12. Opening of the hematokolpos.*

On ultrasound examination, two uteruses are detected, hematokolpos and sometimes hematometra and hematosalpinx are clearly visible from the aplasia side (Fig. 13)

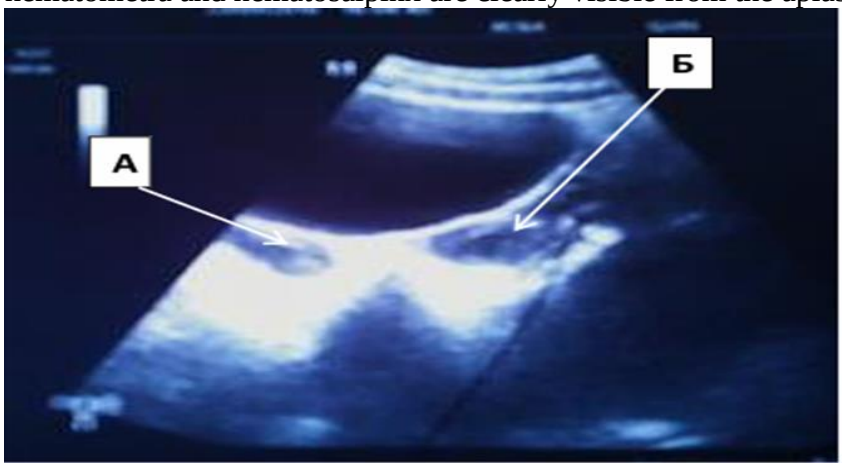


Fig. 13. Echogram of complete uterine and vaginal duplication.

PERVICULAR ATRESIA

Hymen atresia is the absence of a congenital opening in the hymen. This pathology can also be detected in a newborn girl. Due to the production of a large amount of cervical mucus and the accumulation of detached mature superficial cells of the vaginal epithelium, the vagina stretches (mucocolpos) and the hymen bulges (Fig. 14).

In most cases, hymenal atresia is detected at the age of menarche. The vagina is an elastic organ that can hold a large amount of blood, causing pain when the vaginal walls are severely stretched and often accompanied by dysfunction due to compression of adjacent organs.

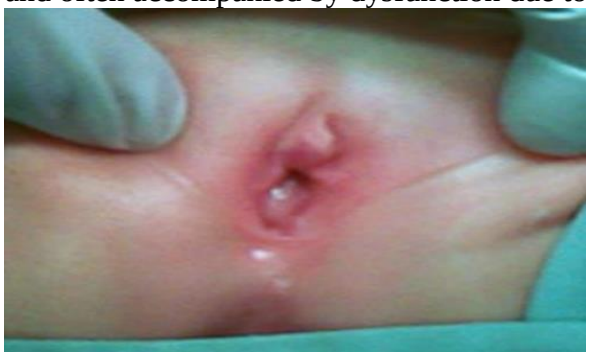


Figure 14. Atresia of the hymen in a girl.

Patients complain of abdominal heaviness, frequent urination, and constipation. Often, abdominal enlargement is observed due to a dense-elastic tumor originating from the pelvis (Fig. 15). Sometimes a patient comes to the hospital complaining of urinary retention.

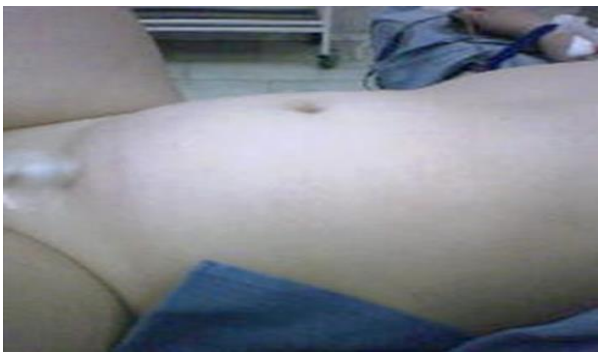
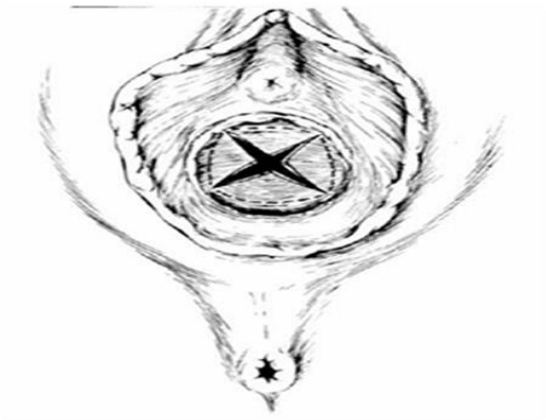


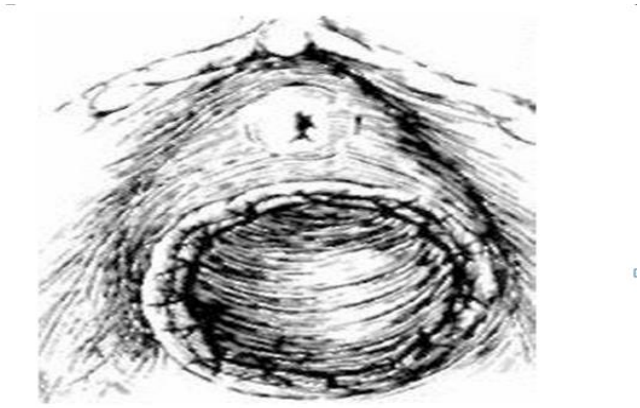
Figure 15. Accumulation of 2 liters of blood in the abdominal cavity in vaginal atresia.

Upon examination of the perineum, the genital cleft is open, the hymen is excessively elongated and protruding (Fig. 16).

Fig. 17. Atresia of the hymen. Hematokolpos.

Treatment: incision of the hymen and emptying of the hematokolpos. The hymen is cut with a cross-section or an oval-shaped window is cut in the middle. To prevent re-healing, the edges of the section are sutured (Figures 18, 19).





Timely diagnosis and selection of the optimal tactics of surgical treatment of girls with uterine and vaginal anomalies with impaired menstrual blood flow (in a hospital with the appropriate license, equipment, and qualified specialists) prevents the development of serious complications. Menstrual blood flow into the abdominal cavity can lead to the formation of pelvic-peritoneal adhesions. Infection of the hematokolpos, hematometers, and hematosalpinx leads to the formation of purulent cavities (piokolpos, piometers, and piosalpinxes) and peritonitis. These complications, in turn, lead to infertility.

Questions:

1. What is meant by congenital developmental anomalies of the female genital organs, and what factors can cause them?
2. How are the degrees of uterine underdevelopment (hypoplasia, aplasia) classified, and what is their clinical significance?
3. How does congenital vaginal aplasia differ from vaginal atresia, and how does it manifest itself clinically in girls and adolescent girls?
4. What typical complaints and symptoms are observed in patients with uterine malposition (retroflection, retroversion, etc.)?
5. How is Kyustner-Rokitansky syndrome (aplasia of the upper third of the uterus and vagina with normal ovaries and preserved secondary sexual characteristics) diagnosed?
6. Which modern visualization methods (ultrasound, MRI, laparoscopy) are the most informative in detecting anomalies in the development of the genitals?
7. What is the management tactics for a teenage girl with normally developed breasts and hair, but without menarche?
8. What psychological and reproductive consequences can arise in young women with Kustner-Rokitansky syndrome?
9. What surgical methods are used for the restoration of vaginal aplasia (neovagination according to the Makintosh method, sigmo-vaginoplasty, etc.)?
10. What is the role of a multidisciplinary approach (gynecologist, endocrinologist, psychologist) in the treatment and observation of patients with congenital anomalies of the genital organs?

Situational tasks:

1. 14-year-old girl. Complaint: absence of menstruation. The mammary glands and pubescence are developed by age. Ultrasound: the uterus is undetectable, the ovaries have a normal structure.
Question: What is your initial diagnosis? What examination methods are needed to confirm the diagnosis?
2. A 16-year-old patient. Complaints: periodic lower abdominal pain, no menstruation. Upon examination: external genitalia are normally developed, the vagina ends blindly at a depth of 2 cm.
Question: Which congenital anomaly is most likely? What is the treatment tactic?
3. 12-year-old girl. Complaints: monthly pain in the lower abdomen. Upon examination: external genitalia are normal, a bluish bump is detected at the vaginal inlet.
Question: Which situation should we think about? What urgent intervention is needed?
4. A 20-year-old woman. Complaint: infertility. Examination: uterus is very small (hypoplasia grade I), ovulation is preserved.
Question: What treatment options are available? Can the patient become pregnant?
5. 13-year-old girl. Complaints: absence of menstruation, periodic abdominal pain. Ultrasound: single-horned uterus (one-cornered uterus) with a hematometer.
Question: What is your diagnosis? What are the tactics and prognosis of reproductive function?
6. A 15-year-old patient. Complaint: absence of menstruation. The mammary glands and appendix are normally developed. Laparoscopy: uterine aplasia, preserved ovaries.
Question: Which syndrome can be predicted? What are the patient's reproductive prospects?
7. A 20-year-old woman. Complaint: infertility. Examination: uterus is very small (hypoplasia grade I), ovulation is preserved.
Question: What treatment options are available? Can the patient become pregnant?
8. 13-year-old girl. Complaints: absence of menstruation, periodic abdominal pain. Ultrasound: single-horned uterus (one-cornered uterus) with a hematometer.
Question: What is your diagnosis? What are the tactics and prognosis of reproductive function?

9. A 15-year-old patient. Complaint: absence of menstruation. The mammary glands and appendix are normally developed. Laparoscopy: uterine aplasia, preserved ovaries. Question: Which syndrome can be predicted? What are the patient's reproductive prospects?

Tests:

1. What are the characteristic signs of Kyustner-Rokitansky syndrome?
A) Aplasia of the ovaries
B) Aplasia of the uterus and upper third of the vagina, ovaries normal
C) Atresia of the hymen
D) Hypoplasia of the mammary glands
2. The main clinical sign of vaginal aplasia in adolescent girls:
A) Primary amenorrhea in normal sexual development
B) Secondary amenorrhea
C) Disruption of the menstrual cycle and profuse bleeding
D) Hypogonadism
3. What is the most informative examination for diagnosing congenital uterine anomalies?
A) Hysterosalpingography
B) pelvic ultrasound
C) Laparoscopy and MRI
D) Hormonal blood test
4. What is characteristic of uterine retroflection?
A) The uterus is curved forward
B) Uterus curved backward
C) No uterus
D) Underdeveloped uterus

5. A 14-year-old girl has no menarche, breasts and hair are normal. Ultrasound: uterus not detected, ovaries normal. What is the most likely diagnosis?
A) Shereshevsky-Turner syndrome
B) Kyustner-Rokitansky syndrome
C) Hypogonadism
D) Atresia of the hymen
6. What is the treatment tactics for adolescents with complete vaginal aplasia?
A) Prescription of hormonal therapy
B) Plastics (creating a neocline)
C) Administration of antibiotics
D) Only dynamic observation
7. What is a characteristic complication of hymen atresia?
A) Hematometra and Hematokolpos
B) Endometrial hypergenesis
C) Ovarian cyst
D) Polycystic ovary syndrome
8. What are the variants of uterine hypoplasia?
A) Aplasia
B) Infantile uterus
C) Juvenile uterus
D) All of the above.
9. What is the correct opinion about Kyustner-Rokitansky syndrome?
A) There are no secondary sexual characteristics.
B) With the help of a surrogate mother, a biological child can be born.
C) No ovaries
D) Independent pregnancy is possible.

10. Which direction is mandatory in the treatment of girls and young women with congenital anomalies of the female genital organs?
A) Only surgical treatment
B) Only hormonal therapy
C) Multidisciplinary approach: gynecologist, endocrinologist, psychologist
D) Treatment with folk medicine

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