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Faculty of international

Department of Obstetrics and Gynecology

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METHODICAL DEVELOPMENT FOR PRACTICAL LESSONS FROM EDUCATIONAL DISCIPLINE

Faculty of international, course IV

Educational discipline "Obstetrics and gynecology"

Practical lesson № 3. Topic: « Neuroendocrine regulation »

Approved:

Meeting of the Department of Obstetrics and Gynecology

Odessa National Medical University

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Practical lesson № 3
Topic: "Neuroendocrine regulation of the function of genital system. Disorders of reproductive system".

Goal: Disorder of the menstrual cycle is one of the most difficult in understanding and mastering topics in gynecology, and the diseases themselves are the most complicated for diagnostics and treatment, because they require of the doctor understanding and knowledge of very difficult mechanisms of regulation of the menstrual function, difficult principles and extreme responsibility in conducting hormone therapy.

Basic concepts: educational (to introduce students to current topics, normal menstrual cycle, regulation of menstrual cycle, the volume of the survey of it.); scientific (logical train student clinical thinking and new methods of diagnosis for abnormal uterine bleeding); creative (see the deontological principles of management of patients with menstrual dysfunction, given the social aspects of the problem); responsible (develop a sense of legal responsibility for the doctor to adequately carried out therapy.).

Equipment: Professional algorithms, structural-logical schemes, tables, models, power point presentations, video and paper media, results of laboratory and instrumental researches, situational tasks, patients, medical histories.

Training time: 4 hours

I. Organizational activities (greetings, checking the audience, announcing the topic, the purpose of the lesson, motivating students to study the topic).

Normal menstrual function is due to the correct synchronous interaction of important parts of neuroendocrine regulation. This system include five levels of regulation and violation of any part of it leads to changes in a woman's menstrual function, varying in nature and severity - from abnormal uterine bleeding to amenorrhea. The following social questions as long incapacity for work, decrease in reproductive function that leads to infertility, high risk of development of precancerous diseases and endometrial cancer are closely connected with this pathology.

II. Control of basic knowledge (written work, written testing, face-to-face interview, etc.) (if necessary):

2.1.Requirements for theoretical readiness of students to perform practical classes:

Knowledge requirements:

- Communication skills and clinical examination of the patient.
- Ability to determine etiological and pathogenetic factors in disorders of the reproductive system and menstrual function.

- Ability to establish a preliminary and clinical diagnosis of the disease.
- Ability to perform medical manipulations.
- Ability to classify of menstrual disorders of patient
- Ability to keep medical records.
- Communication skills and clinical examination of the patient.

List of didactic units:

- Knowledge of the basic concepts of clinical anatomy and physiology of female genitalia.
- Ability to collect Special gynecological anamnesis.
- Possession of necessary methods general and special methods of examination of gynecological patients, methods of functional diagnostics of ovaries.
- Knowledge of classification of function disorders of genital organs (menstrual function).

2.2. Questions (tests, tasks, clinical situations) to test basic knowledge on the topic of the lesson:

Questions:

1. General symptomatics of gynecological pathology.
2. Classification of function disorders of genital organs (menstrual function).
3. Amenorrhea: classification , diagnostics, tactics of GP (general practitioner).
4. Abnormal uterine bleedings: PALM-COEIN classification by FIGO, clinics, diagnostics.
5. Juvenile uterine bleedings: etiology, clinics, diagnostics, tactics of GP, emergency care.
6. Abnornal bleedings of reproductive age: etiology, clinics, diagnostics, tactics of GP, emergency care.
7. Abnornal bleedings of perimenopausal period: etiology, clinics, diagnostics, tactics of GP, emergency care.
8. Dysmenorrhea: etiology, classification, clinics, diagnostics, treatment.

Typical situational tasks:

1. Woman, 37 years old, addressed gynecologist with complaints on heavy menstruations during 3 months. From anamnesis: menstruations since the age of 12 (for 5-6 days, every 28-30 days), moderate, painless; two pregnancies and one abortion in anamnesis; at the age of 25 she had one full-term delivery, uncomplicated. Speculum examination: cervix is cylindrical; epithelium is intact, cervical polyp (size - 5 mm). Bimanual examination: vagina of a parous woman; body of the uterus is enlarged, dense, mobile and painless; appendages are not changed. Ultrasound examination: uterine size 49x40 mm; there is round echo-positive formation in uterine cavity of 18 mm in diameter.

State preliminary diagnosis. What is the further tactics of the patient treatment?

2. A 32-year-old patient consulted the doctor with complaints of the absence of menstruation for 2 years after her second delivery. The delivery was complicated by massive bleeding. After labor the patient noticed hair loss, weight loss. Objectively: the

patient is asthenic, the external genitals are hypoplastic, the cervix uteri is cylindrical, and the corpus uterus is small, painless. The uterine appendages are not palpated.

What is the most possible diagnosis?

3. A 14-year-old patient was admitted to the gynecological department with complaints of heavy bloody discharges from the genital tract. From the anamnesis: menstruations since the age of 15, for the first 4 months they were regulated (3-4 days every 28 days), moderate, painless. She became ill 8 days ago, when after a 3 month absence, bloody discharge appeared that further increased. She does not have a sexual life. Hemoglobin - 92 gr\l. During the rectal examination, pathology of the internal genitals was not revealed.

What is the most rational method of hemostasis for bleeding in this case?

Typical test tasks:

1. For the clinical manifestations of dysmenorrhea are not typical:

A. Headache
B. Nausea
C. Excessive blood loss*
D. Abdominal pain
E. Irritability

2. An 18-year-old girl with normal development of secondary sexual signs complains of primary amenorrhea. Examination revealed that the vagina is underdeveloped, the uterus is absent. Specify the type of amenorrhea:

A. Physiological amenorrhea.
B. Amenorrhea, caused by hyperandrogenia.
C. Hypogonadotric amenorrhea
D. Eugonadotropic amenorrhea. *

3. A 24 year old patient complains of amenorrhea. She had labor 13 months ago. Delivery was by caesarian section due to premature detachment of a normally located placenta and intrauterine asphyxia of the fetus. Labor was complicated with a massive blood loss of approximately 2000 ml due to coagulopathy. What test is indicated in this patient?

A. Ultrasound of the organs of the small pelvis
B. Testosterone blood test
C. Progesterone test
D. Gonadotropins test*
E. Computer tomography of the head

4. A 15 year old girl complains of bloody discharge from the vagina for 2 weeks, which began after a 3 month delay of menstruation. Menarche at 13 years. Irregular menstrual cycle. Blood analysis: Hb - 90 gr/l, erythrocytes - 2,0x1012/l, leukocytes - 5,6x109/l. Rectal exam: the uterus has a normal size, the appendages are not palpated. What diagnosis is most probable?

A. Juvenile bleeding *
B. Incomplete abortion
C. Blood clotting disorder
D. Polyp of the endometrium
E. Cancer of the endometrium

5. A 27 year old patient complains of irregular menstruation, infertility for 4 years. Obesity, hypertrichosis. During bimanual examination: the uterus is small, the ovaries on both sides are enlarged, firm. Discharge - leucorrhoea. Examination showed that the basal temperature is monophase. What is the diagnosis?

A. Shihane syndrome
B. Simmonds syndrome
C. Polycystic ovarian syndrome*
D. Genital tuberculosis
E. Asherman syndrome

6. The uterine form of amenorrhea can result from all specified below diseases, except:
A. None of the below ovarian cyst*
B. Frequent curettage of the uterine cavity
C. Genital infantilism
D. Chronic inflammation nonspecific etiology
E. Tuberculosis of endometrium
7. What is not used for diagnosis of disorders of the menstrual cycle?
A. Tests of functional diagnostics
B. Investigation of the hormone levels in the blood
C. X-ray Turkish saddle
D. Determining the level of TTH
E. Use all of the above*

III. Formation of professional skills, abilities (mastering skills, conducting curation, determining the treatment regimen, conducting laboratory research, etc.).

3.1. Content of tasks (tasks, clinical situations, etc.).

Interactive task:

Students of the group are divided into 3 subgroups of 4-5 people each. We work in women's consultation rooms with gynecological patients, we give tasks:

And the subgroup - to make a preliminary diagnosis.

Subgroup II - to make a plan for the management of a gynecological patient.

Subgroup III - assesses the correctness of the answer of subgroups I and II and makes adjustments.

Atypical situational tasks:

1. Patient M., 53 years old, complains of smearing bleeding within 12 days. Menstruations from 14 years, 3-5 days, 31 days, were regular. Last 3 years of

menstruation irregular, there are delays for 2-3 months. In gynecological examination: vaginal mucosa and cervix without pathological changes. In bimanual examination - the body of the uterus is not painful, mobile, normal size.

Determine algorithm of the doctor's actions.

2. A 49-year-old patient consulted the gynecological department with complaints of bleeding from the genital tract. Anamnesis: menstruations since the age of 14, regulated immediately (4–5 days every 28 days), moderate, painless. In the past 2 years intervals between menstruations were 2–3 months. 15 days ago after a two-month absence of menstruation, the bleeding started which continues till now. Hemoglobin - 100 gr\l. During bimanual examination pathology of the internal genitals was not revealed.

Establish the diagnosis.

Atypical test tasks:

1. A 35-year-old woman was addressed to the doctor 3 months ago with complaints of irregular profuse menstrual bleeding. The doctor administered oral contraceptives for 2 months. Despite of using oral contraceptives, bleeding continued. What is the conducting tactics?
   A. Curettage of the uterus mucous membrane +
   B. Combined oral contraceptives
   C. Estrogen
   D. Nonspecific anti-inflammatory treatment
   E. Progestin.
2. Patient R. 50 years old, complains of intense bleeding from the genital tract for 8 days, which occurred after 2 years of amenorrhea, weakness. If bimanual examination: cervix intact body of the uterus of normal size and painless. Appendages were normal on both sides. With vagina - heavy spotting. Which tactic is most expedient?
   A. Fractional scraping the uterine lining. +
   B. supravaginal amputation of the uterus.
   C. hysterectomy.
   D. Hormone therapy.
   E. hemostatic therapy.

3.2. Recommendations (instructions) for performing tasks (professional algorithms, orientation maps for the formation of practical skills, etc.).

It is necessary to remember the close connection and interdependence in the work of higher nervous centers of the cerebral cortex, hypothalamus, hypothesis and uterus itself. Changes in any of these links according to the principle of direct and reverse connection will cause a reaction of the whole system. The pathogenesis of disorders of the menstrual cycle is also related to a disorder in the amount of hormones. Therefore, destruction to the

ovaries leads to a disorder in the production of steroid hormones, which according to the principle of reverse connection, results in the disorder of secretion of gonadotrophic hormones. Dysfunction of the hypothesis caused by functional or organic destruction, according to the principle of direct connection, results in a change in the secretion of steroid hormone, their uneven and incorrect secretion. Every change in the hormone secretion reflects on the function of the target organs, in this case, the uterus. Damage to any of the organs that take part in the regulation of the menstrual function can result in its disorder. Determining the level of disorder plays an important role in purposeful pathogenetic treatment. Therefore, disorders of the menstrual cycle can be of the central genesis - when the cerebral cortex, hypothalamus, hypothesis are damaged and of the peripheral genesis - when the ovaries and uterus are directly damaged. Disorders of the menstrual cycle of the central genesis can be: cortico-hypothalamic, hypothalamo-hypophysial, hypophysial. There are also disorders of the menstrual function that are caused by a change in the function of the secondary glands of inner secretion: adrenal glands, thyroid gland. The main tasks when examining patients with disorders of the menstrual cycle are the following: 1) presence or absence of organic damage to the hypothalamus and hypothesis, ovaries and uterus, thyroid gland and adrenal gland, and also extragenital diseases; 2) determine the level of functional damage in the regulation of the menstrual function.

The examination is conducted in several stages:

I stage – pre-admission stage: collect the anamnesis, clarify the menogram, general and gynecological examination, blood test, urine test, coagulagram, blood test for RW and HIV. In this stage, functional diagnostic tests, rontgenography of the skull in two projections, check the field of vision and fundus of the eye, ultrasound of the organs of the small pelvis, the level of sugar in the blood and urine, cholesterol in the blood, research of the sex chromatin, toxoplasmin and tuberculin tests, functional tests of the liver, thyroid gland, determine 17–KS, 17-OKS, the level of hormones in the blood plasma are also preformed; consultation with specialists is conducted (neurologist, endocrinologist, therapist, etc.).

II stage – this stage contains additional, the most difficult methods and is performed in the hospital: biopsy of the endometrium, endoscopy of the genitals (hysteroscopy, colposcopy, laparoscopy), Metrosalpingography.

III stage – focused examination: additional X-ray study of the skull, examination of the fundus of the eye and field of vision, quantitative determination of the hormones in the blood plasma in the dynamics of the menstrual cycle and in the dynamics of supervision, functional hormonal tests. As a result, the studies should give information about the state of the target organ; determine the level of disorder in the system.

The absence of menstruation in an adult woman for 6 months is called amenorrhea.

Amenorrhea.

Amenorrhea is the absence of menstruations during 6 months and longer in women aged 16–45 years. The incidence of amenorrhea in population among women of childbearing age makes approximately 3.5 %, and in the structure of reproductive system disorders –

10–15 %. There are differentiated physiological (the absence of menstruations till the pubertal period, during pregnancy, lactation, and in the postmenopause) and pathological types of amenorrhea. The etiology of pathological amenorrhea is very diverse. It is a symptom of a gynecological and extragenital pathology may be primary and secondary: primary amenorrhea is the absence of menstruations at the age older than 16 years; secondary amenorrhea is the absence of menstruations during 6 months and longer after a period of regular and irregular menstruations. Amenorrhea is considered secondary even if there is a history of one menstruation only. If the interval between the episodes of bloody discharge makes less than half a year, the state is considered a hypomenstrual syndrome, a variety of which is the so-called spaniomenorrhea – menstruations take place 2–3 times a year. Besides, there are singled out true and false types of amenorrhea. The reasons for false amenorrhea are: atresia of the virginal membrane, vagina, cervical canal, and transversal membrane of the vagina. This is accompanied by cyclic changes in the hypothalamo-pituitary-ovarian system and uterus, but the outlet of the menstrual blood is blocked. This leads to menstrual blood accumulation in the upper genital tract with the formation of hematocolpos and hematometra accompanied by pain syndrome. Pathological amenorrhea is also classified depending on the level of affection of a certain part of the reproductive system. According to this there are differentiated hypothalamic-pituitary, ovarian, and uterine forms of amenorrhea, and also amenorrhea conditioned by pathology of the adrenal glands, thyroid gland, and the presence of extragenital diseases.

Such forms of amenorrhea are determined:

1. true amenorrhea – the absence of menstruation caused by a disorder in the production of the sexual organs;
2. false amenorrhea – the absence of menstruation because of a disorder in the cyclic changes in the ovaries and with the presence of obstacles in the outflow of menstrual blood;
3. Primary amenorrhea.

 Primary amenorrhea with no sexual development: - gonadal digenesis (Shereshevsky–Turner syndrome, Swayer syndrome); - testicular feminization (Morris syndrome).

 Primary amenorrhea with sexual development delay: - resistant ovary syndrome (in case it arises in the prepubertal period); - hypogonadotropic hypogonadism.

 Primary amenorrhea without sexual maldevelopments: - Maldevelopments of the vagina and uterus (uterine and vaginal aplasia – Rokitansky–Kuestner syndrome; atresia of the hymen, vagina, and cervical canal of uterus).

4. Secondary amenorrhea:

 Asherman’s syndrome (intrauterine synechias as a consequence of traumatic injuries of the uterus);

 hypergonadotropic hypogonadism;

 hypogonadotropic hypogonadism;

 emotional amenorrhea;

 weight loss amenorrhea/

Primary amenorrhea is observed much less frequently than the secondary one and makes 8–10 % in the structure of amenorrhea. Primary amenorrhea is more frequently combined with other signs of sexual development delay (SDD), less frequently it arises at all the signs of sexual development preserved.

Therefore there are singled out two forms of primary amenorrhea:

1. with a derangement of sexual development (SDD, hermaphroditism);
2. Without sexual development disorders.

All over the world much attention is paid to the problem of SDD, which conditioned the fact that this pathology is marked put as a disease entity by the World Health Organization. Underdevelopment or absence of the secondary sexual characters at the age of 13–14 years and absence of menstruation at the age of 15– 16 years should be regarded as SDD. Depending on the primary level of reproductive system affection there are differentiated central (as a result of insufficient gonadotropic stimulation there secondarily arises ovarian insufficiency) and ovarian (primary affection of the gonads accompanied by the increased gonadotropin secretion) forms of SDD. Thus, the central and ovarian forms of SDD are regarded as hypo- and hypergonadotropic. To the ovarian form of SDD we refer gonadal digenesis (GD, hypergonadotropic hypogonadism) – the most widespread reason for primary amenorrhea against the background of SDD. The onset of gonadal digenesis is based on X-chromosome monosomy or mosaicism and X-chromosome aberration. This state is characterized by the absence of the follicular apparatus, which leads to estrogen deficiency and, as a result, to the increase of gonadotropin concentration in blood.

Clinical-diagnostic criteria. The severity of clinical symptoms depends on the quantitative and qualitative pathology of sex chromosomes and the ratio of normal and aberrant clones, which determines the singling out of clinical forms of gonadal digenesis. T

His typical form of GD – Turner's syndrome (45, XO) – is characterized by:

a) the GD phenotype – small stature, wide and short neck, skin folds, which go from the mammillary process to the acromion one, micrognathia, high palate, low-set auricles, numerous pigment spots on the skin, nipples located wide apart, cubitus valgus;
b) evident genital infantilism;
c) primary amenorrhea;
d) anomalies of occlusion;
e) strabismus;
f) shield-shaped chest;
g) winged scapula's;
h) malformations of the kidneys and cardiovascular system;
i) Gonads in the form of connective-tissues bands.

At the pure form of GD (46, XX or 46, XY – Swyer's syndrome) there is observed normal stature, the absence of somatic malformations, eunuchoid or intersexual phenotype at Swyer's syndrome, secondary sexual character underdevelopment, gonad hypoplasia. The mixed form of GD (45, XO/46, XY): - the clinical presentation is characterized by

manifestation variability; - secondary sexual character underdevelopment; - hypoplastic uterus; - gonad asymmetry (a fibrous tissue band on one side, underdeveloped elements of testicles – on the other side). The obliterated form of GD (mosaicism 45, XO/46, XX) is characterized by a variety of clinical signs, whose severity is determined by the ratio of normal and aberrant cell clones. The patients have a small stature less frequently, menarche is possible at normal terms, the development of the secondary sexual characters may be spontaneous (but not complete). Investigation of the hormonal status at all forms detects high concentrations of gonadotropins in the blood plasma and estradiol decrease.

Treatment. The GD therapy depends on the presence of Y-chromosome in the karyotype. Since the risk of gonad malignization is high if Y-chromosome is present, they must be removed surgically. If there is no Y-chromosome in the karyotype or if the gonads have been removed surgically Y-chromosome being present, substitutive hormonotherapy (SHT) is provided aimed at feminization, gonadotropin level lowering, cyclic changes in the endometrium with a menstruation-like reaction, prophylaxis of estrogen deficit conditions, and social adaptation. In order to become pregnant one carries out the program of extracorporal fertilization (in vitro fertilization, IVF) with oocyte donation.

The ovarian forms of SDD in patients with the normal karyotype include the syndrome of resistant ovaries, which develops in the prepubertal period and declares itself with hypoestrogenia, primary amenorrhea, and sexual infantilism. In this disease the morphologically full-value ovaries do not respond to endogenous gonadotropic stimulation, which leads to gonadotropin hypersecretion. The central form of SDD, which is defined as hypogonadotropic hypogonadism, is accompanied by estrogen deficit and primary or, less frequently, secondary amenorrhea. The most common reasons for this disease are genetic factors (congenital hypogonadotropic hypogonadism) and unfavorable exogenous factors (acquired hypogonadotropic hypogonadism against the background of infection-toxic illnesses, pituitary tumors, anorexia nervosa, low body weight, considerable exercise stress). The onset of this pathology may also be conditioned by asphyxia and birth injury of newborn. There is differentiated hypogonadotropic hypogonadism of hypothalamic and hypophysial origin. Hypogonadotropic hypogonadism of hypothalamic origin is based on the disorder of LH formation, which leads to the inhibition of gonadotropin production by the hypothesis and is accompanied by the lack of follicle growth and anovulation. Hypogonadotropic hypogonadism of hypophysial genesis is characterized by violated gonadotropin release.

The diagnostic criteria:

a. primary, less frequently secondary amenorrhea;
b. the eunuchoid type of the organization of the body;
c. underdevelopment of the secondary sexual characters;
d. hypoplasia of the external and internal genital organs;
e. low concentrations of FSH, luteinizing hormone, and E2 in the blood;
f. as a result of low estrogen saturation there is noted a negative progesterone test, a negative clomiphene test;

g. a positive hormonal test with estrogens and gestagens;
h. a positive test with LH at the hypothalamic level of affection;
i. A negative test at hypophysial hypogonadotropic hypogonadism.

The treatment depends on the reasons, which have caused SDD. If the patient has pituitary tumors, the treatment is surgical. The therapy of all the forms of SDD should be complex, aimed at the normalization of the function of the diencephalic area (if there are appropriate indications, the treatment is carried out together with a neurologist, a psychoneurologist). There is recommended general health-improving cyclic vitamin therapy, physiotherapy. If the form of SDD is not full-blown, the mentioned treatment is usually sufficient to normalize the menstrual cycle. If the SDD form is full-blown, which declares itself with underdevelopment or absence of the secondary sexual characters, hormonal treatment is indicated.

Dysfunctional uterine bleedings (DUB) are the bleedings conditioned by disturbances of the cyclic secretion of ovarian hormones and not connected with organic diseases or extragenital pathologies. DUB incidence makes 15–20 % of all gynecological pathologies. DUB development is based on the dysfunction of the hypothalamo-pituitary-ovarian system, which leads to the disturbance of folliculo- and steroidogenesis. DUB may arise at any age. However, they have their peculiarities in different age periods. These differences are the basis of DUB classification. Every period in a woman's life presents an imprint on the possibility of DUB occurring and requires individual approach in conducting the diagnostics and therapy. Therefore, the clinical practice the following are determined:

1. DUB of the pubescence period (juvenile bleeding);
2. DUB of the reproductive period;
3. DUB of the premenopausal period (climacteric bleeding) in women over 40.
4. DUB classification by the character of menstrual irregularities and functional-morphological changes:

1. Anovulatory DUB: a) short-term follicle persistence; b) long-term follicle persistence. c) Immature follicle atresia.
2. Ovulatory DUB. According to the estrogen level DUB divided into hyperestrogenic (most DUB) and hypoestrogenic (more frequent in the puberty, but may also be observed at the childbearing age).

Though all DUB forms are observed at different age periods of the woman's life, in the puberty and premenopausal period anovulatory DUB are more frequent, at the childbearing age – ovulatory.

By contrast, acute AUB was defined as an episode of heavy bleeding that, in the opinion of the clinician, is of sufficient quantity to require immediate intervention to prevent further blood loss. Acute AUB may present in the context of existing chronic AUB or might occur without such a history. Although women of reproductive age with acute AUB require immediate intervention, their follow-up may be largely dependent upon whether they require investigation and ongoing care for an underlying chronic condition. Intermenstrual bleeding (IMB) occurs between clearly defined cyclic and predictable menses. Such bleeding may occur at random times or may manifest in a predictable

fashion at the same day in each cycle. This designation is designed to replace the word “metrorrhagia,” which was one of the terms that the group recommended should be abandoned. The categories were developed based on the group recommendations described earlier; each was designed to facilitate the development of subclassification systems, as necessary. It was envisioned that the most straightforward parts of the system would be used at a primary care level and that the subclassifications would be most relevant at specialist and research levels.

The system has been approved by the FIGO Executive Board as a FIGO classification system.

There are 9 main categories, which are arranged according to the acronym PALM-COEIN (pronounced “pahm-koen”). PALM criteria:

- Polyp (AUB-P) there seems to be little controversy regarding the inclusion of endometrial and endocervical polyps. These epithelial proliferations comprise a variable vascular, glandular, and fibromuscular and connective tissue. Component and are often asymptomatic, but it is generally accepted that at least some contribute to the genesis of AUB.
- Adenomyosis (AUB-A) generally, these criteria have been based on histopathology evaluation of the depth of “endometrial” tissue beneath the endometrial–myometrial interface, as determined via hysterectomy.
- Leiomyoma (AUB-L) Benign fibromuscular tumors of the myometrium are known by several names, including “leiomyoma,” “myoma,” and the frequently used “fibroid.” “Leiomyoma” is generally accepted as the more accurate term and was selected for use in the present system.
- Malignancy and hyperplasia (AUB-M) Although relatively uncommon, atypical hyperplasia and malignancy are important potential causes of, or findings associated with, AUB and must be considered in nearly all women of reproductive age
- Coagulopathy (AUB-C) The term “coagulopathy” encompasses the spectrum of systemic disorders of hemostasis that may be associated with AUB. Highquality evidence demonstrates that approximately 13% of women with HMB have biochemically detectable systemic disorders of hemostasis, most often von Willebrand disease.
- Ovulatory dysfunction (AUB-O) Ovulatory dysfunction can contribute to the genesis of AUB, generally manifesting as a combination of unpredictable timing of bleeding and variable amount of flow (AUB), which in some cases results in HMB
- Endometrial (AUB-E) When AUB occurs in the context of predictable and cyclic menstrual bleeding, typical of ovulatory cycles, and particularly when no other definable causes are identified, the mechanism is probably a primary disorder of the endometrium

- Iatrogenic (AUB-I) There are several mechanisms by which medical interventions or devices can cause or contribute to AUB (AUB-I). These include medicated or inert intrauterine systems and pharmacologic agents that directly impact the endometrium, interfere with blood coagulation mechanisms, or influence the systemic control of ovulation.

In general, the components of the PALM group are discrete (structural) entities that can be measured visually with imaging techniques and/or histopathology, whereas the

COEIN group is related to entities that are not defined by imaging or histopathology (non-structural).

The term "DUB," which was previously used as a diagnosis when there was no systemic or locally definable structural cause for AUB, is not included in the system and should be abandoned, per the agreement process. Women who fit this description generally have 1 or a combination of coagulopathy, disorder of ovulation, or primary endometrial disorder—the last of which is most often a primary or secondary disturbance in local endometrial hemostasis. Abnormal uterine bleeding associated with the use of exogenous gonadal steroids, intrauterine systems or devices, or other systemic or local agents is classified as "iatrogenic." A category of "not yet classified" was created to accommodate entities that are rarely encountered or are ill-defined. For the "malignancy and hyperplasia" group, it is proposed that malignant or premalignant lesions (e.g. atypical endometrial hyperplasia, endometrial carcinoma, and leiomyosarcoma) be categorized as such within the major category, but further dealt with using existent WHO and FIGO classification and staging systems. The system was constructed recognizing that any patient could have 1 or several entities that could cause or contribute to AUB and that definable entities such as adenomyosis, leiomyoma's, and endocervical/ endometrial polyps may frequently be asymptomatic and, therefore, not contribute to the presenting symptoms.

Juvenile Uterine Bleedings

Juvenile uterine bleedings (JUB) are referred to the most frequent pubertal gynecological disorders, their incidence reaches 10 %. Etiology and pathogenesis. JUB pathogenesis is based on the functional immaturity of the hypothalamic pituitary structures in the puberty, which declares itself in the absence of a formed circhoral rhythm of gonadoliberin secretion. This brings to a disbalance of gonadotropin production, and in consequence of that follicle maturing is disturbed, more frequently by the type of immature follicle atresia, and then comes anovulation.

The etiologic factors, which promote JUB development, are very versatile. An important role is played by chronic and acute infectious diseases, hypovitaminoses, psychic traumas, overload, which violate the functioning of the hypothalamo-pituitary-ovarian system. As a result, against the background of low estrogen level a couple of follicles begin to grow to the antral condition. Further development of the follicles is taking place under the action of FSH, whose cyclic production is violated in this case. Owing to this the follicles do not mature completely and undergo atresia (immature follicle atresia). At that, steroidogenesis in the ovaries is disturbed. In immature follicle atresia in the ovaries insufficient amount of estrogens is produced, but their long-term action on the endometrium leads to the development of hyperplastic processes. Anovulation results in yellow body absence, and that accordingly leads to progesterone deficit. Progesterone deficit conditions the absence of the secretory transformation of the endometrium. In case of follicle involution there arises bleeding as a reaction to hormone decrease. Bleedings lead to anemia, which is the most marked in JUB.

Clinico-diagnostic criteria of JUB:

- Bleedings last up to 20–30 days, but usually they are not that voluminous in comparison with follicle persistence. Bleedings are preceded by 2–3-month menstruation delay (usually lasting longer than in case of follicle persistence);
- anemia;
- anovulation;
- functional diagnostic tests: hypothermic single-phase character of the temperature profile, the basal rectal temperature does not reach 37° C; pupil phenomenon "±" or "+";
- the cariopicnotic index (CPI) in this pathology does not exceed 28–35 %;
- pelvic ultrasound may show hypoplastic uterus or endometrium hyperplasia;
- hormone research: low progesterone level in blood;

Dysfunctional Uterine Bleedings in the Premenopausal Period

DUB incidence in the premenopausal period makes 15 % in the structure of gynecological disorders. Etiology and pathogenesis. In most women of this age the main pathological mechanism of DUB is anovulatory dysfunction of the ovary with long-term follicle persistence. Long-term follicle persistence (2–6 weeks) with considerable menstruation delays (up to 1.5 months) followed by severe long-term bleedings is called metropathia hemorrhagica, or Shroeder's disease.

While JUB is a consequence of no steady cyclic function of the hypothalamo-pituitary-ovarian system, premenopausal bleedings are a consequence its involution disturbances. Age-related changes of the hypothalamic structures, which regulate the gonadotropin function, condition disturbance of the rhythm and amount of gonadotropins released. FSH formation and release prevail, the LH level also rises, acquires a monotonous character. The decrease of gonadotropin receptors amount in the ovaries leads to a disorder of the feedback mechanism. This is accompanied by disturbed folliculogenesis and anovulation.

Yellow body absence, decreased progesterone secretion lead to hyperestrogenism development (relative hyperestrogenism against the background of hypoprogesteronemia) and endometrial hyperplasia of different level. In consequence of endometrium growth and insufficient trophism there develop dystrophic changes of the endometrium, which declare themselves with thrombosis, necrosis and irregular desquamation accompanied by long-term bleeding.

Clinico-diagnostic criteria:

- Profuse long-term uterine bleedings with delays up to 1.5 months. It should be noted that menstruation delay is observed in the period of follicle growth and persistence;
- anovulation; - functional diagnostic tests: • hypothermal monophase temperature profile; • the pupil phenomenon, colpocytology study shows a higher degree of estrogen saturation than in short-term follicle persistence; • a higher CPI – 80–100 %;
- gynecological examination and pelvic ultrasound show somewhat oversized uterus and endometrial hyperplasia;

Histological study of the endometrium scrape shows endometrial hyperplasia more often than at the childbearing age – glandular hyperplasia, endometrial polyps. In long-term

bleeding accompanied by mucosa desquamation the scrape may be scanty, but secretion signs are also absent in it.

Treatment DUB is complex and depends on the character of the ovarian menstrual cycle irregularities, age, intensity and remoteness of the bleeding, the degree of anemia severity, the data of the laboratory methods of investigation, particularly hormonal status before the initiation of treatment. The treatment is provided in three stages:

1. Hemostasis.
2. Pathogenetic treatment aimed at rebreeding prevention (hormonal disorder correction, menstrual cycle restoration, or achieving menopause).
3. After treatment (recovery of the reproductive function in women of the childbearing age). Hemostasis (the 1st treatment stage). In order to achieve hemostasis one takes surgical, hormonal, and symptomatic measures.
4. Surgical hemostasis.

Hemostasis (the 1st treatment stage). In order to achieve hemostasis one takes surgical, hormonal, and symptomatic measures. DUB treatment at the childbearing and premenopausal age is begun with diagnostic and therapeutic dilatation and curettage of cervical and uterine mucous membranes. Under modern conditions surgical hemostasis may be conducted using the so-called little-invasive surgical procedures, which are applied under endoscopic control: cryodestruction, laser ablation, and thermal balloon ablation of the endometrium.

In JUB surgical hemostasis is carried out according to the following indications: - profuse uterine bleeding, which threatens the patient's life; - Hb 70 g/L and less, Ht below 25 %; - Suspected pathological changes of the endometrium structures (an endometrial polyp shown by pelvic ultrasound); - In patients with frequent rebreeding's and disease duration exceeding 2 years.

Hormonal hemostasis. For hormonal hemostasis one most often uses estrogens, gestagens and monophase combined estrogen-gestagen preparations, androgens, gonadoliberin agonists, gonadotropin antagonists. The choice of preparations depends on the pathogenetic variety of DUB, the patient's age, and contraindications. The action of the preparations is based on the inhibition of pituitary gonadotropic hormones and maintenance of the steroid hormone concentration at a high level.

Monophase combined oral contraceptives (COCs) are used for hormonal hemostasis the most often. Hemostasis regimen: on the first day 1 COC pill per hour is administered up to 4–6 pills (at the age of 14–15 years – up to 3 pills), then the preparation dosage is reduced daily to 1 pill a day. The preparation is taken during 21 days.

Hormonal hemostasis with COCs is not provided in the premenopausal period. Estrogens have a quick and rather high hemostatic effect.

For hormonal hemostasis one may use preparations of natural estrogens (non-synthetic), for example, progynova (estradiol valerate), estraferm (17β-estradiol). These preparations are administered in the same way as oral contraceptives, but after hemostasis and intake of these preparations for 2 more weeks one should necessarily administer gestagens during 10 days.

Estrogens may be used for hemostasis at any age, but in the premenopausal period their use must be limited and conducted after a histological study of the endometrium. Gestagens have a hemostatic effect at the expense of influencing the endometrium transformation. They block proliferative processes and shift the endometrium into the secretory phase.

For hormonal hemostasis one uses gestagens of two classes: derivatives of 17-OH-progesterone (dydrogesterone – duphaston 10 mg twice a day, medroxyprogesterone acetate – Depo-Provera 200–400 mg i.m. once a week; 17- oxyprogesterone capronate 2 ml 12.5 % i.m., etc.) and derivatives of 19- nortestosterone (levonorgestrel, norgestrel, lynestrenol – orgametryl, norethisterone acetate – primalut-nor, norcalut – 10 mg twice a day, etc.). Unlike estrogen hemostasis, gestagen introduction does not produce a quick bleeding arrest. In 1–2 days after the cessation of gestagen action there is always noted intensive bleeding of the menorrhagia type. Taking into account the ability of gestagens to cause endometrium atrophy and central effect inhibition in the juvenile age, it is not advisable to administer them at this age.

For hormonal hemostasis one may also use antagonists of pituitary gonadotropic hormones: - danazol (danoval, danogen, danol) – 200–400 mg/day, treatment duration makes 3–6 months; - gestrinone (nemestran) – 2.5 mg twice a week during 6 months, etc.

DUB may also be treated with gonadoliberin agonists: - goserelin (zoladex) – 1 injection (3.6 mg) during 28 days subcutaneously; - triptorelin (decapeptyl, dipherelin) – 3.75 mg i.m. once in 28 days. It should be added that androgen hemostasis is resorted to very rarely nowadays because of numerous contraindications and also in connection with pronounced virilization effects. One should remember that administration of hormonal treatment in teenager girls requires special caution and systematic control of the hormonal status of the organism with 3–6-month intervals. The doses of hormonal preparations in the period of menstrual function formation must be rationally limited. In girls one may use estrogens or combined estrogen-gestagen preparations for hormonal hemostasis. In all DUB types there are administered symptomatic hemostatic and uterotonics preparations. There is used sodium etamsylar, ε-aminocapronic acid, tranexamic acid, 10 % calcium chloride solution.

Among uterotonics preference is given to ergot preparations, since unlike oxytocin they do not cause tonic contractions of the uterus (methylergometryl).

The doctor also administers vitamin therapy, tinctures of nettle, water pepper, and buckthorn.

The 2 -nd treatment stage foresees recovery of the menstrual cycle and recurrent bleeding prevention. At this stage there are administered general health improving preparations, hemostimulating and vitamin therapies are continued. Hormonal correction is carried out depending on the patient's age and is determined by the defined goal (menstrual cycle recovery, pregnancy planning, or menopause onset).

At this stage gestagens and COCs are used more often. The 2 -nd treatment stage is aimed at the recovery of the reproductive function in women of the childbearing age. When the rhythmical menstrual cycle is recovered, ovulation is induced with the

application of direct (clomiphene, anestrozol, letrozol) and indirect ovulation inductors (gonadoliberin agonists, recombinant gonadotropins, human menopausal gonadotropins, etc.).

3.3. Requirements for the results of work, including before registration.

- Collect general and special history, an allocation of a typical case-patient data.
- To appoint examination- Analysis and discussion of the results of the patient's examination.
- Show the phantom method of physical examination on organ systems.
- Show on phantom gynecological examination.
- Demonstrate phantom performance tests of functional diagnostics, fractional diagnostic curettage of the uterus.
- Multimedia presentation on the topic of the lesson (review of literature using modern sources; videos, etc.).

3.4. Control materials for the final stage of the lesson: tasks, tasks, tests, etc.

Atypical situational tasks:

1. Woman, 37 years old, addressed is seen in your office with complaints of heavy bloody discharges from the genital tract. From anamnesis - heavy menstruations during last 3 months. From anamnesis: menstruations since the age of 12 (for 5-6 days, every 28-30 days), moderate, painless; two pregnancies and one abortion in anamnesis; at the age of 25 she had one full-term delivery, uncomplicated. Physical examination reveals her height to be 173 cm, her weight to be 69 kg, and her blood pressure to be 96/73 mm Hg. The skin and visible mucous membranes are pale. The abdomen is soft, sensitive to palpation in the lower region. Speculum examination: cervix is cylindrical; epithelium is intact, cervical polyp (size - 5 mm). Bimanual examination: vagina of a parous woman; body of the uterus is enlarged, dense, mobile and painless; appendages are not changed. Ultrasound examination: uterine size 49x40x42 mm; there is round echo-positive formation in uterine cavity of 18 mm in diameter.
   1. **State preliminary diagnosis.**
      - Abnormal uttering bleeding. Polyp of the cervical canal. Polyp of the uterine cavity
   2. **What additional laboratory and instrumental research methods should be prescribed?**
      - General blood test and coagulagram, hormonal examination.
   3. **What treatment tactics will you choose?**
      - Hysteroscopy, Fractional medical-diagnostic scraping of the uterine cavity
   4. **What does the tactics of treatment depend on?**
      - From the results of histological examination of the endometrium.

2. Patient M., 23 years old, complains complaints of delayed menstruation for 3 weeks. Menstruation from 16 years, 3-5 days, scanty, irregular, notes delayed menstruation for 2-3 months. Objectively, the patient is obese, height 162 cm, weight 93 kg. The skin and visible mucous membranes are pink, in the chin and in the area near the nipples, hair growth is noted. In gynecological examination: vaginal mucosa and cervix without pathological changes. In bimanual examination - the body of the uterus is not painful, mobile, normal size; the ovaries are enlarged on both sides up to 5x6 cm and 4x5 cm, dense, sensitive during examination.

1. What is the most likely diagnosis?

- Primary amenorrea

2. What additional diagnostic methods will help you in making the correct diagnosis?

- Examination of the hormonal profile, HOMA index, ultrasound examination of the pelvic organs

3. What are the tactics of further therapy?

- Diet therapy, correction of insulin resistance, combined oral contraceptives

Test tasks KROK-2:

I. A 15 year old girl complains of bloody discharge from the vagina for 2 weeks, which began after a 3 month delay of menstruation. Menarche at 13 years. Irregular menstrual cycle. Blood analysis: Hb - 90 gr/l, erythrocytes - 2,0x1012/l, leukocytes - 5,6x109/l. Rectal exam: the uterus has a normal size, the appendages are not palpated. What diagnosis is most probable?

1. Juvenile bleeding*
2. Incomplete abortion
3. Blood clotting disorder
4. Polyp of the endometrium
5. Cancer of the endometrium

II. A 35-year-old woman was addressed to the doctor 3 months ago with complaints of irregular profuse menstrual bleeding. The doctor administered oral contraceptives for 2 months. Despite of using oral contraceptives, bleeding continued. What is the conducting tactics?

A. Combined oral contraceptives
B. Curettage of the uterus mucous membrane*
C. Estrogen
D. Nonspecific anti-inflammatory treatment
E. Progestin

IV. Summing up (criteria for evaluating learning outcomes).

Current control: oral examination, testing, assessment of practical skills, solving

situational clinical problems, assessment of activity in the classroom, etc.

The structure of the current assessment in the practical lesson:

1. Assessment of theoretical knowledge on the topic of the lesson:

- methods: survey, solution of situational clinical problem;

- maximum grade - 5, minimum grade - 3, unsatisfactory grade - 2.

2. Assessment of practical skills and manipulations on the topic of the lesson:

- methods: assessment of the correctness of practical skills;

- maximum grade - 5, minimum grade - 3, unsatisfactory grade - 2.

3. Evaluation of work with the patient on the topic of the lesson:

- methods: assessment: a) communication skills of communication with the patient, b) the correctness of the appointment and evaluation of laboratory and instrumental studies, c) compliance with the algorithm for differential diagnosis d) justification of clinical diagnosis, e) treatment plan;

- maximum grade - 5, minimum grade - 3, unsatisfactory grade - 2.

Criteria for evaluating the learning outcomes of students during the practical class:

«5»	It is presented to a student who systematically worked during the semester, showed during the exam versatile and deep knowledge of the program, is able to successfully perform the tasks provided by the program, mastered the content of basic and additional literature, realized the relationship of individual sections of the discipline, their importance for future profession. showed creative abilities in understanding and using educational material, showed the ability to independently update and replenish knowledge; level of competence - high (creative);
«4»	It is presented to a student who has shown full knowledge of the curriculum, successfully performs the tasks provided by the program, mastered the basic literature recommended by the program, showed a sufficient level of knowledge in the discipline and is able to independently update and update during further study and professional activities; level of competence - sufficient (constructive-variable)
«3»	Exhibited to a student who has shown knowledge of the basic curriculum in the amount necessary for further study and further work in the profession, copes with the tasks provided by the program, made some mistakes in answering the exam and when performing exam tasks, but has the necessary knowledge to overcoming mistakes under the guidance of a research and teaching staff; level of competence - average (reproductive)

«2»	Exhibited to a student who did not show sufficient knowledge of the basic curriculum, made fundamental mistakes in performing the tasks provided by the program, cannot without the help of the teacher to use the knowledge in further study, failed to master the skills of independent work; level of competence - low (receptive-productive)

LIST OF RECOMMENDED EDUCATIONAL LITERATURE

Basic:

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16. Handbook of Reproductive Health / ed. NG Goidi. - Kyiv: Raevsky Publishing House, 2004. - 127 p.
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19. Small student encyclopedia of obstetrics and gynecology / Markin L.B., Shakhova O.V., Zhemela O.M. et al. - Posvit: 2014. - 203 p.

Additional:

20. Obstetrics: підручник англійською мовою (edit by I.B. Ventskivska).- K.: Medicine,2008.-334 p.
21. Gynecology: підручник англійською мовою (edit by I.B. Ventskivska).- K.: Medicine,2010.-160 p.
22. Progress in Obstetrics and Gynaecology. Vol 10. Ed J Studd. (Pounds sterling 26.50.) Churchill Livingstone, 1993. ISBN 0443-04754-5.
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