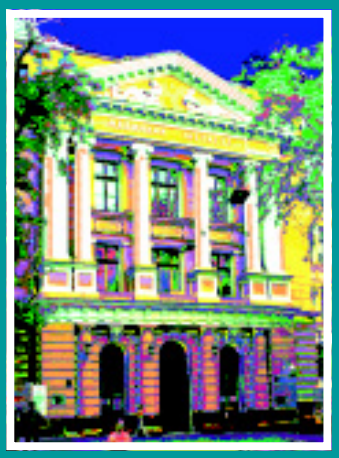

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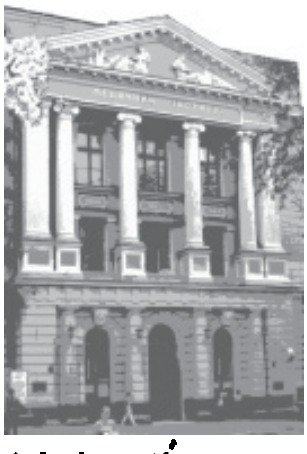

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Editor-in-Chief of the Series "Medical Student's Library"
the State Prize-Winner of Ukraine,
Academician of the Academy of Medical Sciences of Ukraine

V. M. Zaporozhan
V. P. Mishchenko

OBSTETRICS and GYNAECOLOGY

in 2 Books

Book 2
GYNAECOLOGY

Recommended
by the Ministry of Health of Ukraine as a textbook
for English-speaking students of higher medical
educational establishments
of the IV level of accreditation

Odessa
The Odessa State Medical University
2007

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The textbook "Obstetrics and Gynaecology" consists of two books "Obstetrics" and "Gynaecology". The second book highlights the problems of modern methods of examination of gynaecological patients. Specific and non-specific inflammatory diseases and genital tumours, breast diseases are concerned. Great attention is paid to the reproductive system development, its defects, disturbances of the menstrual function, viril and endocrine syndromes. The methods of surgery are presented.

The textbook is intended for higher medical educational establishments of the IV level of accreditation.

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CONTENTS

Chapter 1

COMMON SYMPTOMATOLOGY OF GYNAECOLOGICAL DISEASES. METHODS OF GYNAECOLOGICAL EXAMINATION

A modern stage of the medicine development, as well as the society in a whole, is characterized by the intensification of knowledge acquiring, introduction of newest diagnostic technologies and treatment modes as well as by more awareness of patients which have a possibility to choose a doctor and a clinic on their own accord. Benevolent relations between a doctor and a patient are considered to be the most important factor of the medicine of the future. Therefore the first visit to a doctor is of a special value.

During the initial examination a doctor should get into contact with a patient, based on a mutual trust. It is often a gynaecologist himself who is the first doctor and consultant of a woman. Doctor's communication with a patient during gynaecological consultation touches as a rule on three spheres of her life: 1) anatomophysiological; 2) emotionally personal; 3) interactively social.

A doctor takes anamnesis and other information which is necessary to form a diagnosis and work out the plan of examination and treatment. At the time a patient creates her own impression as for both doctor's awareness and expedience of his recommends. A doctor should foresee a negative reaction of a patient and to react properly at it, especially in case of different interpretation of the disease stated by other specialists including adjacent type. An ability to solve an arising conflict situation in time allows to establish a positive connection with a patient, whereas ignoring of the mentioned moment leads to consolidation of her negative reaction and loss of trust to a doctor.

COMMON OBJECTIVE EXAMINATION

Common objective examination in gynaecology includes anamnesis taking, common inspection of a woman with typo-biological estimation of her organism (growth, weight determination, constitution), physical study by organs systems (with determination of respiration rate, pulse, blood pressure), as well as the use of special (gynaecological) methods of study, functionally diagnostic tests and hormone examinations, ultrasound, endoscopic, roentgenological, radiological and cytological methods of examination.

ANAMNESIS TAKING

Even the most modern methods of diagnosis can not replace the value of initial anamnesis' data. A thorough examination of patient's anamnesis allows to make a provisional diagnosis, to plan a further tactic of patient's inspection.

Anamnesis gathering should be systematized and carried out according to a certain sequence: 1) passport data (name, age, family status, profession, address); 2) main and concomitant complaints; 3) somatic diseases, which the patient suffered from in the past; 4) menstrual, reproductive, secretory and sexual functions; 5) gynaecological diseases and treatment; 6) diseases of a husband; 7) history of this disease and its treatment; 8) life conditions, pernicious habits, occupational hazards.

Complains. While questioning a patient it is necessary to choose main and concomitant complaints. Patients often complain of pain in the lower abdomen and in the waist region, vaginal discharge (leucorrhoea), bleeding from genital tract, dysfunction of adjacent organs, sterility.

If there is pain, they have to pay attention to its character (dull, cutting, stabbing, cramp-like), location (more often at the lower abdomen, in the lumbosacral region) (Fig. 1). Pain can spread to the anus, leg, urethra, upper abdominal region, under the costal arch, etc.

Vaginal discharge are one of the most often complaints of gynaecological patients. Physiological increase of secretion from the genital tract arises in the middle of the ovulatory menstrual cycle (cervical mucus), as well as during pregnancy due to the oestrogene influence. Pathologic discharge from the ge-

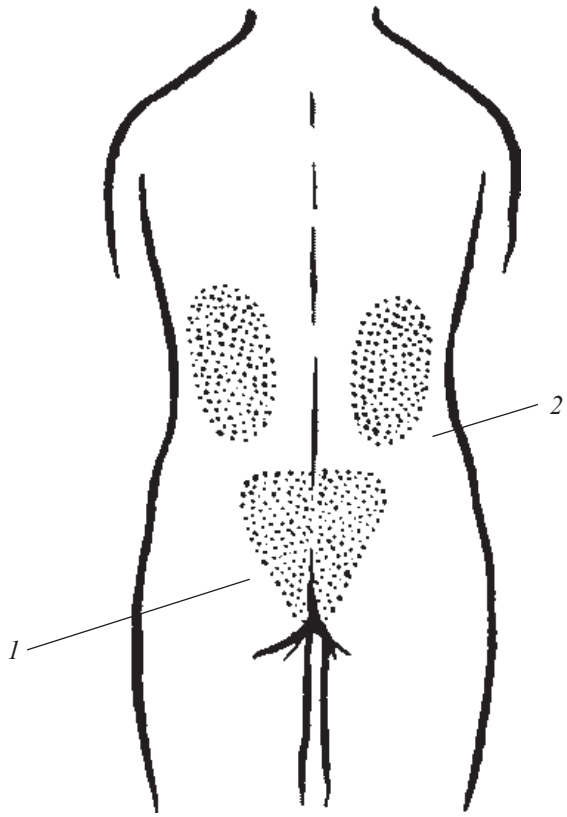


Fig. 1. Localization of the pain:
1 — during the menstruation; *2* — during the renal diseases

nital tract — leucorrhoea — can have an unpleasant odour, cause itching, irritation of external genitalia and internal surface of thighs. The reason of the discharge in most cases is an inflammation of the lower reproductive tract (vaginitis, bacterial vaginosis and cervicitis). Leucorrhoea can be a symptom of malignant diseases (leucorrhroea), oestrogenic or psychogenic stimulation, trauma, consequence of foreign body presence in the vagina, as well as helminthiasis (enterobiasis, ascaridiasis).

Pathologic bleeding from the genital tract can have cyclic *(menorrhagia)* or acyclic *(metrorrhagia)* character, to arise when there is a menstruation delay, after coitus. Bloody discharge can be mild, moderate and profuse. The latter can cause a haemorrhagic shock and are dangerous for the patient's life.

Patients are also disturbed by the dysfunction of adjacent organs — the urinary bladder (frequent strangury, delay of urination, enuresis) and guts (flatulence, constipation, diarrhoea, gas and fecal incontinence of flatus and encopreses).

Anamnesis of the disease. The aim of the further questioning of a patient is to clear up the anamnesis of the disease which has been diagnosed (its onset, first symptoms and consequences of conducted treatment).

Patient's history. ***Gynaecological anamnesis*** is a very important stage of a common examination. The woman's age, the time of first menses appearance, the cycle length (from the 1st day of the previous one to the 1st day of the next menstruation), character of menstrual bleeding. Usually the first menses in the woman's life (menarche) begins at the age of 12–13 years. Its early beginning can be evidence of premature pubescence or development of a hormonally active ovarian tumour. Later menarche (over 15 years) can be a sign of infantilism, other diseases. A normal ovulatory menstrual cycle is characterized by regularity, lasts from 24 to 35 days (28 days on average). Normally the menstrual flow ranges from 3 to 8 days, amount of bloodloss is from 30 to 80 ml, there can be blood clots, the size of which should not exceed the gryvennik's size.

Amenorrhea is an absence of menarche till 16 years *(primary amenorrhea)* or an absence of menstruation during 3–6 months in women who had regular menstruations before *(secondary amenorrhea)*. They find out if there are menstrual dysfunction *(hypomenorrhea, hypermenorrhea, menorrhagia)*, pain during menstruation *(algodismenorrhea)*, as well as intermenstrual *(polymenorrhea, metrorrhagia)* and postcoital bleedings. The date of the first day after the last menstruation is defined . If prolong bleedings occur with often and irregular intervals it is evidence of *menometrorrhagia* or *hyperpolymenorrhea*. Prolongation of the cycle can be evidence of *oligomenorrhea*. Patients are questioned whether they have any signs typical for the *premenstrual syndrome* (enlargement of the mammary glands, mastalgia, fluid delay, increase of the body weight), mastodynia as well as pains which appear in the middle of the menstrual cycle (which may be evidence of ovulation), — ovulatory pain (see Fig. 1).

The anovulatory cycle is characterized by uncontrolled, sudden bleedings of different duration and intensity. In presence of olymenorrhea, anovulatory cycles a patient is examined thoroughly for the purpose to detect possible hyperplastic processes and endometrial cancer.

Besides of information concerning menstrual function, data about sexually transmitted diseases, other gynaecological diseases; carried out treatment including hormone preparations usage; pelvic operations; the age when the first sexual contact happened (sexual debut) are cleared up. The pelvic operations can be the reason of commissural process, which often leads to infertility. A patient is asked about duration and effectiveness of contraceptives using.

While gathering ***obstetrical anamnesis***, they elucidate the number of pregnancies and their consequences: delivery, stillbirth, artificial abortion, multiple or ectopic pregnancy.

Common anamnesis includes the data about common diseases, operations, injuries, haemotransfusion, presence of allergic reactions as well as the drugs used by the patient. The type of the patient's work, possible occupational hazards, conditions of

life, intensity of sports training are ascertained during anamnesis taking. Numerous infectious diseases which the patient suffered from in her childhood and which are bad for reproductive system formation and in the future can be the reason of the pathological neuroendocrine syndromes development are taken into acount. Diseases of the liver, chronic infections can cause sex hormones metabolism abnormalities and afterwards bring to the development of hyperplastic processes in the uterus.

Social anamnesis is based on clarification of the woman's family status, her partner's health, presence of dyspareunia (discomfort during sexual intercourse), children's health, own habits (including using of tobacco, alcohol, drugs).

Taking family anamnesis the presence of congenital diseases, the cause of nearest relatives' death are ascertained. Some gynaecological diseases can be congenitally conditional (delay of menstrual cycle, polycystic ovarian syndrome, uterine myoma, cancer of the uterine cervix, ovary, mammary gland, etc.).

At the end of the questioning, the doctor formulates the provisional diagnosis and defines the course of the further objective examination of the patient (choice of diagnostic modes, succession of their application).

PHYSICAL METHODS OF EXAMINATION

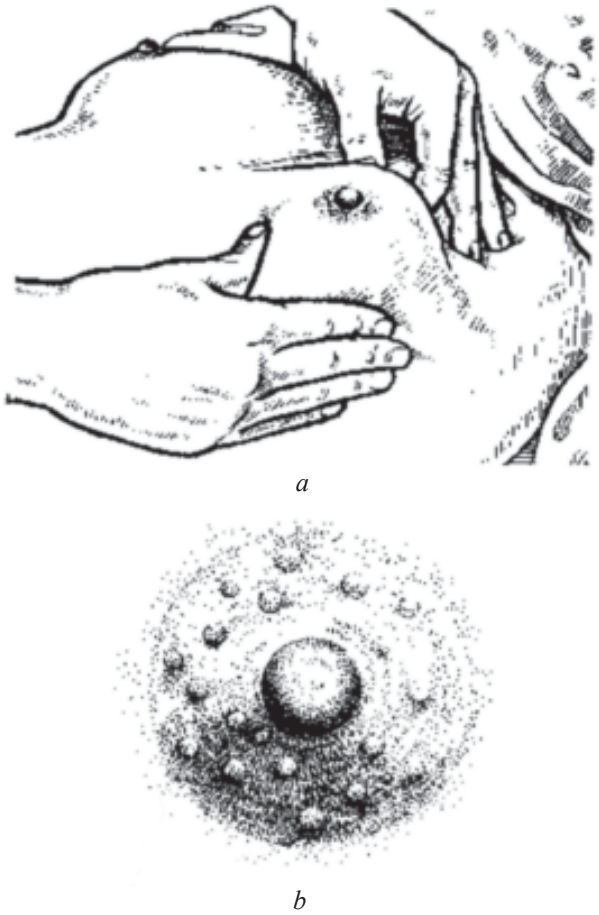
Typobiological estimation. Height, weight and constitution, development of subcutaneous adipose tissue and peculiarities of its allocation should be taken into account while observing a patient. A morphogram which includes measuring indices of the chest circumference, height, distance from the big spit of the femor up to the foot basis, interspital and interacromial sizes are used for definition of the constitution type. Deviations from the normal constitution can be found while mapping these values on a standard monogram. In case of overweight, it is necessary to know when obesity appeared: since childhood, in puberty, after beginning of the sexual life, after abortion or delivery. Phenotypical peculiarities can be evidence of dysmorphies presence peculiar to some syndromes (gonadal dysgenesis).

Common examination. The head, neck (hair, face, oropharynx, tongue, thyroid gland), supraclavicular, axillary, inguinal lymph nodes are inspected; condition and mobility of the extremities, presence of subcutaneous formations, bone and vascular anomalies, oedemata are defined.

Character of pilosis, presence of hirsutism (excessive hair growth in the androgen-sensitive zones: face, lower back part, buttocks, breast, areols, internal femoral surface); skin condition (higher porosity and greasiness, akne); presence of striae atrophicae, their color (purple lines testify to possible adrenal function disorders, pink ones warn against ovarian dysfunction), ammount, location, time of appearance are taking into account.

The mammary glands are examined and palpated — nipples, peripapillary circles, the presence of discharge out of them are taken into account (galactorrhea, benign and malignant diseases).

The mammary glands are divided into 4 quadrants for diagnosis specification (two external — upper and lower and two internal). The mammary glands are a part of the reproductive system, hormone-dependant organ, a target for effect of sex hormones, prolactin, and mediatorily — thyroid glands and adrenal hormones. Examination of the mammary glands by gynaecologist is a necessary screening procedure for diagnosis of benign and malignant tumours of the mammary glands. Examination of a patient is realized in sitting or lying position with consecutive palpation of external or internal quadrants of the glands (Fig. 2, *a*). Presence of nipple discharge, their color should be determined: mild discharge (galactorrhea) are evidence of hyperprolactinemia, dark or bloody — breast cancer. Enlarged glands of the breast areola can be an early sign of pregnancy (Fig. 2, *b*).



a

b

Fig. 2. Examination of the mammary gland:
a — palpation; *b* — enlargement of the glands of the peripapillary rings

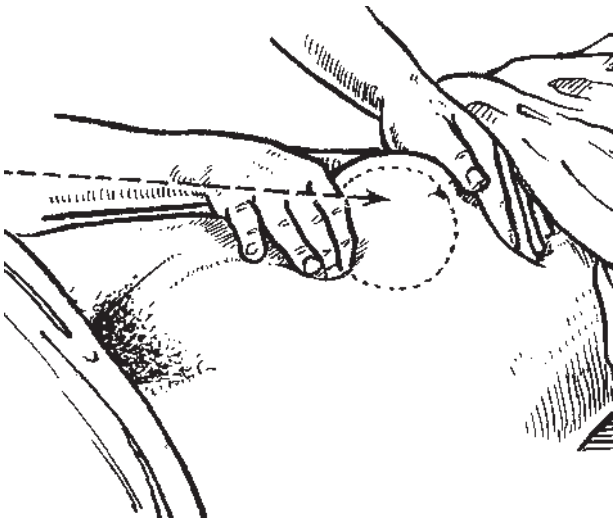


Fig. 3. Palpation of the abdomen

On inspection of the abdomen a patient should be in a supine position with little bit bended lower extremities in knee-joints (for greater relaxation of the anterior abdominal wall) and an empty urinary bladder. The abdomen is also conditionally divided into 3 zones: 1) the epigastric region (epigastrium); 2) the umbilical region (mesogastrium); 3) the pubic region (hypogastrium).

The doctor's hands should be warm not to cause discomfort to a patient during palpation. Presence of space-occupying lesions, line strains, scarring, signs of genital hairiness are found out; auscultation of gut peristalsis is carrying out. Both a big hysteromyoma and an ovarian tumour can be detected during palpation (Fig. 3).

Abdominal percussion is made if there are suspicions of ascites, presence of volumetric masses (formations). Syndrome of peritoneal irritation (Schetkin—Blumberg's) as well as muscular protection are evidence of peritonitis or intraperitoneal haemorrhage most often.

SPECIAL (GYNAECOLOGICAL) METHODS OF OBJECTIVE EXAMINATION

Anxiety of a patient concerning a possible pain aggravation during gynaecological examination make sometimes difficulties for its realization and diagnose. That's why maximum physical and psychical relaxation of a patient during this procedure is very important. On examination a doctor should comment his actions before any procedure execution. Good lighting is a necessary condition.

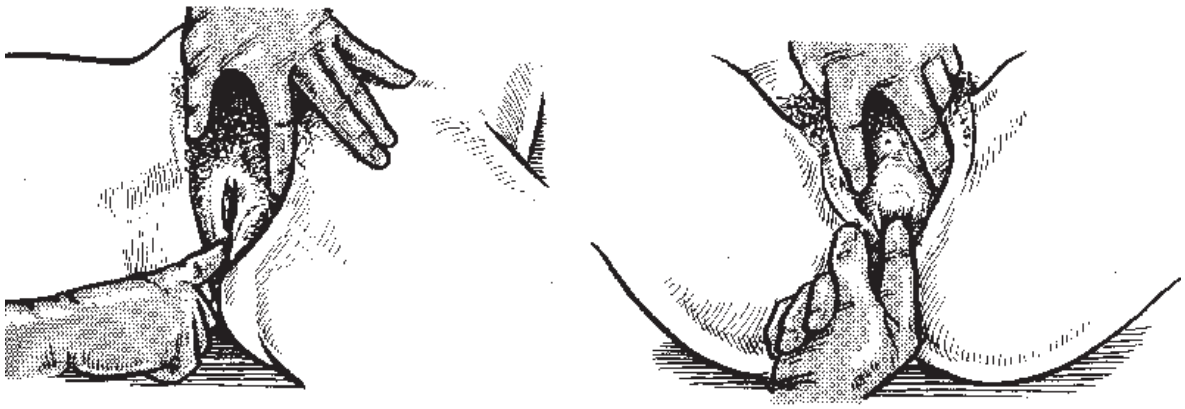
Special (gynaecological) methods of examination can be clinical, laboratory and instrumental.

Gynaecological inspection includes exam of external genitalia; cervix uteri and vaginal walls with the help of vaginal specula; vaginal and bimanual vaginal examination and rectal-vaginal or rectal-abdominal examination if they are necessary.

Inspection is realized in the gynaecological chair in a so called lithotomical position in other words in a position with bended lower extremities in coxal and knee joints, pressed to the abdomen and with empty urinary bladder. A doctor inspects external genitalia (labia, clitoris, greater vestibular glands (Bartholin's), hymen, perineum), carries out examination and palpation (in gloves) of internal genitalia, external urethra's aperture, paraurethral glands, determines the inflammatory changes, pigmentation, space occupying lesions (Fig. 4).

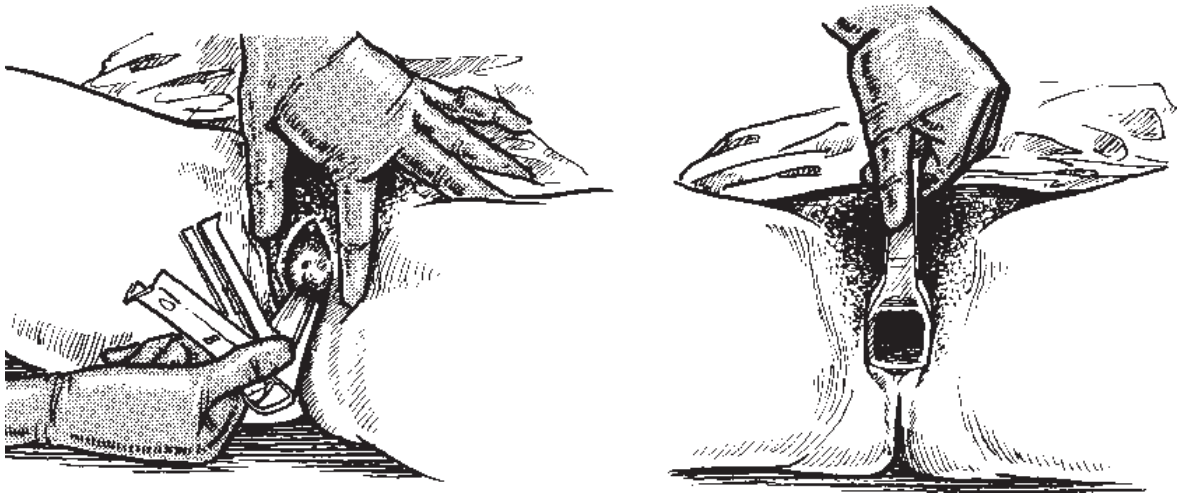
The vagina and cervix are inspected with the help of special specula (Fig. 5). Before their inserting (at an angle about 45º) it is necessary to provide relaxation of muscles which elevate the perineum. For this purpose the following method is used: the forefinger is put in the vagina and carefully pressed down. Specula should be warm and wet with warm water if it is necessary. Disposable specula are used as a rule.

Colour, rugosity of the mucous membrane, presence of space occupying masses are taken into account while inserting specula into the vagina.



a *b*

Fig. 4. Gynaecological examination:
a — of external genital organs (vulva, perineum, external urethral orifice); *b* — of paraurethral glands (with careful pressure on it to eliminate the purulent discharge)



a *b*

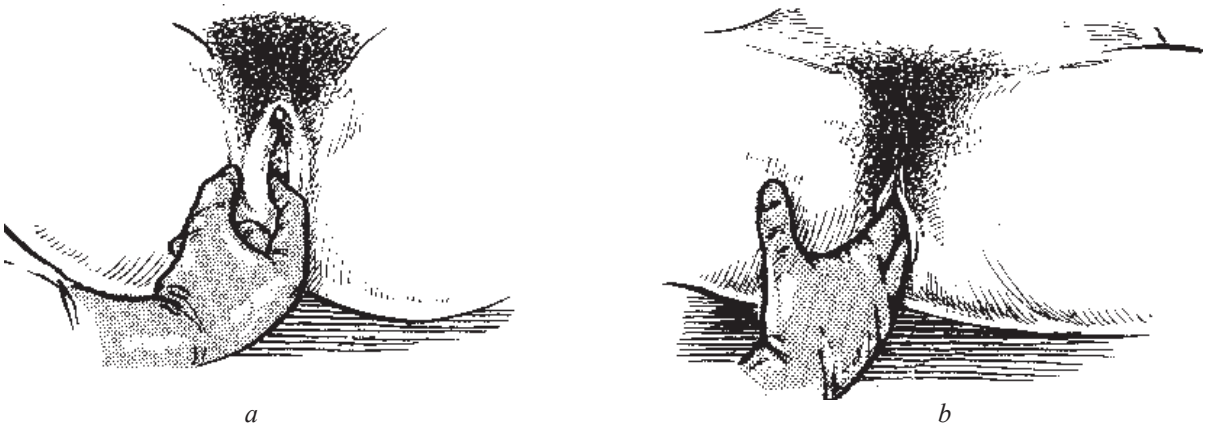
Fig. 5. Examination of the vagina (*a*) and cervix uteri (*b*) with the help of specula

At cervical examination, the form, the look of the ostium uteri (external os), color of the mucous membrane, polyps presence are determined. External os is rounded in women who had never gave birth through natural maternal passages; in those who had vaginal delivery it looks like a horizontal slit sometimes with lateral tears. Both young women and patients who used oral contraceptives can have lateral border displacement between squamous and columnar epithelium on the cervix. After the cervical exam, smears for microscopical, bacteriological (often from cervical canal, urethra and posterior vaginal fornix) and cytological (from the cervical canal) studies are taken. Many precancerous and malignant processes of the cervix start in the zone which delimits squamous and columnar epithelium.

Vaginal examination is realized with a forefinger and a middle finger of one hand. The labia are moved apart with another hand fingers. The location of the greater vestibular glands (Bartholin's) is palpated with a thumb and a forefinger (Fig. 6, *a*). Firstly one finger is put into the vagina carefully pressing on the perineum. The forefinger and the middle one are put into the vagina in such a way that the withdrawn thumb was placed upwards without touching sensitive zones (clitoris) (Fig. 6, *b*).

On *bimanual vaginal examination* the palpation of the uterus, appendages, urethra is carried out with two hands: two fingers of one hand in disposable gloves are put into the vagina; another hand is put in the anterior abdominal wall. Palpation of the pelvic organs is carried out through anterior, posterior (uterus) and lateral vagina's fornices (uterine appendages). In the norm a patient doesn't feel pain during cervical shifts. During palpation of the uterus, its size, form, consistence, location (anteflexion, retroflexion), contours and mobility are revealed (Fig. 7, *a*).

Uterine sizes are estimated approximately in "weeks of pregnancy". Ovarian palpation is difficult and even impossible in pubertal and menopau-



a *b*

Fig. 6. Palpation of the greater vestibular glands of the vagina (*a*), vaginal examination (*b*)

a *b*

Fig. 7. Bimanual vaginal examination: *a* — uterus; *b* — appendages

sal period as well as in cases of oral contraceptives using.

The *rectal* (for estimation of the posterior area of the pelvis, in girls) and *rectal-vaginal* examination (for estimation of sacro-uterine ligaments, during uterine retroflexion, enuresis, genital prolapses) are also carried out if it is necessary (Fig. 8). It is disirable to have empty guts before performing these examinations.

Anamnesis taking and objective examination are carried out for elucidation of problems connected not only with the presence of pathological symptoms but also with an asymptomatic disease course. All given data are fixed in the medical card and are the basis for working out the plan of additional diagnostic and treatment measures.

TESTS OF FUNCTIONAL DIAGNOSIS AND HORMONE EXAMINATIONS

For approximate estimation of ovarian endocrine function, ascertainment of ovulation the **tests of functional diagnosis** do not lose its significance — basal (rectal) temperature measurement, examination of cervical mucus (symptoms of a pupil, fern, crystallisation and mucus tension), colpocytological examination.

The basal temperature is measured in the morning in the rectum. Its analysis reveals two temperature phases of the menstrual cycle: in the 1st half of the cycle (folliculin phase) the temperature is below 37°C; in the 2nd half (lutein phase) is above 37°C as a result of hyperthermic progesterone influence on the thermoregulating hypothalamic centre. Ovulation which occurs approximately at the 13th–14th day in a 28-day cycle takes place between these phases, but can vary very much. The temperature falls dawn on temperature curve the day before the ovulation, which is evidence of the ovule

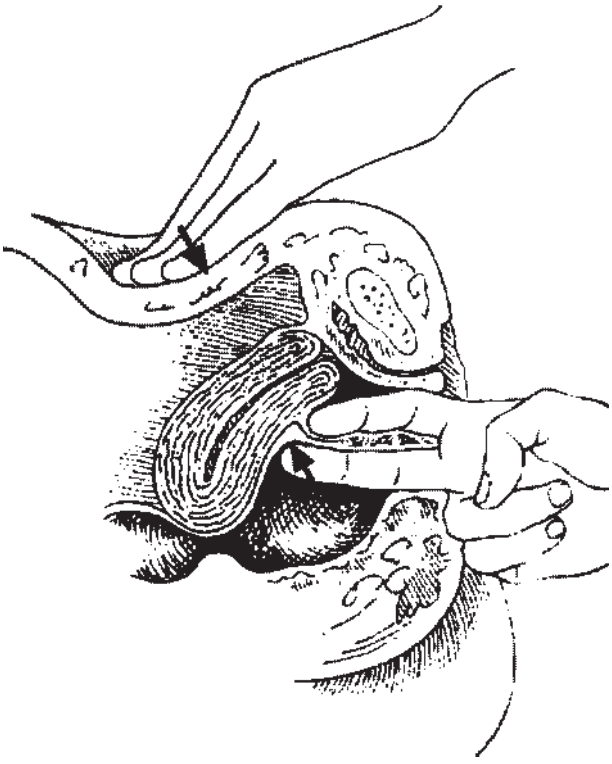
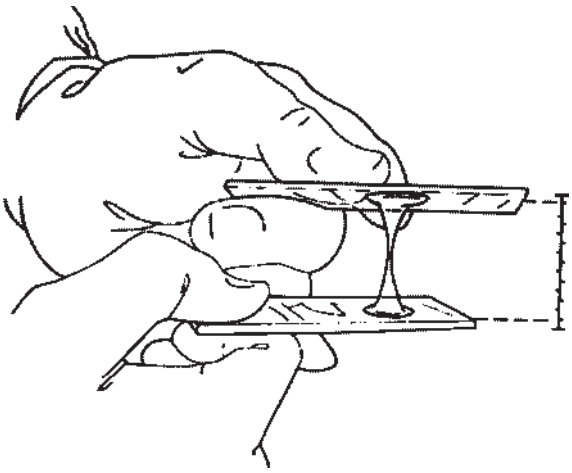


Fig. 8. Rectovaginal examination

leaving the follicle and rises in a day. It is important to determine the difference between the lowest and the highest temperature at different cyclic phases — it should be no less than 0.5–0.8°C. If the hyperthermic phase lasts less than 10–12 days, it is evidence of the lutein phase insufficiency and can cause infertility. The monophase basal temperature curve is evidence of ovulatory absence (anovulatory menstrual cycle).

Examination of the cervical mucus. The *pupil symptom* is conditioned by dilation during ovulation and infill of the ostium of the uterus (external os)



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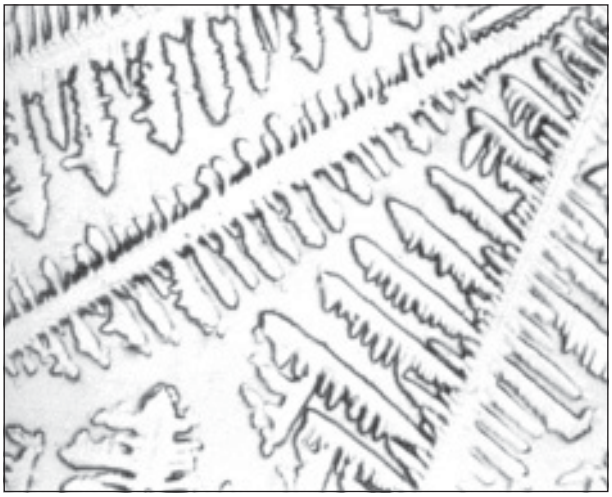


b

Fig. 9. Tests of functional diagnosis:
a — symptom of strain of the mucous; *b* — the fern's symptom

with mucus which is produced by cervical canal glands under the influence of oestrogenic stimulation. Owing to cervical mucus production the cervical canal dilates from 4 mm at the cycle beginning up to 10–12 mm in the ovulating time, then decreases to 4 mm again. The mucus is clear, liquid, well strained *(mucus stretch symptom)* (Fig. 9, *a*) before ovulation and during it. After ovulation the amount of slime decreases, it becomes thick, opaque; external os diameter decreases too. The pupil symptom which is kept for a long time is evidence of anovulatory cycle.

The *fern symptom* (symptom of cervical mucus crystallization) is based on the fact, that the mucus plotted on the glass forms the fern pattern when drying out in the air. The most expressed crystallization is observed in days which correspond to ovulation (Fig. 9, *b*). The nasal mucus is also subjected to similar changes, which can be used when examining girls.

Colpocytological examination. The multilayer squamous vagina's epithelium consists of 5 layers, three of them have clinical meaning: superficial, intermediate and basal. The vagina's epithelium undergoes cyclic changes thanks to receptor's presence of ovarian sex hormones. Superficial epitheliocytes prevail in the I phase of the menstrual cycle — their biggest amount arise in the ovulatory period (about 80%), the biggest amount of intermediate cells is observed in the 2nd cycle phase. Presence of such cyclic changes is evidence of ovulation, i.e. ovulatory cycle. On colpocytological examination the indices are calculated: CPI *(cariopycnotic index)* — percentage of superficial cells with pycnotic nuclei and cells with unpycnotic nuclei; EI — (eosinophilic index) — percentage of acidophilic and basophilic cells; AI (atrophic index) — percentage of basal and parabasal cells and general cellular amount in a smear. KPI and EI show a degree of organism saturation with oestrogens and have a cyclic character. The basal and parabasal cells are absent in smears of healthy women of the reproductive age.

Hormone examinations. ***Estimation of hormones and their metabolites contents.*** Methods of radioimmune, immunoenzymatic and immunofluorescent analysis allowes to determine the contents of albuminous and steroid hormones in the biological fluids and tissues. It might be well to analyse the given results in comparison with tests of functional diagnosis (basal temperature). In case of a 28-day cycle, examinations are carried out on the 5th–9th, 13th–14th, 23rd–25th days of the cycle.

Functional hormone probes are used to reveal the reasons and extent of menstrual dysfunction (hypothalamus—hypophysis—ovaries—uterus). The most wide-spread are probes with gestagens, oestrogens, dexamethasone, clomiphene, luliberin. These methods are based on supression or stimulation of individual components of the endocrine system.

The gestagen (progesterone) probe is used for estimation of extent of oestrogen deficiency, uterine amenorrhoea exclusion and is considered to be positive if in 2–3 days after 6–8-day of intramuscular injection of 1 ml of 1% progesterone solution or in 10–14 days after injection of 1 ml of 2.5% (25 mg) of 17-oxyprogesterone kapronate solution (17-OPK) the patient has a menstrual-like bleeding. The *positive* progesterone probe excludes the uterine form of amenorrhoea and is evidence of sufficient oestrogen activity of ovaries and the *negative* one confirms a deep endometrial lesion or weak oestrogen stimulation.

The *oestrogen and gestagen probe* is applied after receiving a negative progesterone probe result. The patient gets oestrogens (1 ml of 0.1% folliculin oil solution or sinestrol or by 2 tablets of microfollin (ethinylestradiol daily) during 7 days. Then they prescribe progesterone during 8 days. The *positive probe* (appearance of a menstrual-like reaction) allows to exclude the diagnosis of the uterine amenorrhea and is evidence of insufficient endocrine activity of the ovaries.

The probe with *combined oestrogen-gestagen drugs* is used for determination of reserve capacity of the hypothalamic-hypophysial system. The rebound-effect — a recovery of regular menstruations and ovulations — can arise after the medication withdrawal.

The *positive probe with clomiphene* (clomiphene is prescribed by 50–100 mg from the 5th to 9th day of the menstrual cycle) is accompanied by folitrophin and lutrophin increase in blood serum, which provokes ovulation.

The *probe with dexamethasone* is carried out for revealing hyperandrogenism source. It is based on suppression of corticotrophin secretion as a result of dexamethasone use by 5 mg 4 times a day during 2 days. A sudden decrease in 17 ketosteroids (17-KS) excretion with urine is evidence of functional disorders of adrenals (hyperandrogenism of adrenal genesis).

Markers of hyperandrogenism of the ovarian origin are increasing testosterone level in blood serum as well as an increase in 17-oxycorticosteroids secretion with the urine.

DIAGNOSTIC PROCEDURES AND ULTRASOUND STUDY

Diagnostic procedures (minor gynaecological operations) are uterine probing, puncture of the abdominal cavity through the posterior vaginal fornix, cervical biopsy, aspirating biopsy and separated (fractional) diagnostic curretage of the uterine cavity (see page 191).

Histological examination of endometrial aspirate is a quite exact method of the ovarian function estimation. The proliferative phase of the endometrium conforms to the first half of the menstrual cycle, the secretory phase conforms to the second one. Revealing of the proliferative changes in the endometrium in the second half of the cycle is evidence of anovulatory cycle.

A high-informative and wide-spread method of diagnosis is **ultrasound examination** (ultrasonography, echography) with using of transabdominal, transvaginal, rectal sensors. *Transabdominal ultrasonography* is realized with a full urine bladder for acoustic window making. *Transvaginal ultrasonography* allows to use high-frequency sensors, at the same time an examination is carried out with an empty urine bladder, which is convenient for a patient. Obesity and pelvic adhesions do not influence visualization of the uterus and appendages during transvaginal ultrasonography.

The information about the sizes of the uterus (65×51×36 mm on average in the norm), ovaries (29×28×19 mm), a character of space-occupying masses in the abdominal cavity (Fig. 10), congenital malformations of genitalia, pathological formations (adhesions, myoma, polyp, endometriosis, endometrial hyperplasia, cancer), location of an intrauterine device are specified with the help of ultasound; they control follicular growth at ovulatory stimulation.

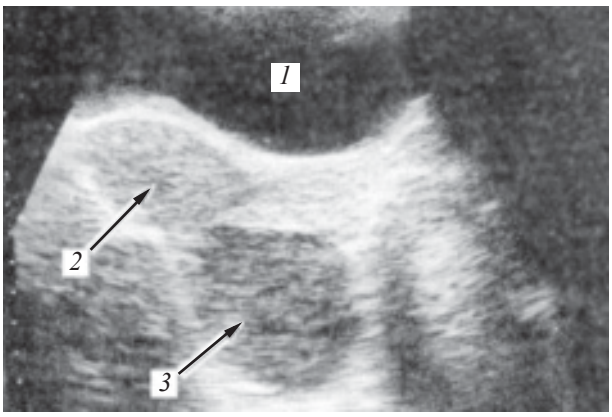


Fig. 10. Ultrasonogramm of the patient with an endometrioid cyst of the ovary:
1 — urinary bladder; *2* — uterus; *3* — ovarian cyst

Ovarian sizes of a healthy woman do not exceed one third of transversal uterine size in echogram.

This correlation is a criterion for determination of normal ovarian sizes, which has an important diagnostic meaning for revealing polycystic ovaries, tumours, tumour-like formations of small sizes.

Increase of a developing follicle size up to 20–26 mm on the 13th cyclic day and a sharp diminution of its size on the 14th day with appearance of liquid in extra-uterine cavity is evidence of ovulation.

Advantages of the method are its noninvasiveness, possibility of using in girls as well as in women with obesity when palpation is difficult.

Modern possibilities of ultrasound (transmission, contrasting echography, hydrosonography) allow to define the tubal patency thanks to administration of sterile fluid or contrast substance (echovist) into the uterus under ultrasound control to define early stages of uterine and ovarian cancer.

ENDOSCOPIC METHODS

Colposcopy is the first endoscopic method widely used in the gynaecological practice. A diagnostic value of the method is great: it allows to examine the vaginal part of the cervix, vaginal walls and vulva in details.

Simple colposcopy is the cervical inspection with a colposcope. The method allows to define sizes of the cervix and external os, color and relief of mucosa, the border between squamous epithelium (ectocervix) and cylindrical epithelium of the cervical canal (endocervix).

Advanced colposcopy is the cerval inspection after its treatment with 3% acetic acid, which causes a short-term oedema of the cylindrical epithelium, cel-

lular swelling of subepithelial vessels and blood sloppy reduction. Acetic acid acts during 4 min. While studying the colposcopic picture of the cervix treated with acetic acid, they pay attention at vessels, their form, size, condition of the cervical glands, presense of cylindrical epithelium ectopia.

The Shiller's probe has an important diagnostic meaning. It is a processing of the cervix with a tampon wetted in 3% Lugol's iodine solution. Iodine, contained in the solution, makes the glycogen of the squamous unaltered cervical epithelium cells brown. Dysplastic and atrophic epithelial changes lead to decrease of glycogen content in cells that's why they are not coloured by the Lugol's iodine solution.

So, the Shiller's probe allows to reveal zones of pathologically changed epithelium to provide a target cervical biopsy.

Chromocolposcopy is an inspection of the cervix after its coloring with different dyes (methylene violet, haematoxylin etc.), which also allow to reveal pathological changes of the cervix, to specify lesion borders, to choose zones for a target biopsy.

Colpomicroscopy is a histological examination of the cervical part of the vagina made in a patient's lifetime which is realized with a contrasting luminescent colposcope.

Colposcopic methods of cervical examination are characterized by high accuracy in diagnosis of cervical diseases, endometriosis, polyps, endocervicitis etc.

Hysteroscopy is a method of endoscopic examination which allows to inspect the cervical canal, uterine cavity, uterine walls with the help of fiber optics. Hysteroscopy is used for detection of intrauterine pathologies (polips, submucousal fibroids, hyperplasia and cancer of the endometrium, reminants of the fetal ovum, intrauterine synechiae), which can cause uterine bleedings in women of any age. Hysteroscopy is not only a diagnostic but also a treatment procedure (hysteroresectoscopy) during which biopsy and endometrial curretage, polyps removal, cryoablation of a polyp's bed, small submucousal peduncular fibroids, dissection of adhesions (synechiae), intrauterine septum, extraction of intrauterine devices or their parts, the Fallopian tubes recanalization are made.

Laparoscopy (Fig. 11) is a method of examination of the pelvis and abdominal cavity against a background of pneumoperitoneum (any gas is inserted into the abdominal cavity: CO_2, NO_2, O_2, air).

The usage of laparoscopy gives an opportunity to reveal and treat patients having mild forms of external endometriosis, chronic pelvic pain, tubal and peritoneal infertility, ectopic pregnancy as well as to carry out differential diagnosis of different pathology of abdominal cavity organs (appendicitis, inflammation of uterine appendages, ovarian cancer, cholecystitis, etc.). Separation of adhesions, vaporization and thermocauterization of endometriodal heterotopias are realized on laparoscopy, ablation of myomatous fibroids, cysts and ovarian tumours, etc. are made.

Culdoscopy is a kind of laparoscopy when the pelvic exam is made with the help of a laparoscope, inserted through the incision in the posterior vaginal fornix. Today this method is almost unavailable being supplanted by a more modern one — abdominal laparoscopy.

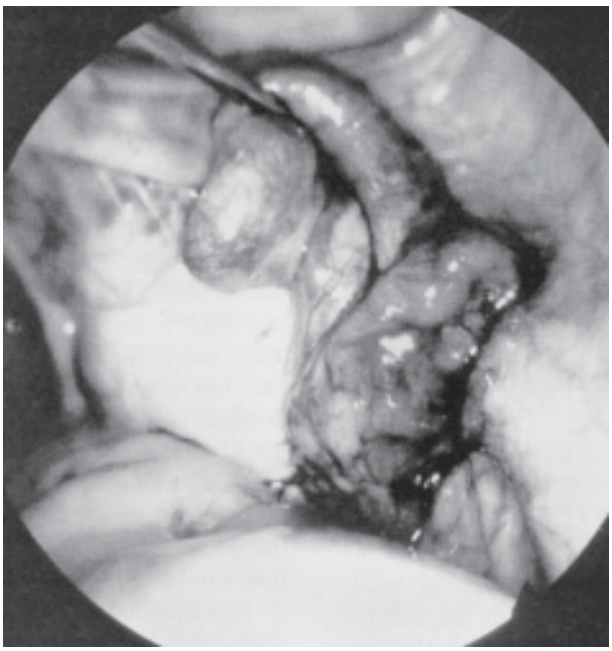


Fig. 11. Normal uterine (Fallopian) tube during laparoscopy

X-RAY AND RADIONUCLIDE METHODS

X-ray methods of examination include hysterosalpingography (metrosalpingography), hysterosalpingography against a background of pneumoperitoneum (bicontrasting pelviography), roentgenological examination of the cranium, adrenals, computer tomography.

Hysterosalpingography is used for determination of the tubal patency, revealing of anatomical changes in the uterine cavity, pelvic adhesions. The examination is carried out on the 5th–7th day of the menstrual cycle with the help of water-soluble (cardiotrast, verotrast, verographin, urotrast, triombrast) or liposoluble (iodinolopol) roentgenocontrasting substances.

The uterine cavity has a triangular form (under the influence of oestrogens) in the 1st cyclic phase, and a pear-shaped one in the 2nd phase (under the influence of progesterones). Analyzing metrosalpingograms, they pay attention at presence of extra shadows (fulfilment defects) in the uterine cavity

(a polyp, myomatous submucousal fibroids), extracontour shadows in adenomyosis, uneven contours in endometrial hyperplasia.

A thin thread of contrast substance which duplicates the tubal contour exceeding its borders and spreading along the pelvis at peristaltic intestinal motions (plural small irregular spots) are evidence of contour tubal patency. If only the uterine cavity is seen at the picture, it must be tubal occlusion in the intramural area; if its contour is seen within a short distance — in the isthmical area; if a Fallopian tube is seen all the way along but there is no free contrast in the abdominal cavity, it is evidence of tubal occlusion in the ampular area (Fig. 12).

Bicontrasting pelviography in contrast to metrosalpingography which allows to see internal organs contours visualizes also external contours and sizes of the uterus, ovaries, hence may be used for diagnosis of polycystic ovaries, submucousal fibroids. Today bicontrasting pelviography is completely displaced by ultrasound examination.

X-ray examination of the adrenals under retropneumoperitoneum conditions is carried out at suspicion of adrenal tumour or hyperplasia, which as a rule is conformed by the clinical picture of virilization.

X-ray examination of the cranium is used for diagnosis of neuroendocrine syndromes. Examination allows to determine the form, sizes of the cella turcica contours — bone bed of the hypophysis. A pituitary tumour is diagnosed in the presence of total or local osteoporosis, local thinning, uneven contour of walls with a corresponding clinical picture. Available digital impressions are evidence of increased intracranial pressure.

Computer tomography allows to do by layers cuts of different body parts with 1 cm pace and to reveal pathological foci of 0.5–1 cm. This method is highly informative especially in case of malignant tumours.

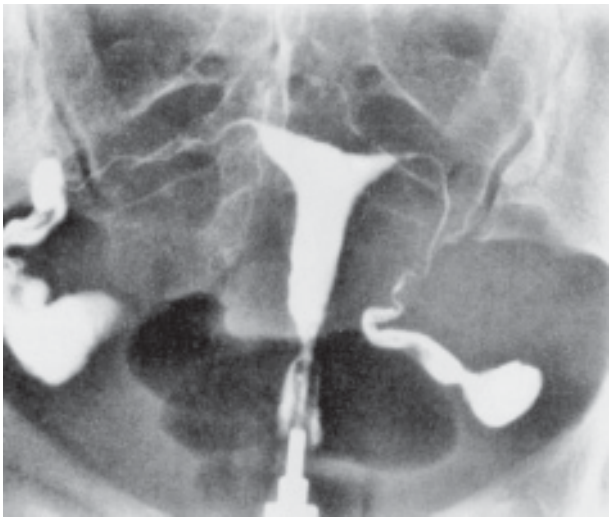


Fig. 12. Hysterosaplingogram: bilateral oedema of the Fallopian tube (hydrosalpinx)

Mammography is an X-ray examination of the mammary glands which has a great value as screening diagnostic method of breast cancer especially in women over 40.

Radionuclide methods of examination are used to detect hyperplastic endometrial processes. The examination is based on the property of radionuclide phosphorus to accumulate in actively dividing cells in a greater quantity than it does in unchanged organ's tissue. Radionuclide examination gives an approximate view about extent of endometrial cellular elements proliferation and the place of the pathological process location in condition of its focal character.

Radionuclide examination (scanning) and dynamic scintigraphy of the uterus and Fallopian tubes allow to model a mechanism of spermatozoons transport in the uterine cavity, Fallopian tubes and through them into the abdominal cavity.

The greatest achievement in ragiology during last three decades is an invention of nuclear magnetic resonance (NMR), which along with computer tomography is ever more used in oncogynaecological practice.

CYTOLOGICAL METHODS

Method of morphological (histological) examination is widely used in gynaecological practice for diagnosis verification, especially in neoplastic processes. Fragments of the endometrium and cervix taken during fractional diagnostic curretage or biopsy; tissues of the cervix and the vagina taken in biopsy; tissues which were ablated during surgical intervention are to be examined. Histological endometrial examination allows to determine the phase of the menstrual cycle (the 5th–6th day — regenerative phase, the 7th–9th day — proliferative phase, the 10th–11th day — late proliferative phase, the 20th–28th — secretory phase), presence of hyperplastic processes, extent of its development (simple glandular hyperplasia, glandular-cystic hyperplasia, atypical hyperplasia, malignant endomenrial transformation).

Cytological examination of the aspirate, taken from the uterine cavity, smears-marks, cells of vaginal epithelium, the material taken during the puncture of the abdominal cavity, tumours, supplements histological cellular examination essentially and allows revealing typical malignant cells. The given methods do not exclude but supplement each other.

The cytological method of examination in gynaecological practice is widely used as a screening method during prophylactic inspections for estimation of hormone and chemotherapy effectiveness in oncological diseases.

Cytogenetic examinations are aimed at definition of X-, Y-chromatin and karyotype ascertainment.

X-chromatine forms by one of X-chromosomes; healthy women have 15% of it; men have no X-chromatin. The content of sex chromatine corpuscles in the germinal epithelium cells' nuclei obtained during scraping the internal cheek surface mucosa is determined with the help of a luminescent microscope. If a quantitative content of sex chromatine changes, a karyotype is examined. The sex chromatin and karyotype are defined in patients having gonadal disgenesis, in short women, in presence of maldevelopment and dysplasia as well as in case of habitual miscarryage of pregnancy. Sex chromosomal abnormalities are mostly observed on women suffering from gonadal dysgenesis.

RECOMMENDED READING

15; 16; 20; 21; 24; 40; 43; 57; 75; 79; 85; 90; 91; 92; 94; 95; 101; 103; 108.

Chapter 2

INFLAMMATORY DISEASES OF FEMALE GENITALIA

Inflammatory diseases of genitalia (IDG) are most often met in the practice of a gynaecologist and compose more than 60% in the structure of gynaecological morbidity. The frequency growth of genital inflammatory diseases all over the world is the result of the migration of the population, urbanization, changing the social norms towards sexual freedom, which leads to spreading of sexually transmitted diseases. Tardy treatment can bring to chronic pelvic pain, infertility, violation of working ability, social activity and even invalidity of reproductive age women.

In modern literature the terms "the sexually transmitted diseases" (trichomoniasis, chlamydiosis, genital herpes, pappilomaviral infection, syphilis, gonorrhoea, AIDS) and "pelvic inflammatory diseases" (endometritis, parametritis, salpingitis, salpingoophoritis, pelvioperitonitis, pelvic absess, etc.) are more often used than the terms "inflammatory diseases of genitalia", "specific and non-specific inflammatory diseases".

NORMAL MICROBIOCENOSIS OF THE VAGINA AND MECHANISMS OF INFECTION DEVELOPMENT

The normal micro flora of genitalia plays a definite part in the appearance of inflammatory diseases. A big number of micro organisms vegetate in the vagina of a healthy woman. In the norm the micro flora of the vagina contains lactobacilli, corinebacteria, diphtheroids; cocci flora — aerobic and anaerobic cocci, hemolytic (β-hemolytic streptococcus) and non-hemolytic streptococci, enterococci; klebsiella, enterobacteria and proteus, colibacillus are rarely observed. The micro flora of the vagina contains aerobic and anaerobic flora in equal quantity. Micro organisms which constantly vegetate in the genital tract can become virulent under certain conditions and take part in the development of IDG.

The ecology of the vagina depends on the glycogen contents in the epithelium, concentration of lactobacilli, acid-base balance and local immunity.

It is typical for the normal microbiocenosis: 1) domination of lactobacteria supporting the acid pH, so protecting the organism from pathogenic flora; 2) the low content of colibacillus, korinebacteria, staphylococci, streptococci, obligate anaerobes. During the reproductive period there are from 3 to 8 main types of pathogenic micro organisms which vegetate in the content of the vagina (Table 1). The presence of pathogenic flora is not a sign of the pathologic process when the inflammatory reaction is absent.

Women can have vaginal discharge (leucorrhoea) at any age. Vaginal mucous discharge are physiological and can be observed in most cases. The physiological secretion of the vagina mainly consists of cervical mucus, the vagina's desquamated epithelium, products of micro flora's metabolism, exudation of sebaceous, sudoriferous glands, greater vestibular glands (Bartholin's), paraurethral glands, endomethrial and tubal secretion. The mechanisms which shift the normal ecosystem are hormone effects which influence the glycogen contents in the vaginal epithelium; microbial antagonism; disorders of general and local immunity; features of woman's sexual behaviour. If the hormone effect is absent, the epithelium is thin, atrophied and contains a little amount of glycogen. Vaginal discharge have a high pH. That's why in minimal hormone stimilation (puberty, postmenopausal period), the amount of vaginal discharge is little. When there is an adequate oestrogenic and progesterone stimulation, the amount of glycogen increases and pH decreases (milk acid is produced during glycogen utilization). The amount of cervical mucus and vaginal discharge is growing under the influence of oestrogen production increase, during ovulation, pregnancy, sexual or any other emotional stimulation.

Table 1. **Vaginal microbiocenosis in different periods of woman's life**

Indices	Period			
	newborn	prepubertal	pubertal and reproductive	menopausal
Hormonal effect	Oestrogens progesteron	Absent	Oestrogens, progesteron	Minimal or absent
Vaginal pH	3.7–6.3	6.0–8.0	3.5–4.5	6.8–8.0
Vaginal microflora	Anaerobes and aerobes	Gram-positive cocci and bacilli	*Aerobes, %:* lactobacilli (70–90), epidermal staphylococcus (30–60), dyphtheroids (30–60), streptococci (α-, β- hemolytic, non-hemolytic (10–40), colon bacillus (20–25) *Anaerobes, %*: bacteroides (5–40), peptococci (5–60), peptostreptococci (5–40), closridia (5–15)	Gram-positive cocci and bacilli

The protective mechanisms, acting in the area of the cervical canal and endometrium have a special meaning for the upper female reproductive tract. In most cases the normal vaginal flora prevents from the invasion of other pathogenic micro organisms.

The cervical mucus which contains antibacterial matters (lysozyme), antibodies to colibacillus, gonococci, salmonellas is a barrier that divides the upper and lower female reproductive tracts.

The endometrium plays a protective function in the uterus and hinders from the penetration of micro organisms thanks to periodical sloughing of its functional layer during the menstruation.

The leucocytic infiltration of endometrial basal layer is also a protecting function in the menstrual period.

Candida albicans, Trichomonas vaginalis, Gardnerella vaginalis and *Chlamydia trachomatis* can often cause vaginitis and leucorrhoea.

The penetration of infectious agents into the upper female reproductive tract can be realized with the help of spermatozoons and *Trichomonae*, the passive transport is possible, rarely there are hemato- and lymphogenous ways of infection. Intrauterine procedures (hysterometry, metrosalpingography, hysteroscopy, pertubation, hydrotubation, genital operations, abortions, delivery) as well as intrauterine contraception promote spreading of the infection into the upper female reproductive tract.

NON-SPECIFIC INFLAMMATORY DISEASES

VAGINITIS

The presence of the vaginal discharge simultaneously with pelvic pain and haemorrhage relate to the most wide-spread complaints of gynaecological patients. In most cases the reason of these discharge is the inflammation of the lower female reproductive tract (vaginitis, cervicitis). The pathologic discharge are characterized by the vulva irritation, dirtying of clothes and often have an odour.

Vaginitis (colpitis) is an infectious inflammatory disease of the vagina, caused by the influence of conditionally pathogenic micro organisms (colibacillus, strepto-, staphylococci, etc.). There are *acute, subacute, chronic, recurrent* as well as *simple serous-purulent* and *granulous diffuse vaginitis*.

Clinical picture. The main symptoms of vaginitis are discharge (leucorrhoea), which can be liquid, watery, purulent. In presence of epithelial desquamation, the white discharge have a thick consistence, an odour, sometimes with streaks of blood. Itching, burning, sometimes dysuria can arise during the acute form of the disease. The vaginal examination causes pain due to hypostasis and sensitivity of the vaginal walls. In patients suffering from chronic vaginitis the pain as a rule is not promoted. The manifestations are white discharge, itching and burning; sometimes there are small ulcers on the vulva and in the low third of the vagina. The granulous vaginitis is characterized by the presence of red spots which slightly jutted out above the mucous membrane of the vagina. The patients complain of dyspareunia (pain during sexual intercourse).

Diagnosis of vaginitis is based on the data of bacterioscopic and bacteriological examination. As a rule, they reveal some types of microorganisms, a big amount of leucocytes, desquamated cells of the vaginal epithelium.

Treatment should be complex and include etiotropal antiphlogistics, directed to the elimination of concomitant metabolic and endocrine disorders. Besides, a necessary condition is to stop sexual in-

tercourse and to treat the partner. Antibacterial therapy, mainly local, is realized taking into account the micro flora sensitivity. It is recommended to wash external genitalia three times a day with a weak solution of potassium permanganate, tinctures of camomile and sage; during the acute form the vagina should be syringed with solutions of antiseptics (potassium permanganate 1:6000–1:8000, camomile, salvin, recutan, furaciline, chlorophillipte) during 3–4 days with a subsequent use of local antiphlogistics (vaginal suppositories "Betadin", "Polyzynax", "Terzinan", "Gino-Pevaril", etc.) as well as oestrogens usage if it is necessary (tampons with 0.1% phlliculin oil solution in 20 ml of synthomycin emultion; suppositories and cream "Ovestin"). Prolong and frequent syringes can hamper the normalization of the vaginal pH, reinforce the process of the epithelial desquamation. The local use of biologicals (lactobacterin, bifidumbacterin, "Vagilac") is recommended for the recovery of normal vagina's microbiocenosis after the application of the mentioned treatment.

BACTERIAL VAGINOSIS

Bacterial vaginosis is an infectious noninflammatory syndrome connected with dysbacteriosis of the vagina which manifests itself in excessively high content of obligately and optionally anaerobe conditionally pathogenic bacteria against a background of significant decrease or absence of lactobacilli in the vagina. Conditionally pathogenic micro organisms dominate: gardnerella (40% of cases), bacteroides, peptostreptococci, micoplasmae; vaginal pH is above 4.5. Vaginal dysbiosis can be determined by immune, hormone changes, irrational antibiotic therapy and quite often combines with intestinal dysbacteriosis.

Bacterial vaginosis is the most wide-spread type of genital infectious pathology in reproductive age women (30–50% of all vaginal infections).

Clinical picture. The main symptoms are the white discharge with "fishy" odour, viscous, sometimes foamy, sticky, their amount is about 20 ml per day (the norm is under 10 ml) as well as the feeling of burning, itching, the presence of dyspareunia. The signs of bacterial vaginosis during the examination are the absence of inflammatory signs, oedema, hyperaemia of the vaginal and vulvar walls.

Diagnosis of bacterial vaginosis is based on the presence of 3–4 signs:

1) pathologic vaginal discharge with an odour;

2) the presence of typical crucial cells in the vaginal swab, the cells of vaginal epithelium covered with Gram-variable bacteria;

3) an elevated vaginal pH over 4.5;

4) the whiff test (while adding 10% solution of KOH to a vaginal prep, a specific amine "fishy" odour arises). A little amount of leucocytes is found out in the vaginal prep, lactobacilli number is sharply reduced.

Treatment. The question concerning treatment of patients suffering from bacterial vaginosis and their sexual partners is debatable. The majority of specialists think that it is necessary to treat those patients who have clinical manifestations of the disease.

The aim of the treatment is to recover the normal ecosystem of the vagina and lactoflora, to eliminate obligate anaerobe component of micro flora, in order to prevent from the superinfection by conditionally pathogenic micro organisms (by fungi, enterobacteria and etc.).

Ethiotrophic therapy of patients with bacterial vaginosis is carried out with antianaerobic antibiotics. The most effective are both oral and topical treatment with metronidazole and clindamycin. The fact of the same efficacy of both methods is established but thanks to topical usage of these preparations the side-effect is greatly decreased or is completely absent.

Metronidazole is prescribed in a dose of 500 mg 2 times a day orally during 7 days. Immediate effectiveness of such treatment composes 98.8%, deferred — 60–95%. A 2 g single dose of metronidazole therapy (effectiveness is 85%) is possible. In case of recurrence of the disease after a single 2 g of metronidazole, the patients take a 7-day course of treatment with this drug.

The topical use of metronidazole has fewer side-effects and becomes a drug of choice for treatment of pregnant and breast-feeding women.

The most wide-spread complication during the metronidazole therapy is the development of mycotic vulvovaginitis (6–16%). That's why diphlucan (a single dose of 150 mg orally) is prescribed together with metronidazole to prevent candidiasis, or nizoral — 0.2 g 2 times a day or nystatin — 500,000 U 4 times a day per os during the metronidazole course. Trichopol is used by 0.5 mg 3 times a day orally during 6 days. Metronidazole is used intravaginally as a 75% gel, 1-2 applications a day during 5 days or as suppositories — "Metronidazole", "Flagil", "Macmiror".

The combination of imidazole internal introduction with local medical procedures is effective: daily irrigations of the vagina with solutions of anticeptics, 1% hydrogen peroxide solution, 0.05% solution of chlorhexidine bigluconate.

Clindamycin is prescribed by 300 mg 2 times a day orally during 7 days or 1–2% cream ("Dalacin") by 5 g once a day topically, better before going to bed during 7 days. "Dalacin" is effective in 92–94% of cases and practically has no side-effects.

Naxogin, tiberal, tinidazole, cephadroxil, amoxicyllin, nimorozol, unazin, augmentin can also be used for treatment of patients suffering from bacterial vaginosis.

The last stage of ethiotrophic treatment of patients with bacterial vaginosis is the use of biologicals — eubiotics for stimulations of the vagina's lactoflora. Lactobacterin, acilact, bifidumbacterin, bifidin, "Narine" are used as vaginal tampons or as suppositories once a day for 7–10 days. The preparations of lactate bacteria should be prescribed only if fungi *Candida* are absent in vagina; otherwise the development of acute candidiasis (increase of vaginal pH) can be provoked. Pregnants are recommended to use lactate-gel (pH 3.8) — 1 dose before going to bed during 7 days.

The treatment mode of bacterial vaginosis is elaborated by I. F. Kira (1994), it includes daily vaginal instillation of 100 ml 2–3% solution of lactic or boric acid for 7 days; then the application of vaginal suppositories or tampons with metronidazole (0.5 mg), sinestrol (0.005 g) or folliculin (10,000 U), ascorbic (0.3 g) or lactic (0.05 g) acid. The suppositories or tampons are used twice a day during 7–10 days. If there is pain, itching, burning, ointment with anesthesin, novocaine and dicaine (on basis of seabuckthorn, olive or oil of dog-rose) are prescribed.

VULVITIS

Vulvitis is an inflammation of external genitalia which can be primary (traumatic) and secondary (if there is any inflammatory process in internal genitalia — the vagina, cervix, etc). A steady injury of external genitalia during itching of the vulva, helminthiasis, enuresis, diabetes mellitus can promote the appearance of vulvitis.

The conditionally pathogenic flora of the vagina and perineum is an agent of vulvitis as a rule; the combination of vulvitis with condyloma acuminata may also take place.

Clinical picture. Itching, burning in the area of external genitalia, especially after urination, purulent discharge, pain during walking, dyspareunia are typical.

Diagnosis is based on the clinical data as well as on the results of bacteriological and colposcopic examinations. In collibacillar infection the discharge are liquid, yellow and green, with unpleasant odour and in staphilococcal infection they are thick, white and yellow.

The treatment includes local therapy: toilet of external genitalia 3 times a day with warm solutions of anticeptics: camomile (a tablespoon is flooded-with a glass of boiling water and drawing for 20 min), sage, furaciline (1:5000), potassium permanganate (1:10,000); the use of hip-baths with potassium permanganate, ethiotrophic ointments; treatment of concomitant inflammatory and metabolic diseases. In case of strong itching, the vulva is dubbed with 5% anaesthesin liniment.

BARTHOLINITIS

Bartholinitis is an inflammation of the greater vestibular glands which can be caused by the conditionally pathogenic flora, as well as by gonococci, trichomonadae, micoplasms, other micro organisms and their associations. The disease cause can be acute or chronic, relapses can be often observed.

Clinical picture. Microbes can affect both the excretory duct (canaliculitis) and the gland itself (bartholinitis). The latter enlarges and becomes painful during palpation, the purulent secretion is exuding from the excretory duct while pressing. Pseudoabscess of the Bartholin's gland arises in cases of excretory duct occlusion and accumulation of serous purulent exudate. The enlarged gland throws out the internal surface of a labium, closes the income to the vagina (Fig. 13). A tight and elastic formation is palpated in the thickness of a swelled labium.

If pseudoabscess of the Bartholin's gland develops, the general condition of the patient can be the same. When inflammation involves the adjoint tissues, the true abscess with a severe course (hyperaemia of the vulva, fever, acute pain) takes place. Chronic bartholinitis often recurs, which is characterized by vague signs of inflammation, the pain can be absent. During the prolonged treatment of chronic bartholinitis the fluid exudation, mucus are accumulating in the cavity of the gland.

A painless retentional cyst of the greater vestibular gland (Bartholin's) forms.

Fig. 13. Bartholinitis

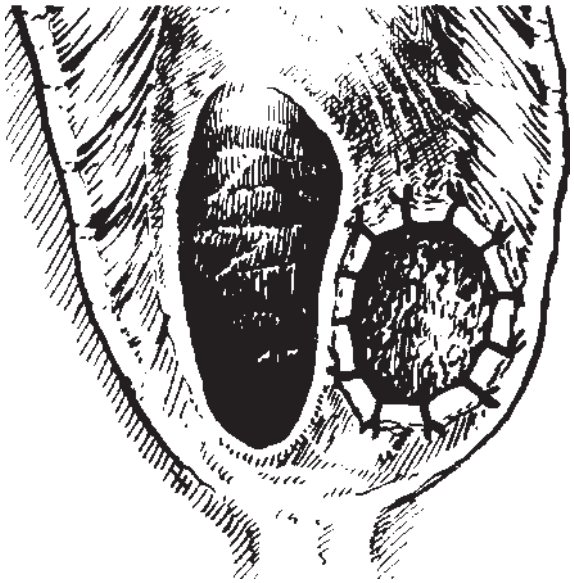


Fig. 14. Marsupialization of the cyst of the greater vestibular gland of the vagina (Bartholin's)

Treatment of patients suffering from the acute form of canaliculitis includes antibiotics, analgesics; within first days — local hypotermia (ice) separately (per 20 min alternating with 30 min breaks) then since the 3rd–4th day — UHF magnetic field, ultraviolet radiation. The surgical treatment presents the incision of the abscess with subsequent drainage, antibacterial and roborant therapy. In cases of pseudoabscess or cyst in a cold stage, the duct of the greater vestibular gland is opened, the mucous membrane is turned out and anchors to the vulvar mucous membrane (marsupialization of cyst) (Fig. 14).

SPECIFIC INFLAMMATORY DISEASES

GONORRHOEA

Aetiology and Pathogenesis. Gonorrhoea is related to sexually transmitted diseases and caused by gram-negative diplococcus and gonococcus *(Neisseria gonorrhoeae)*, adapted for being in cylindrical and transition epithelium. The common way of infection (linen, bast whisp, towel) is met seldom (mostly in girls).

Gonococci affect the parts of genital system, covered with monolayer cylindric epithelium (the urethra, para urethral ducts, excretory ducts of greater vestibular glands, the cervical duct, endometrium, endocervix) and endothelium (synovial membranes, peritoneum, embryonic endothelium, ovaries), as well as the urinary bladder, the rectum, fauces, conjunctiva. In most cases the primary place of gonococci location is endocervix, the distal part of the urethra, pararectal ducts. However, gonococci as well as chlamydiae are those few micro organisms capable cause infectious lesion of the Fallopian tubes.

During the microscopic examination of the prep taken from the cervical duct and the distal part of the urethra, the typical signs for gonococci are revealed: the intracellular location (in protoplasm of polinuclear leucocytes), bean-like form.

Phagocytosis of gonococcus by trichomonas bringing to persistence of the infection has an important meaning.

The vaginal mucosa, covered with multilayer cylindrical epithelium is stable to gonorrhoeal infection as a rule. Gonorrhoea spreads to directly mucous membranes (the canalicular way of spreading without preliminary damage of tissues) more often, though gonococci may get into the blood as well. There is no immunity to gonorrhoea, the reinfection can have the same acute course as the primary disease has.

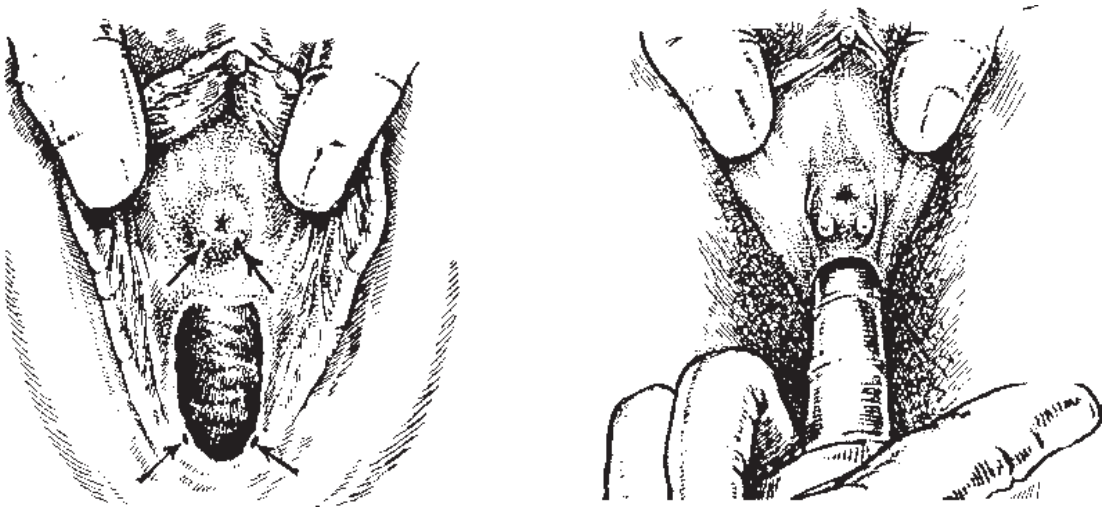
Gonococci are sensible to high temperature (above 55ºC), drying out, the effect of chemical compounds (salts of silver and mercury). During the treatment with sulfonamides and antibiotics in small doses, L-forms of bacteria can form.

Clinical picture. The incubation period lasts from 3 to 15 days. It is distinguished a *fresh* gonorrhoea (which lasts up to 2 months) and chronic (more than 2 months). A fresh gonorrhoea in its part is divided in acute, subacute and torpid (less symptomatically).

According to location there are the gonorrhoea of the lower genital and urethral tracts (urethritis, the infection of paraurethral ducts, excretory ducts of greater vestibular glands, endocervicitis, seldom — vulvitis and vaginitis) and ascending gonorrhoea (inflammatory diseases of the uterus, appendages, peritoneum).

Gonorrhoea of the lower urinogenital tract. The urethra, mucous membrane of the cervical duct, the urethral glands (urethral, paraurethral) and the greater vestibular glands (Bartholin's) are more often affected (Fig. 15, *a*), the rectum is seldom affected. The clinical symptoms are not promoted even in fresh gonorrhoea cases. In urethritis the patients complain of pain and colic, which appear at the beginning of urination; during lesion of the cervix of the urinary bladder they complain of the acceleration of urination which completes with colic. Hypostasis and hyperaemia of urethral lips, sensitivity during palpation are found out during the objective examination. When the infection involves the *urethral glands*, local hyperaemia arises, yellow pus is observed while pressing the excretory ducts area (Fig. 15, *b*).

The patients suffering from chronic urethritis have no discharge, the urethra's induration is palpated through the anterior vaginal wall.



a *b*

Fig. 15. Gonorrhoea of the lower urogenital tract:
a — typical localization of primary focus of infection: excretory ducts of the glands of the urethra (urethral) and greater vestibular glands of the vagina (Bartholin's); *b* — purulent discharge while pressing on the paraurethral ducts from the vagina's side

When the *greater vestibular glands are injured*, hyperaemia appears around the external duct's aperture (gonorrhoeal spots), little mucous purulent discharge appear, the ducts are sensitive and oedematous on palpation. The discharge are absent during the chronic form. In case of occlusion of external duct's aperture the pus is accumulating in the duct itself and strains it, making a pseudoabscess of the gland and the true abscess originates during the joining of another pathogenic flora and spreading of the infection.

In *gonorrhoeal endocervicitis* the patients complain of mucous purulent discharge (leucorrhoea), nagging pain in the lower abdomen and sacrum. Oedema and hyperaemia of the uterine cervix, quite often erosion around the external os, mucopurulent discharge are revealed with the acute form of the disease during the examination with the help of the vaginal specula.

Hypertrophy, erosion of the cervix**,** poor mucous discharge from the cervical duct can be observed during the chronic form.

Gonorrhoeal vaginitis and vulvovaginitis can arise in infancy, pregnancy, postmenopausal period. There are complaints of pus, burning, vaginal itching. During the acute process, the vaginal mucosa is hyperaemic, often cyanotic with green and yellow discharge.

The acute form *gonorrhoeal proctitis* is accompanied by unpleasant sensations, tenesmus**,** burning, itching in the anus, poor mucous purulent discharge. Skin hyperemia, chaps, fold oedema are observed around the anus.

Gonorrhoea of the upper genital tract. Untimely diagnosis and improper treatment of patients suffering from gonorrhoea of the lower urino-genital tract, intrauterine manipulations, cervical biopsy, menstruation, postpartum and postabortive periods, hygiene neglect promote the infection spreading above the cervical internal os. Pathologic processes which take place during gonorrhoeal endometritis, salpingitis, adnexitis (salpingoophoritis), pelvioperitonitis and peritonitis are similar to those in inflammatory diseases of another aetiology. The presence of bloody and purulent discharge from the genital tract, bilateral lesion of the uterine appendages, the onset of the disease just after the menstruation or intrauterine interferences, fast clinical remission (during 1–2 days) under condition of a proper treatment are evidence of a gonorrhoeal character of the inflammatory disease.

Gonorrhoeal endometritis as a rule is characterized by lesion of the basal endometrial layer (after menstruation, delivery, abortion), gonococci penetrate less often in the period of proliferative and secretory changes in the endometrium. The inflammatory process inhibits the regeneration and subsequent cyclic processes in the endometrium, that's why delay of menstruation is possible. Endomyometritis develops in presence of the chronic process.

At the acute form of the disease patients feel heaviness at the lower abdomen, weakness, they complain of headache, thick serous purulent, saneous or bloody discharge. Purperant women have the body temperature rise, spasmodic pain due to uterine outflow disorders. On bimanual gynaecological examination the enlarged tender uterus of a soft consistence is palpated. Slight leukocytosis or a normal leucocytes number against a background of considerably elevated ESR are marked in the blood. Chronic endometritis presents with disorders of menstruation and reproductive functions, miscarriage. Postpartum gonorrhoeal endometritis is noted for lat-

er presentation (on the 2nd–3rd week after delivery) the temperature rise up to 38ºC once or twice within first days of the postpartum period.

As a rule, *gonorrhoeal salpingitis and adnexitis (salpingoophoritis)* are bilateral. The excretion of serous purulent exudate brings to fimbriae adhesion of the Fallopian tubes with the sactosalpinx formation. The chronic stage is characterized by catricial and adhesive processes, the Fallopian tube's motor function and permeability are disturbed. Hydro-, piosalpinx, pio-ovarium develop, though these processes are not specific. The disease can be revealed only on examination of the patient on occasion of infertility or menstrual dysfunction. Purulent adnexitis is characterized by disorders of general condition, pain at the lower abdomen, chill, the temperature rise (38ºC), leukocytosis, increased ESR (till 40–60 mm/h). Bilateral tubo-ovarian inflammatory formations and abscesses develop in case of prolong treatment. On bimanual gynaecological examination the bilateral adnexal enlargement is determined; pelvic adhesions prevail in chronic adnexitis (Fig. 16).

As a rule*, gonorrhoeal pelvioperitonitis* starts in peritoneal membrane of the Fallopian tubes, involving the uterine peritoneum, pelvis and abdominal cavity (seldom). The disease is characterized by a sudden onset (acute pain at the lower abdomen, nausea, vomiting, constipation, flatulence, temperature rise above 38ºC). Abdominal pain during palpation, promoted muscular protection, peritoneal irritation symptoms are observed. The tongue is dry, covered with a patch. Bimanual examination presents difficulty due to acute vaginal tenderness.

Because of the increase of peritoneal symptoms, in spite of treatment, the patients' state becomes worse, the pain spreads to the mesogastrium, the fever continues, the peritoneal irritating symptoms are growing, the leucocytes and ESR amount elevates. Extended pain in the abdominal area, nausea, vomiting, fever (above 38ºC), tachycardia (above 90–100 b/min), chill, watery stool, rapid painful urination, general weakness, purulent bloody discharge from the genital tract can appear during diffuse gonorrhoeal peritonitis.

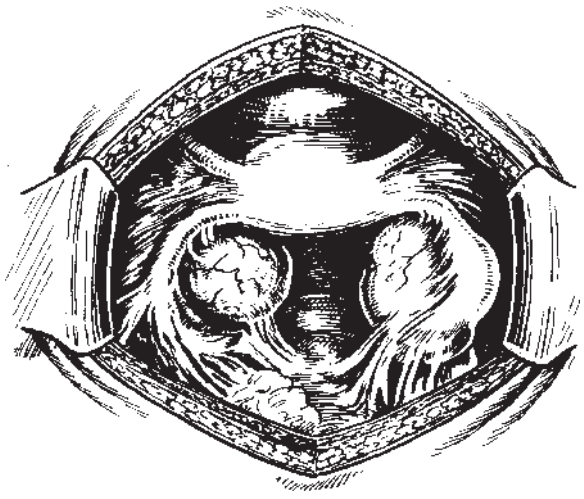


Fig. 16. Adhesive process in the pelvis and enlargement of the uterine appendages during gonorrheal adnexitis (salpingoophoritis)

The *diagnosis* is based on the anamnesis data, clinical symptoms, results of gynaecological and laboratory examinations. The analysis for bacterioscopic and bacteriological examinations is taken from the cervical duct, greater vestibular glands, the duct of the urethral glands. The wash-outs from the rectum and abdominal cavity are taken if it is necessary. In case of long and torpid treatment of the disease, the bacterioscopic and bacteriological examinations are made three times (during three days) with preliminary provocation.

There are some ways of provocation:

1) *chemical* (smearing of the urethra with 1–2% silver nitrate solution 1–2 cm deep, lower part of the rectum 4 cm deep with 1% Lugol's iodine solution in glycerine, cervical duct 1–1.5 cm deep with 2–5% silver nitrate solution);

2) *biological* — intramuscular gonovaccine injections (500 mln of microbic bodies) or gonovaccine with pyrogenal at the same time (200 minimal pyrogenic doses — MPG);

3) *physiological* (swabs are taken on the 2nd–4th menstruation day);

4) *alimentary* (piquant, salty food, beer and etc.);

5) *combined*.

The most effective combined provocation is a provocation when chemical and biological provocations are made at the same day against a background of physiotherapy treatment. The swabs from the infectious foci are taken every 24–48 h, inoculations are taken every 72 h. If a big amount of leucocytes and epithelial cells are found on bacterioscopy when the bacterial flora is absent, the smear is considered to be gonorrhoea suspicious and another bacterioscopy is carried out after a combined provocation and bacteriological examination.

Treatment should be complex and aetiopathogenetic. Bed rest in the acute period; ice on the abdomen off and on, light diet; complete failure of using alcohol; the regulation of gut function are recommended. The use of liquid is limited. Infussion (dextrans, crystalloids, albuminous and potassium preparations), desensitizing, vitaminous therapy in accordance with common treatment principles is prescribed if there are any signs of general intoxication, temperature rise.

Antibacterial therapy is realized taking into account the possible microbic aerobic-anaerobic associations. The doses of antibiotics are increased twice, the parenteral administration of the preparations is recommended in case of ascending gonorrhoea. Penicillins do not lose their meaning during the treatment of gonorrhoeal patients: benzylpenicillin (natrium and potassium salts) in a single dose from 1,000,000 to 2,000,000 U, in a daily dose till

20,000,000 U during 5 days if there is an ascending process; oxacillin, ampicillin — 1 g 4 times intramuscularly during 7 days with the ascending process. Bicillin-1, bicillin-3 are used if there is gonorrhoea of the lower female reproductive tract. Cephalosporins (ceporin, kefzol) are taken in a dose of 1 g 4 times a day intramuscularly, tetracycline (doxycycline) — 100 mg 2 times a day per os or intravenously during 10 days; macrolids (erythromicin) — 500 mg 4 times a day during 7 days; aminoglycosides (gentamicin, tobramicin) — 1.5 mg/kg 3 times a day during 7 days; fluorinequinolones (cyproby, cyprinol) — 250–500 mg 2 times a day during 10 days. Taking into account the possibility of microbial associations, the most effective is the use of antibiotic combinations in generally accepted doses: doxycycline + cephoxitin, clindamycin + gentamicin; doxycycline + metronidazole.

The specific gonococcal vaccination and non-specific immune modulating remedies (pyrogenal, prodigiosan, autohemotherapy) are used in immune therapy. It is recommended to carry out the immune therapy in cases of torpid and chronic course of the disease with subsequent prescription of antibacterial medication. Contraindications to immune therapy are tuberculosis, cardiovascular system disorders, essential hypertension, severe hepatic and renal illnesses, exhaustion, anemia, allergy, menstruation, pregnancy, serious forms of diabetes mellitus, lesion of the central nervous system.

Gonovaccine is injected intramuscularly or intracutaneously; the reaction on the administration can be general (indisposition, headache, weakness), temperature, focal (discharge reinforcement, sensitivity in the affected area) and local (sensitivity and hyperaemia in the injection place). The first dose is 150–250 mg of microbe bodies; the injections are made in 1–2 days (it depends on a patient's organism reaction), gradually increase the dose by 150–250 mln of microbe bodies (6–8 injections in a whole).

Pyrogenal is prescribed intramusculary by 20–50 MPD with the administration in 1–2 days gradually increase the dose in 25–75–100 MPD according to the reaction (a maximal single dose is 1,000 MPD).

The *local treatment* includes hot hip-baths with permanganate potassium solution (1:8,000), camomile decoction (1 table-spoon for 2 glasses of water); vaginal baths with 3% protargol and colargol solutions; microenema with 50 mg of 1% protargol solution; urinary bladder's ablution with permanganate potassium solution (1:10,000); instillations with 1–2% protargol solution, 0.5% silver nitrate solution.

Physiotherapy treatment is used in all gonorrhoeal forms (UHF therapy, ultrasound, inductothermy, diathermy, medicine electrophoresis, mud cure).

If the complex antiphlogistic therapy is ineffective, patients with pelvioperitonitis are performed laparascopy (specification of inflammatory process location, abdominal cavity drainage, the administration of antimicrobic and disintoxicating preparations, the pathologic exudation evacuation) with diagnostic and medicinal purpose during 12–48 h. Patients with diffuse peritonitis need the urgent surgical intervention the extent of which depends on destructive changes in the pelvis, woman's age and her health condition.

The recovery criterion of gonorrhoeal patients is the gonococci absence in smears after realized provocation complex within three menstrual cycles. If it is impossible to detect the disease origin, the patients should be under gynaecological observation during 6 months.

GENITAL TUBERCULOSIS

Female genital tuberculosis is observed quite seldom and is the second nonpulmonary disease and relates to so called "true" chronic IDLPO. The infection gets into the genitalia hemato- or lymphogenously from the primary tubercular focus (lungs, guts). The disease arises in the childhood or youthful age most often and frequently remains undetected. In most cases the clinical presentations of genital tuberculosis coincide with hormonal change periods in a female organism, puberty, pregnancy, menopause.

Infertility is observed in 90–95% of women suffering from genital tuberculosis. Tuberculosis is revealed in 10–22% on the examination of such patients.

Tubercular micobacteria affect the Fallopian tubes (97%), endo- and miometrium (33%) most often. At present vaginal and vulvar tuberculosis cases are almost absent, and is evidence of a neglected disease form.

Clinical picture. Vaginal tuberculosis manifests itself as superficial ulcers on mucous membrane mainly localized at fornices area. The ulcers presence on the internal surface of the small pudendal lips, which are sensitive during palpation, is typical for vulvar tuberculosis.

In most cases tubercular endometritis has no characteristic symptomatology. The main complaint is infertility, often primary. The abdominal and waist pain is not connected with menstruation pain and caused by pelvic adhesions. Menstrual cycle abnormality can have the character of amenorrhea, algodys- or oligoamenorrhea.

In case of adnexal tuberculosis, the tuboovarian inflammatory masses should be surgically ablated (Fig. 17).

Diagnosis of the disease is difficult as the clinical signs are similar to those observed in non-specific inflammatory diseases. Anamnestic data (pul-

Fig. 17. Tuberculosis of the appendages and peritoneum of the uterus

monary tuberculosis in the past, a contact with patients suffering from the open tubercular form), positive results of the tuberculin test, data of bacteriological and histological examinations, radiography, metrosalpingography, (uterine cavity deformation, synechiae formation) play a great role. Non-specific cervical pathology is often diagnosed at colposcopy.

The subcutaneous tuberculin test with 20 or 59 TU (tuberculin U) is the most valuable of the tuberculin reactions. The clinical blood examination is realized during 5 days against a background of the tuberculin test; blood albuminous fractions, C-reactive protein are examined, the cellular and humeral antitubercular immunity is estimated 48 h before and after subcutaneous tuberculin administration. A diagnostic uterine curretge is carried out 2–3 days before the menstruation (if there are no contraindications) in suspicion at genital tuberculosis. The taken swabs are histologically and bacteriologically examined.

Multiple adhesions are found out on laparoscopy; calcified Fallopian tubes' surface, peritoneum, and lymph nodes; tuberculoma; contraction, thickening, segmentation, the peristalsis absence of the Fallopian tubes; peritoneal miliary eruptions.

Treatment. The specific treatment is indicated in the following cases: 1) active tubercular process, 2) histologically confirmed tubercular endometritis and adnexitis; 3) separation of tubercular micobacteria; 4) nidal reaction on subcutaneous tuberculin administration; 5) the presence of tubercular intoxication. A continuous antibacterial therapy in the antitubercular prophylactic centre lasts for 12–24 months depending on affection extent. Riphampicin, isoniazid, ethambutol combinations are used in doses depending on a woman's body weight. Lidaze, zinc electrophoresis or sodium thiosulphate are used from the first treatment days; sinusoidal modulated currents, cortisol phonophoresis (12–15 procedures) are used in series after perifocal inflammation liquidation in 4 weeks after the last physiotherapeutic procedure. It is expedient to realize the patients rehabilitation in a specialized sanatorium after completing the main treatment course in the hospital.

Patients should be under medical observation for 2 years on average; if relapses are absent they are struck off the register.

TRICHOMONIASIS

Trichomononiasis is one of the most wide-spread inflammatory diseases of the lower female reproductive tract caused by vaginal trichomonas —flagellated oviform protozoans. *Trichomonas vaginalis* is little bigger than a white blood cell and has four flagella on anteriolateral undulating membrane. Among all protozoan parasites trichomonas trophozoits are very stable to temperature shifts and keep vitality at 0ºC during 5 days.

Trichomonas vaginalis inhibits a human. The infection is predominantly sexually transmitted. A nonsexual way (quite seldom!) is possible by way of medical staff's hands if they do not follow asepsis rules as well as through personal hygiene goods (sponges, towels, bed-clothes). A non-sexual way of infection is observed mostly in girls.

Trichomonas invade predominantly the vagina and the cervix; the most auspicious conditions for their penetration is pH which exceeds 5.0. The inflammatory process can involve the urethra, urinary bladder, paraurethral glands as well. Trichomonas get into the greater vestibular glands (Bartholin's), rectum, uterus and its appendages rarely.

Trichomonal infection arise in 25% of women, but only 20% of them can have symptoms of the disease. Most infected partners have asymptomatic disease course.

Clinical picture. There is trichomononiasis with acute, subacute and torpid (less symptomatic) course, chronic (which lasts more than 2 months) and asymptomatic (trichomonal carrying). The incubation period ranges from 3 days to 3–4 weeks, on average 10–14 days.

Trichomonal vulvitis and vestibulitis are met in girls more often. If there is an acute inflammation, the patients complain of burning in external genitalia, watery, purulent, frothy yellow and green discharge, itching, sometimes imperative feeling of urination. The exam reveales edematic hyperaemic mucosa of the vulva and vestibule of the vagina, covered with thin pus: punctate eputhelial papillae can also be observed. If the process has a chronic character, the patients complain of itching, vaginal discharge with unpleasant odour. A typical clinical picture of the disease can not be observed in 80% of infected women.

In case of *trichomonal urethritis* development the patients may have colic and pain during urination. On the vaginal examination the lips of urethral external aperture look oedematic, hyperaemic, pus ex-

udes when pressing. The chronic process is often asymptomatic.

In acute trichomonal colpitis (vaginitis) profuse purulent frothy green discharge with unpleasant odour, sometimes with blood admixture, itching, burning, dyspareunia can disturb patients. Poor intermenstrual ("spotting") and postcoital bloody discharge can also be the symptoms of trichomonal infection. Vaginal mucosa is intensely hyperaemic, edematous, with punctated haemorrhages. In chronic trichomoniasis, patients complain mainly of periodical itching and leucorrhoea.

Patients suffering from *trichomonal cervicitis* have an edematous hyperaemic cervix with subepithelial haemorrhages ("strawberry cervix"); the true erosion can be formed.

Diagnosis is based on complains of patients, anamnesis data, clinical picture of the disease and the *trichomonae vaginalis* presence via microscopic examinations of pathologic material (discharge from the vagina, cervical canal, urine analysis, etc.). Trichomonas are found in wet prep (with solidum chloride isotonic solution) or with the help of immune-fluorescent examination.

Treatment is necessary for both sexual partners. Sexual intercourse is not allowed during the treatment and subsequent control period. The mainstay of treatment is metronidazole (trichopol, flagyl, efloran), other metronidazole and ornidazole derivatives (tiberal, artican, naxogin) are used. Both partners should refuse alcohol during the treatment course with metronidazole (the appearance of abdominal pains, hot flushes are possible). 5.5 g of preparation are used for the therapy course (the maximal course dose is up to 7.5–10 g). Different treatment regimens with metronidazole are used: (1) 250 mg 3 times a day during 7 days; (2) 500 mg 2 times a day during 7 days; (3) a single dose of 2 g orally; (4) two doses by 1 mg each during 12 h; (5) within first 4 days — 250 mg 3 times a day, the next four days — 250 mg 2 times a day; (6) the first day — 500 mg 2 times a day, the second — 250 mg 3 times a day and the next day — 250 mg 2 times a day. Tinidazole (fazigin) is prescribed orally in a dose of 2 g (4 tablets by 500 mg each). The effectiveness of each treatment regimen is about 95%.

75% of metronidazole or dalacyn gel are used topically by 5 g once a day during 5 days; Klion-D, 1 Table a day intravaginally during 7 days; vaginal suppositories "Metronidazole", "Flagyl", "Terzinan" — 1 suppository into the vagina before going to bed during 6–10 days, a preliminary vaginal antiseptic irrigation (0.05% chlorinehexidine solution, cammomile, sage infusions, etc.) is recommended. The metronidazole treatment is contraindicated in the first trimester of pregnancy). If the trichomoniasis symptoms are marked in the II–III trimester of pregnancy, a single metronidazole dose (2 g) can be prescribed as well as the topical treatment.

Girls at the age of 1–5 years old are applied metronidazole in a dose of 1/3 of tablet (0.083 g) 2–3 times a day ; at 6–10 years — 1/2 of tablet (125 mg) 2 times a day; at 11–15 years — 250 mg 2 times a day. The treatment course is 10 days.

Girls with acute vaginitis receive the vaginal irrigation with cammomile and sage infusions, the vaginal walls processing with 4% methylene blue using a thin catheter.

The treatment of patients suffering from resistant forms of trichomonal vaginitis is carried out according to the following scheme: 1 g of metronidazole orally 2 times a day for 7 days, or metrogil (contains 500 mg of metronidazole) intravenously during 20 min 3 times a day for 5–7 days.

Recovery criterion. The first control (swabs taking) is performed in 7–10 days after treatment ending, later on during three menstrual cycles (3 months). The examinations are carried out before and after menstruation, once a month in girls. If trichomonas are absent in smears during next three menstrual cycles, the patients make a complete recovery.

Immune solcotrichovac — a system vaccine which contains some variable lactobacteria cultures obtained from trichomonas infected patients is recommended for a long-term prophylaxis of recurring infections and relapses.

CANDIDOSIS

Candidosis (candidiasis) is a wide-spread disease of the lower female reproductive tract, caused by yeast-like fungi of *Candida albicans* in 67–95% of cases. Candidosis is characterized by lesion of the vaginal mucosa which spreads to the vulva (candidosis vulvovaginitis) and the cervix. The pathogens — fungi of Candida are normal enteric and perineal flora and can be secreted from the vagina of practically healthy women if the clinical signs of vaginitis are absent. Pregnancy, the use of broad spectrum antibiotics, oral contraceptives as well as the immunosupression, diabetes mellitus, intestinal dysbacteriosis can be the factors which are favourable for mycosis development.

The Candida fungi get into the female reproductive tracts out of guts or exogenous sources of infection during immediate contact as well as through infected objects. The infection can be the result of a sexual intercourse, though it is not the main way.

Clinical picture. Patients complain of itching, burning in external genitalia, sometimes strongly pronounced. As a rule itching intensifies after long walking during menstruation. The vulva and vagina are hyperaemic, edematous with excoriations from scratchings. The white discharge can be watery, profuse, cottage cheese-like plaques adjoined to the vaginal mucosa or thick, cream-like green and white.

The odour of the vaginal discharge is sourish or absolutely absent. There is a dependence between the extent of the process spreading and the amount of the vaginal discharge is observed. Urination delay and the infection of urine tracts may arise during vulvitis.

Diagnosis. A typical sign of the disease is grey and white plaques on the affected vaginal mucosa and ectocervix. They are of oval or irregular form, 3–5 mm in diameter, locate separately or merge together. The results of bacterioscopic smear (wet KCl prep, Gramm's coloring) confirm the candidosis diagnosis.

The plaques consist of fungal pseudomycelium, epithelial and white blood cells. At the acute stage, the vaginal mucosa is hyperaemic, edematous, and unchanged — at the chronic stage. Strongly hyperaemic mucosa inclined to haemorrhage appears at the place of a removed plaque. In acute candidosis such changes can be observed in the area of big and small labia, clitoris, around the urethra's aperture. The mentioned symptoms are less expressed at the chronic stage.

The hidden forms of the disease have an almost asymptomatic course from the very onset with unsteady and non-intense itching or discharge which appear from time to time and don't disturb a woman very much.

The candidosis course is long (often during months and even years). The acute condition is often observed before menstuation or during intercurrent disease. The treatment doesn't often give stable results, relapses are possible after therapy courses, especially in the presence of other candidosis foci in the organism. Another development of the disease in 1 month and more after the effective treatment is considered to be a reinfection.

Treatment should be complex and aimed at liquidation of the agent and concomitant diseases therapy. The sexual partner treatment is carried out in persistant cases or infection relapses in women even if the disease symptoms are absent. Suppositories, vaginal tablets, gels, creams are prescribed topically; syringes with 2% natrii hydrogen carbonate solution, potassium permanganate (1:5000), vaginal tampon wetted with 10–20% natrii tetraborate (barax) solution in glycerin. Ointments with antimycotic preparations are effective: nystatin, levorin, klotrimazole, micomazole, econazole, terconazole, butoconazole, tioconazole, which are prescribed before going to bed during 3–7 days. "Kandibene" (suppositories, tablets, gel, 1% cream, ointment); "Pimafucin" (vaginal and oral tablets, suppositories, cream); "Poliginax" (suppositories), "Nisoral" (tablets, ointment), Hyno-Travohen (suppositories, ointment) and etc. are used locally. Tablets, suppositories and cream are inserted in the vagina's back fornix with the help of a special applicator once a day before going to bed; the vulva is treated with cream, ointment, gel. Klotrimozole cream (1%) is also used for instillation in the urethra daily during 5–6 months.

Nystatin is prescribed in a daily dose of 2,000,000 U (500,000 U 4 times a day), Diphlucan (Fluconasol) — 150 mg (1 tablet) at once, if it is necessary — 150 mg more once a day for 3–4 days. If necessary 150 mg of diphlucan for prophylaxis once a month. Pimaphucin (tablets) is prescribed orally, 0.1 g 4 times a day for 5 days, orungal capsules if there are often relapses.

Cream, tablets which contain klotrimazole are not used during pregnancy; it is recommended to use such preparations as "Pimaphucin", "Pimaphucort", "Polizinax", "Terzinan", "Hyno-Paveril".

Water-soluble levorin's or nystatin's sodium salts (20,000 U per 1 ml of water) are used for girls' treatment with candidose vulvovaginitis. Solutions are injected into the vagina with the help of thin elastic catheter daily (1–2 times a day) during 2–3 weeks. Vulva's area is treated with actinomycotic creams or ointments (levorine, nystatine, "Klotrimazole", "Pimaphucin", "Nisoral" and etc.). 1% solution of gentian violet and methylene blue are also used, vitamin therapy is realized.

In prolong treatment, topical preparations are prescribed during 14–28 days and to continue the therapy during the next menstrual cycle. In failure of topical drugs, ketoconazole or diphlucan (150 mg orally once a month) are prescribed.

CHLAMYDIOSIS

Aetiology and Pathogenesis. Chlamydiosis' agent is *Chlamydia trachomatis*, the bacteria similar to Gram-negative bacilli which can grow only in tissue culture. Chlamydiae have some properties inherent to viruses and a capability for obligate intracellular parasitizing. Chlamydia invade only cycindrical epithelium except for L-form bacteria. Chlamydial infection incidence reaches 50% in women suffering from inflammatory diseases of the pelvis and the lower female reproductive tract. The disease is sexually transmitted, that's why young single women who have many sexual partners make up a risk group of chlamydial infection.

Chlamydial cervicitis occurs in women with cervical ectopia as well as changes of cervical mucosa due to oral intrauterine contraceptives using. Chlamydia are often found in microbic associations of patients suffering from gonorrhoea and trichomoniasis, and pelvioperitonitis, tuboovarial abscess as well. If the treatment is not carried out, chlamydia penetrate from the cervical duct to the uterus and get into the Fallopian tubes (endosalpinx) by an intracanicular way. Abortions, intrauterine contraception are conductive to chlamydial endometritis development.

If gonorrhoea was the main reason of salpingitis and tubal infertility in 60s of the XX century, today

salpingitis of chlamydial aetiology is observed in 30–67% of cases (till 80%) and gonorrhoeal infection provoke the development of this disease only in 10% of cases.

Obligate intracellular cyclic development is typical for chlamydia. Chlamydial microcolonies — intracellular inclusions which are composed of elementary intermediate and reticular bodies — are forming in host cells. Intracellular cyclic development lasts for 2–3 days whereupon an infected cell is destroying and newly formed chlamydia get into the intracellular area. Under certain conditions chlamydiae can be transformed in L-forms of little sensitivity to antibiotics and cause a slow-acting and a long-lasting infection. Chlamydia are not sensitive to antibiotics, which leads to less symptomatic subclinical or latent chlamydial course.

Clinical picture. The incubation period lasts for 20–30 days. The disease is characterized by a prolong course, unexpressed symptoms, susceptibility to relapses. The clinical chlamydial manifestations are non-specific, the disease proceeds often asymptomatically. The patients complain of pain in the affected area and discharge. Chlamydia can infect the cervix (endocervix), the urethra, the greater vestibular glands (Bartholin's), endometrium, Fallopian tubes, rectum, conjunctive, oropharynx, etc. Chlamydiae are the etiological factor of *venereal lymphogranuloma*.

Cervical mucosa is a primary nidus of the infection. An acute stage of chlamydial endocervicitis is characterized by serous purulent discharge from the cervical duct, hyperaemia around the uterine aperture (external pharynx), hypostasis of the vaginal part of the cervix. In a chronic stage of the disease discharge become muco-purulent, a cervical pseudoerosion often arises (ectopia of the cylindrical epithelium). The patients with chronic chlamydial infection are suffering from cervicitis, which is accompanied by cervical thickening and induration.

Chlamydial urethritis can be accompanied by dysuria or have an asymptomatic course.

Salpingitis of chlamydial origin also has no specific symptoms. However, it can cause tubal infertility almost in 50% of cases.

Diagnosis. Anamnesis data (urethritis, epididymitis and other urogenital diseases of a sexual partner), infertility, infectious urogenital diseases in the patient's history, gonorrhoea in particular are the reason for making diagnosis.

Laboratory diagnosis of chlamydiosis is difficult, expensive, and needs special equipment. The most wide-spread modern methods include swabs taking and revealing of the agent, its antigen or antibodies to chlamydiae with the use of immune fluorescent and immunoenzymatic methods (test sensitivity — over 90%, specificity — 95% in case of symptomatic infection and correctly taken smear). Many cells of the cylindrical epithelium, some erythrocytes, a little of mucus are revealed in the analysis. The "golden standard" of diagnosis is chlamydial culture allocation. However, this method is more expensive and needs much time. The DNA-probe diagnosis, polymerase chain reaction approximates to the cultural one by sensitivity and specificity, but its shortcoming is a big per cent of wrongly-positive results. Modern method of chlamydial diagnosis is the use of antigens to albumens of thermal shock proteins, which are exuded by the chlamydial membrane.

Infertility, abdominal pregnancy, chronic pelvic pain as a result of multiple adhesions are *the complications* of chlamydial salpingitis. Chlamydial infection of the Fallopian tubes can cause infertility (even at patency) when the ciliary epithelium is damaged and incapable to provide an ovule's transport. According to up-to-date conceptions, tubal infertility is associated with chlamydial infection in 70% of cases. The negative influence of chlamydial infection on ovogenesis, spermatogenesis and fertilization process is proved. Endometrial lesion, pathologic processes in the cervix (endocervicitis) can be the reasons of chlamydial infertility.

During salpingitis the peritoneal dissemination of chlamydial infection can bring to appearance of perisalpingitis, perihepatitis (the formation of ribbon-like scarring or Fitz-Hue—Curtis syndrome) as well as owing to gonorrhoeal infection, peritonitis.

Pregnant women suffering from chlamydiosis can have spontaneous miscarriage, premature birth, pre-natal infection of newborns (conjunctivitis, pneumonia, urethritis, vulvitis).

Treatment is directed to prevention of severe complications (infertility, ectopic pregnancy), prophylaxis of a sexual partner's infection and prenatal fetus' infection during pregnancy. Synchronous examination and treatment of a woman's sexual partner, as well as cessation of sexual intercourses untill full recovery, prohibition of using alcohol, pungent food, excessive physical and psychical activity are necessary.

Tetracyclines (vibramicin, doxycyclin, tetracyclin) and antibiotics — macrolides (erythromycin, rovomycin, azithromycin, roxytromycin) are most effective for etiotrophic treatment. Owing to peculiarity of bacterial growth (formation of elementary and reticular bodies) the treatment should continue no less than 7 days.

Doxycycline (vibramicin) is the preparation of choice — 100 mg 2 times a day during 7–14 days, or tetracycline — 500 mg orally 4 times a day for 7–14 days.

An alternative drug for treatment of pregnants with allergy to tetracyclines is erythromycin (500–800 mg orally 4 times a day during 7 days or sulfoxazol — 500–800 mg orally 4 times a day during 10 days if the organism is unresponsive to erythromycin).

Azithromycin (Sumamed) is prescribed during acute infection in a single 1 g dose; at the chronic process the following treatment plan is applied: the 1st day — 1 g of the drug, then — 500 mg once a day for 4 days.

Roxytromycin (Rulid) is prescribed in 150 mg 2 times a day, the course of treatment is 8–10 days.

Among the preparations of fluorinequinolones the most effective against chlamydiosis are ofloxacin (Tarivid) — 300 mg orally 2 times a day for 7–10 days and lomefloxacin — 600 mg once a day during 7 days. Taking into account undesirability of antibiotic long use, a pulse-therapy is used as 7–10 day courses; then, if it is necessary, (in chronic disease forms) the course of treatment should be repeated 2–3 times more after the same interval (7–10 days).

A simultaneous candidosis prophylaxis includes prescription of 150 mg of diphlucan orally or nystatin in a dose of 2,000,000 U daily, or nizoral — 0.02 g 2 times a day during the first treatment period of patients with chlamydiosis.

ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS)

Aetiology and Pathogenesis. This syndrome was described for the first time in 1981, and some years later, in 1983 the agent of this disease was discovered. According to statistical data, the HIV-infection incidence is growing steadily. Homosexuals and bisexuals, drug addicts, prostitutes, patients suffering from haemophilia, recipients of untested blood preparations, single young women who have many sexual partners make up a group of risk. The main ways of HIV-infection transmission are the following: 1) sexual; 2) transplacental (from mother to fetus); 3) parenteral (via infected blood). Due to high virus consentration in sperm, microtraumas of female genitalia mucous membrane during a sexual intercourse as well as concomitent diseases can promote the infection. Due to the fact the viral transmission from male to female occurs more often than from female to male.

Virus has tropism to cells of a lymphoid line: T-lymphosytes-helpers, macrophages, monocytes. Viral lesion of T-helpers causes functional immune abnormalities. After a period of compensatory changes a decompensatory period begins, the clinical signs of which are decrease in resistibility to conditionally pathogenic microorganisms, tumours formation, lethal encephalitis development.

Clinical picture. Duration of the incubation period between viral penitration and seroconversion lasts about 12 weeks; then periods of primary and secondary manifestations and a lesion period follow. The *primary manifestation period* lasts for 1.5 months and manifests itself as a temperature rise, enlarged lymph nodes, liver, spleen, irruptions, diarrhoea, sometimes encephalitis.

The secondary manifestations period continues from some months till 8–10 years. The most characteristic sign is lymphoadenomatosis with the lesion of the nervous system (encephalitis with dementia). T-helpers decrease, immunoglobulin increase are found out in the blood.

The last period lasts from some months to 3–5 years and characterized by abrupt fall in immunity, development of recurrent oral cavity candidosis, herpes, pyoderma, furunculosis, cachexy, constant fever (typical AIDS manifestations).

Typical AIDS symptoms are pneumocystic pneumonia; tracheal, lung candidosis; criptosporidiosis with diarrhoea; cytomegaloviral affection of organs; plural ulcers on mucous membranes and skin caused by herpes simplex; herpetic pneumonia; brain lymphoma; Kaposi's sarcoma in persons who are under 60; sepsis, abscesses of the internal organs, bones and joints. Children who were born from infected mothers have enlarged lymph nodes, liver, spleen, diarrhoea, fever, viral and bacterial infections. Hypotrophy, cranial malformations arise during prenatal fetus' infection. In view of infection's danger during beeding with breast infected milk, donory of the last one should be under severe control as indications to haemotransfusion.

Diagnosis. All patients with a high risk to sexually transmitted diseases, drug addicts, blood recipients are subjected to serologic testing on HIV. Screening test is the definition of antiviral antibodies with the help of enzyme-linked immunosorbent assay (ELISA). If the test result is positive, it should be repeated and confirmed by blood examination on virus' antigen (Western blot).

Treatment. Zidovudine (azidothymidine) which blocks the viral replication is used. Zidovudine is prescribed to pregnant women by 100 mg 5 times a day for the whole gestational period for prophylaxis of prenatal fetal infection. Patients and women with positive serologic reaction are to be examined every 6 months.

Today *prophylaxis* of HIV-infection is the only possible method which controls this disease, and its basis is to reduce a number of sexual partners, prevent sexual contacts with persons from the group of high risk, the use of condoms with nonoxinol-9 (lubricant, inactivating virus *in vitro*), disposable syringes.

The patients having a seropositive reaction are recommended to avoid pregnancy (sterilization, barrier contraception).

OTHER INFLAMMATORY DISEASES OF GENITALIA

Syphilis. The incidence of syphilis in young and pregnant women has a tendency to rise in Ukraine. So, the syphilis incidence among girls under 18 years old through 1990–1996 increased 12–13 times.

That's why all the patients from the risk group of sexually transmitted diseases must pass syphilis testing (Wassermann reaction).

Venereologists manage the patients suffering from syphilis in Ukraine. However, in most cases a woman who doesn't suspect her disease turns to a gynaecologist first of all, that's why one should know symptomatology of this disease.

Aetiology and Pathogenesis. Treponema pallidum is the causative agent of syphilis. In the period between 10 and 90 days after treponema penetration into the lymphatic system and circulation of the blood through the damaged skin or intact mucous membrane a firm chancre, the focus of primary infection, appears at the site of inoculation. If treatment is absent a secondary syphilis sign — generalized rash — appears 2–6 weeks later (from 2 to 6 months). Even without treatment the rash disappears within 2–6 weeks. Then the infection can transform to a latent form. The tertiary syphilis develops in 4–20 and more years after uncured primary infection. Sexual partners of a patient with primary syphilis are to be examined and treated if a contact period with a patient is till 90 days.

Clinical picture of syphilis depends on the infection stage. The *primary stage* of syphilis is characterized by formation of painless firm papules or ulcer with raised edges at the skin or mucous membranes as well as inguinal lymphoadenopathy (Fig. 18, *a*).

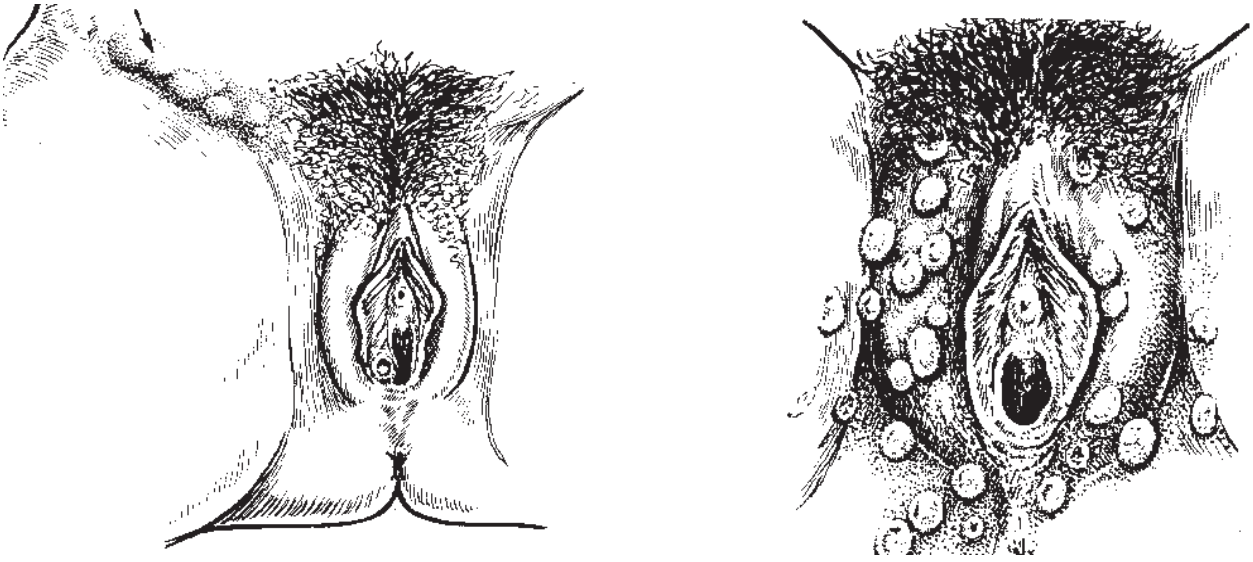
The chancres are small and hardly visible around the vagina's entrance; on cervix the firm chancre often localizes on the anterior labium, vermilion in colour. Papular rash which spreads on palms of the hands and soles of the feet are typical for the *secondary syphilis*; macular, maculopapular or pustular rash can appear on external genitalia — flat condylomas *(candyloma lata)* (Fig. 18, *b*). Non-specific polyadenopathy symptoms or virus-like syndrome often join. In latent syphilis the clinical episodes similar to those ones of secondary syphilis can be repeated but in most cases it flows asymptomatically.

Diagnosis. Only 30% of infected have clinical syphilis manifestations. Diagnosis is established on the basis of fluorescent antibodies' exposure on microscopy in a dark vision field, the Wassermann reaction. Many syphilis complications are due to untimely diagnosis and lack of treatment. These complications may develop in the cardiovascular and central nervous system as well as in skeleton, upper respiratory tract (nose, gullet, larynx), tunica mucosa of the mouth, in the eyes, liver, stomach and lymph nodes.

Treatment depends on the stage of the disease and as a rule includes a prolong penicillin use. If there is penicillin allergy, the alternative drugs are doxycycline (100 mg orally 2 times a day for 14 days), erythromycin (500 mg orally 4 times a day for 14 days) and cephthriaxone (250 mg intramuscularly once a day for 10 days). Chancroid, inguinal granuloma, venereal granuloma, contagious mollusc, parasites (pediculosis pubis, scabies) belong to so called small sexually transmitted diseases.

Chancroid (soft chancre) is caused by *Haemophilus ducreui*; the incidence of this infection is rising during last years is related to the increase in HIV infection. Chancroid can also attend to other sexually transmitted diseases. The incubation period is 2–5 days. Patients with chancroid are to be registered.

Clinical picture. Painful ulcer's appearance on the vulva with profuse contact purulent bloody discharge is typical; painful inguinal lymphadenitis is



a *b*

Fig. 18. Manifestation of syphilis:
a — primary: ulcer in the region of small pudendal lips, inguinal lymphadenopathy;
b — secondary: wide condylomas

observed more than in half of cases. On exam pustules are observed, which in a due course turn into ulcers with rough surface surrounded with erythematic vesicles and accompained by regional lymphadenopathy. Diagnosis presents a certain difficulty because of the complexity of microorganism's isolation that's why in most cases the diagnosis is clinical.

Treatment consists in keeping personal hygiene and conducting antibiotic therapy: erythromycin — 500 mg orally four times a day for 7 days or cephthriaxone — a single dose of 250 mg. Prescription of trimetoprim-sulfametoxazole (in a dose of 160/800 mg orally 2 times a day for 7 days), or amoxicilline-klavulane acid (500/125 mg orally 3 times a day for 7 days), or ciprophloxacin (500 mg orally 2 times a day for 3 days) belong to alternative treatment regimens.

As a rule ulcers are healing up within 7 days, adenopathy regression lasts for a long time. The need in lymph nodes drainage may arise as a result of their fluctuation. It is better to realize this procedure by aspiration with the needle which is injected through healthy adjoining tissues, which lowers the risk of fistulas formation.

Treatment of patient's sexual partners is obligatory like in all sexually transmitted diseases.

Inguinal granuloma is caused by *Calymmatobacterium granulomatis* and is a chronic infection which affects the vulva, the peritoneum and the inguinal area. In cases of bacterial encapsulation with mononuclear phagocytes Donovann's corpuscles which are a specific diagnostic sign of inguinal granuloma are formed. The incubation period is 8–12 weeks.

Clinical picture. Painful ulcers which are accompanied by the discharge with an odour appear on the vulva, peritoneum, inguinal area. Ulcers have a red base and clear sharp edges. In the late disease stage the festering of inguinal lymph nodes and buboes are forming. The cervical lesion can resemble carcinoma.

Diagnosis is confirmed in case of Donovann's corpuscles identification during bacterioscopy.

Treatment foresees the use of one or some bacteriostatical agents during 14–21 days: tetracycline — 500 mg 4 times a day; doxycycline — 100 mg 2 times a day or erythromycin — 500 mg 4 times a day. Contagious mollusc (*Molluscum contagiosum*) is caused by *Proxviridae* and characterized by the formation of small domes papules with a umbilicate centre and a soft middle.

Diagnosis is based on clinical data.

Treatment consists in drainage, cryotherapy or curettage of papules.

Pediculosis pubis is caused by *Phtiriius pubis* colonization. The main clinical symptom of parasitosis is itching of the vulva. It is recommended to use 1% lindane solution, aerosol "Spray-Pax" (contains natural piretrines and butoxide piperonil).

Scabies is caused by *Sarcoptes hominis*. Disease symptoms are similar to pediculosis pubis manifestations. Aerosol "Spregal" (contains esdepaletrine and piperanil butoxide.

Actinomycosis. Actinomycosis — deep mycosis is caused by radiant fungi — actinomycetes belong to very rare forms of "true" chronic specific diseases of female genitalia. The uterine appendages are affected most often. The disease is characterized by a long course, formation of infiltrations and fistulas, treatment resistance, menstrual and reproductive function disorders (tubal and ovulatory infertility) and unfavourable prognosis.

Treatment is carried out with iodine preparations, intravenous injections of penicillin, cephalosporin, aminoglycozide, tetracycline high doses, etc.; immune and vitaminic therapy (disintoxication therapy) is carried out, surgical treatment is recommended if there are purulent masses in the pelvis. Coccidioidomycosis, rinosporidosis, blastomycosis, torulopsosis belong to the deep mycosis group. Owing to parasitical diseases the pathologic genital changes can appear when there are brucellosis, echinococcosis, schistosomiasis, mixed parasitisms.

VIRAL DISEASES

Viruses can cause diseases of the vulva, vagina, cervix. Some forms of viruses penetrate to the upper genitalia, bringing to inflammatory process development including associations with other agents (conditionally pathogenic flora, chlamydiae, mycoplasms, etc.). Infections caused by herpes simplex virus and cytomegalovirus will define the development of infectious pathology in future according to estimates of the WHO's European bureau.

Viral infections are often latent, chronic, long-term. Infections caused by herpes simplex virus type 2 (genital herpes) and papillomavirus (they belong to the group of sexually transmitted diseases) are most spread in gynaecological practice. Cytomegalovirus, hepatitis B virus do not bring to pathologic changes in genitalia of pregnant women. However, they expose the fetus to intrauterine infection causing congenital malformations.

Viral income doesn't always cause local (inflammation and tissue destruction) and general organism reactions. Endogenous and exogenous factors (sudden temperature changes, ultraviolet light, overfatigue, stress situations, general disease) promote appearance of viral infecion relapses. The possibility of such relapses is connected with viral persistence in the regional lymph nodes, nerve ganglions (herpes simplex virus).

HERPETIC INFECTION

Herpes simplex virus type 2 (HVS-2) is the reason of 90% of genital herpes, whereas herpes simplex virus type 1 causes only 10% of cases. HVS-1 affects predominantly the skin, mucous membrane of the face and lips. Development of genital herpes owing to mixed infection (HVS-1 and HVS-2) is possible. Genital herpes is a persistant sexually transmitted infection and observed in young sexually active women. Both the patients with clinical presentation of symptoms and viral carriers can be the source of infection. In men the main infection reservoir is urino-genital tract, in women — the cervical duct. Genital herpes belong to permanently persistant infectons.

Clinical picture. Genital herpes is often asymptomatic. The incubation period lasts for 3–7 days. Local infection's manifestations appear mostly in the area of vulva, vagina, cervix, peritoneum. HVS is also found in the uterine contents, Fallopian tubes and urinary bladder.

The primary infection of seronegative patients is characterized by severe pain in the area of the vulva, itching which is accompanied by accelerated urination, dysuria. Fever, headache, general indisposition, enlargement and sensitivity of regional lymph nodes can arise. If seropositive patients have clinical infection, so symptoms are less expressed.

Typical sign of herpetic infection is the appearance of single or multiple vesicles, 2–3 mm in diameter on hyperaemic, hydropic mucous tunic of the affected area. In 2–3 days vesicles break evolving into irregular ulcers. They are covered with yellow deposit and heal up within 2–4 weeks without scarring. The vesicles may evolve into ulcers persisting for a long time and covered with purulent deposit owing to adjoining secondary infection.

Maximum antibodies titres are found out within first 3 days of infection. After replication in sensory neurons HSV transports thanks to unmyelinizated nerves into the genital skin again where its subsequent replication causes typical lesions.

On account of viral persistence the disease relapses in 50–70% of cases. Overcooling, sexual intercourse, stress situations, overfatigue, other diseases, pregnancy promote the recurrence. HVS-2 prossesses oncogenic properties. At present genital herpes' association with cervical cancer is researched.

Diagnosis. Algorithms of diagnostic examination are based on clinical symptoms and laboratory tests. Smears-imprints from mucous tunic of affected organs (cervix, vagina, urethra) or aspirate (endometrium) are examined stuff.

Herpetic infection's clinical criteria are the presence of no less than two general (extragenital) symptoms (fever, myalgia, headache, nausea); genital eruptions with expressed local pain and hyperaemia for 10 days and more; herpetic eruptions of the other location (fingers, buttocks, oropharynx). However, 66% of diagnosed genital herpes are accompanied by atypical clinical picture (vaginitis which is resistant to a common therapy; skin hypostasis; feeling of dyscomfort in the vagina, urethra and urinary bladder; vulvodinia, burning, itching; relapsing disease of the cervix — ectopia, leukoplakia; pelvic ganglioneuritis; condylomatosis).

Though viral cultures (sensitivity — 80–100%, specificity — 100%) are considered to be a "golden standard" of any viral infection, its practical use is rather limited by many reasons. Combination of some methods is used most often: viral antigens reveling with the help of immunefluorescent, immunenzymatic or immuneperoxidase examinations; viral genome definition (polimerase chain reaction or PCR); cytological, electron-microscopical and serologic diagnostic methods. Every of the mentioned methods has its defects.

Only antigens detection may be insufficient as there is a possibility of transit or viral transfer without affecting organism. PCR is highly sensitive (95%) and specific (90–100%). However, it gives wrongly-positive results when contaminated by alien DNA, nuclease interferences, blood or in suboptimal primer-matrix correlation. Revealing of antibodies to HVS is not an exact diagnostic criterion as their presence can be caused by herpetic infection in anamnesis. It is impossible to reveal an active infection (till 80% of population can have antibodies to HSV or CMV) on serological examination, though the absence of antibodies excludes viral infection diagnosis. Reveal of IgG class antibodies means that an organism had already collided with this type of virus (it is important for pregnant: in this case fetus' primary infection won't develop). Presence of IgM-antibodies may be evidence of acute infection. However, they disappear fast or on the contrary they persist for a long time. If in blood samples obtained in acute period of the disease, antibodies to viruses were not revealed and in 2–3 weeks they appeared, it is possible to diagnose the primary infection. Only IgG titre growth or IgM appearance is evidence of relapse. The antibody titre is lower in case of viral infection's reccurent form.

Treatment of patients with genital herpes is palliative and directed to viral reproduction blockade, stimulation of specific and non-specific organism resistance, painful syndrome liquidation. Action mechanism of antiviral preparations can be based on suppression of nucleinic acids replication (acyclovir, zovirax; alpizarine, helepin, foscarnet, trianten), endogenous interferon induction (antiviral albumen), etc.

In primary infection acyclovir is prescribed in 200 mg orally 5 times a day for 7–10 days or 5 mg/kg intravenously every 8 h for 5–7 days or till disappearance of disease symptoms. Cream "Zovirax",

3% ointment "Trianten" as well as such ointments as "Alpizarine", "Hissopol", "Megasin" are used topically.

For relapsing herpes in case of expressed symptoms of the disease acyclovir is prescribed in a dose of 200 mg orally 5 times a day for 5 days or by 800 mg 2 times a day for 5 days or alpizarine — 100 mg 5 times a day for 5 days. Additional therapy is with: vitamins — thiamine (vit. B_1), pyridixine (vit. B_6) — 1 ml, ascorbic acid — 1 g 2 times a day during 15 days; specific antiherpetic immunoglobulin — 1 dose intramuscularly once for 3–7 days (the course of treatment is 5 injections), or antimeasles gamma globulin — a single dose of 3 ml for 3 days (4 injections), or sandoglobulin (normal human immunoglobulin for intravenous injections). Complex treatment includes the use of immunomodulators (T-activin 0.01% — 1 mkg/kg subcutaneously 2 times a week, 10 injections; licopid — 10 mg a day during 6 days, 3 courses with 14 days intervals; "Laferon", "Viferon", "Reaferon", etc.); desensitizing and sedative remedies (calcium gluconate — 500 mg 3 times a day; tavegil, suprastin, tazepam). Creams, ointments are used locally — "Zovirax", "Alpizarine", "Gossipol", "Megasin", etc.

PAPILLOMAVIRAL INFECTION

Papillomaviral infection (PVI) also belongs to the sexually transmitted diseases and often affects young women, who have active sexual life with many partners. PVI is also known as "condyloma acuminata" or "genital warts" and is one of leading reasons of benign diseases of the vulva, vagina and cervix.

Aetiology. About 50 subspecies of human papillomaviruses are known. Last ten years PVI incidence increased 5 times in developed countries of the world. Virus infects the squamous epithelium and brings to its proliferation, which manifests itself as condyloma acuminatum formation (warts). This disease is predominantly caused by the 6th and 11th types of virus. Viral types 16, 18, 31, 33 cause condylomata formation but more seriously is correlated with cellular atypia development, dysplasia, carcinoma *in situ* and invasive cancer. Malignant changes are often associated with the development of not candylomata acuminata but condylomata lata. In most cases candylomata acuminata are forming on the vulva, flat and inverted ones are on the cervix. Condylomata acuminata are characterized by exophytic growth at any place of the vulva, peritoneum and prianal area and in big overgrowths which resemble cauliflower. Condylomata can be multiple, of small sizes in the vagina (most often in entrance area) and they visualize better with the help of colposcopy. Condylomata of external genitalia skin are white or brown and condylomata of mucosa are pale pink or reddish. Microscopically condylomata consist of epithelium (stratified) and connective-tissue stroma which is pierced through with vessels.

Clinical picture. The disease has a prolong clinical course, secondary bacterial and protozoal infection addition, which is accompained by pain, itching, pathologic vaginal discharge (white discharge), often with an odour. Condylomata overgrowth on external genitalia hinders walking, dispirits a patient.

Accelerated growth of condylomata acuminata is observed during pregnancy and can be connected with immunodeficiency, insufficient hygiene observance. Spontaneous regression is possible even without treatment (after delivery) or on the contrary, intensive growth is observed. In this case surgery is necessary. Diagnosis of condylomata acuminata offers no difficulty, though sometimes they have to be differentiated with syphilitic condylomata (with the help of serologic reaction — Wassermann's reaction). On colposcopy condylomata acuminata look like finger-shaped white epithelial formations with clear visible contours of capillaries when processing with acetic acid. In colposcopic picture condylomata lata and inverted condylomata are similar to intraepithelial carcinoma: capillaries are not seen, dilated vessels as red dots are noticeable. Iodine negative zones are found out with the help of Shiller's test. Diagnosis is established on the basis of histological examination of biopsy.

Treatment is carried out according to the character of the lesion (benign, dysplasia) providing a synchronous therapy on the occasion of concomitant diseases (vaginitis, cervicitis, cervical pseudoerosion, etc.). The use of interferon is ineffective. Cryoablation, electrocauterization, laservaporization with the help of CO_2-laser are widely used, surgical ablation, local applique of cauterized substances (20% podophyllin, condyllin, resorcinol, 5-fluorineuracil cream and, etc.) are made. Patients with papillomaviral genital infection have a high risk to develop intraepithelial cervical cancer.

CYTOMEGALOVIRAL INFECTION

Aetiology, pathogenesis. Cytomegaloviruses (CMV) are representatives of Herpes family.

After primary infection (infection's source are saliva, urine, cervical, vaginal secretion, sperm, tears, blood) cytomegalovirus persists during the whole life and can reactivate. Long and tight contact is needed for horizontal virus' trasmission owing to agent's lability and influence of environmental factors. Duration of incubatory period is not finally ascertained. Disease symptoms are non-specific: fever, enlargement of the lymph nodes (clinical picture is similar to mononucleosis). Specific antibodies — antibodies of A, M, E classes are forming at the onset of the disease and found out in blood during 8–12 weeks after infection. IgG are keeping during the whole life long in titres which are gradually diminish.

However, the antigen's presence to both CMV and SHV doesn't prevent viral reactivation. The viral titres are lower in the asymptomatic form of infection than in a clinically active one. Maternal immunity is not able to prevent neither reinfection in case of existence of different antigenic CMV cultures nor latent infection reactivation during pregnancy nor CMV transmission to the fetus. An acute CMV-infection or its relapse in the I trimester of pregnancy can bring to miscarriage, congenital malformations (microcephaly, ablepsia, deafness), in the III trimester it can bring to premature birth, intrauterine infection, the lesion of the children's central nervous system).

For a long time (from some weeks to some years) CMV infection can be in the latent state; it is inclined to relapses, often has a subclinical form. CMV is secreted from the cervix in 5–24% of women. Pneumonia, CNS lesion, thrombocytopenia, hepatitis can appear in severe form of CMV infection.

Diagnosis of CMV-infection in cervical mucus, urine, blood is based on revealing of intranuclear inclusions which greatly enlarge the infected cells ("cytomegal cells", an "owl's eye"). Serological diagnosis is used (reaction with the titre 1:4 is negative, 1:8 is poorly positive, 1:16 and more is positive), immunofluorescent and immunoenzyme methods.

Treatment. The use of specific antiviral preparations (acyclovir, zovirax, virazol) is not effective. The use of hyperimmune gamma-globulin with a high titre of anti-CMV-antibodies (cytotec), other immunomodulators are recommended: decaris (levamizol); T-activin, tymalin, reaferon, viferon, etc. The courses of metabolic therapy with the use of B-group vitamins, ascorbic acid (vit. C), α-tocopherol (vit. E), folic acid, anabolics as well as enzyme therapy with the use of "Vobenzim", 5 dragee 3 times a day 35–40 min before meal during 2 weeks, then 3 dragee 3 times a day during 2 weeks.

MYCOPLASMOSIS AND UREAPLASMOSIS

The role of mycoplasmal infections in aetiology of inflammatory genital diseases has been effectively studied last years. Micoplasmas participate in microbic associations with trichomonae, gonococci, chlamydiae, anaerobes, especially with bacteroides. Micro organisms of Mycoplasmae genus (75 species), including *Mycoplasma urealiticum* (10 serotypes) belong to *Mycoplasmaticea* family. The name "ureoplasma" is connected with a capability of these micro organisms to produce urease enzyme which splits the urea. Ureaplasmas are little gram-negative microorganisms, about 0.3 μm in diameter which are excreted from genitalia if there are any inflammatory diseses (vaginitis, cervicitis) as well as practically healthy women.

Ureaplasmas' pathogenic properties appear if there is the lowering of organism's resistance and is determined by their adhesiveness, in other words an ability to fasten onto epithelial mucosa, leucocytes, spermatozoons as well as to take part in endo- and exotoxins' formation. Ureoplasmas are not characterized by high invasive ability and are predominantly detected in superficial epithelial layers. The latent ureaplasmic infection can cause an infringement of cellular chromosomal apparatus.

Clinical picture. Ureaplasmal genital infection often has a latent course without specific symptoms. Ureaplasmas are revealed in patients suffering from vaginitis, cervicitis, urethritis, bartholinitis, salpingitis as well as in tuboovarial abscess, tubal infertility, often in microbial associations. Mycoplasmal infection entails spontaneous abortion in late terms (II trimester) of pregnancy, premature birth which are accompanied by fetal membranes rupture as well as intrauterine infection, postpartum purulent septic complications.

Diagnosis of mycoplasmal and ureaplasmal genital infection is difficult due to the fact that mycoplasmas are often associated with the other microbic flora and a special analysis is necessary. The bacteriological method is used for ureaplasmas identification. Clinical examples are subject to the urease test (colour test), the direct test-spot for urease with indicator is carried out (mangan sulphate) or inoculation of dense medium which contains mangan sulphate. In consequence of ureaplasmas growth in fluid nutrient medium, the micro organisms split urea onto carbonic gas and ammonia, the reaction turns from acid into alkaline and at the same time indicator's color changes (bromidethymol dark blue) from lemon-yellow till green and dark blue.

Teatment. Tetracyclines (doxycyclin, vibramicin and, etc.) and macrolids (erithromycin, macropen, rulid, sumamed) are used for etiotropal treatment.

PELVIC INFLAMMATORY DISESES

Pelvic inflammatory diseases (PID) are internal genital infections: acute chronic inflammation of the endometrium and myometrium (endometritis, endomyometritis), Fallopian tubes and ovaries (salpingitis, oophoritis, adnexitis or salpingoophoritis), pelvic fat (parametritis, pelviocellulitis) and peritoneum (pelvioperitonitis, peritonitis).

PID result mostly from sexually transmitted diseases and are caused by microbial associations of aerobe and anaerobe flora: gonococci, chlamydiae, streptococci, staphilicocci, mycoplasmas, colon bacillus, enterococci, proteus, bacteroides. Acute PID often arise in young sexually active women who start sexual life early. Intrauterine contraception (chronic

endometritis) increases PID risk, the use of the barrier and oral contraceptives decrease it. PID don't develop in women who have no sexual intercourse and do not use intrauterine contraceptives.

Incidence of abdominal pregnancy in patients suffering form PID increases 6–10 times as much, chronic pelvic pain — 4 times. Other PID complications include tubal infertility especially in recurring PID cases, dyspareunia.

ENDOMETRITIS

Aetiology. Non-specific bacterial endometritis is caused by pathogenic and conditionally pathogenic microorganisms. In most cases the basal endometrium layer is affected.

Acute endometritis arises after abortion, diagnostic uterine curretage, delivery. The presence of blood, reminents of decidual membrane and fetal ovum promote the infection development.

Inflammatory process of the uterine mucosa often involves adjoining layers of the myometrium (endomyometritis). Owing to aerobic flora appearance the necrotic destructive changes can arise in the myometrium.

Clinical picture. Acute endometritis develops on the 3rd–4th day after infection and accompanied by fever, tachycardia, elevated white blood cells count, left shift of leukocytal formula, pain in the lower abdomen, elevated ESR. The uterus can be enlarged, tender by palpation in the vascular fascicle area in particular. Discharge are serous purulent, often with a touch of blood (delay of mucosa regeneration). The acute stage of endometritis lasts for 8–10 days, the process is resolved if a proper treatment is provided, rarely it turns into a chronic form. Against a background of antibiotic therapy, endometritis can have a mild or abortive form.

Chronic endometritis. Chronic endometritis can start and proceed without signs of acute inflammation. Specific changes in the endometrium are absent most often, sometimes thickening of the endometrium with stroma's fibrosis are observed, fibrous adhesions in the uterine cavity are forming; inflammatory process often involves the myometrium. Nidal or diffuse infiltrates composed of plasmatic cells and lymphocytes are found out in the endometrium. Sometimes chronic endometritis can result in pyometra formation. Chronic salpingitis, ovarian hypofunction, infertility may accompany chronic endometritis.

Clinical picture. Chronic endometritis symptoms are moderate enlargement of the uterus, secretory and menstrual dysfunction (intermenstrual bloody discharge, "spotting" before or after menstruation, leucorrhoea). These changes can be associated with concomitant functional ovarian disorders.

Treatment is with broad-spectrum antibiotics with taking into account the susceptibility of infection agents (semisynthetic penicillins, amynoglycosides — kanamycin, gentamicin, cephalosporins, fluorinequinolone) as well as often addition of aerobic infection (metronidazole, clindamycin). Antibiotic treatment regimens are determined by severity of the disease. Complex treatment is performed according to the extent of organism's regulatory systems disorders and includes infusion, desensitizing and roborant therapy.

A complex treatment should be used in chronic endometritis with antibacterial (in exacerbation), sedative, desensitizing therapy, vitamin- and physiotherapy, normalization of ovarian function (cyclic hormone substitutive therapy with oestrogen-gestagenic preparations depending on a patient's age and concomitant diseases). If the disease lasts less than 2 years, the microwave therapy of a centimetric diapason or UHF therapy is recommended. If the disease course is over 2 years, impulse ultrasound or zinc electrophoresis as well as iodine electrophoresis at ovarian hypofunction are used. Sanatorium and spa treatment (pelo-, balneotherapy) is effective.

SALPINGITIS AND ADNEXITIS (SALPINGOOPHORITIS)

Inflammatory lesions of uterine appendages and ovaries — salpingitis and adnexitis (salpingoophoritis) are the most wide-spread genital inflammatory diseases caused by aerobic-anaerobic microbial associations as well as other sexual diseases. Recently the role of chlamydiae and mycoplasmas has greatly increased in salpingitis development (up to 80% of cases). At first, inflammatory process develops in the Fallopian tube's mucosa (endosalpingitis), and then it spreads to the muscular membrane, serous integument of the tube (perisalpingitis), ovary (adnexitis or salpingoophoritis). Owing to Fallopian tube's fimbriae adhesion under inflammatory exudation influence and adhesions development, tumour-like serous (hydrosalpinx) or purulent (pyosalpinx) masses, tuboovarian inflammatory "tumours" and abscesses arise in ampular part of the tube. Purulent tuboovarian masses are accompanied by the development of unions with intestines, epiploon, and the parietal peritoneum of the pelvis and can bring to pelvioperitonitis and peritonitis.

Acute adnexitis (salpingoophoritis). *Clinical picture* depends on the severity of the process (serous, purulent), characterized by the temperature rise, worsening of general health condition, abdominal pain, chill at purulent process, sometimes there are dysuria and dyspeptic symptoms. During first days of the disease the abdomen is strained, tender by palpation; the muscular defence phenomenon may arise. Gynaecological exam is painful, adnexal contours are not clearly defined (oedema, perifocal

processes); they are enlarged, confined in mobility. Typical blood changes for acute inflammation are following: leukocytosis, lelt shift of the leukocytar formula, elevated ESR and C-reactive albumin. Acute inflammatory process may result in full recovery in a timely adequate treatment or get a character of subacute or chronic process which lasts for years.

Diagnosis is based on anamnesis data (genital inflammatory diseases, intrauterine manipulations, and intrauterine contraception), results of common objective and gynaecological examinations, data of ultrasound and laparoscopy. Laparoscopic picture of acute adnexitis (salpingoophoritis) is characterized by hyperaemia of serous integument of the Fallopian tubes, exudates presence, fibrous deposit on the tubal surface and in the pouch of Douglas. On laparoscopy the exudate is taken from the Fallopian tube for bacteriologic examination.

In acute adnexitis treatment includes bed, physical and mental rest, adequate diet, antibacterial therapy taking into account the agent's susceptibility (Table 2).

If microbial associations are revealed in patients suffering from acute adnexitis (salpingoophoritis), they are prescribed penicillin in a dose of 20,000,000–30,000,000 U intramuscularly with synchronous administration of aminoglycosides (kanamicin) — 500 mg intramuscularly 2 times a day or gentamicin — 1 mg/kg intavenously 3 times a day). If the effect is absent within 72 h, clindamycin is added by 600 mg intravenously 4 times a day untill the body temperature falls and peritoneal irritation symptoms disappear, then penicillins and aminoglycosides are used for 5 days.

Metronidazole has a bactericidal effect on obligate anaerobes and *B. fragilis* (daily dose is 1–1.5 g intravenously for 5–8 days) and is used in suspicions at anaerobic flora presence; in less severe cases — 500 mg orally 3 times a day for 7–8 days.

If the agent is unknown, different combinations of antibacterial preparations are used parenterally:

— clindamycin — 600–900 mg 3 times a day intramuscularly or intravenously + gentamicin or

Table 2. **Antimicrobial drugs used in genital inflammatory diseases**

Causative agent	Drugs of choice	Other drugs
Staphylococci:	Benzylpenicillin, oxacillin, naphcillin, dicloxacillin	Cephalosporins of I and II line
β-lactamazonegative, penicillin susceptible		Erythromycin
β-lactamazopositive, penicillin resistant		Clindamycin
Streptococci hemolytic	Benzylpenicillin	Cephalosporins of I and II line
		Erythromycin
		Clindamycin
Enterococci	Ampicillin + Amoxicillin	Vancomycin
	Aminoglycosides	Mezlocillin
		Piperacillin
		Azlocillin
Klebsiella	Amoxicillin	Cephalosporins of III line
	Cephalosporins of I and II line	Fluorquinolones
	Aminoglycosides	
Bacteroides	Clindamycin	Lincomycin
	Metrodidazole	Cephoxitin
Peptococci, peptostreptococci	Benzylpenicillin	Tetracycline
		Erythromycin
		Cephoxitin
		Clindamycin
Gonococci	Cephamizin	Tetracycline
	Benzylpenicillin	Cephalosporins of II line
Gardnerellas	Metronidazol	Amoxicillin
Mycoplasmas	Erythromycin	
	Tetracyclines	
Clamydias	Tetracyclines	Macrolides
		Fluorquinolones

tobramicin — 1.5 mg/kg 2–3 times a day intramuscularly ("golden standard");

— metronidazole — 500 mg 3 times a day intravenously + gentamicin or tobramicin — 1.5 mg/kg 2–3 times a day intramuscularly;

— cephotaxim (Claphoran) — 1–2 g 3 times a day intravenously or intramuscularly + doxycycline — 0.1 g 2 times a day orally;

— cephtazidim — 1–2 g 2–3 times a day intravenously or intramuscularly + amoxycycline-klavulane acid (augmentin) — 500 mg 2 times a day orally;

— imipenem-cylastatin (Tienam) — 500–1000 mg 3–4 times a day intravenously;

— cyprophloxacin (Cyprobai) — 200–400 mg 2 times a day intravenously + augmentin — 500 mg 3 times a day orally.

Infusion therapy is realized in case of expressed intoxication (parenteral administration of 5% glucose solution, Ringer solution, isotonic solution of chloride natrium with vitamins, antihistamines; low- and middle molecular dextrans, albuminous preparations in a full volume of 2–2.5 l). Hypothermia is used *locally* (antiphlogistic, anaesthetic and haemostatic effects). Tubal irrigation with isotonic chloride natrium solution which contains antiseptics and antibiotics; fresh adhesions removal; adhesiotomy of the fimbrial part of the tubes and ovaries; pus aspiration, abscess cavity lavage with antiseptic solutions and antibiotics are performed during laparoscopy. A need in radical surgery often occurs in presence of tuboovarian purulent masses with the threat of perforation.

Chronic adnexitis (salpingoophoritis) is one of the most wide-spread forms of PID, develops because of untimely or insufficient treatment of patients with acute salpingoophoritis. It is characterized by the presence of infiltrations, loss of physiological functions of the Fallopian tube's mucous and muscular membranes, connective tissue forming, vascular lumen constriction, sclerous processes. The Fallopian tubes occlusion with hydrosalpinx formation can arise during long disease course.

Clinical picture of chronic salpingoophoritis is non-specific; the main patients' complaint is chronic pelvic pain (at the lower abdomen, in the groin, at the sacrum area, in the vagina). So called pelvic nerves neuralgia, vegetative ganglioneuritis, develop according to chronic inflammatory and adhesive processes, and the pain intensity doesn't often correspond to genital changes extent. Each second patient has menstrual, sexual, secretory, reproductive dysfunction (polymenorrhea, algodismenorrhea, dyspareunia, anovulation, infertility) as well as of adjacent organs dysfunction (colitis, bacteriuria, cystitis, pyelonephritis), hepatobiliary system.

Chronic salpingoophoritis is characterized by a prolong course with exacerbations (with predominance of exudative or pain components), often adding of neurotic reactions, endocrine and vascular disorders.

Diagnosis is based on anamnesis data, reveal of pelvic adhesions. Laparoscopy plays a decisive part in differential diagnosis of chronic salpingoophoritis with minor forms of endometriosis. Chlamydiae and anaerobic flora are often found out on bacteriological examination of aspirate taken from the pouch of Douglas.

Treatment should be directed to attainment of antiphlogistic and anaesthetic effect, rise of organism's protective power, recovery of disturbed genital functions, liquidation of neuroendocrine or other organism system disorders (anaesthetics, sedative, desensitizing, tonic). Antibiotics are used in a period of inflammatory reaction aggravation as well as while using drugs which intensify the metabolism, activating enzyme systems (pyrogenal, prodigiosan, gonovaccine, etc.). Non-drug factors (gynaecological, vibratory massage, therapeutic physical training, acupuncture, psychotherapy), rational food (prophylaxis of constipation), sanatorium-and-spa treatment play the main part in complex treatment.

PARAMETRITIS

Parametritis is an inflammation of parametrium; depending on location it can be lateral, posterior or front. In 2/3 of cases this disease is associated with postpartum infection but it can arise after abortion, uterine scraping, other surgical manipulations in genitalia and the rectum (haemorrhoids, anus chaps).

Aetiology. Parametritis is caused by pathogenic or conditionally pathogenic flora (staphylococci, streptococci, enterococci, microbial associations). The infection gets into parametrium in consequence of injury as well as by lymphogenous or hematogenic (seldom) way from the endometrium, endocervix, and vagina. Inflammatory process comes to nothing more than the parametrium, but it can involve all the pelvic fat (pelviocellulitis or pelvic cellulitis). When inflammatory process goes over to the paravesical fat, the infiltration spreads along the posterior surface of the anterior abdominal wall and gets a triangular form with an apex directed to umbilicus. Posterior parametritis can spread upwards extraperitoneally till the renal area and downwards to the paravaginal fat.

A diffuse inflammatory reaction happens after infection penetration in to the parametrium. During the 1st stage (serous parametritis) the infiltration is soft, with serous exudation; at the 2nd stage as a result of fibrin formation the infiltration becomes dense; melting of the infiltration with an abscess formation takes place at the 3rd stage.

Clinical picture is typical for inflammatory process: at the acute stage — fever, tachycardia, pain at the lower abdomen, especially at the place of the affected parametrium but general health condition doesn't deteriorate acutely; leukocytosis, elevated ERS in the blood; signs of peritoneal irritation are absent.

On gynaecological examination at first the resistance of vaginal fornix is found out at the affected area, then less sensitive infiltration at the side of the uterus as a rule (rarely behind it or from the front), which stretches to the pelvic wall (Fig. 19). In a unilateral infiltration, the uterus shifts to another side, in bilateral — upwards and to the front. Infiltration desorbs as a result of adequate treatment. However, the tissue scarring is possible, which displace the uterus to the affected side.

Infiltrate infection occurs seldom under conditions of up-to-date antibacterial therapy. In case of infection the abscess is opened, often through the vaginal fornix, rarely through the anterior abdominal wall with a subsequent drainage and administration of antibacterial preparations. An abscess can burst open into the urine bladder, rectum, renal area, buttocks.

Treatment is in accordance with general therapeutic principles of management of patients suffering from pelvic inflammatory diseases (etiotrophic antibiotic combinations, desensitizing, common roborant remedies, disintoxicating, and infusive therapy). Antibacterial therapy is made intravenously at first using big antibiotic doses, acting on aerobic and anaerobic flora (metronidazole, tinidazole, clyndamicin, lyncomicin) in combination with cephalosporins of the II and III generation or broad-spectrum penicillins (ampicillin, unasin, piperacillin) as well as with aminoglycosides (gentamicin, amykacin, torbamicin). Fluorinequinolone group drugs are effective: abactal, cyprophloxacin, etc. (Table 3).

When a clinical remission is achieved, intramuscular and oral drugs are prescribed for 7–14 days, supportive therapy is realized.

PELVIOPERITONITIS AND PERITONITIS

Pelvioperitonitis and peritonitis often arise secondarily, as a result of infection spread from the uterus, appendages or pelvic fat to the peritoneum. The onset of the disease is often provoked by intrauterine manipulations; prolong using of intrauterine device, abortion, uterine perforation during curettage, posterior vaginal laceration or rupture of purulent masses of uterine appendages with contents pouring out to the abdominal cavity.

These diseases are caused mostly by aerobic-anaerobic associations, including staphylococci, colon bacillus, gonococci, anaerobes, chlamydiae, viruses.

Clinical picture of pelvioperitonitis and peritonitis is almost the same (of the inflammation spreading outside the pelvic peritoneum). However, more expressed intoxication symptoms are typical for peritonitis: fever, tachycardia, and chill, dry tongue, nausea, hiccup, profuse diarrhoea, heavy breathing, and general weakness. Tension of the anterior abdominal wall, bloating are also observed, positive peritoneal irritating symptoms appear (Schetkin—Blumberg's), intestinal peristalsis weakens, leukocytosis and ESR elevate. Pelvioperitonitis can be se-

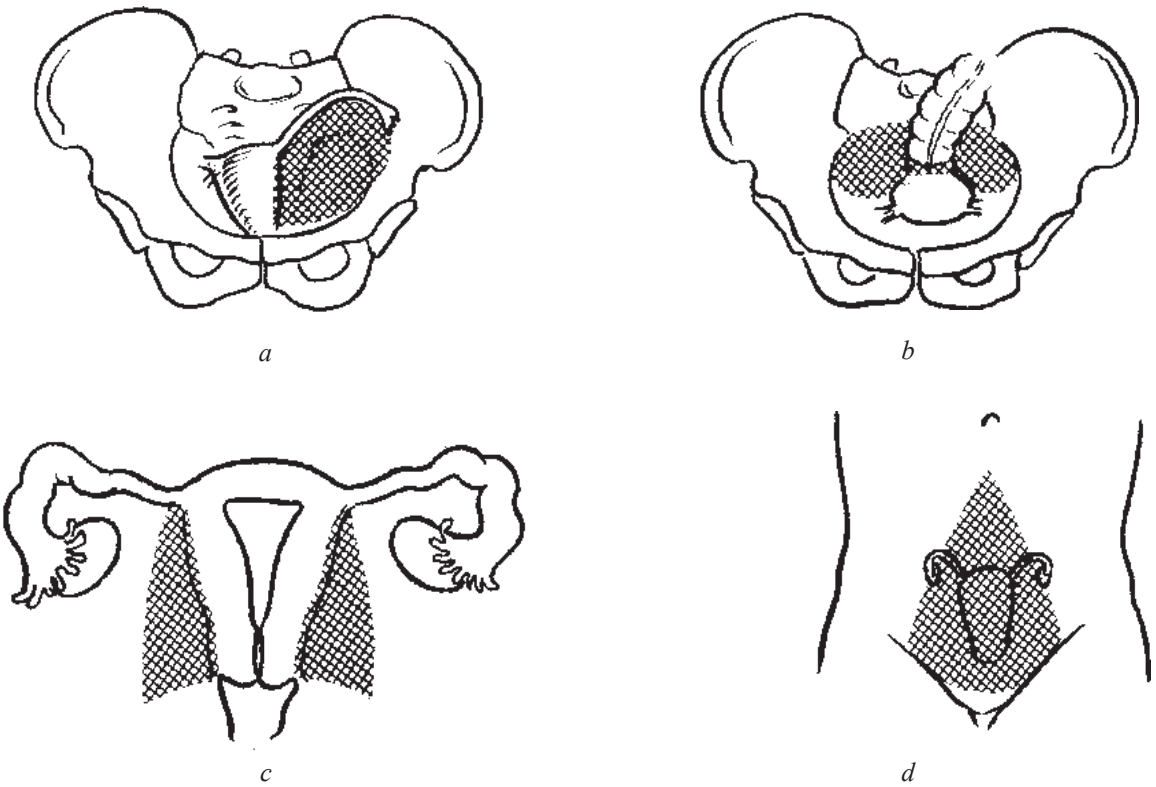


Fig. 19. Kinds of parametritis (localization of infiltration):
a — one-sided lateral; *b* — posterior; *c* — two-sided lateral; *d* — anterior

Table 3. **Standard doses and methods of antibacterial drugs introduction in treatment of pelvic inflammatory diseases**

Drugs	Dose, g		Method of introduction
	single	day	
Penicillins:			
Ampiox	1	4	I/m, i/v
Unazin	1.5–3	1.5–3	I/m, i/v
Augmentin	0.5	1.5	Per os
Imipenem	0.5–1	2–4	i/v
Cephalosporins:			
Cefoxitin	1–2	4–6	
Cefthriaxone (Logocef)	1–2	2–4	I/v, i/m
Ceftazidim (Fortum)	1–2	2–6	
Cephotaxim (Claphoran)	1–2	4–6	
Aminoglycosides:			
Gentamicin	0.8	1.6–2.4	I/m
Sizomicin	0.6	0.8	I/v, i/m
Amicacin	0.5	2	I/v, i/m
Tobramicin	0.8	2.4	I/v, i/m
Macrolides:			
Erythromycin	0.5–1	3–6	Per os
Azythromycin (Summamed)	0.25	0.75–1	
Tetracyclines:			
Doxycycline	0.1	0.2	I/v, per os
Other drugs:			
Clindamycin (Dalacin C)	0.6–0.9	1.8–2.7	I/m
Lincomycins	0.6	1.8	I/v, i/m
Metronidasole	0.5	1.5–2	I/v
Metrogil	0.5	1.5	I/v
Efloran	0.5	1.5	I/v
Klion	0.5	1.5	I/v
Rifampicin	0.2–0.3	0.6–0.9	Per os
Ofloxacin (Tarivid, Zanocin)	0.2–0.4	0.4–0.8	Per os
Perfloxacin (Abactal)	0.4	0.4	I/v, per os
Ciproby	0.25–0.4	0.8	I/v
Nistatin	500,000 U	2,000,000 U	Per os
Diflucan	0.15	0.15	Per os

rous-fibrous (adhesive with adhesions development) or purulent (exudative). In chlamydial aetiology of the disease intoxication symptoms are less expressed with a tendencies to adhesions. A big amount of fibrinogenous precipitation and fast process' limitation are signs which are peculiar to gonorrhoeal pelvioperitonitis. In case of purulent pelvioperitonitis, pus delimits slowly, purulent exudation gets into the rectal-uterine pouch (Douglas').

Diagnosis. The causative agent is identified using common bacteriological and serological methods. The stuff for exam is taken from the cervix, the posterior vaginal fornix, and urethra. It is necessary to remember that micro flora of the lower female reproductive tract conforms to that one of the upper parts only in 50% of cases which is evidence of the importance of laparoscopy during which the affected organs are directly examined. Ultrasound examination, laparoscopy are used for specification of process spreading area, location of purulent masses.

Treatment is realized in the hospital and should be complex, active: etiotropal parenteral antibiotic therapy, disintoxicating, infusible transfuse therapy; antiphlogistics, anaesthetics (analgin, reopyrin, voltaren, and dychlophenac) and desensitizing medications; normalization of intestinal functions, cardiovascular and respiratory system. Radical ablation of the purulent focus (tuboovarian abscess) is made.

It is recommended to put cold on the lower the abdomen to prevent inflammatory process spreading. *Infusive therapy* consists in dextrans administration (5% glucose solution, Ringer solution, Ringer—Lock solution, isotonic sodium chloride solution with

B group vitamins, ascorbic acid (vit. C), bioflavonoids (vit. P), plasma and other albuminous preparations), correction of acid-base and water-electrolytic condition (alkaline solutions, potassium chloride are used for hypokaliemia correction).

Broad-spectrum antibiotics are prescribed concerning to possible agents (gonococci, chlamydiae, grampositive and gramnegative aerobes and anaerobes), especially if the etiological factor couldn't be defined fast and exactly. The main agents in tuboovarian abscess are anaerobic bacteria (in 85–90% of cases) — bacteroides, peptococci, peptostreptococci, often in connection with aerobes — esherichias, enterococci, goldish staphylococcus and, etc.

Intensive antibiotic therapy should be certainly realized during 48 h after disappearance of fever, general intoxication symptoms; full course of antibiotic treatment with should be no less than 10 days. The following combined schemes of antibiotic treatment are also recommended:

— doxycycline (100 mg in 12 h) + cephoxitin (2 g in 6 h);

— clindamycin (600 g in 6 h) + gentamycin (2 mg/kg in 8 h with severe condition, but renal function preservation; later on — 1.5 mg/kg in 8 h)

— doxycycline (100 mg in 12 h) + motronidazole (1g in 12 h).

Cardiac glycosides are administrated for supporting of cardio-vascular system activity. Proserin, cerucal, hypertensive enemas are used to stimulate gut peristalsis.

In PID laparoscopy is performed in the next cases: 1) for specification of inflammatory process location and extent; 2) if antibacterial and disintoxicative therapy in ineffective during 48 h; 3) for removal of tuboovarian formation's contents, pelvic cavity drainage, ablation of abdominal cavity with antiseptic solutions, antibiotics administration and to settle the question about the need in radical treatment.

Puncture through the posterior vaginal fornix is made with the purpose of drugs introduction if irritating peritoneal symptoms are absent. The puncture is contraindicated if there are bilateral tuboovarian abscesses and irritating peritoneal symptoms.

Laparoscopy is recommended if tuboovarian abscess perforation is suspected, intensive treatment and laparoscopic drainage failure during 24–36 h as well as if there is peritonitis.

Surgical treatment includes uterine extirpation with injured appendages (supravaginal amputation is made if uterine lesions are absent), drainage of the abdominal cavity with colpotomy; inserting of drainages, microirrigators for intra-abdominal drop infusions and permanent evacuation of pathologic exudation (peritoneal dialysis).

Physical methods, quantum haemotherapy in particular (blood reinfusion after ultraviolet irradiation), intravascular blood irradiation with helium-neon laser, hyperbaric oxygenation (especially in anaerobic infections) to remove immunodeficiency, normalize rheological blood properties, indices of haemostasis and proteolysis, to reduce antibiotic doses and shorten the treatment course as well as relapses incidence are effectively used.

Physiotherapy is used for aftercare: ultrasound, UHF-therapy, SHF, dynamic currents, iodine, zinc electrophoresis, phonophoresis with cortisol, lidase, massage, hydro- and balneotherapy. Local treatment includes the vagina's treatment with antiseptic solutions (0.5% clorhexidine) with inserting of dymexin tampons, Vishnevsky ointment as well as the use of microenemas with antibacterial and antiphlogistic drugs (dimexid, dioxidin, cortisol, rhiphampicin, etc.).

RECOMMENDED READING

3; 7; 16; 19; 21; 23; 24; 25; 27; 29; 37; 38; 43; 59; 69; 75; 79; 90; 92; 93; 94; 101; 103; 108.

Chapter 3

DISORDERS OF THE MENSTRUAL FUNCTION

REGULATION OF THE FUNCTIONS OF THE REPRODUCTIVE SYSTEM

The activity of the reproductive system is directed upon reproduction, preservation of the existing species, which causes exclusive reliability of its functioning. The reproductive system, as well as other systems of the organ, is functional and is constructed by the hierarchical principle, consisting of five central and peripheral levels of regulation, which cooperate by the principle of direct and inverse relations (Fig. 20).

The first level of regulation consists of *organs and tissue* (genitalia, mammary glands, hair follicles, skin, bones, and adipose tissue). The cells of these organs and tissues have receptors for sexual steroid hormones (estradiol, progesterone, and testosterone). The contents of steroid hormones in the blood change depending upon the phase of the menstrual cycle. The hormone molecule is seized by the cytoplasmatic receptor, and the hormone-receptor complex is transferred to the cell nucleus. In the nucleus, the complex unites with chromatin, regulating the transcription processes. Cyclic adenosine monophosphate (cAMP) and prostaglandin, playing the role of intercellular regulators, are also referred to the first level of regulation of the reproductive system. On the first level of regulation the most expressed cyclic changes occur in the endometrium *(uterine* or *endometrial cycle)* — its preparation for menstruation or the implantation of fertilized ovum (Fig. 20, I).

The second level of regulation of the reproductive system — *ovaries* (Fig. 20, II). The cyclic changes in the ovaries are referred to as the *ovarian cycle.* In the first (follicular) phase the development of primary and secondary follicles occurs, in the second phase (luteal or corpus luteum phase) from the cells of the tertiary (Graafian) follicle, where ovulation has occurred, an endocrine gland is formed — the corpus luteum.

The third level of regulation — *adenohypophysis* (the anterior lobe of the hypophysis; Fig. 20, III). In the adenohypophysis the secretion of gonadotrophin is carried out: lutrophin, follitrophin, prolactin, thyrotrophin, somatotrophin, corticotrophin, melanotrophin and lipotrophin. Follitrophin and lutrophin have a glycoprotein nature, prolactin — a polypeptide one. The half-life period for lutrophin consists of about 30 min, follitrophin — up to 30 min. These hormones in the humoral way stimulate the growth of a follicle, synthesis of steroids and maturing of the ovum. An increase in the level of estradiol in the pre-ovular follicle causes the emission of lutrophin and follitrophin, ovulation. The ovarian hormone-inhibin inhibits the release of follitrophin. In ovular cells under the action of lutrophin, progesterone is formed. Lutrophin also stimulates the synthesis of androgens in the external theca cells. Prolactin stimulates the growth of mammary glands and regulates the processes of lactation. An increase in the level of prolactin oppresses the steroid genesis in ovaries and the development of follicles.

The fourth level of regulation of the reproductive system — *hypothalamus.* In the neurons of the hypothalamus, a pulsating secretion of gonadotrophin releasing-hormones (GN-RH) occurs in the circhoral mode. Through the axons of neural cells neurosecretion (GN-RH) enters the portal system and the blood is transferred to the anterior lobe of the hypophysis (Fig. 20, IV).

Neurons of the hypothalamus integrate exo- and endogenous information, arriving from various departments of the central nervous system. Through the hypothalamus such factors as starvation, stress and so forth can influence the menstrual cycle. The hypothalamus takes part in the regulation of sexual behaviour, body temperature, consumption of food and water. Small amplitude and frequency fluctuations during the secretion of GN-RH (gonadoliberins) testify of the changes occurring in hypothalamus. Normally the frequency of pulsating secretion of GN-RH in the follicular phase is one pulse per 1 h (circhoral rhythm of secretion), and in the luteum phase — one pulse per 90 min. GN-RH does not

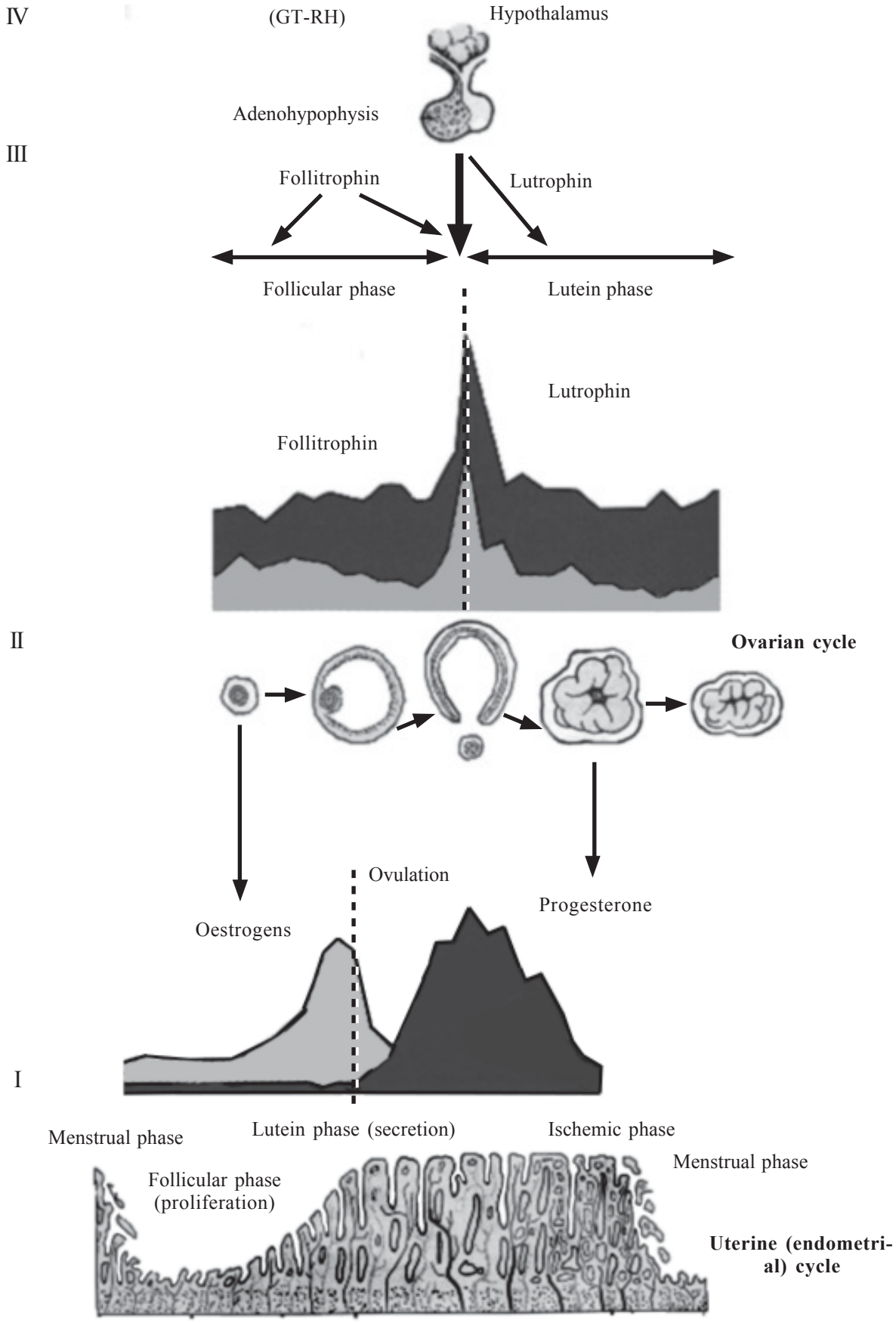


Fig. 20. Levels of regulation and cyclic changes in the reproductive system during the menstrual cycle

participate in the increase of folli- and lutrophin levels in the middle of the cycle. These changes occur under the influence of a positive inverse relation between the concentration of circulating oestrogens, progesterone and hypophysis, that, in turn, causes the response of the hypothalamus.

Secretion of gonadoliberins is under the influence of neuromediators: dopamin, norepinephrin, α-endorphin, concentration which also depends upon the action of oestrogens and progesterone. Therefore, medical products, influencing the metabolism of neurotransmitters, can act on the secretion of GN-RH and prolactin of the hypothalamus (methyldopa, reserpin, antidepressants).

The fifth level of regulation — *supra-hypothalamic structures of the brain.*

A classical example of the cyclic processes occurring in the reproductive system of a woman during maturity is the ovarian-menstrual cycle. The mechanisms of direct and inverse relations acting during the menstrual cycle are submitted in fig. 21.

The first day of menstruation (menstrual bleeding) is considered the first day of the menstrual cycle and is the beginning of the first phase (menstrual) of the uterine (endometrial) cycle. This phase is characterized by the disintegration and discharge from the uterus of the functional superficial layer of the endometrium, caused by an acute decrease in estradiol and progesterone levels in the blood. The disintegration of the whole external layer of the endometrium proceeds a few days.

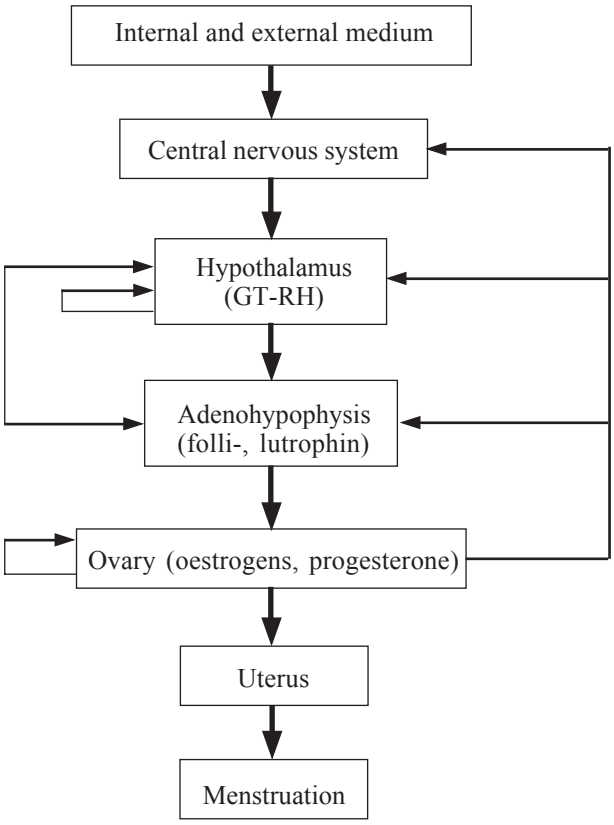


Fig. 21. Mechanisms of direct and reverse neurohumoral connections during the menstrual cycle (direct connection, reverse connection)

Low levels of oestrogens and progesterone during the last days of the menstrual cycle cause corresponding cyclic changes at the level of the hypothalamus and hypophysis, serving as the reason for the beginning of a new menstrual cycle. Pulsating secretion promotes an increase of gonadotrophin secretion by the hypophysis (follitrophin and, to a lesser degree, lutrophin). Follitrophin stimulates folliculogenesis in the ovaries. The developing follicles allocate oestrogens. On the 5th–7th day of the menstrual cycle one follicle starts to dominate and intensively allocate estradiol; other follicles are subjected to inverse development (atresia). This phase is referred to as the follicular phase and corresponds to the proliferative phase of the menstrual cycle.

The endometrium reacts to the production of oestrogen by the ovaries by the renewal of cyclic changes and development of the uterine mucous membrane. Regeneration begins with the basal layer of the endometrium on the second day of the menstrual cycle and is accompanied by an increase in the level of oestrogen, which stimulates the proliferation process of endometrial cells. During the preparation process for implantation of fertilized ovum (blastocysts), during proliferation glycogen accumulates in the cells of the endometrium.

The hypophysis and hypothalamus react to the decrease in allocation of follitrophin by an increase in the level of oestrogen in the blood (negative inverse relation). In the middle of the cycle, when the development of the follicle and ovocyte nears the period of full maturity, the high level of oestrogen causes a sudden and substantial increase in the level of lutrophin. Ovulation occurs 10–16 h after the peak of lutrophin. The peak of lutrophin is a major reference point for morphological and hormonal changes 13–15 days after its attainment. Unlike the second phase, the duration of the first phase of the menstrual cycle is very variable.

The peak of lutrophin is evidence of the final stage of maturity for the ovocyte (completion of the first meiotic division). Follicular epithelial cells of the granular shell of the follicle absorb lipids and lutein pigment; acquiring a yellow color (the corpus luteum is formed). The corpus leteum phase of the ovarian cycle begins.

In the first half of the corpus luteum (lutein) phase the production of progesterone and the oestrogen formation amplifies. At this time the corpus luteum develops up to 80% of all the produced progesterone in the letein phase. The level of progesterone in blood serum more than 3 ng/ml is proof that ovulation occurred. If the concentration of progesterone does not reach 8–10 ng/ml approximately 7 days after ovulation, it is evidence of the insufficient function of the corpus luteum.

An increase in the levels of oestrogen and progesterone results in changes to the endometrium, directed upon the preparation of implantation of the fertilized ovum. The reserves of glycogen considerably increase, vascularization increases (lutein or secretory phase), and the glandular structure of the mucous membrane of the uterus reaches the mature form, is capable of providing the blastocyst with glucose.

The concentration of oestrogen and progesterone reaches a maximum level in the middle of the lutein (secretory) phase of the menstrual cycle. In reply to the increasing levels of oestrogen and progesterone, the secretion by the hypophysis of follitrophin and lutrophin decreases. The corpus luteum is subjected to retrogression if it is not stimulated with an adequate level of chorionic gonadotrophin (CG), formed in a significant amount the 7th day after fertilization. If a pregnancy occurs, the chorionic gonadotrophin supports the function of the corpus luteum, prevents the tearing away of the endometrium prior to the beginning of synthesis of the corresponding hormones in the placenta (sixth-eighth week of pregnancy). If fertilization does not occur, the function of the corpus luteum, the levels of progesterone and oestrogen are essentially reduced, a new menstrual cycle begins.

Disorders of the menstrual cycle can be caused by an increase in the production of oestrogen and progesterone by functional cysts of the ovaries (for example, persistency of the corpus luteum and so forth).

The *menarche* age (first menstruation) normally fluctuates from 10 to 16 years and on average is 12–13 years of age. The beginning of the ***ovulary menstrual cycle*** is characterized by regular, cyclic, predicted menstruations with an interval of 24–35 days, duration of bleeding of 3–8 days and the general blood loss of 30–80 ml. Blood clots in menstrual blood should not exceed a ten cent coin in size.

Disorders of the menstrual cycle include:

amenorrhoea — absence of menstrual flow during at least 6 months;

oligomenorrhoea — an interval between menstruation more than 35-40 days;

polymenorrhoea — uterine bleeding with intervals between menstruation less than 21 days;

metrorrhagia — uterine bleedings with irregular short intervals;

menorrhagia (hypermenorrhoea) — menstrual bleeding, occurring with regular intervals and lasting more than 8 days, with a loss of more than 80 ml of blood;

menometrorrhagia — strong long bleedings with short and irregular intervals;

hypomenorrhoea — menstrual bleeding with a duration of less than 3 days;

opsomenorrhoea — rare (an interval more than 35 days) and small (bleeding less than 3 days) menstrual bleeding;

Inter-menstrual bleedings occur during the period between regular menstruations.

AMENORRHOEA

Amenorrhoea — absence of menses for 6 months and more. Amenorrhoea is the symptom testifying to anatomic, genetic, physiological and emotional disorders. With **true amenorrhoea** there are no cyclic changes in the ovaries, endometrium, etc. ***False amenorrhoea*** is characterized by the absence of menses with the presence of cyclic changes in the gonads and in the whole organism (anomaly of genitalia development).

The absence of menarche till the age of 14 with the absence of secondary sexual attributes or till 16 with normal growth and development of secondary sexual attributes is referred to as ***primary amenorrhoea;*** the absence of menstruation in women with previous regular menstruation periods — ***secondary amenorrhoea.***

About 80% of amenorrhoea cases are connected with chronic anovulation. Anovulation normally causes amenorrhoea during puberty, pregnancy, lactation and after menopause. Pathologic amenorrhoea can be a symptom of multiple organic and functional disorders at any level of the reproductive system. The most complete classification of amenorrhoea is by the level of disorder, which unites the basic syndromes accompanying anovulation (S. S. Jen et al., 1986).

The reasons for amenorrhoea:

1. Anatomical defects of the reproductive system (developmental anomalies of the uterus, vagina, synechia).

2. Insufficient ovarian function (agenesia, disgenesis).

3. Chronic anovulation syndrome.

Hypothalamic forms:

1) disorders in the CNS-hypothalamus system;

2) hypothalamic (isolated) disorders of lutrophin-releasing-hormone secretion.

Pituitary forms:

defect or dysfunction gonadotrophins, including disorder of reception or defect of subunit synthesis.

Disorder of the inverse relation law:

1) application of oestrogen or contraceptives;

2) excessive extraglandular secretion of oestrogen;

3) disorder of the “buffer” system;

4) functional hyperandrogenesis (adrenal or ovarian);

5) steroid-producing tumours;

6) autoimmune diseases.

Recurring disorders of the inverse relation law due to combination central and peripheral disorders:

1) excessive secretion of corticosteroid or androgen (Cushing's disease);

2) hypo- or hyperthyroidism;

3) excessive secretion of prolactin (galactorrhoea-amenorrhoea syndrome) or somatotrophin;

4) eating disorder. Amenorrhoea can be normo-, hyper- and hypogonadotrophic.

Normo- or eugonadotrophic amenorrhoea is connected with inborn and acquired anomalies of the genitalia (Mullerian anomalies, imperforate hymen, transverse vaginal septum, Asherman's syndrome, tubercular endometritis), as well as with the diseases accompanying the overproduction of androgens (tumours of the adrenal glands, congenital hyperplasia of the cortex of the adrenal glands; polycystic ovarian syndrome, androgen-producing tumours of the ovaries). The ovaries thus secrete the normal amount of oestrogen and progesterone, and the inverse relation with the hypophysis provides the normal amount of gonadotrophin.

Hypergonadotrophic amenorrhoea includes chromosomal (gonadal dysgenesis), gonadal (testicular feminization syndrome, resistant ovarian syndrome) and genetic defects, disrupting the mechanism of inverse hormonal relations, necessary for the oppression of gonadotrophin secretion.

Hypogonadotrophic amenorrhoea develops secondarily, after the period of regular menstruation: under the influence of emotional stress, use of medical drugs, during diseases and tumours of the hypophysis, in cases of eating disorders, excessive physical loads, dysfunction of the adrenal glands and thyroid gland. As a rule, hypogonadotrophic amenorrhoea is also hypoestrogenic.

PRIMARY AMENORRHOEA

Depending upon the level of disorder of the reproductive system, cerebral (cortico-hypothalamic), hypothalamic (hypothalamo-pituitary), pituitary amenorrhoea, caused by diseases of the adrenal glands and thyroid gland, ovarian and uterine are distinguished. Sometimes the reasons for primary amenorrhoea are considered connected with gonadal disorders (Turner's syndrome, testicular feminization syndrome, resistant ovarian syndrome and non-gonadal.

The examination of patients with primary amenorrhoea includes gathering anamnesis; general (short height, stigmas of dysembryogenesis) and gynaecologic examination; research of the hormone levels; radiological examination (computer tomography) of the skull and sella turcica; ultrasonic and laparoscopic examinations; if necessary — gonadal biopsy. In the presence of signs of virilization, the levels of androgen of the ovaries and adrenal glands are determined in blood serum. With the purpose of diagnosis of the reasons of sexual maturity delay, functional tests with oestrogen, progesterone, gonadotrophin and releasing-hormones are conducted.

In clinical practice it is accepted to distinguish such forms of primary amenorrhoea: 1) with the absence of attributes of sexual development; 2) due to a delay of puberty; 3) against a background of virilescence; 4) with a normal female phenotype.

Primary amenorrhoea with the absence of attributes of sexual maturity takes place during gonadal dysgenesis — genetically caused by ovarian maldevelopment (instead of ovaries — bands of connective tissue, fig. 22, *a*) due to a defect of the sexual chromosomes (karyotype X0, or mosaicism).

Primary amenorrhoea due to a delay of puberty (underdevelopment of secondary sexual attributes, sexual infantility) is caused by an organic and functional pathology of the hypothalamo-pituitary systems, at which the formation and release of gonadotrophin-releasing-hormones are broken, as a result there are changes in the gonadotrophic functions of the hypophysis and ovarian function (see "Sexual development delay" p. 112). As a result of a delay in puberty, hypogonadotrophic amenorrhoea develops, characterized by a decrease in the levels of gonadotrophins (folli- and lutrophin) in the blood. Tests with progesterone and lutrophin-releasing-hormones are negative. Patients differ with eunuchoidal constitution features, hypoplasia of the mammary glands, hyperostosis of the spine of a reduced ephippium; the sizes of the uterus and ovaries correspond to those in the childhood period.

Primary amenorrhoea against a background of virilization is caused by *congenital adrenogenital syndrome* as a result of genetically caused disorders of androgen synthesis in the cortex of the adrenal glands (see "Virilization of adrenal genesis").

Amenorrhoea, caused by adiposogenital dystrophy (Pehkranz—Babinski—Frohlich syndrome) develops due to tumours or traumas of the hypothalamus, accompanied by a decrease in the secretion of releasing-hormones and gonadotrophins.

The *clinical picture* is characterized by obesity, growth inhibition and hypoplasia of the genitalia. After the elimination of the organic reason of the syndrome (tumour) the patients are appointed gonadotrophins, and further — cyclic oestrogen-gestagen therapy.

Cranyopharyngioma arises in 3% of tumour cases of the skull, more often — in the second decade of life. Sexual infantility, sexual development delay, amenorrhoea and gonadotrophin deficiency is marked in patients. Cranyopharyngioma can result in the disorder of secretion of thyro-, adreno-, somatotrophin and vasopressin.

Primary amenorrhoea with a normal female phenotype is caused *by anatomic defects of devel-*

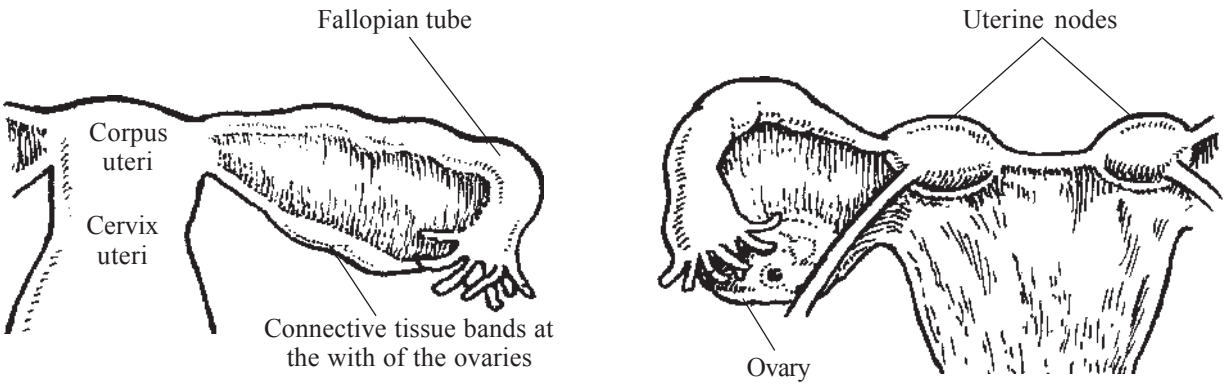


Fig. 22. Anomalies of the development of genital organs:
a — gonadal dysgenesis (connective tissue bands instead of the ovaries, decrease of the uterine seizes if the large cervix uteri exists); *b* — Mullerian agenesis (absence of the uterus and vagina during the normal development of ovaries and Fallopian tubes)

opment of the uterus and vagina. With the presence of the imperforate hymen, transverse vaginal sputum there is a delay in menstrual blood above the place of obstruction: hematocolpos, hematometer, hematosalpinx *(cryptomenorrhoea)*. In cases of *mullerian agenesis* anomaly (Mayer—Rokitansky—Custer—Hauser syndrome) with the presence of ovaries, the uterus and vagina are not present (Fig. 22, *b;* see also "Developmental anomalies of the sexual glands and disorders of sexual differentiation" p. 100).

A difficult diagnostic problem is differential diagnosis of mullerian anomalies and *testicular feminization syndrome* (tolerance to the action of androgens), at which the man's karyotype (with the presence of testicles) is combined with the female phenotype (with the presence of a blind vaginal sac and aplasia of the uterus).

Patients have developed mammary glands with an insufficient development of the peripapillary circles and papilla (the development of the mammary glands under the influence of oestrogen secretion begins at 12–13 years), insufficient pubic and axillar pilosis (in connection with the absence of receptors for androgens in target tissues). The syndrome is observed seldom (1:12,000–1:15,000), is a monogenic disease and is accompanied by androgen reception disorder, causing sever resistance to the testosterone action. The disease is diagnosed with the presence of a normal man's level of testosterone in the blood serum or by determining karyotype 46, XY while Mullarian agenesis is characterized by karyotype 46, XX, biphase ovulatory curve of the basal temperature and an increase in the level of progesterone during the lutein phase of a cycle (normal ovarian function).

The appearance of the patients, the presence of a vaginal blind ending, the absence of sexual pilosis have great value in the diagnosis of the testicular feminization syndrome. The congenital inguinal hernia where the testicle is located has diagnostic meaning. The testicles can be located in the abdominal cavity, in the depth of the labia majora. For specification of the diagnosis, ultrasonic examination, laparoscopy, biopsy of the gonads are used.

Treatment. Defective testicles are subject to obligatory removal because of the high risk of malignancy. The operation is carried out on patients at the age of 16–18 (after the completion of growth and the development of secondary sexual attributes) with subsequent hormone replacement therapy for the prevention of postcastration syndrome and genital atrophies. **Primary amenorrhoea** can develop on the background of **enzymopathy:** deficiency of 17-hydroxylase (symptoms of the disease are amenorrhoea, sexual infantility and hypertension as a result of an increase in the production of desoxy- corticosterone), as well as a deficiency of 17, 20-desmolase (primary amenorrhoea and sexual infantility).

SECONDARY AMENORRHOEA

Secondary amenorrhoea also can be caused by disorders at various levels of the reproductive system. The following forms are distinguished:

1) central — on the central nervous system level (psychogenic amenorrhoea, stress amenorrhoea, pseudo-pregnancy);

2) hypothalamic (on the background of weight loss, due to neural anorexia);

3) hypothalamo-pituitary:

— hyperprolactinemia (functional, organic);

— hypogonadotrophic amenorrhoea;

— postpartum hypopituitarism (Sheen's syndrome);

4) adrenal:

— postpubertal adrenogenital syndrome;

— virilizing tumours of the adrenal glands;

5) ovarian:

— gonadal dysgenesis, testicular feminization;

— premature ovarian failure syndrome;

— ovarian resistance syndrome;

— ovarian virilizing tumours;

6) uterine:

— endometrial synechia (Asherman's syndrome);

— tubercular endometritis.

For patients with secondary amenorrhoea it is necessary to rule out pregnancy first of all. Secondary amenorrhoea can cause severe somatic diseases (for example, autoimmune), neuroendocrine syndromes (for example, polycystic ovaries), the use of some medicines (gonadotrophin-releasing-hormone analogues, combined oral and gestagen alone contraceptives).

The central form of amenorrhoea. *Psychogenic amenorrhoea (stress-amenorrhoea)* among other forms makes about 10%, it is connected with the stress-induced increase in the synthesis of β-endorphin and the oppression of dofamin and gonadoliberin allocation, that, in turn, results in the reduction of gonadotrophin secretion. Psychogenic amenorrhoea is accompanied by the development of asthenoneurotic or asthenodepressive syndrome.

Monotonous levels of folli- and lutrophin, estradiol, the amount of which changes within the lower limits of the basal level, are observed in the blood. During gynaecologic and ultrasonic examination, the normal development of internal genitalia is observed. Due to long-term amenorrhoea the sizes of the uterus can change a little. The gonadoliberin test is positive, which confirms the hypothalamic genesis of amenorrhoea.

The treatment of patients is carried out by the gynaecologist together with the neuropsychiatrist. Antidepressants, neuroleptics, vitamin therapy with the obligatory elimination of stress factors are prescribed.

Hypothalamic amenorrhoea. *Amenorrhoea against a background of weight loss* (about 10% of the cases) can be observed in girls and young women, keeping a strict diet, intensively go in for sports, ballet. The decrease of the mass of adipose tissue results in a decrease of non-gonadal secretion of oestrogen.

The peculiar sings are a decrease in body weight 15–25% from the normal, moderate hypoplasia of the mammary glands, external and internal genitalia, absence of appetite. The level of gonadotrophic hormones is determined on the lower limit of basal secretions. During ultrasonic examination, a reduction in the size of the uterus with normal sizes of the ovaries is observed.

Amenorrhoea due to neural anorexia arises in young women and girls after mental trauma, starvation. Thus, a decrease in the secretion of lutrophin and oestrogen on the background of an increased level of follitrophin is observed.

The treatment of such patients is advisable to be carried out by a gynaecologist together with a psychotherapist, high-grade, fractional portion meals, vitamins, sedative means are prescribed. If these measures are inefficient, hormone therapy combined with oral contraceptives for the course of 2–3 cycles is prescribed.

Amenorrhoea during pseudo-pregnancy is observed in women, strongly wishing to have a child or, on the contrary, afraid of becoming pregnant. The pathogenesis is connected with a stressful increase in the secretion of lutrophin and prolactin. This amenorrhoea is always secondary; attributes of pregnancy are absent. The diagnosis is confirmed with ultrasonic examination.

Treatment: psychotherapy, sedative means, hypnosis.

Amenorrhoea with Morgagni—Stuwart—Morel syndrome (frontal hyperostosis) is a rather rare pathology and is characterized by a triad of symptoms: internal frontal hyperostosis, obesity and virilism. In women over the age of 35, secondary amenorrhoea develops; the carbohydrate metabolism is broken; convulsive attacks, mental disorders begin. Treatment is symptomatic; hormone therapy in these cases is not prescribed.

Hypothalamic-pituitary form of secondary amenorrhoea. ***Hyperprolactinemia —*** an increase in the production of prolactin in the anterior lobe of the hypophysis and its level in the blood; it is found in 15–50% of women with secondary amenorrhoea and anovulatory infertility.

Physiological hyperprolactinemia is observed during pregnancy and lactation period. *Pathologic hyperprolactinemia* develops due to anatomic or functional disorders of the hypothalamo-pituitary systems. An increase in the level of prolactin causes the oppression of oestrogen production, secretion disorders of GN-RH of the hypothalamus, thus the formation and allocation of gonadotrophin, first of all lutrophin decreases, resulting in the disorder of folliculogenesis, anovulation, insufficient lutein phase, disorders of the menstrual cycle, infertility.

The reasons for *functional hyperprolactinemia* may be the following functional disorders in the prolactin synthesis regulation system:

— oppression of the dofamin secretion— the basic inhibitor of prolactin synthesis;

— hypothyroidism, accompanied by an increase in the level of thyrotrophin-stimulator of prolactin synthesis;

— a long-term application of drugs (psychotropic, neuroleptic, hormones, oestrogen-gestagenic contraceptives);

— stress, hyperandrogeny, post-operative period and traumas of the thorax, as well as the consequences of durable lactation and abortions.

Functional hyperprolactinemia in 30% of the cases is accompanied by primary amenorrhoea and galactorrhoea (galactorrhoea-amenorrhoea syndrome).

Galactorrhoea is revealed by squeezing the papilla of the mammary glands. General weakness, increased fatigability, delay in mental reaction, chills, constipation, drowsiness, dryness of the skin, and fragility of the nails are characteristic for hypothyroidism. The first attribute of hypothyroidism can sometimes be galactorrhoea. General (total) obesity inherent in patients with hyperprolactinemia is caused by psychotrophic and antipsychotic preparations.

During the examination of patients with hyperprolactinemia, hypoplasia of the uterus, swelling of the mammary glands can be observed.

Organic hyperprolactinemia is caused by prolactin-secreting tumours of the hypophysis — micro- and macroprolactinoma. Amenorrhoea-galactorrhoea and infertility are observed in 70–100% of the patients. Macroprolactinoma (diameter more than 10 mm) is accompanied by hypoestrogeny symptoms, vision disorders due to the compression of the optic nerves, changes of the cella turcica (seen at the roentgenogram), the eye fundus and colour visual fields.

Other forms of hyperprolactinemia are amenorrhoea-galactorrhoea, connected with pregnancy and labor (Chiari—Frommel syndrome); idiopathic amenorrhoea-lactorrhoea, not connected with pregnancy, labor and tumour of the hypophysis (Argons del Castillo syndrome); tumour-induces amenorrhoea-galactorrhoea (Forbes—Albright syndrome).

The screening method of diagnosis of hyperprolactinemia is used to determine the initial level of prolactin in the blood serum. With the clinical picture of hypothyroidism, the levels of thyrotrophin, triiodidothyronin and thyroxine are determined. Prolactinomas are revealed during radiological examination of the skull and cella turcica. Symptoms of tumour development of the hypophysis can be osteoporosis of the cella turcica walls, its "double floor", jagged sites of its internal contour under unchanged structure of the cranial bones. With the presence of microprolactinoma (the most often pathology) the sizes of the cella turcica can not increase, therefore computer tomography, nuclear magnetic resonance are used with a diagnostic purpose.

Treatment depends upon the reason of the disease. With a macroadenoma of the hypophysis patients are subject to neurosurgical or radiation treatment under the conditions of a specialized hospital.

Patients with functional hyperprolactinemia, disorders of the menstrual and reproductive functions are prescribed inhibitors of prolactin synthesis — parlodel (bromcriptin), carbegolin (dostinex), serocriptin, norprolak. The action mechanism of parlodel consists of the stimulation of receptors and increase in the level of dofamin; it restores the cyclic secretion of gonadotrophin and ovarian hormones. The preparation is appointed in a doze of 2.5–7.5 mg per day depending upon the level of prolactin in the blood and the parameters of functional diagnosis. Restoration of ovulatory cycles while treating patients with parlodel, as a rule, is observed in 1–2 months of continuous therapy; pregnancy–in 1–3 months (70–80% of patients). The efficiency of the treatment depends upon the duration of amenorrhoea. With insufficient effectiveness of parlodel for 3–4 months, in addition prescribe ovulation stimulation with clomiphene (50–100 mg a day starting with the 5th till the 9th day of the menstrual cycle). If pregnancy does not occur, the preparation is combined with chorionic gonadotrophin by 1,500–3,000 U on the 2nd, 4th, 6th day of increased basal temperatures. The control of ovulation, except for the tests of functional diagnosis, is carried out with the help of ultrasonic monitoring of follicle growth with transvaginal sonograph (occurrence of a dominant follicle with a diameter of 18–20 mm), laparoscopy.

With primary hypothyroidism thyroid hormones are prescribed: thyreoidin, triiodothyronin, etc. Parlodel is also used in cases of prolactin-secreting adenomas of the hypophysis (1.25–2.5 mg and more 3 times day) until the normalization of prolactin levels, the discontinuance of pathologic lactation and restoration of reproductive function.

Pregnant women with prolactin-secreting adenoma of the hypophysis should be under the supervision of the oculist, neuropathologist and neurosurgeon.

Panhypopituitarism can occur spontaneously or due to surgical or radiation treatment of patients with adenoma of the hypophysis, as well as after a massive postpartum bleeding (Sheen syndrome). The disease is characterized by lactation disorder, anovulation, and loss of sexual pilosis, hypothyroidism and adrenal glands failure.

Hypogonadotrophic secondary amenorrhoea (15–20% of all amenorrhoea cases) is characterised by the absence of independent menstruations, infertility, disproportional constitution, and hypoplasia of the internal and external genitalia. The disease is caused by congenital mild or moderate insufficiency of the hypothalamo-pituitary system (20–25% of patients); it may be hereditary-caused. In the blood, low levels of gonadotrophin and estradiol are determined, which corresponds with the lower limit of the early follicular phase, the normal contents of prolactin, cortisole and testosterone. Hypogonadotrophic amenorrhoea occurs in patients with the Sheen syndrome (see "Neuroendocrine syndromes" p. 67).

The patients with *hypogonadotrophic amenorrhoea of the mild degree* have proportional constitution, developed mammary glands (adipose tissue instead of glandular), radiological changes in the cranial bones (the main sinus hyperpneumatization, hyperostosis of the normal-sized dorsum sellae), insignificant decrease in the level of gonadotrophin in the blood serum. The uterus and ovaries are underdeveloped (corresponding to the age of 12–13);

late menarche is observed; oligomenorrhoea turns into amenorrhoea. Tests with progesterone and luliberin are positive; the use of clomiphene is inefficient.

With *hypogonadotrophic amenerrhoea of the moderate degree* there are observed disproportional body structure, hypoplasia of the breasts, hyperostosis and a reduction in the size of the cella turcica; a moderate decrease in the level of gonadotrophin in the blood serum; the uterus and ovaries resemble those of a 10–11 year old.

Hypogonadotrophic hypogonadism, accompanying olfaction defects (bulbus olfactorios), is known as Calman's syndrome. Sexual infantilism, eunuchoid constitution, disorder of the synthesis or allocation of the lutrophin-releasing-hormone (LT-RH) are observed.

The destruction of the hypothalamus by tumours, trauma of the central nervous system, influence of radionuclides also can serve as the reason for hypothalamic amenorrhoea, deficiency of somatotrophin, thyroid hormones.

The *treatment* of such patients provides cyclic hormone replacement therapy for the restoration of menstrual-like reactions. The restoration of ovulation and the reproductive function is carried out by expert gynaecologist-endocrinologists by the use of menopausal gonadotrophin, human chorionic gonadotrophin and analogues of gonadoliberins. The latter is given intravenously at a pulsating rhythm with an interval of 60 min (circhoral rhythm) for 2–3 weeks. Treatment with gonadotrophin matters only if there is the absence of hypophysis disorders and is more effective in cases of mild hypogonadotrophic amenorrhoea.

Amenorrhoea with acromegalia and giantism is caused by the hyperproduction of somatotrophin due to adenoma, trauma or infection of the hypophysis. An increased production of somatotrophin oppresses the secretion of gonadotrophin.

Treatment is carried out in endocrinological hospitals.

Amenorrhoea with the Itsenko—Cushing's disease is caused by increased production of corticotrophin (basophilic adenoma of the hypophysis, trauma to the skull, encephalitis); with the Cushing's syndrome — overproduction of hormones by a tumour of adrenal glands.

Amenorrhoea with the "empty" cella turcica syndrome can be combined with diplopia, narrowing of the visual field. It is connected with congenital developmental anomaly of the diaphragm of the cella turcica; it can develop after the surgical removal of a tumour of the hypophysis or due to its necrosis. Thus the secretion of pituitary hormones, including gonadotrophin, are oppressed.

Ovarian amenorrhoea can be primary (gonadal dysgenesis, testicular feminization) or secondary (premature menopause, resistant ovarian syndrome).

The premature ovarian failure syndrome (premature menopause) is diagnosed when menopause occurs before the age of 40. The disease makes 3–8% among the reasons of secondary amenorrhoea .

The *clinical picture* of the disease is characterized by symptoms of ovarian function loss (congestion, sweating, and palpitation). In the ovaries, elevated atresia of the follicles takes place. The premature ovarian failure due to the action of antiovarian antibodies can be an attribute of polyorgan autoimmune disorders (together with insufficiency of the adrenal glands, hypothyroidism, etc.).

Diagnosis. A drastic increase in levels of folli- and lutrophin (5–10 times) with a significant reduction of oestrogen concentration in the blood serum has great value. Negative tests with progesterone, clomiphene, gonadotrophin and gonadoliberin testify to the irreversible changes in the endometrium and ovaries.

Treatment. Patients with ovarian failure syndrome are prescribed cyclic hormone replacement therapy (oral contraceptives, containing estradiol ≤ 0.03 mg or preparations of natural oestrogens and progestagen, used in replacement therapy during menopause). The purpose of substitution therapy is the restoration of menopause-like reactions, removal of vegetative disorders, prevention of cardiovascular disease and osteoporosis.

The resistant ovarian syndrome is the reason for amenorrhoea (3–5%) in women before the age of 35. It is associated with the ovarian resistance to the action of gonadotrophin (follitrophin). The development of the follicles in the ovaries stops before they achieve the antral stage. The exact reason of this disease is unknown and, probably, is connected with autoimmune disorders (production of antibodies, blocking the gonadotrophin receptors in the ovaries). During differential diagnosis the absence of climacteric symptoms, a substantial increase in the gonadotrophin level, and the normal prolactin level in the blood have great meaning. The contents of estradiol keeps on the lower limit for the follicular phase norm. The progesterone test is positive, which is evidence of sufficient oestrogenic saturation.

Treatment is similar to that of premature ovarian failure symptom, and consists of cyclic hormone replacement therapy.

Iatrogenic amenorrhoea can be caused by the application of hormonal contraceptives, ganglioblockers, reserpin and derivatives of fenothyazin.

In less than 1% of women amenorrhoea occurs after oral contraceptives withdrawel. However, the majority of such patients as a rule had irregular menstrual cycles prior to the use of hormonal contraceptives. Simultaneously, preparations are prescribed: derivatives of fenothyazin, reserpin, narcotics. This condition is referred to as the *excessive inhibition of gonadotrophic function of the hypophysis syndrome,*

appearing as amenorrhoea, anovulation for 3–6 months and more after oral contraceptives withdrawal.

Amenorrhoea can develop due to the application of especially gestagenic contraceptives of long action (depot-provera, norplant), which causes the development of endometrial atrophy.

Derivatives of fenothyazin, reserpin and ganglioblockers influence the hypothalamus through the dysbalance of dofamin and noradrenaline, which can lead to the development of amenorrhoea-galactorrhoea syndrome.

Diagnosis. Hormonal researches, ultrasonography, hystero- and laparoscopy are conducted.

Treatment (cyclic hormone therapy, clomiphene, gonadotrophin preparations, parlodel, inter-uterine contraceptives) begins after they rule out organic reasons of amenorrhoea, establish the hormonal status of the organism and the condition of the endometrium.

Forms of adrenal amenorrhoea, amenorrhoea due to the polycystic ovarian syndrome, neuroendocrine syndromes, uterine forms of amenorrhoea are considered accordingly in the chapter "Virilization syndromes", "Neuroendocrine syndromes" and "Developmental disorders of the reproductive system".

Diagnosis. The examination of patients with amenorrhoea begins with the lower female reproductive tract according to the stage-by-stage diagram:

1) Sexual labium (adhasion)
2) Hymen (absence of aperture)
3) Vagina (agenesia, partition)
4) Uterus (agenesia, cervix stenosis, Asherman's syndrome)
5) Hypothalamo-pituitary and central forms of amenorrhoea

During the first examination it is necessary to pay attention to three major characteristics:

— Degree of breast development
— Level of oestrogen in the blood serum
— Presence of the uterus

The level of chorionic gonadotrophin allows to diagnose pregnancy or excludes it. The presence of uterine curettage in the anamnesis of women with secondary amenorrhoea allows to suspect the Asherman's syndrome. Hysteroscopy is conducted for specification of the diagnosis.

In the case of primary amenorrhoea and delay of sexual development, the differential diagnosis of gonadal dysgenesis with hypopituitarism is conducted. The diagnosis of gonadal dysgenesis (Turner's syndrome) or anatomic anomalies (mullarian agenesis, testicular feminization, and cervix stenosis) are frequently established during objective examination. Additional examinations (prolactin level, gonadotrophin level in the blood, karyotype) are conducted if there is suspicion on a specific reason of the disorder.

The oestrogenic status is examined by determining the moisture content and foldings of the vaginal mucosa, phenomenon of cervical mucosa crystallization. In case of uncertainty of these criteria the progesterone challenge test with is conducted: 10 mg medroxyprogesterone acetate orally 1–2 times a day for 5 days or 100 mg of oil solution of progesterone intramuscularly. Menstrual bleeding occurs in a week after progestin withdrawal indicating an adequate level of oestrogen and intactness of the lower sexual tract. The diagnosis of chronic anovulation is established with the occurrence of withdrawal bleeding and the presence of oestrogens, usually connected with polycystic ovarian syndrome.

If the withdrawal bleeding does not occur, the following stages of examination depend upon the result of the prolactin level determination in the blood serum. The studies (computer tomography, nuclear magnetic resonance) are conducted in case of elevated prolactin level or the presence of galactorrhoea to rule out the diagnosis of prolactin-producing macro- or microadenomas of the hypophysis.

In case of a normal prolactin level with the absence of withdrawal bleeding after progestin challenge, the gonadotrophin level in blood plasma is determined. In elevated gonadotrophin level, the reason for amenorrhoea should be considered ovarian disorders. If the gonadotrophin level is low or normal, amenorrhoea is connected with hypothalamo-pituitary frustration or anatomic defects.

With indistinct data of the objective examination and to eliminate the diagnosis of the Asherman's syndrome it is recommended to conduct cyclic oestrogen-gestagene therapy. The absence of bleeding confirms the diagnosis of the Asherman's syndrome or other anatomic defects. With the occurrence of withdrawal bleeding after oestrogen-progestin therapy, chronic anovulation with the absence of oestrogens (functional hypothalamic amenorrhoea) is possible to be diagnosed. Radiological examination of the hypothalamus and hypophysis is conducted to rule out tumour-like processes (functional hypothalamic amenorrhoea is determined by the method of exclusion).

ALGODYSMENORRHOEA

Algodysmenorrhoea is defined as an acute pain in the lower abdomen, lumbar and sacral areas (dysmenorrhoea, algomenorrhoea) during menstruation. Algodysmenorrhoea appears in 10–30% of cases and depends upon the threshold of pain sensitivity in woman. The strong pain can result in a nervous breakdown, decrease in work capacity during menstruation.

Primary and secondary algodysmenorrhoea are distinguished. Primary algodysmenorrhoea is a phys-

iological pain during menstruation of the uterine origin; secondary — pain during the menstruation, associated with organic disorders (inflammation, ischemia, hyper-strain, compression of the organs, bleedings, etc.).

Algodysmenorrhoea is characterised by the spasmodic pain located in the lower abdomen, back, sacral area, radiating to the hips, thighs, rectum.

Primary algodysmenorrhoea. The menstrual pain which begins from menarche or later (after the formation of ovulatory cycles), does not increase from cycle to cycle, has physiological nature and is associated with the uterine contraction under the influence of prostaglandin, mainly $F_{2\alpha}$ (potential stimulator of smooth muscles and vasoconstrictor) and E_2 (potential vasodilator and aggregation inhibitor of thrombocytes). Intrauterine pressure before the beginning of menstruation can reach 53 kPa (400 mm Hg). Individual sensitivity of an organism to pain, caused by endogenic opioid substances blocking the pain receptors in tissues of the central nervous system, plays a certain role.

The pain can begin 24 h before menstrual bleedings. However, more often it coincides with the beginning and is accompanied by other symptoms of the smooth muscles spasm: migraine headache, vomiting, diarrhoea, and, as a rule, subsides on the 2nd day of the cycle, before the end of menstruation.

Primary algodysmenorrhoea never occurs during anovulatory cycles. The physiological pain during menstruation is evidence of ovulation.

Treatment is with inhibitors of prostaglandin-synthetase (naproxen, ibuprofen, diclophenak-voltaren, methindol-indometacin, brufen, mephenamin acids, and aspirin) for 3 days prior to the onset of menstruation and during the first day of the cycle in such doses:

— aspirin — 600–1200 mg every 4–6 h;

— ibuprofen (advil, buran) — 400–600 mg every 6 h;

— indometacin (methindol) — 25–50 mg every 8 h;

— mephenamin acid — first 500 mg, then — 250 mg every 6 h;

— naproxen — first 550 mg, then — 275 mg every 8 h;

— diclophenak — 75 mg every 8 h.

If the dose of antiprostaglandin agents is efficient, it can be reduced.

The physiological pain during menstruation is usually eased by the cessation of ovulation by the use of combined oral contraceptives with low contents of oestrogen and progesterone. Other methods of action: sedative preparations (valeriana, trioxazin), acupuncture, homeopathic therapy (menalgyn — 1–2 tablets 1–3 times a day for 7–10 days prior to the menstruation onset; dysmenorm — 1–2 tablets 3 times a day for 1–3 months or more), "Remens" drops — 10–20 drops 3 times a day 30 min before meals or 1 h after meals for 2–3 months.

Secondary algodysmenorrhoea can have uterine, intramural and extrauterine reasons.

Reasons for secondary algodysmenorrhoea

Uterine	*Intramural*	*Extrauterine*
Myomatous	Adenomyosis	Endometriosis
Polyps	Myomatous	Tumours
Intrauterine spiral		Inflammation
Endomyometritis		Adhesions
Cervical stenosis		Psychogenic reasons
Damage to the cervix		Other (non-gynaecological) reasons
Developmental anomalies of the uterus		

More often secondary algodysmenorrhoea is caused by adenomyosis, retrocervical endometriosis, inflammatory diseases of the uterus and appendages with accompanying neuralgia of the pelvic nerves, pelvic adhesions.

Symptoms of adenomyosis can be insignificant discharge ("spotting") before and after menstruation. The pain, as a rule, is not accompanied by nausea, vomiting, migraines, and diarrhoea. Secondary algodysmenorrhoea occurs in women with developmental anomalies of genitalia complicating the menstrual outflow, uterine myoma, large polyps of the endometrium. The reasons for painful menstruation can be also intrauterine contraceptives resulting in the contraction of the myometrium, varix dilatation of the uterine broad ligament, ovarian ligament, rupture of the posterior branch of the uterine broad ligament (Allen—Masters' syndrome).

Diagnosis is based on the anamnesis data, results of ultrasound research and laparoscopy (revealing endometriosis, adhesions, etc.).

Treatment of patients with secondary algodysmenorrhoea depends upon its reason. When impossible to establish the reason of the disease, symptomatic therapy is conducted. Analgesics and combined oral contraceptives are prescribed.

UTERINE BLEEDINGS

Bloody discharge from the uterus is one of the most common symptoms of gynaecologic diseases and can occur in women of any age. Uterine bleedings conditionally are divided into two big groups.

Dysfunctional uterine bleedings (DUB) are caused by changes in the endometrium due to the

disorder of ovarian hormonal function, as a rule, on against a background of absolute or relative hyperoestrogenism and progesterone deficiency. DUB can develop during puberty (juvenile bleeding), in the reproductive period and perimenopause due to the disorders of the functional condition of the hypothalamic-hypophyseal-ovarian axis. More than 80% of the cases of dysfunctional uterine bleedings are connected with chronic anovulation.

Anovulatory dysfunctional uterine bleedings occur acyclic, with intervals of 1.5–6 months, prolonging, as a rule, more than 10 days. They are observed during the beginning or fading of the function of the reproductive system when there are disorders of circhoral emission of luliberin (juvenile, perimenopausal bleedings). Anovulatory DUB can be observed during the reproductive period due to disorders on any level of function of the hypothalamic-hypophyseal-ovarian axis.

The anovulatory endometrium, because of an insufficiency of the progesterone phases of the cycle, is at a stage of chronic oestrogen-stimulated proliferation. The thickened endometrium disintegrates not completely, resulting in irregular bleedings.

Organic uterine bleedings have an anatomic substratum: fetal egg or its remnants; tumours of the cervix, endometrium, and ovaries; an internal endometriosis (adenomyosis) and so forth.

JUVENILE BLEEDINGS

Juvenile bleedings make about 10–12% of all gynaecologic diseases in patients of the pubertal1 age and occur due to anovulation. The risk factors are infectious-toxic influences on the hypothalamic structures, stress, excessive physical loads, and irrational eating style. Anovulation, being the reason for juvenile bleedings, is caused by atresia of the follicles, which have not reached maturity. Thus, the production of oestrogen and progesterone is reduced, secretory transformations of the endometrium do not occur, which prevents its timely sloughing off and causes long bleeding without expressed endometrial hyperplasia. The reason for bleeding is also insufficient uterine contraction activity in this period of development.

Clinical picture. Juvenile bleedings, as a rule, are observed within first 2 years after menarche. The condition of the patient depends upon the degree of blood loss and severity of the accompanying anemia. The expressed anemia is characterized by weakness, absence of appetite, fatigue, paleness of the skin and mucous membranes, tachycardia, headache, changes of rheological and coagulation parameters of the blood.

Diagnosis is based on the hystory (age of the patient, the onset of menstruation), the typical clinical picture. The anovulatory character of cycles is confirmed with the help of functional diagnosis tests, hormonal examination.

The differential diagnosis is conducted with diseases of blood system (thrombocytopenic purpura), hormone-active tumours of the ovaries, uterus, cervical cancer (very rare!), abortion. For diagnosis ultrasonography, rectal and rectoabdominal examinations with the emptied intestines and bladder are used. If necessary, the cervix is examined by means of children's specula or vaginoscope.

To rule out the diagnosis of pregnancy examination of the chorionic gonadotrophin β-subunit level in the blood serum, ultrasonic examinations are conducted. With the presence of nose bleedings, bleedings after extraction of teeth, from the gums, as well as hypodermic haemorrhages, carefully examine the condition of the coagulation blood system. In the case of anomaly revealing the patient is recommended a consultation with the hematologist.

Treatment of patients with juvenile bleedings is complex and includes arrest of bleedings (hemostasis) and prevention of its relapse. The choice of method of haemostasis depends upon the condition of the patient. With a severe condition, expressed oligemia (paleness of the skin and mucous membranes, contents of haemoglobin in the blood lower than 80 g/l, hematocrit — less than 25%) and strong bleedings, *surgical haemostasis* — curettage of the uterine mucosa with subsequent hystologic examination of the endometrium, is recommended. The hymen before the operation is cut away with a 0.25% solution of novocain in a mix with 64 U of lydasum.

Infusion-transfusion therapy is conducted for the liquidation of oligemia and anemia (by indications — transfusion of the erythrocyte mass, albuminous preparations, dextran, and crystalloid). Extended oral introduction of iron preparations (ferroplex, tardyferon, conferon, ferrogradumet), vitamins of group B, ascorbic acid, rutin (quercetin), folic acid, uterotonic agents, gluconate or calcium chloride — by 10 ml of a 10% solution intravenously — are prescribed. Abundant drinking, juices and a rational diet are recommended.

In 26–28 days after surgical haemostasis it is necessary to induce menstrual-like reactions. With this purpose, girls with hyperplastic processes of the endometrium are prescribed dufaston, gestagen preparations (norcolut — 5–10 mg from the 11th (16th) till 25th day of the cycle).

If the patient's condition is average or satisfactory (when symptoms of anemia and oligemia are not vividly expressed), conservative haemostasis with oestrogen-gestagen drugs (oral contraceptives) or oestrogen alone with the further application of gestagen are prescribed.

Oestrogen-gestagen drugs with the contents of 50 mg of estradiol are prescribed — 4–5 tablets a day till the bleeding arrest (as a rule, it stops by the end of the first day). Then the doses are reduced by a tablet a day, leading up to 1 tablet, and then con-

tinue treatment for 16–18 days (general oestrogen-gestagen therapy course should be 21 days).

Microfollin (ethynylestradiol) is prescribed at 0.05 mg orally 4–6 times a day till the bleeding stops, further, the dose is reduced daily, leading up to 0.05 mg a day for 8–10 days and then at once prescribe gestagen (norcolut — 5 mg for 10 days or progesterone — 1 ml of a 1% solution intramuscularly for 6 days; 17-oxyprogesterone capronate — 1 ml of a 12.5% solution intramuscularly 2 times with an interval of 2–3 days (on the 17th and 21st days of the cycle); medroxyprogesterone acetate — 10 mg a day for 10 days).

Prevention of relapses of juvenile DUB with the presence of endometrial hyperplasia is conducted by prescribing combined oral contraceptives during three menstrual cycles. Gestagen may also be used — 5 mg a day from the 16th till the 25th day of the menstrual cycle for 4-6 months.

Sanitary measures have great value in the prevention of juvenile bleedings: sanitation of the centers of infection (caries of the teeth, tonsillitis, etc.), physical training (outdoor games, gymnastics, skiing, swimming), high-grade meals with the restriction of fat and sweets, vitamin therapy in the spring-fall seasons (aevit, B vitamins, ascorbic acid, tocopherol).

The prognosis is favorable under the conditions of adequate therapy. With the absence of treatment endometrial hyperplasia can progress, chronic anovulation, infertility develop.

DYSFUNCTIONAL UTERINE BLEEDINGS DURING THE REPRODUCTIVE PERIOD

Dysfunctional uterine bleedings in women of the reproductive period between the ages of 18–45 make approximately 30% of all gynaecologic diseases.

Etiology and pathogenesis of DUB in the reproductive period are connected with functional disorder in the hypothalamic-hypophyseal-adrenal axis, resulting in anovulation. The risk factors of these disorders can be abortions, endocrine and infectious diseases, intoxications, stress, medications intake (for example, derivatives of fenotyazine).

Hence, contrary to juvenile bleedings, more often atresia does not occur but persistency of the follicles in the ovaries with the excessive oestrogen production. Ovulation does not occur, the corpus luteum is not formed, progesterone-deficiency condition takes place against a background of hyperoestrogenism. In the endometrium, proliferative processes and hyperplastic changes progress. The bleeding begins from necrotic infarction sites of the hyperplastic endometrium.

Diagnosis is based on the hystory, objective examination, as well as on the exclusion of other pathologic conditions, accompanying uterine bleeding (disorder of uterine or ectopic pregnancy, delay in parts of the fetus egg, placental polyp, submucous node of uterine myoma, polyp of the endometrium, adenomyosis, cancer of the endometrium, ovarian polycystic syndrome, complications due to the use of intrauterine devices applications). Ultrasonography is used; the levels of hormones in the blood serum are determined; functional diagnostic tests are used.

Hysteroscopy and medical-diagnostic fractional currettage of the cervical canal and uterus with further analysis play an important role in diagnosis of uterine bleedings. Reproductive age women with DUB have as a rule hyperplastic processes in the endometrium: glandular, glandular — cystic, atypical endometrial hyperplasia. During hysteroscopy it is possible to find polyps, myomatous nodes, endometrioid paths.

Hysterosalpingography is conducted with the help of water-soluble X-ray contrast substances 1–2 days after curettage; however, it is less informative than hysteroscopy. Ultrasonic examination (especially three-dimensional emission-contrast echography) allows estimating the myometrium structure, revealing and determining the sizes of the myomatous nodes, adenomyosis, diagnose polycystic changes in the ovaries (increase in their sizes, thickening of the capsule, multiple small cysts with a diameter of 8–10 mm) find and specify the position of an intrauterine device or its parts, conduct differential diagnosis of pregnancy.

Colposcopy and cytologic inspection of the smears, taken from the cervical canal, allow excluding the diagnosis of cervical cancer.

Treatment depends upon the reason of the bleeding, includes obligatory surgical haemostasis and prevention of DUB relapses. Fractional curettage of the mucous membrane of the cervical canal and the uterus with subsequent hystologic exam of the received material is conducted. Anemia, oligemia are managed by infusion and antianemic therapy similar to those of juvenile bleedings. If present uterine myoma or endometrial polyps are deleted surgically (conservative myomectomy, hysterectomy). Small submucous peduncular myomas, polyps can be removed by performing hysteroresectoscopy.

For the prevention of DUB relapses the patient is prescribed hormone therapy, depending upon her age, reproductive anamnesis, desire of pregnancy, as well as the results of hystologic exam of the endometrium.

For the treatment of patients with *dysfunctional anovulatory uterine bleedings* a necessary condition is the stabilization of the endometrium before reaching the controllable episodes of bleeding.

Last years for the *treatment* of patients with hyperplastic processes in the endometrium, such preparations are successfully prescribed (see also “Endometrial hyperplasia” p. 133):

— Derivatives of hydroxyprogesterone — 17-oxyprogesterone capronate (17-OPC)

— Derivatives of acetooxyprogesterone — medroxyprogesterone acetate ("Provera", "Depot-Provera", megestrol acetate, cyproteron acetate androcure)

— Derivatives of ethynyltestosterone — danazole, pregnin

— Derivatives of 19-norsteroid — gestrinon (nemestran)

— Combined oral contraceptives

— Stimulators of ovulation (clomiphene, menopausal and chorionic gonadotrophin)

At the outpatient setting patients are prescribed oestrogen-gestagen drugs with a great number of hormones (1 tablet 3 times a day for 7 days), that, as a rule, results in bleeding stop, then — the combined oral contraceptives — 1 tablet a day for 21 days, as a result withdrawal bleeding occurs. Therapy with *progestin* for 10 days promotes a rather full detachment of the endometrium, and it is recommended to patients with hyperoestrogenism. For the stabilization of the endometrium in patients with intense bleedings, anemia accompanying by extragenital diseases, foreign gynaecologists advise intravenous introduction of conjugated oestrogens (25 mg every 6 h for 24 h). Controllable episodes of bleeding are further reached with the help of combined oral contraceptives.

If there is no necessity for contraception, cyclic therapy of medroxyprogesterone acetate is prescribed (10 mg daily during the first 10 days of each month), causing the expected bleeding. Oral contraceptives provide both contraception and stabilization of the endometrium.

With glandular-cystic endometrial hyperplasia, patients take monophase or biphase oestrogen-gestagen drugs — 1 tablet the 5th through the 25th day after curettage, further — the 5th through the 25th day of the menstrual cycle for 3–4 months, for relapsing hyperplasia — for 4–6 months. Gestagens alone are also used (norcolut, preparations of progesterone). Norcolut is given 5 mg orally the 16th through the 25th day after curettage, further — the same days during the menstrual cycle, the treatment course— 3–6 months. Oxyprogesterone capronate is given intramuscularly 1 ml of a 12.5% solution on the 14th, 17th and 21st day after curettage, further — the same days during the menstrual cycle for 3–4 months (for relapsing hyperplasia — 4–6 months). For the stimulation of ovulation clomiphen is prescribed — 50–150 mg the 5th through the 9th day of the cycle for 3 cycles. Upon the termination of the course of hormone therapy, control cytologic research of a smear of the endometrium or control curettage of the uterine mucosa with further hystologic research of the taken material are conducted.

The patient with adenomatosis or atypical endometrial hyperplasia is recommended to take a 12.5% solution of oxyprogesterone carpronate — 4 ml intramuscularly 2 times a week for 3 months, further — 2 ml 2 times a week for 3 months.

Danazol and gestrinon render anti-oestrogenic and anti-gonadotrophic action; oppress the synthesis of steroids in the ovaries and the formation of gonadotrophin in the adenohypophysis. The preparations should be taken continuously by women 40 years and older: danazol — 400–800 mg a day, gestrinon (nemestran) — 2.5 mg 2 times a week for 3–6 months, monitoring the condition of the endometrium (ultrasound of the endometrium, control curettage the first 3 months after ending the course of treatment and hystologic examination of the smears).

Contraindications for hormonal treatment are thrombembolia, jaundice during pregnancy, varix dilation of the lower extremities and rectum, chronic diseases of the liver and biliary tract.

The prognosis with adequate treatment, as a rule, is favorable. If the treatment is inefficient, in 3–4% of the cases endometrial hyperplasia progresses (adenomatosis, atypical hyperplasia, adenocarcinoma). In many women with DUB fibro-cystic mastopathy, myoma of the uterus, adenomyosis, and anovulatory infertility are revealed.

Prevention of DUB in women of the reproductive period includes proper diagnosis and treatment of chronic anovulation, hyperplastic processes in the endometrium. One of methods of DUB preventing is using oral contraceptives, which promote reduction of proliferative processes in the endometrium.

DYSFUNCTIONAL UTERINE BLEEDINGS DURING THE TERMINATION OF MENSTRUATION

Etiology, pathogenesis. DUB during the termination of menstruation (climacteric period, premenopause) occurs due to the age changes in the functional condition of the hypothalamic-hypophyseal-ovarian axis. Aging of these structures results in disorder in the cyclic emission of lutrophin-RH, lutrophin and follitrophin. Changes in ovarian functions consist of disorder in the growth and maturing of follicles, their atresia or persistent anovulation, insufficient function of the corpus luteum, progesterone-deficient condition on the background of relative hyperoestrogenism. These changes, as well as the ageing function disorders of the immune system, promote the development of hyperplastic processes in the endometrium in women at the transition age and increase the risk of their malignant transformation.

The *clinical picture* is similar to DUB in the reproductive period, and depends upon the volume of blood loss, degree of anemia and oligemia. However, it can be worsen due to the accompanying extragenital and neuroendocrine disorders (adiposity, hypertension, diabetes).

Diagnosis is conducted by eliminating organic pathology, the incidence of which rises in women of this age (uterine myoma, adenomyosis, and endometrium polyps, hyperplasia and cancer of the endometrium, hormone-active ovarian tumours). Diagnostic opportunities extend due to the use of modern methods of ultrasonography (transvaginal, emission, contrast and so forth), diagnostic fractional curettage of the mucous membrane of the cervical canal and uterus with subsequent hysteroscopy in a liquid medium; hysterography with water-soluble contrast substances, laparoscopy. Echoscopic attributes of endometrial hyperplasia are its thickness more than 15 mm, heterogeneity of structure, presence of hyperechogenic inclusions. In women with regular menstruations, examination is conducted during menses, on the 20th–25th day and repeated — on the 5th–7th day of the cycle.

Treatment should begin with fractional medical-diagnostic curettage of the mucous membrane of the cervical canal and the uterus. Further treatment tactics depends upon the results of hystologic examination of the endometrium, age of the patient, presence of accompanying gynaecologic and extragenital pathologies.

Indications to *surgical treatment* (hysterectomy) are adenocarcinoma of the endometrium, a combination of DUB with relapsing adenomatosis or atypical endometrial hyperplasia, the central form of adenomyosis, uterine myoma, an increase in ovarian sizes; relative indications — relapsing endometrial glandular-cystic hyperplasia, metabolic-endocrine disorders.

Conservative treatment of patients is conducted under the conditions of isolated hyperplastic processes in the endometrium, the absence of other pathology, as well as in the case of a combination of hyperplastic processes in the endometrium with small intramural-subserous myomatous nodes, the diffuse form of adenomyosis (an increase in the uterus untill it reaches the size of a 8 week pregnancy).

To prevent the relapses of DUB after curettage, mainly gestagen drugs are used: 17-OPC — 1–2 ml of a 12.5% solution intramuscularly for the 14th, 17th and 21st day after curettage, further — the same days of the cycle for 6 months. In women up to the age of 50 17- OPC is given by 250 mg 2 times a week for 6 months. With the purpose of endometrial hyperplasia regressing, the preparation "Provera" is used — 30–50 mg the 14th through the 25th day of the cycle, dufaston — 10–20 mg the 11th–16th through the 25th day of the cycle for 6 months, danazole — 200–400 mg a day for 3 months, gestrinon — 2.5 mg 2 times a week for 4–6 months. Norcolut, orgametril are also used (5–10 mg orally the 16th through the 25th day of the cycle after curettage, and further — the same days of the cycle for 4–6 months). With atypical endometrial hyperplasia it is recommended to apply the preparation "Depot-provera" (medroxyprogesterone acetate) by 200–400 mg intramuscularly once a week for 6 months.

Contraindications for taking gestagen, danazole, gestrinon are thrombembolia disease in the anamnesis, varix dilation, and diseases of the kidneys, hepatobiliary and cardiovascular systems, accompanied oedemas.

Recently preparations of androgen are not used for the oppression of menstrual functions, because they cause symptoms of virilism, arterial hypertension. Besides, their metabolization to oestrogens in adipose tissue, endometrium and other tissues, having receptors for sexual steroids is possible. Modern methods of treatment of patients with DUB with endometrial hyperplasia are so-called *minimally invasive surgical procedures* which are conducted under endoscopic (hysteroscopic) control: cryolysis of the endometrium, transcervical resection (ablation), laser ablation of the endometrium with the help of YAG-Nd-lazer.

Cryolysis is conducted with a special device working by the principle of compulsory circulation of liquid nitrogen (the cooling of the cryozone reaches 170–180°C). After cryolysis, the content of cytozol-receptors of estradiol in the endometrial tissue, which hinders its proliferation, is normalized. In 2–3 months the endometrium is replaced with cicatricial tissue and amenorrhoea develops. Cryolysis has no contraindications and gives a sound therapeutic effect.

Ablation of the endometrium is conducted by means of special instruments — resectoscope — under the control of a hysteroscopy. The endometrium is removed, including its basal layer, and the myometrium at the depth of 1–2 mm, after which the uterine form of amenorrhoea develops.

The complex of medical means consists of the normalization of endocrine-metabolic disorders by keeping an adequate diet with the restriction of animal fats, carbohydrates, liquids and salts; the use of hypocholesterinemic (cetamyphene, miscleron), hypolipoprotein (linaethol), lipotrophic (methionine, lipoid acid) drugs, immune-modulators and vitamins.

The prognosis under the conditions of adequate treatment in many cases is favorable. The risk factors for the progressing of hyperplastic processes and endometrial cancer development are obesity, diabetes, a high calorie diet abundant in animal fats, heredity factor.

The disease *prevention* for DUB is similar to that used for women of the reproductive age.

Bloody discharge during menopause when the function of the ovaries has stopped, should be examined as a symptom of an organic pathology and, first of all, it is necessary to rule out malignant tumours (cervical cancer or (more often) of the uterus, hormone-active tumours of the ovaries; (see "Uterine bleedings of the organic nature", p. 59).

OVULATORY UTERINE BLEEDINGS

Ovulatory bleedings are observed in 20% of the cases of uterine bleedings. Intermenstrual ovulatory bleedings and ovulatory bleedings caused by persistent corpus luteum, are distinguished.

Intermenstrual uterine bleedings occur in the middle of the menstrual cycle, the days corresponding with ovulation, lasting 2–3 days and are not intensive; they are accompanied by the ovulatory syndrome. The *pathogenesis* is connected with a decrease in the level of oestrogen in the blood serum after the ovulatory hormonal peak.

The *clinical picture* is characterized by significant bloody discharge in the middle of the menstrual cycle, which can be accompanied by pain in the lower abdomen from the side where ovulation is taking place.

The *diagnosis* presents no difficulties. The control for the ovulatory character of the bleeding is conducted with functional diagnostic tests (measurement of the basal temperature, examination of the levels of hormones — estriol, progesterone, folli- and lutrophin in the blood serum). The differential diagnosis is made with polyps of the endometrium and cervical canal, cervical endometriosis, adenomyosis, erosion and cervical cancer. For diagnosis colposcopy, hysteroscopy (after the bleeding has stopped), hysterography (on the 5–7th day of the menstrual cycle) are used.

Treatment is conducted only with the presence of profuse discharge. Oral contraceptives — 1 tablet the 5th through the 25th day of the menstrual cycle for 3–4 months, in the case of accompanying pain syndrome — inhibitors of prostaglandin- synthetase (indometacin, naproxen, ibuprofen, and aspirin) are prescribed to suppress ovulation.

Dysfunctional uterine bleedings, caused by persistent corpus luteum, are rarely observed and are connected with disorders of the gonadotrophic stimulations of progesterone synthesis. The increase in the contents of progesterone in the blood interferes with the normal endometrial sloughing off during menstruation.

The *clinical picture* is characterized by a delay in menstruation by 4–6 weeks with subsequent moderate bleeding.

Diagnosis. Bimanual examination reveals some softening of the uterus (influence of progesterone) and unilateral small increase of the ovary, in which during ultrasonic examination it is possible to find lutein cysts, are determined. The diagnosis proves to be true by the data from the hystologic examination of the endometrium (secretory changes in glands and decidual reaction of the endometrial stroma).

The treatment of patients begins with fractional curettage of the mucous membrane of the cervical canal and uterus. Regulation of the ovarian functions is conducted with the help of cyclic use of oestrogen-gestagen drugs such as oral contraceptives for three menstrual cycles.

UTERINE BLEEDINGS OF ORGANIC NATURE

Uterine bleedings for organic reasons (Fig. 23) can occur at different age periods. In girls they can be caused by hormone-active tumours of the ovaries (granular-, theca-, granular- and thecacellular). These bleedings are not strong and are accompanied by clinical symptoms, premature development of secondary sexual attributes (see "Developmental disorders of the reproductive system" p. 96). For diagnosis, ultrasonic examination, hystero- and laparoscopy are used.

In women of the reproductive age uterine bleedings are mainly connected with disturbed uterine or

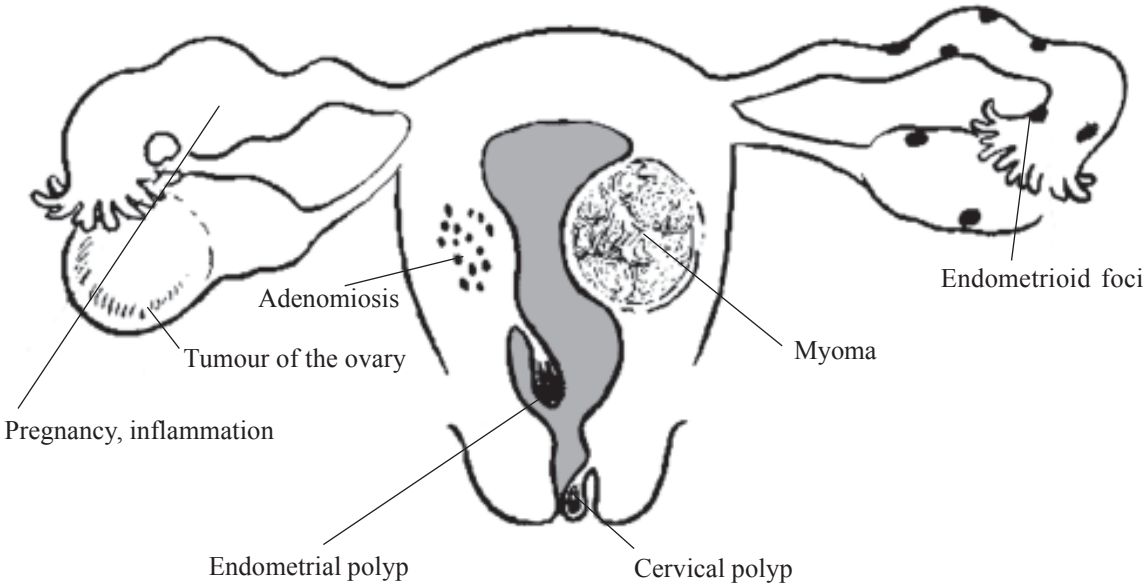


Fig. 23. Organic reasons for uterine bleedings

ectopic pregnancies, tumours of the cervix and uterus, hyperplastic processes in the endometrium, adenomyosis, trophoblastic disease, complications due to the use of intrauterine contraceptives.

The main cause of uterine bleedings during the termination of menstruation is hyperplastic processes and tumours of the cervix and uterus (benign and malignant), adenomyosis.

Bloody discharge during menopause are more often connected with endometrial or cervical cancer, sometimes — polyps, inflammatory processes on the background of atrophy of the epithelium of the uterus and vagina.

The *diagnosis* of the reasons for bleeding during menopause includes obligatory fractional diagnostic curettage of the mucous membrane of the cervical canal and uterus under the control of hysteroscopy, aspiration or biopsy with further hystologic research of the taken material; ultrasonic examination of the uterus and ovaries to eliminate the diagnosis of neoplastic processes. For diagnosis of cervical diseases colposcopy and cervical biopsy are used.

Feminization (oestrogen-producing) tumours of the ovaries can be accompanied by an increase in the elasticity of the skin, improvement in the trophicity of the nails, hair, which gives women a younger look.

Polyps are tolerant to hormone therapy (hormone independent) and are subject to surgical removal during hysteroscopy. To prevent relapses, cryolysis of the polyp is conducted. In the case of a relapsing polyp of the endometrium, hysterectomy is conducted.

Bloody discharge during menopause can be caused by atrophic colpitis as a result of hypoestrogenism and the addition of an infection.

For treatment a 5–10% emulsion of synthomycin with the addition of a 0.1% oil solution of 1 ml folliculin or sinestrol in 10 g of emulsion are prescribed. Orally estriol is prescribed by 0.5 mg 2 times a day for 10–12 days; locally suppositories, “Ovestin” cream, lactobacillin (”Vagilak”) preparation are prescribed after anti-inflammatory therapy.

RECOMMENDED READING

7; 15; 16; 18; 20; 24; 38; 75; 79; 92; 94; 95; 108.

Chapter 4
VIRIL SYNDROMES

Viril syndromes (virilism) consist of various adrenogenital disorders of the adrenal and ovarian genesis, basic clinical display being virilization.

Virilism is understood as the occurrence of man's secondary sexual characters in women, namely: hirsutism (excessive hair in the adrenal-sensitive zones — the face, the lower half of the back, breast, buttocks, peripapillary circles, inner thighs, external genitalia, pubis — fig. 24), acne, disorders of the menstrual cycle (oligo- and amenorrhoea, dysfunctional uterine bleedings), deepening of the voice, hair loss in the temporal zones, hypertrophy of the clitoris, loss of female body habitus, infertility. Such symptoms are observed in the case of disorder of the ovarian function and function of the adrenal glands as a result of androgen-secreting tumours of the ovaries and adrenal glands, congenital hyperplasia of the cortex of the adrenal glands (congenital adrenogenital syndrome).

Evaluating the degree of hirsutism, it is necessary to take into account significant racial and genetic distinctions in the amount of hair follicles and hair, especially above the upper lip and on the lower extremities.

The influence of androgen on a woman's organism depends upon several factors:

— degrees of their production;

— susceptibility of tissue (organs);

— speed of their metabolism;

— level of androgen-linked proteins in the blood plasma.

Androgens metabolism. In the ovaries and adrenal glands in women some androgens are secreted: testosterone, androstendion, dehydroepiandrosterone. Primary ovarian androgens are *androstendion* and *testosterone,* secreted by stroma and theca endocrinocytes (theca cells) of the ovaries. The reticular zone and cortex of the adrenal glands produce *dehydroepiandrosterone* (DHEA) and *dehydroepiandrosterone-sulphate* (DHEAS). The influence of androgen of the ovaries and adrenal glands depends upon the phase of the menstrual cycle and pathologic changes. Normally, in a women's organism about 870–1040 nmole (250–300 mg) of testosterone (in men — 20,800 nmole/day or 6,000 mg/day) are produced daily. Approximately 50% of testosterone is formed as a result of glandular secretion and 50% — peripheral conversion of androstendion. From 3 mg/dl of androstendion half of its amount is produced by the ovaries, the rest — by adrenal glands; 14% of this amount is converted into testosterone in the liver, skin, blood, skeletal muscles under the action of 17-ketosteroidreductase.

The influence of androgen on androgen-dependent tissue is shown by the stimulation of growth of hair follicles under the action of *dehydrotestosterone,* which is formed from testosterone with the participation of enzyme 5T-reductase. The basic metabolite of dehydrotestosterone — *androstendiolglucuronide* — also produced in peripheral tissue, and its levels are frequently increased in women with hirsutism. The contents of testosterone in blood plasma (in a free and a bound form) normally for women do not exceed 30–35 ng/dl. Only 1% of testosterone normally is in a free (unbound) form, and about 80% of it connects with testosterone-binding globulin. The binding activity of the latter decreases with the increase of androgen levels, in particular, with obesity.

Clinical displays of hyperandrogenism can be caused by the following factors:

1) Hyperproduction of androgenism or their predecessors.

2) Reduction in the level of testosterone-connecting globulin.

3) Increase in the fermental activity of androgen receptors in hormone-dependent tissue.

Hair growth. Hair follicles appear about the 8th week of the gestation period as a derivative of the epidermis. The amount of hair is determined by genetic factors. Men and women have approximately identical amounts of hair follicles. Three types of hair are distinguished:

1) *lanugo* — short, tender hair, covering the body of the fetus and newborn;

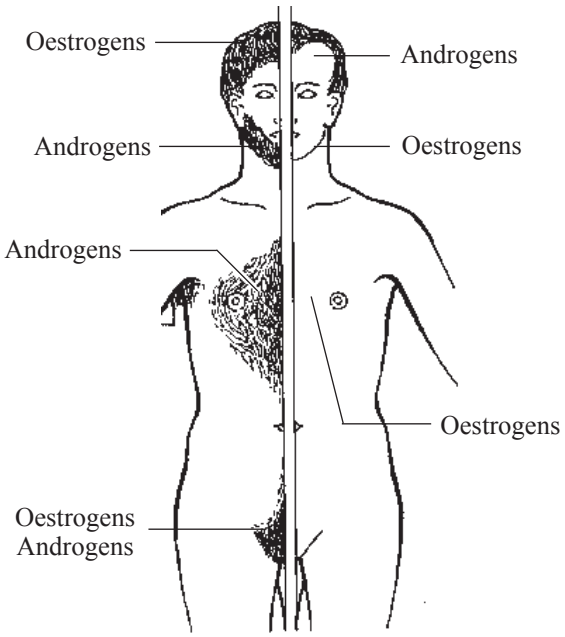


Fig. 24. Stimulation and suppression of the hair growth under the influence of oestrogens and androgens

2) *vellus hair* — soft, short, nonpigmented hair;

3) *terminal (final) hair* — long, thick, pigmented (on the scalp, in hormone-sensitive zones).

Vellus hair can be transformed into terminal under the influence of androgenic stimulations (growth of a beard in young men during puberty).

Hair growth is cyclic: the periods of growth are replaced by dormant periods (inactive periods), which has value when determining the term for therapy in patients with hirsutism. These periods include growth phases, fast involution and rest.

Diagnosis. The examination of patients with hyperandrogenism begins with the elimination of life-threatening diseases (adrenal glands or ovarian tumour). With the presence of hirsutism and disorders of the menstrual rhythm, since puberty, it is possible to suspect ovarian polycystic syndrome or congenital hyperplasia of the adrenal cortex with subsequent display in the advanced age. Cases of family hirsutism can testify about ethnic, or idiopathic, hirsutism with an increase in the level of 5α-reductase or androgen receptors in the skin. In women with congenital hyperplasia of the adrenal cortex, there may also be a burdened familial hystory. In the case of an acute onset and fast progressing hirsutism with displays of virilism, it is necessary to suspect the development of a tumour.

Objective examination of the patient has great value. Acanthosis can testify to the ovarian polycystic syndrome; insulin-resistent, abdominal strips of stretching of the skin and obesity of the trunk are characteristic for the Cushing's syndrome; galactorrhoea associated with hyperprolactinemia. Careful abdominal and gynaecologic examinations allow the finding of space occupying lesions in appendages. Additional methods of exam include laboratory analysis of the level of DHEAS or testosterone in blood plasma, ultrasonograph, laparoscopy, computer tomography or nuclear magnetic resonance.

Idiopathic hirsutism can be observed in women with normal ovulatory menstrual cycles and normal serum levels of androgen. However, in the peripheral androgen-sensitive tissue (hair bulbs, sebaceous glands), the activity of enzymatic conversion of testosterone into dehydrotestosterone increases. The contents of androstendiol glucuronide in blood serum are increased more than in 80% of the women with hirsutism, having a normal menstrual rhythm, and the degree of its increase corresponds with the intensity of hirsutism.

ADRENAL VIRILIZATION

Congenital (pubertal) adrenogenital syndrome (congenital hyperplasia of the adrenal cortex), is found during puberty, is observed in patients with hirsutism in 1.2–20% of the cases and can be connected with a deficiency of 21-hydroxylase or other enzymes. As a result of the deficiency, a reduction in the production of cortisol results in the increased release of corticotrophin of the hypophysis, stimulations of steroidgenesis in the adrenal glands and hyperproduction of androgens. Differential diagnosis is conducted with ovarian polycystic syndrome. An increase in the level of 17-hydroxyprogesterone as a reply to the stimulation of corticotrophin allows the distinction of congenital adrenogenital syndrome from ovarian polycystic syndrome.

Post-pubertal adrenogenital syndrome comes to light in women over the age of 20. Attributes of virilism are expressed moderately (hypertrichosis, acne), the phenomena of defeminization is not observed. Disorders of the ovarian functions are characterized by anovulation, insufficiency of the lutein phase of the menstrual cycle (insignificant decrease in the production of estradiol, pronounced — progesterone). Disorders of the menstrual cycle are shown as hypo-, oligomenorrhoea, rarely — amenorrhoea. Infertility or premature labor due to hyperandrogenism and insufficiency of the lutein phase of the cycle are observed. Differential diagnosis is conducted with the ovarian polycystic syndrome. In the blood, an increase in the level of androgen of the adrenal genesis, in the urine — their metabolites are found. After the test with dexamethasone, a reduction in the contents of DHEA in the blood and 17-KS — in the urine is observed.

Treatment is directed on the oppression of androgen secretion by the use of dexamethasone (0.25 mg/day). With the normalization of androgen levels,

but the preservation of anovulatory cycles and insufficiency of the lutein phase, the stimulation of ovulation with clomifen (50–100 mg from 5th day of the cycle till the 9th day) is prescribed. During treatment, ovulation is controlled by using functional diagnosis tests, ultrasonic monitoring of follicle growth, laparoscopy.

Hyperandrogenism of the adrenal genesis can develop in patients with **Cushing's syndrome** caused by central hyperproduction of corticotrophin or the presence of an adenoma of the hypophysis **(Itsenko—Cushing's disease).** Other, rarer, reasons are ectopic production of corticotrophin by tumours of the lungs, extra-sternal or pancreas, or independent of the corticotrophin level cases of adenoma or carcinoma of the adrenal glands. Hyperandrogenism causes an increase in the level of glycocorticoids, which, in turn, results in the production of androgen by the adrenal glands. Obesity, menstrual cycle irregularities, hirsutism, virilism, infertility which demand differential diagnosis with ovarian polycystic disease can be observed in patients. Red stripes of stretching on the abdomen, breasts, arterial hypertension, muscular weakness, and osteoporosis are characteristic for Cushing's syndrome. The specific test for this pathology is an increase in the cortisol level in a 24-hour urine portion or an absence of reduction of its contents in the morning urine (at 8.00 o'clock) after receiving dexamethasone by 1 mg on the eve at 23.00 o'clock.

Adenoma or carcinoma of the adrenal glands. Virilizing tumours of the adrenal glands in women are observed rather seldom. The diagnosis is based on the clinical displays of virilism (hirsutism, amenorrhoea, etc.) and proves an increase in the contents of DHEA, DHEAS in the blood serum and 17-ketosteroid in the urine. Large tumours can also produce cortisol and androstendion. The test with night suppression of cortisol level, as a rule, is negative. To confirm the diagnosis of a tumour of the adrenal glands, computer tomography or nuclear magnetic resonance is used. The adenoma of adrenal glands sometimes can primarily produce testosterone. In this case, the level of 17-ketosteroids is normal, and testosterone is considerably increased.

Disorder of testosterone-binding globulin production results in an increase in the level of active androgens and can be accompanied by the development of obesity, hyperthyroidism and hypertrichosis.

The treatment of patients with adrenal tumours, tumours of the hypophysis is conducted in specialized surgical hospitals.

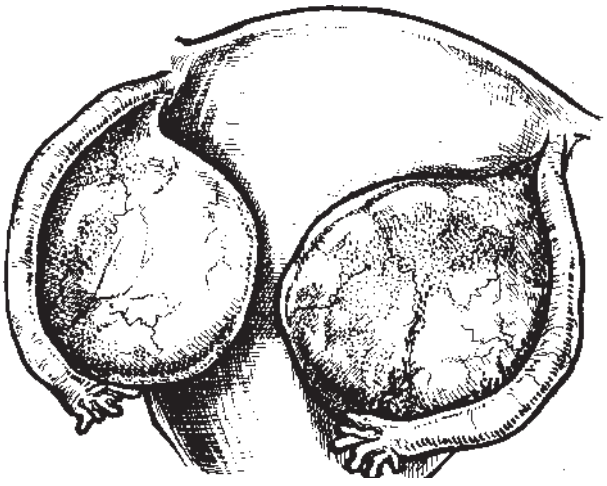
OVARIAN VIRILIZATION

The ovarian polycystic syndrome (disease), or Stein—Leventhal syndrome (disease) is characterized by a bilateral increase and sclerocystic (polycystic) changes in the ovaries and is revealed as chronic anovulation, obesity (not always), hirsutism, oligo- or amenorrhoea, and frequently connected with the increase in ovarian secretion of androstendion and testosterone.

The ovarian polycystic syndrome (disease) (primary ovarian polycystic or Stein-Leventhal syndrome) for the first time was described by Stein and Leventhal in 1935. It is revealed in 3–7% of women of the reproductive age.

Now, conditions with various pathogenesis, revealed as hyperandrogenism and polycystic changes of the ovaries are united under this name.

Most frequently, increased, white, with a smooth surface and thick capsule ovaries, which contain multiple follicular cysts in different stages of atresia (Fig. 25), hyperplasia, theca-shell and stroma, frequently — the absence of white bodies, are observed.



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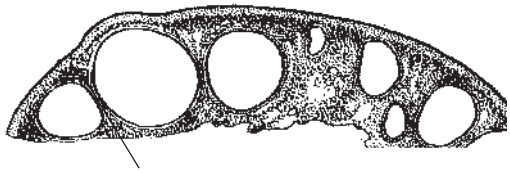

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Fig. 25. Typical manifestation of the polycystic ovarian syndrome: enlargement of the ovaries, enlargement of the capsule, hyperplasia of the cortex and multiple follicles in different stages of atresia

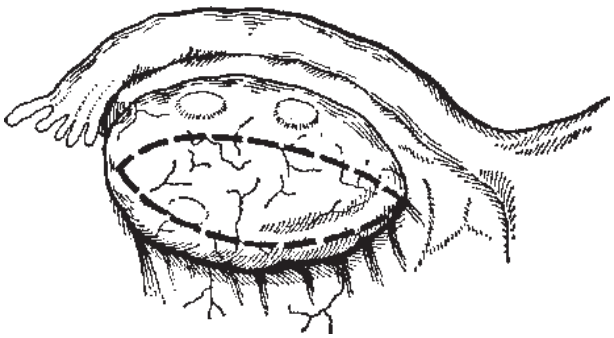


Fig. 26. Clinoid resection of polycystic ovaries

Etiology, pathogenesis. The etiological factor of the disease is unknown. It can be presumed that it can be connected with a constant, instead of cyclic lutrophin secretion in the hypothalamic-hypophyseal axis or excessive secretion of androgen by the ovaries or adrenal glands *(secondary polycystic ovaries, or ovarian polycystic syndrome)*. The disease can be transmitted by the autosomal-dominant and X-linked types. Androgens (mainly androstendion), which are secreted in excessive amounts by the ovaries, are transformed in fatty and other tissue of the organism into estrone. The increased contents of androstendion and other androgens interfere with the maturing of follicles, causing anovulation.

The increased contents of estrone, circulating in the blood, result in an increase in the luntrophin secretion by the hypophysis and a decrease in the follitrophin secretion. High concentrations of lutrophin cause hyperplasia of the theca endocrinocytes and stroma of the ovaries, as well as an increase in the androgens secretion, resulting in chronic anovulation. The decreased follitrophin secretion delays the maturing of follicles. With obesity the amount of sex steroids grows as a result of the decrease in contents of steroid-binding globulin (increase in concentration of free testosterone), and in connection with increased transformation of androstendion into estrone. The more the degree of obesity, the more cycles will be broken in connection with the aromatization of androgens into oestrogens in fat cells, which, in turn, results in an inadequate production of lutrophin by the mechanism of positive inverse relation. The termination of the development of follicles serves as the reason for an increase in the sizes of the ovaries, thickening of their capsule, the occurrence of multiple follicular cysts. The ovarian production of androgens is accompanied by an increase in the adrenal synthesis of androgens.

Clinical picture. The disease is characterized by disorders in the menstrual cycle (oligo-, amenorrhoea), chronic anovulation, infertility, obesity (in 40% of the cases), hirsutism, acne, an increased fat content of the skin, connected with androgens excess. Sings of true virilism (deepening of the voice, enlarged clitoris) are observed seldom.

An intensifying growth of hair in such patients is usually observed during puberty and can progress or remain at one level. Sometimes virilism develops. Dysfunctional uterine bleedings, as a rule, are caused by the influence of oestrogens and arise without any cyclicity, begin at various times, are characterized by various duration and volume of blood loss.

In a majority of the patients with ovarian polycystic syndrome menarche occurs on time. However, further menstrual bleedings are irregular, oligo- and amenorrhoea develop. Long and acyclic stimulation of the endometrium by oestrogen results in its hyperplasia, dysfunctional bleedings; the risk of uterine cancer development increases.

Diagnosis is based on the history data, the clinical picture, inspection of ovarian (testosterone, etc.) and adrenal androgens level, ultrasound and laparoscopy study. Ultrasonographic criteria of polycystic ovaries are their enlargement (volume more than 9 cm^3), the presence of 8–10 follicular cysts with a diameter of 3–8 mm, an increase in stromal density. During laparoscopy (or laparotomy) the smooth white capsule, enlarged ovaries — up to 5–6 cm in length and 4 cm in width, multiple follicular cysts are found.

An increase in the ratio of lutrophin/follitrophin > 2–2.5 in the blood plasma is a marker of the ovarian polycystic syndrome. In the case of fast progressing hirsutism more detailed researches to eliminate the diagnosis of virilising ovarian tumour are conducted.

Treatment should be individual, consists of cessation of inadequate cycles and depends on the patient's desire for future fertility. Treatment can be conducted in several ways: 1) reduction of androgen production by the ovaries (wedge resection — fig. 26, laparoscopic resection, thermocautherization, laser vaporization, diathermocoagulation of the ovaries, use of combined oral contraceptives); 2) oppression of peripheral synthesis of oestrogen (reduction of body weight); 3) with desire of pregnancy — increase the secretion of follitrophin and achieve ovulation by means of using antioestrogen clomiphen citrat (clostilbegit) which causes ovulation in 3/4 of the cases. With other patients wedge resection (pregnancy within first 6 months after the operation is desirable), laparoscopic thermocauterization, laser vaporization of the ovaries or the use of menopausal gonadotrophin can be effective.

The restoration of ovulatory cycles after the operation is temporary. Fertility fades already at the end of 1st year after the operation, and in 3–5 years constant anovulation is observed. The absence of pregnancy for 6 months after operation with the presence of an ovulatory cycle (by functional diagnosis tests) confirms the peritoneal or tubal factor of infertility.

The normalization of body weight in patients with obesity has special value. In non-obese patients

and those who are not interested in pregnancy periodic withdrawal bleedings can be achieved by the use of medroxyprogesterone acetate ("Depot-Provera") once a month, which can prevent the development of endometrial hyperplasia. In the case of hirsutism and unwillingness of pregnancy, suppression of the ovarian and adrenal androgen secretion with the help of combined oral contraceptives with antiandrogen action ("Diane-35", etc.) is conducted.

Hyperthecosis is characterized by the presence islets of luteinizing theca-cells in the stroma of the ovaries. The level of androgen with hyperthecosis is usually higher than in patients with ovarian polycystic disease; cases of virilism are observed. The lutrophin/follitrophin ratio, as a rule, equals 1 in comparison with the increased one (> 2) with ovarian polycystic disease. A majority of the patients have anovulatory cycles and the inefficient induction of ovulation by the use of clomiphene citrate are observed.

The diagnosis is based on the history data, extent of virilism, microscopic confirmation of stromal hyperthecosis after wedge resection of the ovaries.

Androgen-secreting ovarian tumours should be suspected with the presence of patients' complaints of fast progressing hirsutism and other displays of virilism. Solid hormone-active ovarian tumours are found in 3% of the cases. Granulosa-theca-cell tumour, which usually secretes oestrogens, in some cases can cause virilism while the tumours from Sertoli—Leydig's cells, secreting, as a rule, androgen, sometimes results in feminization.

Such ovarian tumours as thecoma, luteoma, arrhenoblastoma (tumour from Sertoli—Leydig cells), Leydig's tumour and (rarely) granulosa-cell tumours are usually related to hirsutism and virilism. The incilence of malignant tumours of this group (as a rule, small size) makes up 20–30% of the cases.

After removing the androgen-producing tumours, all displays of virilism regress within several months, except for the timbre of the voice which remains low and hoarse. Menstruation, as a rule, restarts in 3 months; in 10% of the patients pregnancy and the birth of healthy children are possible.

Treatment. In patients with hyperandrogenism the disease management depends on the reason of the androgenic crisis. Ovarian and adrenal tumours are subject to surgical removal. The patient with thyroid disorders and Cushing's syndrome is prescribed the corresponding hormonal drugs. In the case of obesity, an adequate diet is necessary; a loss of the body weight is in most cases accompanied by the decrease in the androgens level. However, conversion of vellus into terminal hair can be irreversible even with the restoration of ovulatory cycles.

Cosmetic treatment includes the removal, shaving of hair, the use of depilatory creams, and electrolysis in combination with drugs. Acne, as a rule, is responsive to the reduction of the androgen level under influence of drugs.

In most cases, displays of hirsutism may only ablate. Treatment should continue 8–10 months, shorter courses are ineffective.

The oppression of gonadotrophin secretion is necessary for adequate suppression of the androgen production by the ovaries, for example in the case of polycystic ovaries. Oral contraceptives reduce the cyclic and basal levels of lutrophin, promote the growth of testosterone-binding globulin, which reduces the level of active testosterone. In addition, oral contraceptives strengthen the clearance of testosterone in the liver and in this connection reduce the contents of DHEAS.

The correction of hyperandrogenism with hyperplasia of the adrenal glands is conducted with the help of glucocorticoids, which promote a decrease in the level of corticotrophin (prednisone at a dose of 7.5–10 mg/day provides maximal suppression of androgens after 2-month's therapy; dexamethasone — 0.5 mg at night inhibit the night level of ACTH secretion and results in a less expressed hold up of liquid than prednisone).

Antiandrogens are effective due to the influence on androgens in target organs. Cyproterone acetate and spironolactons bind with the androgen receptors and inhibit binding of dehydrotestosterone. "Diane-35" is prescribed the 5th through the 25th day of the menstrual cycle for 6 months; if necessary the treatment courses are repeated. As feminization of a male fetus is possible, the use of antiandrogens is discontinued during pregnancy.

Spironolacton (veroshpiron) is the antagonist of aldosterone, potassium-saving diuretic; in addition it is capable of competing with androgens while bonding with their androgenic receptors. Spironolacton also inhibits enzyme P-450 in steroid-producing cells that results in a decrease in the androgens level in the plasma. Clinical efficiency is achieved when a preparation is used in a dose of 50–200 mg daily; satisfactory results are observed in 2–6 months. Upon the discontinuance of therapy hirsutism can recur. In the case of tolerance to spironolacton, it is used in combination with oral contraceptives or dexamethasone.

In *patients with hirsutism* treatment can be therapeutic and cosmetic. Therapeutic treatment provides:

1) suppression of androgen secretions by the ovaries or adrenal glands by the use of oral contraceptives, glycocorticoids or analogues of gonadotrophin-releasing hormones;

2) prescription of antiandrogens which influence the amount of hair follicles and sebaceous glands (cyproterone acetate — "Diane-35", "Androcure").

Depilatory creams are applied both for shaving, and for mechanical removal of hair (new growing

hair is usually softer). The pulling out of hair yields unstable results and can be accompanied by the development of folliculitis and irritation of the skin.

Electrolysis is used for the destruction of dermal papilla with the help of electric vibration and possesses permanent effect. For greater efficiency treatment should be conducted after 9–10 month medicamentous therapy for the achievement of synchronization of terminal hair. Side effects can be the formation of scars, pigmentation, and papilloma virus or hepatitis B virus infection during the use of bacterial instruments.

RECOMMENDED READING

7; 15; 16; 18; 20; 24; 38; 75; 79; 92; 94; 95; 108.

Chapter 5
NEUROENDOCRINE SYNDROMES

Neuroendocrine gynaecological syndromes are connected with the disorders of the hypothalamic-hypophyseal axis as a major link in the regulation of specific functions of the female organism. However, each of these syndromes with the presence of a general pathogenesis is characterized by specific symptoms.

POSTPARTUM NEUROENDOCRINE SYNDROME (POSTPARTUM OBESITY)

Postpartum neuroendocrine syndrome (PNES, postpartum obesity), described for the first time by V. M. Serov in 1970, is characterized by a disorder of the menstrual and reproductive functions against a background of an increase in body weight after an abortion or labor (in 3–12 months). The development of the syndrome is observed in 4–5% of women after an interrupted pregnancy or labor complicated by gestosis (arterial hypertension, pre-eclampsia), as well as surgical interventions and manifest itself by an excessive increase in the body weight, bleedings.

The pathogenesis of PNES is not completely clear. A hereditary burden of endocrine diseases, obesity, infections and intoxications during puberty can be an adverse premorbidal background. After labor hypophysotrophic functions of the hypothalamus do not restore and metabolic disorders remain, resulting in the development of the clinical picture of PNES.

Family anamnesis is characterized by obesity, diabetes, arterial hypertension. Women with PNES, as a rule, have menstrual cycle disorders, excessive body weight from childhood, as well as often infectious diseases. The gain of the body weight after pregnancy is 8–10 kg and more.

Due to the increase of the corticotrophin level, there is an increase in the concentration of cortisol in the blood, the development of prolactin increases, the level of testosterone increases, the level of estradiol and to a greater extent — progesterone that is connected with anovulation is a little reduced. The carbohydrate (hyperglycemia) and lipid metabolism (increase in the contents of cholesterol, triglyceride, lipoproteins of low and very low density, increase in the atherogenous factor in the blood serum) are broken.

The *clinical picture* of PNES is shown as obesity (weight-height index — above 30), chronic anovulation, moderate hypertrichosis, tendency to arterial hypertension, hyperglycemia. The so-called Cushing distribution of adipose tissue to the areas of the humeral zone (climacteric tubercle), in the lower abdomen is observed. The skin of the stomach, hips and buttocks are covered by multi-coloured stretch marks — from pale to bright pink; hypertrichosis, acne are observed. The subthalamic disorder symptoms include headache, fast fatigue, dizziness, polyuria, polydipsia, polyphagia, and hyperthermia.

15–20% of women have oligo- or amenorrhoea, anovulatory uterine bleedings occur. The disorder of the subthalamic regulation of lutrophin and follitrophin discharge of the hypophysis results in the disorder of folliculogenesis and the maturing of the ovum, and anovulation.

Hyperoestrogenism in patients with PNES promotes the development of proliferative changes in the endometrium (hyperplasia), mammary glands (fibrocystic disease). Without adequate treatment of women with PNES secondary polycystic ovaries (PCO) of the hypothalamic (central) genesis are gradually formed. The source of hyperandrogenism can also be the adrenal glands, as moderate hypercorticoidism takes place, and the ovaries.

Diagnosis. Data from the anamnesis, objective examination, the presence of an increased level of corticotrophin, cortisol, and testosterone have great value; the tendency to elevated levels of prolactin and lutrophin is also observed. The levels of the FSH, oestrogen change within the normal limits; the con-

centration of progesterone is reduced. Additional methods of research include ultrasonic examination of the ovaries (determine their sizes and structures), roentgenography of the skull and cella turcica, endometrial biopsy, EEG, glucose tolerance test.

Differential diagnosis of PNES is carried out with the Cushing's disease (together with the endocrinologist), ovarian polycystic syndrome, and constitutional obesity.

NEUROMETABOLIC ENDOCRINE SYNDROME UNCONNECTED WITH PREGNANCY

The symptoms, characteristic for PNES, sometimes develop in girls and women who has not been pregnant, as well as against a background of obesity during puberty, after infections, stress, etc. The basis of the pathogenesis of these neuroendocrine syndromes is disorder of the hypothalamic structure function, in particular disorder of synthesis and degradation of neuro-transmitters (dofamin, serotonin, endorphin), the sensitivity of neurosecretory structures of the hypothalamus to them.

The *clinical picture* is similar to that of PNES: anovulation, oligo- or amenorrhoea, progressing obesity, hypertrichosis, infertility (can be primary as opposed to PNES), hypothalamic disorders (polyuria, polyphagia, hyperthermia, and sleep disorders), hyperfunction of the adrenal cortex (stretch marks).

The *diagnosis* is confirmed by the increased levels of cortisol, testosterone, corticotrophin and prolactin with a normal level of follitrophin and increased contents of lutrophin, having a definitive tendency to increase. The increased contents of testosterone are connected with the development of polycystic ovaries.

The treatment of neuro-metabolic-endocrine syndromes, connected and unconnected with pregnancy, is difficult and long. The criteria of efficient treatment are following: 1) reduction of the body weight; 2) restoration of ovulatory menstrual cycles without the application of ovulation stimulators; 3) restoration of ovulatory menstrual cycles on the background of direct ovulation stimulators; 4) pregnancy as a parameter of restoration of the reproductive function.

The first stage of treatment is *reduction diet,* directed at the reduction of body weight (5024–7536 kJ, or 1200–1800 kcal) while observing the principles of a balanced diet: eating 5–6 times, replacement of animal fats with vegetative ones, limited use of sugar, honey, flour products, normalization of gastrointestinal tract function, observing of days of limited intake of food — dairy, cheese, apple, meat-vegetable). The reduction of body weight by 5–6 kg the 1st month of treatment is considered satisfactory. The restoration of a regular ovulatory cycle on the background of diet-therapy occurs in 8–9% of women. Necessary components of treatment are physical exercises, muscular loads — long walking, run, and swimming. From medicamentous preparations, simultaneously with the diet veroshpiron at a dose of 0.025 g 3–4 times day for 2 months is prescribed. Regulators of neuro-mediatory metabolism (chloracon, diphenin, parlodel) are prescribed.

The use of these preparations against a background of a reduction diet normalizes the exchange and promotes additional reduction in body weight of 8–10 kg. Approximately 40–50% under the influence of such treatment has a renewal in regular ovulatory menstrual cycles and fertility. The absence of ovulation and pregnancy, against a background of normalized body weight and metabolism, is evidence of the development of secondary polycystic ovaries, which is proven by the results of echoscopic examinations or laparoscopy.

Clomiphene, using the usual schema (the 5th through the 9th day of the cycle at a dose of 50–150 mg, controlling with the basal temperature) is prescribed to stimulate ovulation; the dose can be increased up to 150 mg day. Surgical stimulation of ovulation (wedge resection or thermocauterisation of the ovaries) is recommended with the inefficiency of clomiphene and the presence of laparoscopic picture of polycystic ovaries.

The *prognosis* of recovery for patients is favourable under the conditions of adequate therapy. With the absence of treatment, patients are in the risk group for the development of endometrial cancer.

Prevention consists of duly revealing and removal of the disorders, which have occurred during puberty, pregnancy and labor.

POSTPARTUM HYPOPITUITARISM (SHEEN'S SYNDROME)

The incidence of postpartum hypopituitarism, or Sheen syndrome, makes 0.1% of the cases. However, after massive postpartum bleedings it can reach 40%.

Etiology, pathogenesis. The syndrome develops as a result of necrotic changes in the hypophysis, occurring against a background of spasm or intravascular coagulation of blood in the frontal lobe of the hypophysis after bleedings or bacterial shock during labor and abortions. The development of these changes is promoted by the feature of blood supply of the hypophysis, the mass of the frontal lobe which increases 2 times during pregnancy; the complication of pregnancy by late gestosis with the development of chronic DIV-syndrome; a short

intergenetic interval (less than 2 years). Preparations of ergot (methyloestradiol), used for postpartum bleedings play a certain role.

Clinical picture. Displays of the disease depend upon the extent of affection of the hypophysis. The expressed clinical picture is observed with the affection of 80% of the tissue of the adenohypophysis. Necrotic changes in the adenohypophysis, as a result of intravascular thromboses, are accompanied by trophic changes in other organs and systems — kidneys, liver, brain.

The syndrome is characterized by a various degree of hypofunction of the adrenal glands, thyroid and sexual glands. Depending upon the insufficiency of trophin hormones of the hypophysis, different forms of the syndrome are distinguished: 1) complete — with clinical displays of TTH, gonadotrophin, ACTH insufficiency (the disease can proceed in a light or severe form); 2) partial — with gonadotrophic, thyrotrophic, corticotrophic function insufficiency; 3) combined (gonadotrophic and thyrotrophic; thyrotrophic and adrenocorticotrophic) insufficiency.

By the degree of severity three forms of Sheen's syndrome are distinguished — mild, moderate and severe. *The mild form* of the syndrome is characterized by headaches, fast fatigue, fever, tendency to arterial hypotension. During careful examination, a decrease in the function of the thyroid gland and glycocorticoid functions of the adrenal glands is found in patients.

For the *moderate forms* of the Sheen's syndrome, a decrease in the hormonal function of the ovaries — oligomenorrhoea, anovulatory infertility; thyroid gland — pastous, tendency to swelling, nail fragility, dryness of the skin, fatigue, arterial hypotension with predisposition to loss of consciousness are characteristic; these symptoms can be observed in various combinations.

The severe form of the Sheen's syndrome is shown by symptoms of complete hypofunction of the hypophysis with the insufficiency of gonadotrophic hormones (hypogonadotrophic amenorrhoea, oligotrophy of the genitalia and mammary glands), thyrotrophin (hypothyroidism, myxedema, baldness, drowsiness, decline in memory), corticotrophin (arterial hypotension, adynamia, weakness, hyperpigmentation of the skin). Expressed reduction of the body weight, stable anemia is characteristic for the severe form.

Diagnosis. The characteristic anamnesis and the connection of the onset of the disease with bleeding or septic shock during abortion or labor are important. A distinctive attribute of the syndrome is agalactia. Hypoglycemia, a decrease in the levels of gonadrotrophic hormones, corticotrophic, thyrotrophic, estradiol, cortisol, sex hormones, T_3 and T_4 are found in the blood. With the use of gonadotrophic hormones the level of peripheral hormones in blood accordingly increases.

Differential diagnosis is conducted with neural anorexia, tumour of the hypophysis, Addison's disease, myxedema.

The *treatment* consists of glycocorticoids and thyrotrophic preparations replacement therapy with the presence of clinical displays of hypofunction of the thyroid gland and adrenal glands. Prednisolon is prescribed by 5 mg 2 times a day for 2–3 weeks, while supervising the level of adrenal hormones. Patients with oligo- and amenorrhoea before the age of 40 are prescribed cyclic hormone-therapy, vitamins of the B group, ascorbic acid (vitamin C), tocopherol acetate (vitamin E), nicotinic acid (vitamin P), preparations of iron for anemia, as well as a high-grade protein diet.

Prevention of the disease consists of rational tactics of observing pregnant women with gestosis, prevention of obstetric bleedings and adequate treatment.

PREMENSTRUAL SYNDROME

Premenstrual syndrome (PMS) — a compound constellation of psychological, vegetovascular and metabolic-endocrine disorders which occurs cyclically, 1–14 days prior to menstruation, stop with its beginning and do not manifest themselves at least during first 7 days of the menstrual cycle. Usually premenstrual syndrome accompanies ovulatory cycles.

The frequency of PMS increases with the years: up till 30 years it is about 20%, after 40 years with the presence of a regular menstrual cycle it reaches 55%.

Pathogenesis of PMS has not been elucidated yet; hyperoestrogenism (relative with a deficiency of progesterone or absolute) and the delay caused by it of sodium and liquids in the tissues of the organism, first of all in the central nervous system, play an important role. However, a significant reduction of the contents of progesterone in the blood of patients with PMS is not found. According to other hypotheses, prolactin, functional disturbance of renin-angiotensin-aldosteron pathway, secretion of prolactin or vasopressin, which promotes the delay of liquids, as well as prostaglandin, β-endorphins, serotonin, deficiency of vitamins — retinol (vitamin A,), tocopherol acetate (vitamin A) and pyridoxine (vitamin B_6), which are co-factors to the production of serotonin and prostaglandin, play a main role. Possible reasons for PMS may also be disorders of thyroid hormones secretion, hypoglycemia, and infectious processes in the ovaries. The primary neurohormonal disorders at the level of the hypothalamus allow the cure of PMS before the development of hypothalamic syndrome.

In the opinion of the majority of gynaecologists, premenstrual syndrome includes multiple physiological, instead of psychological symptoms. Some

authors, depending on the clinical picture of the disease, allocate light and severe stages of premenstrual syndrome, as well as four clinical forms: neuro-psychological, hydropic, cephalgetic and crisis — although they are hardly distinguished in the practical work.

The neuropsychological form is characterized by irritability (depression, aggression), general weakness, increased sensitivity to sounds and smells, tenderness of the breasts.

For *hydropic forms* of the syndrome the following are peculiar: tenderness and sensitivity of the breasts, swelling of the face, shins, fingers of the hands, bloating of the stomach, irritability, weakness, sweating, of skin itching, negative diuresis (delay of liquid of up to 500–700 ml).

Cephalgetic form of PMS is characterized by the pulsating migraine-like headaches beginning in the temporal area and irradiating to the eyeball, irritability, nausea and vomiting, sensitivity to sounds and smells, dizziness, expressed depression, pain in the heart area, sweating, numbness of the hands, tenderness of the breasts, edema with the presence of positive diuresis.

The crisis form develops, as a rule, with the absence of treatment with any form of PMS, and is connected with the dysfunction of dophamin structures of the hypothalamus and especially advances severely during pre-menopause. The crisis has a sympathoadrenal character, develops against a background of stressful situations, is accompanied by the feeling of fear, an increase in arterial pressure, tachycardia, sweating.

Rare forms of PMS are the atypical form (similar to hyperthermal and ophthalmoplegic forms of migraines), cyclic allergic reactions, as severe as Quincke's edema, cyclic trench mouth and stomatitis, cyclic "bronchial asthma", vomiting, i.e. typical displays of psychosomatic pathologies.

Diagnosis is based on data of the anamnesis, cyclic character of the pathologic symptoms. Objective inspection allows eliminating the organic pathology.

Treatment is conducted according to the age of the patient, duration of the disease, the clinical form of PMS, accompanying extragenital pathologies. With an obscure etiology and physiopathology syndrome, a broad spectrum of medicamentous, physical and psychotherapeutic methods of treatment, which, however, are insufficiently effective, are used. In 40–50% of the cases the temporary positive effect is achieved due to the use of placebo.

A necessary component of treatment is *psychotherapy;* the basis of which includes the explanation to the woman of the essence of her disease, recommendations concerning auto-training, a regime of work and rest, keeping to a diet, especially during the II phase of the menstrual cycle. The diet provides the use of fresh vegetables and fruit, restriction of sweets and fat dishes, frequent meals of small portions for the prevention of hypoglycemia, as well as the reduction of the use of salt (prevention of meteorism) and coffee (reduction of nervousness). *Physical exercises* (promote the increase of the production of β-endorphin), *general massage* and *massage of the collar area, balneotherapy, endonasal electrophoresis with thiamin* (vit. B1), *central electroanalgesia* from the 5th till the 14th day of the cycle are also recommended. With hyperoestrogenism and the sensitivity of receptors to progesterone, gestagen (pregnyl internally, progesterone (utrojestan) — as rectal or vaginal suppository; norcolut or duphaston — by 5–10 mg starting the 16th day of the cycle for 10 days) are recommended.

The *induction of anovulation* is achieved with the help of oral contraceptives, danazol, agonists of gonadotrophin-releasing-hormone. However, danazol and agonists of gonadotrophin-releasing-hormone — zoladex (goselerin), decapeptil give an unstable positive effect. With allergic reactions, antihistamine preparations (tavegil, suprastin, pipolphen, diazolin), which are taken 2 days prior to menstruation and within its first day, are prescribed.

With an increase in the level of prolactin, mastodynia, parlodel (1.25 mg day in the second phase of the cycle for 8–10 days) is prescribed. Diuretics are applied for the reduction of symptoms of delay of liquid and salt in the organism (veroshpiron, spironolacton — antagonists of aldosteron — 4 days prior to the display of symptoms by 25 mg 2 times a day prior to the beginning of menstruation). Tocopherol acetate (vitamin A) promotes the reduction of sensitivity of the breasts, and pyridoxine (vitamin B_6) improves the exchange of histamine; it is prescribed appointed at 40 mg 2 times day in the second phase of the cycle for 10 days. An overdose of pyridoxine can lead to the development of peripheral neuropathy.

Symptomatic treatment consists in the application of non-steroid anti-inflammatory means, inhibitors of prostaglandin synthetase (oral or suppository): ibuprofen at a dose of 400–600 mg 2–4 times a day, indometacin — 25–50 mg 3 times a day, diclofenac — by 75 mg 3 times a day from the 14–16 day of the cycle till the beginning of menstruation.

By indications, sedative means (valeriana), tranquilizers (trioxazin, relanium, sibazon) are prescribed. Treatment is useful by conducting in cycles (no less than 3), with 2–3 month breaks. If necessary, experts of adjacent profile (neuropathologist, psychotherapist, etc.) are involved in the conducting of treatment. If the symptoms of PMS recur, treatment by cycles should be repeated. From homeopathic preparations, "Dysmenorm" — 1–2 tablets 3 times a day (30 min before eating) for a long period of time, "Remens" — by 10–20 drops 3 times a day (30 min before eating or 1 h after) for 2–3 months, are applied.

Patients with premenstrual syndrome, especially in the premenopause period, are in the group of risk for the development of climacteric syndrome.

POSTCASTRATION SYNDROME

Postcastration syndrome (PCS) is understood as a constellation of pathologic vegetovascular, psychological and metabolic-endocrine symptoms developing after total or subtotal ovariectomy in women of the reproductive age. The frequency of PCS with the absence of preventive therapy reaches 80% of all cases of this disease.

Pathogenesis. Surgical removal of the ovaries promotes a sudden decrease in the level of sex hormones, disorder of neuro-transmitter secretion, accompanied by hypergonadotrophic conditions, resulting in pathological symptoms, characteristic for the climacteric syndrome.

Clinical picture of PCS is characterized by vegetovascular symptoms, the expressiveness of which is a parameter of the severity of PCS: hot flashes, reddening of the face, sweating, tachycardia, arterial hypertension, heart pain and headache. Metabolic-endocrine disturbances include obesity, hypercholesterinemia, hepatocholecystitis, atherosclerosis, osteoporosis, atrophic changes in the breasts and urinogenital system (cystitis, urethritis, atrophic vaginitis, kraurosis and leukoplakia of the vulva). The development of osteoporosis is shown by pain in the lumbar or thoracic department of the spine, knees, radiocarpal, humeral joints, and muscles. The density of bone tissue decreases in 2 years after ovariectomy; the risk of fractures rises.

Displays of PCS (neurovegetative, psychoemotional, metabolic-endocrine, and osteoporosis) develop already in 2–3 weeks after the operation and reach full development in a few months.

Diagnosis of PCS does not represent difficulties, it is revealed on the basis of the anamnesis and typical clinical picture.

Treatment. In modern gynaecology, preventive therapy for patients with PCS within 1 year (no less) after the operation is conducted. Treatment is conducted stage by stage, depending on the age of the patient and volume of operative intervention. It consists of the use of cyclic hormone replacement therapy (in view of contraindications), the use of phytoestrogens, non-hormonal medicamentous and nonmedicamentous means. For hormone replacement therapy natural oestrogens ("Divigel"), combined oestrogen-gestagen drugs ("Divina", "Climen", "Climonorm", "Cyclo-proginova" — by 1 dragee a day with 21 day cycles, with breaks between them for 7 days, begin the packet with the 5th day from the beginning of menstrual-like reactions) are used. Phytopreparation "Climadinon" (active component is an extract of the cimicifuga root — related to the receptors of oestrogen in the hypothalamus, reduces the stimulating influence of the latter on the gonadotrophic function of the hypophysis), promotes the elimination of psychoemotional and vegetovascular disorders. The specified preparations are recommended for 3–4 months with the subsequent break for 1 month. Preparations of calcium, vitamins of the B group, ascorbic acid, tocopherol acetate, nicotinic acid, sedative preparations, tranquilizers are also prescribed; microwave therapy on the area of the adrenal glands, tonic and fortifying physiotherapeutic procedures (coniferous, sea baths, cold shower, rubdowns) are conducted; measured physical loads, sanatorium treatment are recommended.

The prognosis is favorable under the conditions of duly beginning of preventive therapy.

CLIMACTERIC SYNDROME

Climacteric syndrome (CS) is a symptom-complex, developing in 40–70% of cases due to the fading function of the reproductive system against a background of general age involution of the organism.

The term ***menopause*** denotes the termination of menstruation, or the final menstruation in a woman's life. The transitional period between ovulatory cycles and menopause, during which the functional activity of the ovaries progressively decreases, is called ***climacteric*** or ***pre-menopausal*** period (climacterium). The term ***"pre-menopausal period"*** or ***"menopausal period"*** means the time after menopause. During this period numerous endocrine, somatic and psychological changes take place in a woman's organism.

The average age of women at menopause is 50–51 years and does not depend on the time of the occurrence of menarche, social and economic status, race, parity, age and body weight. Smoking promotes an earlier beginning of spontaneous menopause.

Endocrine changes associated with ageing. Endocrine changes, characteristic for female climacteric, are caused by a reduction in the oestrogen secretion by the ovaries and an increase in the gonadotrophin level. The absence of oestrogen influence causes atresia of the follicles, reduction in the sizes and mass of the ovaries (up to 2.5 g). The cortical zone of the ovaries decreases as a result of germ and follicular cells loss, which results in a relative increase of the amount of stromal cells. Against a background of oestrogen deficiency in target organs, containing oestrogen receptors (uterus, mammary glands, vagina, muscles of the pelvic floor, urethra, bladder, arteries, heart, skin, bones, brain, mucous membranes of the throat, mouth, conjunctiva), there can be pathological changes (Fig. 27).

The level of follitrophin during the beginning of menopause grows to the greater degree than the level of lutrophin, which explains the cancellation of sup-

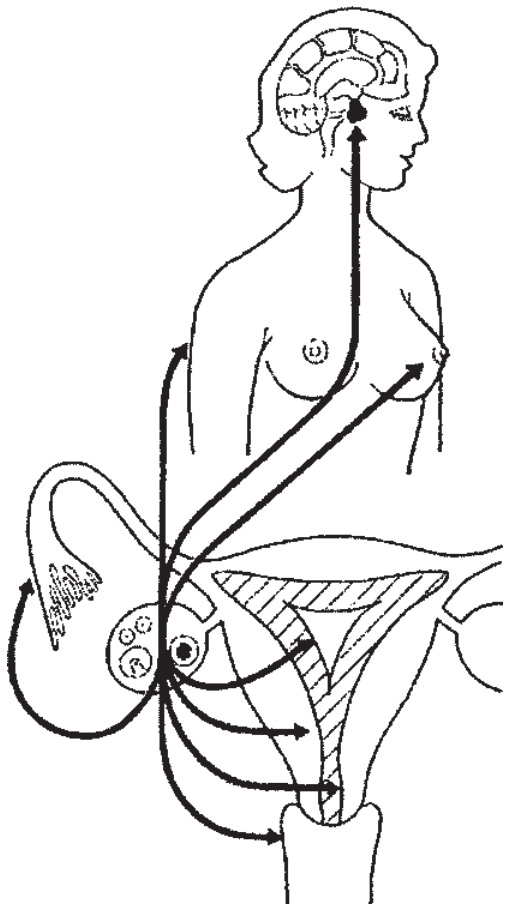


Fig. 27. Scheme of the effect of the estrogens on estrogen-sensitive zones

pression of follitrophin by the follicular inhibitors. The levels of oestrogen and androgen are reduced. After menopause the dominant way of synthesis of oestrogen becomes their extraglandular formation. The extraglandular aromatization of androstendion mainly occurs in the adipose tissue, bones, muscles, skin and brain. Because the basic place for the production of oestrogen is adipose tissue, in women with obesity the aromatization of androgen increases.

Clinical picture. The concept "climacteric syndrome" or "menstrual syndrome" includes a broad spectrum of symptoms which can occur within 4–6 years before and after the last menstruation. These symptoms can be divided into three groups.

The first group of symptoms contains vasculomotor and emotional-mental disorders: hot flashes, vasculomotor instability, sweating, headache, tachycardia, pain in the heart area, arterial hyper- or hypotension, drowsiness, or, on the contrary, sleeplessness, irritability, nervousness, depression, absentmindedness, decrease in libido.

The second group of symptoms (connected with urinogenital organs, skin and its appendages) includes dryness and atrophy of the epithelium of the vagina, uterus, dyspareunia, accelerated urination, dryness, and fragility of the nails, dryness and loss of hair, increased formation of wrinkles. The expressiveness of the vasculomotor symptoms and the atrophy of the urinogenital epithelium correlate with the oestrogen deficiency.

Metabolic disorders (for example, osteoporosis) belong to the third group of pathologic symptoms.

Hot flashes are observed in 30–80% of women, in 40% of them symptoms can be severe, which demands therapeutic help. Hot flashes are accompanied by the sensation of warmth, heat and end with profuse sweating. The frequency, duration and intensity of vasculomotor disorders widely vary, but, in most cases they decrease in 4–6 years after menopause.

The pathogenesis of hot flashes is not completely known. The researches, conducted recently, have established the connection between the flashes and pulsating emission of lutrophin. However, this mechanism is not the only. The application of oestrogen in most cases promotes the reduction of pathologic displays, but under the condition of the absence of full suppression of the level of gonadotrophic hormones. Probably, the trigger of vasculomotor disorder is the central nervous system (hypothalamus). In some women the hot flashes do not disappear after the use of oestrogen; on the other hand, 25% of the patients respond to placebo-therapy. Obviously, the reason of hot flashes does not only consist of oestrogen deficiency.

Urogenital atrophy occurs due to a decrease in the oestrogen level and is characterized by symptoms of atrophic vaginitis (itching, discomfort, burning in the vagina, dyspareunia, bloody discharge due to trauma to the thin epithelium). The oestrogen deficiency can result in the weakening of the supporting device of the uterus, pelvic floor that causes descent and prolapse of genitalia. Other symptoms of oestrogen insufficiency are enuresis (involuntary and with pressure), dysuria, accelerated urination.

Pain in the heart area, quite often, demands differential diagnosis of urogenital atrophy with angina pectoris and myocardial infarction. The attack is preceded, quite often, with attributes of hypothalamic disorders (nausea, hot flashes, cold sweats, numbness of the extremities, and sensation of lack of air). The pain in the heart area is connected with the metabolic disorders occurring in the myocardium (climacteric cardiomyopathy).

Diagnosis, as a rule, offers no difficulties. In case of prevalence of cardiovascular symptoms in patients with hypertension, the diagnosis is sometimes difficult to determine. While studying the general anamnesis, it is necessary to pay attention to the diseases of the patient which can promote a complicated course of the climacteric period: chronic infections, cardiovascular and other extragenital pathologies, neurologic disorders.

Treatment should be complex, early, individualized, with the use of dietary, physical and medicamentous factors and the conduction of hormone replacement therapy with absence of contraindications

(prevention of cardiovascular complications and osteoporosis).

Nonmedicamentous therapy is applied usually for the mild forms of the climacteric syndrome. Physiotherapy exercises (homocybernetics), a balanced diet (fresh vegetables, fruit, limited consumption of fats and carbohydrates), hydropathy (dousing, showers, mineral baths), physiotherapeutic procedures (galvanizing of cervical-facial area, massage of the collar zones) render a positive influence on the organism.

Medicamentous non-hormone therapy is conducted with spasmolytics, reserpin, vitamins of the B group, ascorbic acid (vit. E), tocopherol acetate (vit. E), weak tranquilizers, neuroleptics, psychotrophic means (cerebrolysin, aminalon, nootropil, pyroxicam).

Hormone therapy is recommended mainly for expressed forms of climacteric syndrome and is conducted with natural oestrogen with the inclusion of progestagens (gestagens). Natural oestrogens include 17-estradiol and its derivatives (estradiol valerat, microionized estradiol), conjugated oestrogens (estrone sulphate, etc.), estriol and estriol succinate. Natural oestrogens, as opposed to synthetic, are used in contraceptives, do not cause proliferative changes in the endometrium, normalize the lipid spectrum of the blood (reduce the contents of lipoproteins of low and very low density, having an atherogenous action, and increase coagulative properties of the blood).

For *combined treatment* the derivatives of progesterone (medroxyprogesterone acetate, cyproterone acetate, duphastone, megestrol acetate) and synthetic progestagens, derivatives of 19-norsteroids (norgestrel, desgestrel, levonorgestrel, noretisterone acetate) are used.

For hormone therapy the following may also be applied: climen (estradiol valerat — 2 mg and cyproterone acetate — 1mg), cycloprogenon (estradiol valerat — 2 mg and norgestrel — 0.5 mg), divina, divitren (estradiol valerat — 2 mg and medroxyprogesterone acetate — 20 mg), climonorm (estradiol valerat — 2 mg and levonorgestrel — 0.15 mg). The drugs are taken in a cyclic method.

With urinogenital disorders and atrophic vaginitis, estriol (0.5 mg in tablets) and "Ovestin" (by 1–2 mg in tablets, suppositories and creams) are most effective.

The risk of oestrogentherapy. *Influence on the cardiovascular system (cardiovascular effect).* Today, there is no evidence that the oestrogen replacement therapy results in an increased risk for thrombembolia, stroke or arterial hypertension. There has been the assumption, that replacement therapy with the use of oestrogens reduces the risk of ischemic heart disease. It can be connected with more favourable ratio of lipid fractions: decrease in the levels of cholesterol and low density lipoproteins and an increase in the contents of lipoprotein of high density.

Diseases of the gallbladder. The purpose of replacement therapy with the use of conjugated oestrogens can increase the risk of the formation of gallstones due to an increase in the cholesterol level in the bile.

Breast diseases. The breast as the target for oestrogen influence can react to their use by the development of benign and malignant processes. The recent researches testify that long use of low doses of oestrogens does not increase the risk of breast cancer development. However, even in view of this fact, oestrogen treatment is not prescribed to women with previous malignant breast diseases and is stopped with the breast cancer development.

Endometrial cancer. Women with obesity (adipose tissue is the basic extraglandular place of aromatization of androgens), liver diseases have a higher risk of endometrial cancer, which as a result of oestrogen therapy increases 7 times and grows due to both an increase in the dose, and duration of therapy. However, the death rate among women with this complication does not increase, that, probably, is connected with a low malignancy.

A combined prescription of progesterone for 10–13 days is recommended in order reduce the risk of hyperplasia and endometrial cancer during monotherapy with oestrogens in women in menopause, as well as to reduce their influence on the uterus. The use of progesterone both during cyclic and permanent oestrogen therapy reduces the frequency of cases of hyperplasia and endometrial cancer. The loss of ovarian functional activity results in an increase in the contents of low density lipoproteins and decrease the level of high density lipoproteins in the blood. The use of oestrogen will neutralize these changes. Progesterone, on the contrary, renders the opposite influence on the level of lipoproteins and increases the risk of heart ischemic disease, depending on the dose and duration of progesterone therapy. Additional use of progesterone in a dose of 200 mg a day orally for 10 days does not result in authentic growth in the level of atherogenous lipid fractions.

An increase in the frequency of cancer of the ovaries, cervix, Fallopian tubes, vagina or vulva was not observed in women who had replacement therapy during menopause.

Before prescribing hormone therapy and during it, the anamnesis is studied; gynaecologic and ultrasonographic researches of the genitalia and mammary glands, colposcopy, cytologic research of smears from the cervical canal are conducted; the levels of cholesterol, lipoprotein, coagulation factors are determined in the blood; arterial pressure is measured.

Contraindications to hormone therapy during climacteric syndrome are following: 1) tumours of the uterus, ovaries, breasts; 2) uterine bleedings of unknown genesis; 3) acute thrombophlebitis, thrombem-

bolic disorders connected with the use of oestrogens in the anamnesis; 4) liver and kidney insufficiency; 5) severe forms of diabetes. With extra care, hormone therapy is used with diseases complicated by symptoms of delay of liquid (asthma, migraine, epilepsy), as well as with endometriosis, asymptomatic uterine myoma, jaundice of pregnant women and depression in the anamnesis.

The duration of the use of preparations depends on the clinical displays and specific features of a woman's organism.

Prevention of complications during the climacteric period should begin with women of the reproductive age and consist of duly treatment of patients with somatic and gynaecologic diseases, as well as the keeping of an adequate diet, regime of work and rest.

OSTEOPOROSIS

Osteoporosis is the severest complication of postmenopausal hypoestrogenism. It is characterized by a decrease in the density of bone tissue, a reduction of the contents of calcium in it, a loss of structural support (bone mass) in the trabecula bones, mainly in the spine. The prevalence of osteoporosis in women over the age of 50 is 50%, and in 40% of the patients osteoporosis can result in bones fractures.

The loss of bone mass progresses with the speed of 1–2% a year. By the age 80 up to 50% of bone mass can be lost. With the absence of treatment osteoporosis causes the most sever suffering in elderly women. It is established, that 25% of women over the age of 60 have radiological confirmation of compression fractures of the spine. Such fractures and their complications frequently are one of principal causes of invalidity and death in elderly women.

The major factors causing the development of osteoporosis are the white race, low body weight, hypoestrogenism, early menopause, cases of osteoporosis in the family, diet with low contents of calcium and calciferol (vitamin D) or with high contents of caffeine, phosphates, alcohol and proteins, smoking, and work in the sitting position. During the menopausal period a woman should use 1,500 mg of elementary calcium daily to maintain the calcium balance. It is established, that a reduction in the amount of endogenic oestrogen is connected with an increase discharge of calcium with urine. Oestrogen promotes the reduction of osteoporosis displays, even though the mechanism of this phenomenon remains obscure. In the bones there are receptors for oestrogen, i.e. the influence of the latter can be direct. Oestrogen deficiency also can promote an increase of sensitivity of the bones, kidneys and intestines to parathyroid hormones. At the end, there is an increase in bone resorption and mobilization of calcium without increase in its excretion by the intestines or with urine.

In women over 40 the frequency of bone fractures increases and by the age of 60 it exceeds 4 times the parameter for men, and later on continues to increase. The resorption of the bone tissue in young women is observed after ovariectomy, during ovarian forms of amenorrhoea (premature ovarian depletion, resistant ovarian syndrome, gonadal dysgenesis). Genetically caused reasons of the development of osteoporosis play a certain role.

Clinical picture. Attributes of osteoporosis are pain in the bones, especially in the spine; micro- and macrofractures testifying to the late stages of the process. The pain, quite often, is regarded as a symptom of osteochondrosis or radiculitis, which results in an inadequate treatment. A decrease in height by some centimeters, decrease in mobility, chronic pain in the back, a spinal curvature as a "widow's hump" are the symptoms of osteoporosis. The most severe displays of osteoporosis are hip fractures (every seventh woman), which in 50% of the cases results in restriction of mobility, deterioration of life, in 20% of the cases — death due to accompanying complications.

Diagnosis of osteoporosis presents significant difficulties. A computer tomography and absorptiometry can be used to determine the density of the bone mass. Radiologically, osteoporosis is diagnosed in the case of the loss of no less than 25–30% of the bone tissue when treatment is already ineffective. Mono- and biphoton absorptiometry are difficult and expensive methods of diagnosis, allowing the estimation of the bone density with a loss of bone tissue within the limits of 1–2%.

Treatment. Preparations of natural free and conjugated oestrogens in combination with progestagen are used, just like during the treatment of patients with climacteric syndrome. Oestrogen-therapy inhibits the decrease in the level of calcium in an organism, promotes the normalization of its balance and increases the density of bones, reduces the probability of spinal fractures. Hormone therapy reduces the frequency of hip fractures in women by 50%. The medical regime can include 0.625 mg of conjugated oestrogen, or estrone sulphate, or 1 mg of estradiol for the first 25 days of each month. Estradiol can be prescribed transdermal (hypodermic implants), as well as as vaginal suppositories and creams. Preparations of cycloproginova, climen by 1 dragee daily for 21 days, then a break of 7 days are recommended; the course of treatment is 6 months. After hysterectomy, oestrogens are possible to use without accompanying progesterone therapy.

Indications of treatment with preparations of sex hormones are bone fractures (even single) in women over 45. The "golden" standard for antiresorption therapy is the combination of sex hormones, calci-

tonin (miacalcic — synthetic calcitonin of salmon) and biphosphonate — inhibitors of resorption of bone tissue (phosamax, xidiphon). Phosamax is prescribed in a dose of 10 mg (1 tablet) a day. It is necessary also to take calcium (1,500 mg a day) and calciferol (vitamin D).

Means, stimulating the formation of bone tissue, are anabolic steroids, preparations of sodium fluoride (ossin, coreberon), osteohin (ipriphlavon). Osteohin is in the class of flavonoides, improves the metabolic processes in the bone tissue, stimulates the formation of bone mass, reduces the processes of osteolysis, renders analgesic action, and improves motor activity with osteoporosis. Ossin is prescribed by 1 dragee 2 times a day after meals for 1–2 years (the preparation cannot be given simultaneously with calcium, as well as with medical products containing magnesium and aluminium).

RECOMMENDED READING

7; 15; 16; 24; 38; 56; 75; 79; 92; 94; 95; 108.

Chapter 6
INFERTILITY

Infertility is an inability of a married couple to conceive after 1 year of unprotected intercourse. Women over 35 or with a known reason of infertility should be examined and given corresponding treatment.

Primary infertility is diagnosed with the absence of conception in a married couple. ***Secondary infertility*** is the absence of pregnancy in married couples having conception in the past.

The incidence of infertility is more than 15% among all married couples. According to experts of the WHO (World Health Organisation, 1995), in the world about 100 mln married couples are infertile, and their amount annually increases. It is connected with the tendency to conception delay by many married couples, more often anovulation in women of the older age groups, as well as the growth of sexually transmitted diseases.

Improving of the society standards of living, certainly, should promote the growth of social importance of the problem of infertility. Infertility can render a deep emotional influence on a married couple. The infertile spouses are frustrated; they stay angry, signs of depression, grief, alarm, which demands psychological and even psychiatric help.

Etiology. The most often reasons for infertility are: disorder of spermatogenesis (40%); ovulation disorders (30%); disorders of the normal structure of the reproductive system (30%). Approximately 15% of the reasons for infertility remain obscure.

During examination of the married couple (it should not precede more than 2–6 months) it is necessary to find the reason (or reasons) for infertility, which appears possible in 85–90% of the cases. The course of treatment should last no more than 2 years. It is necessary to inform the patients, that the incidence of pregnancy due to treatment averages about 40%.

The basic conditions necessary for successful conception and pregnancy are as follows:

Conditions for conception

• Presence of ovulation (a cyclic exit of the ovum from the ovaries)

• Sufficient amount of mobile spermatozoons in the ejaculate

• Ejaculation close to the cervical canal

• Normal movement of spermatozoons in the direction of the Fallopian tubes

• Penetration of the ovum, capable of fertilization, in the Fallopian tubes

• Patency of the Fallopian tubes

• Physiological value of PH medium in the uterine cavity, providing active movement of the spermatozoons

• Corresponding conditions for sex cells in the Fallopian tubes

Conditions for pregnancy

• Spermatogenesis (male factor)

• Ovulation (ovarian factor)

• Interaction of the cervical mucous and sperm (cervical factor)

• Normal size and form of the uterus, structure and integrity of the endometrium (uterine factor)

• Patency of the Fallopian tubes and their normal anatomic relations with the ovaries (tubal factor)

• Fertilization (coital factor)

FEMALE INFERTILITY

The following forms of female infertility are distinguished:

— endocrine (anovulatory) — 30% of the cases;

— tubal and peritoneal-tubal — 30%;

— connected with various gynaecological diseases (endocrine-tubal, uterine factor, etc.) — 25%;

— immunological — 2–5%;

— psychogenic — 3%;

— unexplained — 6–10%.

Endocrine (anovulatory) **infertility** is connected with ovulatory abnormalities. Chronic anovulation can be a symptom of multiple endocrine disorders,

gynaecologic diseases, neuro-enodocrine syndromes, such as ovarian polycystic syndrome, hyperprolactinemia, adrenogenital or postpartum neuro-enodocrinal syndromes, disorder of the thyroid gland functions (hyper- and hypothyroidism), of the hypophysis and adrenal gland functions (Cushing's disease and Cushing's syndrome). Anovulation can be a result of stress, sharp loss of weight, brain traumas, and long use of some medical products.

Among the disorders of the hormonal ovarian function, being the reason for infertility, such conditions, as lutein phase defects (about 15%) and the syndrome of non-ovulatory follicle luteinization (up to 5%) are distinguished.

Insufficiency of the lutein (II) phase of the menstrual cycle (ILP) or hypofunction of the corpus luteum is characterized by a decrease in progesterone synthesis that results in defective secretory transformation of the endometrium, the absence of conditions necessary for implantation of the fertilized ovum, a decrease in the peristaltic activity of the Fallopian tubes. The reasons for insufficiency of the II phase of the menstrual cycle can be hyperandrogenism, hyperprolactinemia, hypothyroidism, inflammatory diseases of the uterus and appendages. ILP can be observed as a temporary phenomenon within the first year after menarche, as well as after labor, abortion. Characteristic attributes of the syndrome are: shortening of the hyperthermal phase of the basal body temperature up to 4–8 days with the reduction of the difference between temperature parameters at the I and II phases of the cycle less than 0.4°C; bloody discharge (”spotting”) 4–7 days prior to the expected menstruation, a decrease in the level of progesterone to less than 10 ng/ml in the middle of the II phase of the cycle.

Treatment. Pathogenetic gestagen replacement therapy in the II phase of the cycle is conducted: progesterone by 1 ml of a 1% solution intramuscularly starting the 18–20 day of the menstrual cycle for 6–8 days, or utrojestan, or rectal suppositories with progesterone, norcolut — by 5–10 mg the 16th through the 25th day of the cycle, dufaston — by 10 mg the 11th through the 25th day of the cycle. Chorionic gonadotrophin is prescribed by 1,000–1,500 U intramuscularly on the 2nd, 4th, 6th day the basal temperatures rise for 3–4 menstrual cycles.

Luteinization of non-ovulatory follicle syndrome (LNF) is connected with stressful factors, hyperprolactinemia, inflammatory processes in the ovaries. Diagnosis of this condition are difficult; functional diagnostic tests are uninformative. During ultrasonic monitoring of the growth of the follicle, a gradual decrease in the size of the dominant follicle instead of its bursting and disappearance after ovulation. During laparoscopic examination in the middle of the cycle, the corpus luteum which does not have the ovulation stigma is found.

Treatment consists in induction of ovulation.

Tubal and peritoneal-tubal infertility is caused by organic and functional pathology of the Fallopian tubes.

The functional pathology of the Fallopian tubes is caused by stressful factors, hypofunction of the ovaries, hyperandrogenism, and disorder in the balance of prostaglandins.

The organic pathology of the Fallopian tubes results in the tubal occlusion; it is accompanied by adhesions, which are frequently observed after inflammatory diseases of the internal genitalia (more often of the chlamydial, gonorrhoeal etiology).

The tubal factor of infertility is observed in 30% of the cases and is proven by the results of hysterosalpingography or laparoscopy. The tubal occlusion can result from pelvic inflammatory diseases, adhesions, endometriosis, operations on the pelvic organs and organs of the abdominal cavity.

Pelvic adhesions can interfere with fertilization due to obstruction, and twisting of the Fallopian tubes. The adhesions are cut during laparoscopy with the application of microsurgical technics with careful haemostasis.

For the *diagnosis* of tubal infertility hysterosalpingography (HSG) on the 6th –7th day of the menstrual cycle, with water-soluble radiopaque substances (triombrast, verografin, urografin) is conducted; on the 6th–7th day of the menstrual cycle echo-contrast substances (”Echovist”) are entered into the uterus under the control of ultrasonograph; laparoscopy with chromoperturbation is done. On the basis of the laparoscopic pictures the stage of the adhesions is estimated according to the Hulka's classification (from each side): I stage — isolated thin adhesions; II stage — dense adhesions occupying less than half of the ovarian surface; III stage — multiple dense adhesions occupying more than half of the ovarian surface; IV stage — dense plane adhesions occupying the whole surface of the ovary, which is not visible.

Treatment. A patient with functional tubal infertility is prescribed sedative means, inhibitors of prostaglandin synthesis (ibuprofen, naproxen, indometacin), spasmolytic means, psychotherapy. As physiotherapeutic procedures they use ultrasound in a pulse mode on the uterine appendages area, carry out gynaecologic massage, hydro- and balneotherapy.

The treatment of patients with tubal infertility of the inflammatory genesis begins with the liquidation of the inflammatory process. With chronic relapsing inflammatory processes, treatment should begin with the application of preparations like pyrogenal, prodigiosan with further antibiotic therapy, depending upon the activator of the infection. In the case that bacteriological research can not be done, treatment with tetracyclines, taking into account the high incidence of chlamydial salpingitis, should be conducted. The complex of treatment includes adap-

togens, immunomodulating factors, physiotherapeutic procedures, depending upon the stage of the disease.

Recently many clinical physicians have refused hydrotubation as a method of treatment for tubal infertility because it is traumatic, gives unsatisfactory results, frequent complications (hydrosalpinx). Short (2–3 procedures) courses of hydrotubation are justified after laparoscopic operations for tubal patency restoration.

The further treatment of such patients, as a rule, is surgical. The microsurgical treatment of patients with tubal and peritoneal-tubal infertility (operative laparoscopy, laser surgery) has received wide development. Laparoscopy is recommended to all patients with infertility after negative results form hysterosalpingography.

Contraindications to surgical treatment are genital tuberculosis, age over 38, the duration of tubal infertility more than 5 years, acute inflammatory processes, IV stage of adhesive process (by the Hulka's classification).

Operative laparoscopy allows adhesiolysis, salpingoovariolysis (separation of the adhesions formed around the tubes and ovaries, the elimination of bends and distortions); neosalpingostomy, salpingostomatography (creation of a new aperture in the Fallopian tubes with impassable ampullar department); fimbrioplastic. A repeated laparoscopy is recommended in 6–30 days for the separation of postoperative adhesions. For this purpose, diathermocoagulation, thermocoagulation, Nd-YAG-laser, CO_2-laser are used. The efficiency of the operation (20–50%) depends on the surgeon's professional skill, quality of material and surgical instruments.

With severe disorders of the Fallopian tubes methods of fertilization *in vitro* are applied. The incidence of pregnancy in such cases is 15–40% and depends on the disorder severity.

Prevention of tubal and peritoneal-tubal infertility consists of duly adequate treatment of patients with inflammatory processes of the genitalia and other pelvic organs, restriction of the amount of hydrotubations, the conduction of hysterosalpingography with water-soluble contrast substances.

Infertility associated with various gynaecologic diseases. The reason for infertility can be anatomic disorders in the cervical area of the uterus (polyps, deformations, ruptures, the consequences of conization) and inflammatory processes (chlamydial, micoplasmal, gonorrhoeal cervicitis).

In these cases, the cervical factor of infertility takes place (Fig. 28).

Cervical mucus thus can present a significant barrier for the penetration of spermatozoon. The presence of abnormal cervical mucous is revealed in women with ovulatory cycles with the help of

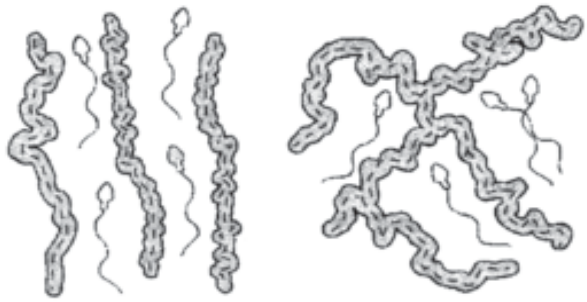


Fig. 28. Cervical factor: normal migration of spermatozoones in the cervical mucous and its disturbance

postcoital tests. The time for the exam (during the ovulatory period) is determined by an ovulatory elevated lutrophin level in the urine or the parameters of the basal body temperature. The postcoital test is abnormal if motionless or "trembling" spermatozoons are found. The test for the presence of antispermal antibodies is conducted in both partners.

The treatment of patients with the cervical factor of infertility consists of the use of conjugated oestrogens (0.325 mg a day on the 3rd–12th day of the cycle) or intrauterine insemination.

Endometriosis can cause infertility approximately in 30% of the cases with the presence of Fallopian tubes affection (Fig. 29), disorders of the lutein phase, increases in the activity of macrophages.

Treatment should be individual. Laparoscopic treatment of patients with mild forms of endometriosis consists of the removal of endometrioid peritoneal heterotopias by excision, electrocauterization, laser vaporization, ligation of adhesions. Coagulation of the capsule of the endometrioid cysts should be conducted with the help of Nd-YAG laser. Med-

Fig. 29. Endometriosis of the ovaries and Fallopian tubes

icamentous treatment is conducted with the mild forms of endometriosis or after the operation with the purpose of suppressing residual disorders. For this purpose, combined oral contraceptives, progestin, derivatives of testosterone (danazol), analogues of GN-RH antiprogestin (gestrinon, zoladex, decapeptil) are prescribed. Pregnancy rate depends on the extent of endometriosis (40% — fir the I stage and about 30% — for the II and III stages) (see "Endometriosis" p. 87).

The uterine factor of infertility can be intrauterine synechiae (the Asherman's syndrome), polyps, submucous leiomyoma.

Infertility caused by intrauterine synechia (Asherman's syndrome) develops in women with frequent miscarriages in the anamnesis, currettage of the uterine cavity during uterine bleedings, due to tubercular endometritis and is accompanied by the hypomenstrual syndrome or amenorrhoea with the preservation of the ovarian function.

The diagnosis is established according to the anamnesis and results of hysteroscopy.

Treatment consists of the ligation of the adhesions under the control hysteroscopy after the termination of menstruation with further prescription of cyclic hormone therapy for 2–6 months with two or three-phase oral contraceptives. Monophase oral contraceptives are not recommended, because they can cause hypoplastic changes in the endometrium. The question concerning the use of an intrauterine spiral to prevent relapses of the the Asherman's syndrome remains debatable.

A large submucousal myoma is removed by laparotomy, a small one — hysteroresectoscopy. Congenital anomalies of the uterus (septum) can cause primary miscarriages. Correction is done with the help of hysteroresectoscopy or uterine metroplastic.

Immunological infertility can be caused by the formation of antispermal antibodies (antibodies formed in the plasma of sperm and resulting in the agglutination of spermatozoons — the male form of infertility), as well as antibodies formed in the cervical mucous, causing immobilization of the spermatozoons.

Diagnosis is conducted with postcoital tests (see "Male infertility").

Treatment. Use of condoms is recommended for 6 months (efficiency — about 60%), glycocorticoids are prescribed (efficiency — 20%); intrauterine fertilization (efficiency — up to 40%); *in vitro* fertilization and embryo transfer.

Psychogenic infertility can be connected with the stressful oppression of ovulation (family conflicts, professional problems, pregnancy expectation syndrome).

Treatment — psychotherapy, sedative means.

Unexplained infertility is observed in 10–15% of cases; fertilization frequently occurs irregardless of treatment. In the case of obscure infertility during objective examination of the married couple, pathologic symptoms are not found. So, the pregnancy rate in one year is 30%, in 3 years — 60%. In these cases, additional examinations should be conducted. With the absence of pregnancy during the period of observation, empiric treatment with the use of ovulation induction, intrauterine insemination and assisted reproductive technologies are conducted.

MALE INFERTILITY

Male infertility is understood as the inability of a mature male organism to conceive. Male infertility can be secretory (spermatogenesis abnormality) and excretory (disorder of sperm excretion). The principal causes of male infertility are infections of the genital tract (25%), varicocele (20%), and idiopathic oligoasthenoteratozoospermia (31%). The combination of several factors of infertility is found in 32% of the cases. In 21% of the cases male infertility is caused by endocrine factors, in 7% — congenital or acquired anomalies of the genitalia, in 3% — immunological factors.

Andrologists, urologists are engaged in the diagnosis of male infertility and treatment. Primary examination of men begins with the analysis of sperm and the postcoital test. The main criteria of a normal sperm are resulted in Table 4.

Analysis of sperm is conducted twice with an interval of 14–15 days after sexual abstention for 3–7 days. If the results of the two analyses have significant differences, a third one is conducted.

The results of the sperm analysis can be as follows:

— oligozoospermia — decrease in the concentration of spermatozoons < 20 mln;

— teratozoospermia — normal spermatozoons are less than 50%;

— asthenozoospermia — forwardly moving spermatozoons are less than 50%;

— oligoasthenoteratozoospermia — combination of the mentioned disorders;

Table 4. **Criteria of normal sperm**

Parameters	Normal values
Volume of ejaculate, ml	2–6
pH	7.0–8.0
Total amount of spermatozoons	20 mln
Underpressure	Complete for 1 h
Mobility	50% and more
Normal form	60% and more

— azoospermia — absence of spermatozoons in the ejaculate;

— aspermia — sperm volume is 0 ml.

Biochemical parameters, such as the contents of general zinc in the ejaculate (normal > 2.4 μmole/l), citric acid (> 10 mmole/l), fructose (> 13 mmole/l) have great value for the quality of the sperm.

Postcoital test (PCT, Shuvarsky—Sims—Huhner test) determines the amount of mobile spermatozoons in the cervical mucus. The test is conducted during ovulation, within 8 h after the sexual intercourse, after a three-day sexual abstention. With a tuberculin or insulin syringe mucous is taken from the cervical canal, put on glass and under a microscope (×400) the amount of spermatozoons are counted. With negative results from the postcoital test (absence of spermatozoons in the mucous) the antispermal antibodies level is analyzed.

The male hormone estimation (the level of follitrophin and testosterone in the blood plasma) is conducted with the amount of spermatozoons less than 5 mln in 1 ml and normal testicle size. In case of sexual insufficiency, the prolactin level is determined.

Instrumental methods of examination include *thermography of the scrotum, ultrasound of prostate and seminal vesicles.*

The opportunities of treatment of male infertility are limited and depend on the reason of infertility. Men with azoospermia, as a rule, are not subject to treatment. An increase in the level of follitrophin in the blood serum is evidence of a loss of functional germinative tissue. In such cases, the spouses are recommended insemination of a donor sperm or the adoption of a child. Obstruction of the ejaculate canals or retrograde ejaculation into the bladder is observed with a normal follitrophin level.

Oligozoospermia is usually idiopathic though in some cases it can be connected with testicular stroke, trauma, infection or varicocele (in 40% of infertile men). Varicocele — the dilatation of the internal testicle vein. The mechanism of infertility in this case is connected with an increase in testicular temperatures and venous stasis. The quality of the sperm increases in 50–90% of men after surgical dressing or radiological occlusion of the internal testicle vein; however, the incidence of fertilization is only 25–50%.

Conservative treatment of patients with spermatogenesis disturbances consists of the use of andorgens, antioestrogens, gonadotrophin (menotrophin, humegon, pergonal), chorionic gonadotrophin (prophase, pregnyl), inhibitors of prolactin secretion (parlodel), immunomodulating factors, angio-protectors, biogenic preparations (solcoseril), means for the correction of sexual function (caverject, tentex, viagra, yohimbine, etc.).

Routine use of thyroid hormones, clomiphenecitrate and testosterone is irrational due to the development of subsequent paradoxal oppression of spermatogenesis.

Surgical treatment is recommended for varicocele, cryptorchism, inguinal and inguinal-scrotal hernias, congenital anomalies, stricture and obliterations of the urethra, occlusive azoospermia.

EXAMINATION OF AN INFERTILE COUPLE

The history and objective examination have very great value in the establishment of the condition of the female patient and her partner.

The age the woman began sexual (puberty) development and menarche is clarified. The menstrual anamnesis includes data concerning duration, frequency of cycles, and amount of blood loss. Regular, cyclic, predicted mences in the majority of cases are proof of ovulatory type cycles, while the presence of amenorrhoea, menometrorrhagia in the anamnesis is evidence of anovulatory type cycles and possible uterus pathologies.

A woman is asked about the presence of dyspareunia (pain during sexual relations that reduces their frequency and quality), severe algodysmenorrhoea that is an evidence of endometriosis. The presence of inflammatory diseases of the pelvic organs, ruptured appendix, surgical interventions on the organs of the abdominal cavity or long use of the intrauterine spiral in the patient's history can be connected with the Fallopian tubes injury.

The features of a previous pregnancy course, labours, their complication, duration of infertility, application of contraception methods, presence of chronic diseases and methods of their treatment; harmful habits, professional harm, as well as hereditary diseases of relatives of the I and II degrees of consanguinity are elucidated.

Galactorrhoea can be an evidence of hyperprolactinemia. The development of hirsutism during puberty, the presence of acne and greasy skin allow the exclusion of the diagnosis of ovarian polycystic syndrome or other disorders connected with hyperandrogenism. The information on previous infertility of the woman and methods of treatment is also important.

During examination they pay attention to the weight-height factor, degree of hirsutism, breast development, acanthosis (dark pigmentation on the neck), abdominal stretch marks, obesity (Cushing's disease and Cushing's syndrome, adrenogenital syndrome), increase in the thyroid gland, surgical scars, anomalies of body constitution, which can help to establish the cause of infertility.

The degree of vaginal oestrogenization (pink color, moisture, foldings, percentage of superficial cells), as well as the amount and quality of the cer-

vical mucus are obligatory components of the examination.

The cervical colposcopy is carried out. During bimanual gynaecologic examination, the sensitivity and morbidity of the cervix, uterus, appendages, their size and mobility are determined.

The man is asked about his previous ability to fertilization (fertility), general state of health, operative interventions on the genitalia, use of medicaments, use of alcohol or drugs, frequency of hot baths, presence of strong physical and mental stress, presence of chronic fatigue, frequency of sexual intercourse.

During objective examination of the men, they pay attention to the degree of secondary sexual characters development, the presence of gynecomastia, cryptorchism, varicocele or hydrocele.

Diagnosis of ovulation. The presence of regular, cyclic menstruation in the anamnesis with some displays of premenstrual syndrome (insignificant morbidity, fatigue) in most cases is proof of ovulation. To confirm ovulation, the basal body temperature is measured starting the first day of the menstrual cycle (Fig. 30).

For the best accuracy, a special basal thermometer is used. The temperature is measured every morning, while lying in bed, approximately at the same time, before eating, drinking, smoking or brushing teeth.

On the basal temperature map the episodes of fever, diseases, sexual intercourse, bloody discharge ("spotting") or vaginal bleeding are marked.

The normal curve of the basal temperature is characterized by such attributes:

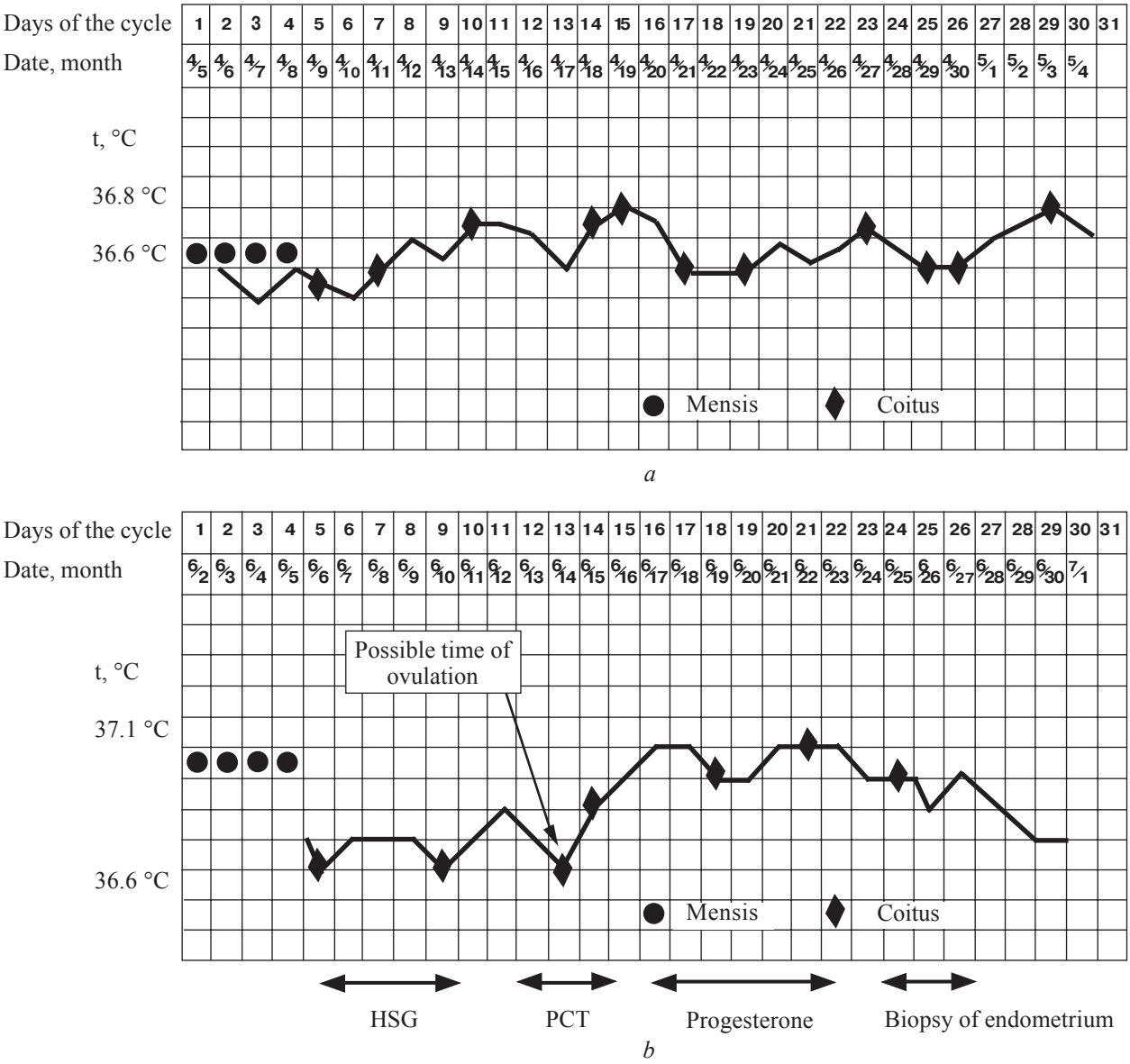


Fig. 30. Curvature of the basal temperature:
a — anovulatory cycle; *b* — ovulatory cycle; time of the performing of diagnostic tests:
HSG — hysterosalpingography, PCT — postcoital test

1. In the follicular (proliferative) phase the basal temperature, as a rule, is less than 36,7ºC.

2. During ovulation in some women there is a decrease in the basal temperature (during a 28 day cycle usually between the 13th and 14th days).

3. In the lutein phase the basal temperature, as a rule, rises by 0.6–0.7ºC under the influence of the thermogenic actions of progesterone. The lutein phase proceeds from the middle of the cycle till the beginning of following menstruation, normally — during 11–16 days.

The approximate time of ovulation can be calculated with the help of the basal temperature curve; sexual intercourse is recommended every 36–48 h for 3–4 days before ovulation and 2–3 days after it (according to the change in the temperature curve).

With the laboratory methods ovulation is estimated by the lutrophin level in the urine in the middle of the cycle and progesterone — in the middle of II phase of the cycle. An increase in the lutrophin level in the blood is a sign of ovulation. Sexual intercourse is recommended 12–24 h after the elevated lutrophin level.

Though progesterone is not the basic product which the corpus luteum secretes, its level in the lutein phase > 3–4 ng/ml, as a rule, is evidence of ovulation. In the middle of the lutein phase the progesterone level should exceed 10 ng/ml. If it is lower than 10 ng/ml, it can be evidence of the lutein phase insufficiency or other hormonal disorders.

A high incidence of inflammatory diseases among the reasons of infertility causes a necessity in screening of sexually transmitted diseases with the use of bacterioscopic, bacteriological, virologic and other methods of laboratory diagnosis (revealing of chlamydiosis, mycoplasmosis, trichomoniasis, gonorrhoea, genital herpes, etc.). These exams are conducted after provocation (physiological — menstruation, medicamentous — gonovaccine, pyrogenal).

With the detection of intrauterine synechiae, exam for the presence of tuberculosis is conducted.

Radiography of the skull and cella turcica is conducted in patient with disorders of the menstrual rhythm (oligo-, amenorrhoea) hyperprolactinemia for the diagnosis of neuroendocrine diseases. The form, size, contours of the cella turcica are evaluated. The enlarged size, occurrence of a double floor, expansion of the entrance, thinning of the walls can testify to a tumour of the hypophysis.

In cases of hyperprolactinemia and the absence of changes on the roentgenogram of the skull ***computer tomography*** and ***nuclear magnetic resonance*** for the diagnosis of micro-adenomas of the hypophysis are conducted.

Hormonal screening with the presence of regular menstruation allows the revealing of endocrine infertility and includes the research of the levels of prolactin, testosterone (marker of ovarian hyperandrogenism), cortisol, dehydroepiandrosterone sulphate (adrenal hyperandrogenism) in the blood plasma in the early follicular phase (on the 5th–7th day of the cycle). At the II phase of the cycle (on the 20th–22th day) the progesterone level is determined for an estimation of the full value of ovulation and function of the corpus luteum. With oligo- and amenorrhoea it is necessary to determine the levels of prolactin, folliand lutrophin, estradiol, testosterone, cortisol, DEAS, thyroid hormones (thyrotrophin, T_3, T_4).

Ultrasonic examination of the pelvic organs and mammary glands is conducted in all patients on the 5th–7th day of the cycle to reveal tumours, developmental anomalies of the genitalia. Ultrasonic examination of the thyroid gland is recommended to patients with oligo- and amenorrhoea.

Hysterosalpingography. Disorders of the Fallopian tubes can be secondary due to pelvic inflammatory diseases, septic abortion, application of intrauterine spirals, rupture of the appendix or surgical operations on the uterus and tubes. Hysterosalpingography is conducted by introducing radiopaque (water-soluble) substance in the uterus 3–6 days after the termination of menstruation. Normal results of hysterosalpingography are characterized by the absence of filling defects to the uterus, tubes as well as attributes testifying of the contrast substance (urografin, triombrast 76% or 60%) getting into the abdominal cavity (through the Fallopian tubes).

Endometrial biopsy is conducted 2–3 days prior to the onset of mences to determine the attributes of ovulation. Progesterone stimulates the secretory changes in the endometrium, found out during hystologic research. Insufficiency of the lutein phase of the cycle is characterized by a delay in the endometrial secretory changes in response to an increase in the lutrophin level or a delay in the menstrual period for more than 2 days within 2 cycles or more. During dysfunctional uterine bleedings, irregular menstruations, diagnostic currettage of the uterus under the control of hysteroscopy is conducted.

Hysteroscopy is recommended during menometrorrhagia, suspicion of a polyp or endometrial hyperplasia, submucous uterine myoma, intrauterine synechia, developmental anomalies of the uterus, as well as to determine the condition of the uterine apertures of the Fallopian tubes, in connection with obscure infertility (in combination with laparoscopy).

Immunological study provides the carrying out of the postcoital test that helps to determine the quality of the cervical ovulatory mucous. Under the influence of an increased level of oestrogen during ovulation the cervical mucus should be liquid, nonsaturated, and transparent; the phenomena of crystallization (”fern”) and stretching are characteristic. The presence of more than 10–20 mobile spermatozoons correlates with the normal data of the sperm analysis and the greater incidence of pregnancy than with a

lesser amount. The pathologic values of postcoital test can even be observed in fertile patients. The absence of spermatozoon or the presence of motionless or "trembling" forms is considered to be abnormal and demands a further inspection. Negative PCT is evidence of a possible presence of antispermal antibodies.

Diagnostic laparoscopy is conducted to diagnose endometriosis or suspecting it, in the case of any pelvic inflammatory diseases which the patient had had before, as well as with abnormal data from hysterosalpingography and obscure reasons of infertility. With the help of laparoscopy, adhesions, endometriosis, tubal occlusion in the ampullar department (distal occlusion), ovarian cysts are found. *Chromoperturbation* (injection of methylene blue through the cervix) can be conducted during laparoscopy with the purpose of confirming tubal patency. During laparoscopy, if it is necessary, surgical medical procedures can be carried out (thermocauterization of polycystic ovaries, laser vaporization of the center of endometriosis, ligation of adhesions, etc.).

Examination of men begins with the analysis of clinical-anamnestic data, general examination, evaluation of the condition of the urinogenital system, exam of the spermogram (see "Male infertility").

TREATMENT OF PATIENTS WITH ENDOCRINE INFERTILITY

Treatment of patients with infertility depends upon its reason. Before beginning treatment the doctor should be convinced of the absence of disorders of the hypophysis, ovaries, uterus, adrenal glands and thyroid gland.

Patients with endocrine infertility are prescribed gestagens, oral contraceptives, clomiphen, clomid, human menopausal gonadotrophin in combination with chorionic gonadotrophin, agonists of gonadoliberins (efficiency in 45–82% of the cases). Laparoscopic microsurgery, nemestran, danazol, agonists of gonadoliberins (efficiency — 42–60%) are prescribed for patients with endometriosis; with a uterine myoma — operative laparoscopy, agonists of gonadoliberins, ovulation stimulation (18–32%).

Clomiphenecitrate is rather harmless, effective and widely used to induce ovulation. This nonsteroid preparation with weak oestrogen and antioestrogen effects promotes the development by the hypophysis of lutrophin and follitrophin. An increase in the levels of these hormones results in the growth and maturing of follicles in the ovaries. Clomiphenecitrate is not a direct stimulator of ovulation, and only promotes physiological hormonal changes, characteristic for a normal ovulatory cycle. The preparation is prescribed in a dose of 50-200 mg the 5th through the 9th day of the menstrual cycle, which causes an increase in the level of lutrophin and follitrophin in the blood serum. Treatment begins with the introduction of a dose of 50 mg, which can be increased to 200 mg and more in a day. Ovulation occurs between the 15th and 20th day of the ovarian cycle.

The most often indication for the use of clomiphenecitrate is ovarian polycystic syndrome and insufficiency of the lutein phase of the menstrual cycle. Patients with sufficient oestrogen activity (positive test with progestin) are sensitive to this preparation. Patients with hypoestrogenism, as a rule, do not react to treatment with clomiphenecitrate.

The time of ovulation and the efficiency of clomiphenecitrate are established by means of exam of the cervical mucus in the middle of the cycle, monitoring the lutrophin level in the urine, ultrasonic documentation of the development and rupture of the tertiary (dominant) follicle. The level of progesterone in the blood is determined or endometrial biopsy on the 27th–28th day of the menstrual cycle is conducted with the purpose of confirming ovulation and determining the adequacy of the lutein phase. The absence of ovulation after receiving the corresponding doses of the preparation is corrected by additional intramuscular introduction of chorionic gonadotrophin (CG) — 5,000–10,000 U after ultrasonic identification of the ruptured follicle.

Side-effects of the action of clomiphenecitrate can include: vasomotor flushes (10%); multiple gestation pregnancy (7%); abdominal swelling (5.5%); morbidity of the breasts (2%); nausea and vomiting (2.2%); headache (1.3%); vision disorder (1%); dryness and hair loss (0.3%).

After receiving sufficient doses of clomiphenecitrate ovulation occurs in 80% of the women. The pregnancy rate in these cases is the same as for healthy women with ovulatory cycles. Without significant side-effects therapy with clomiphenecitrate can be continued for 36 months. With the absence of pregnancy during this period it is necessary to carry out further research for revealing other reasons of infertility.

Menotrophin (human menopausal gonadotrophin, HMG) is received by extraction from urine of women during menopause. The preparation of HMG pergonal contains 75 U of follitrophin and 75 U of lutrophin, it is used intramuscularly. In connection with the possible side-effects and the necessity for clinical and laboratory monitoring, the preparation is prescribed carefully to only selected patients. Candidates for receiving HMG are patients unresponsive to clomiphenecitrate, with hypopituitarism or those to whom "superovulation" is prescribed. The incidence of pregnancy with superovulation with the use of HMG and subsequent insemination of the husband's sperm is 20–30%.

Menotrophin, as a rule, is given on the 3rd day of a spontaneous cycle or withdrawal bleeding induced by medoxyprogesterone acetate or at any time for women with hypogonadotrophic hypogonadism and amenorrhoea. The initial dose is 1–3 ampoules (150–300 U) a day, duration — till the 7th day of the menstrual cycle. Simultaneously, ultrasound investigation of the follicle growth or the estradiol level in the blood serum is conducted; having achieved proper results CG is introduced in addition. Adequate stimulation of the follicle, as a rule, is achieved within 7–14 days of permanent therapy with HMG. With the maturity of the follicle, the cervical mucus becomes liquid, transparent; the stretching and "fern" phenomena are visible; the level of estradiol in the blood serum increases up to 200–300 pg/ml, the diameter of the follicle, by ultrasound is 16–20 mm. At this time, ovulation is achieved with the help of an injection of CG (5,000–10,000 U) 24–48 h after the last injection of HMG. Chorionic gonadotrophin is biologically and structurally similar to lutrophin and is capable of stimulating an ovulatory increase in the lutrophin level. Ovulation occurs 32–36 h after the introduction of CG.

If the level of estradiol exceeds 2,000 pg/ml or the sizes of the ovaries are increased, CG is not used: such displays testify to *hyperstimulation of the ovaries* and usually — about the absence of ovulation. Hyperstimulation of the ovaries also is accompanied by such symptoms, as abdominal swelling, increase in the body weight. In severe cases, ascites, pleural exudate, electrolyte disbalance, oligemia, arterial hypotension, oliguria can be observed. Such patients require hospitalization and intensive infusion therapies.

With the help of menotrophin, ovulation is achieved in about 90% of carefully selected women. The frequency of pregnancy is 25% of all the cases of ovulation. Multiple gestation pregnancies are observed in 20% (with two fetuses — 15% of the cases, three and more — 5% of the cases). Ectopic pregnancy occurs in 1–3% of the cases; the combination of uterine and ectopic pregnancy is possible. The use of menotrophin can be repeated during 3–6 cycles. If pregnancy does not occur, treatment is temporarily stopped to find the reason for failure.

The combination of clomiphenecitrate and menotrophin, in comparison with monotherapy, gives additional opportunities during treatment. Clomiphenecitrate is given by 100 mg a day on the 3rd–7th day after the introduction of 1–2 ampoules of menotrophin. Monitoring and time for the use of CG are the same, as for treatment with only menotrophin. Such ways allow the prevention of hyperstimulation of the ovaries and is cheaper than treatment only with menotrophin.

Urofollitrophin (follicle-stimulating hormone). In women with ovarian polycystic syndrome, an increase in the level of lutrophin is observed during the normal or a bit reduced level of follitrophin. Clomiphene citrate serves usually as a preparation of choice for the ovarian polycystic syndrome. However, with ineffectiveness of the latter the following step in the treatment of such patients is prescribing menotrophin or urofollitrophin. Each ampoule of urofollitrophin contains 75 U of folli- and < 1 U of lutrophin. Urofollitrophin is prescribed intramuscularly by 1–2 ampoules a day under the control of the similar with the use of menotrophin. In approximately 80% of women with the ovarian polycystic syndrome ovulation occurs due to the use of urofollitrophin; in 10–40% — pregnancy takes place. Side-effects including hyperstimulation of the ovaries and multiple gestation pregnancies occur with the same incidence as with the use of menotrophin.

Gonadorelin (gonadotrophic-releasing hormone, Gn-RH). The pulsating use of Gn-RH is caused by the releasing of folli- and lutrophin by the hypophysis and ovulation in women with anovulatory cycles. The best candidates for treatment with Gn-RH are women with hypogonadotrophic hypogonadism. The advantage of taking gonadorelin in comparison with menotrophin is the rarity of the ovarian hyperstimulation. The development of a large amount of follicles is achieved due to the use of large doses of Gn-RH entered with short intervals (every 60 min).

In connection with a short half-life period and rhythmic character of secretion, gonadorelin is prescribed intravenously or hypodermically in a pulsating rhythm under ultrasound for 10–14 days. Ovulation occurs as a result of endogenic lutrophin rise.

Bromcryptin (parlodel). Complex research of the reason for infertility necessarily includes the determination of the prolactin level in the blood serum, which is increased in 10–15% of the women with chronic anovulation (hyperprolactinemia). With hyperprolactinemia and the presence of amenorrhoea (galactorrhoea-amenorrhoea syndrome), the use of 2.5–7.5 mg of bromcryptin (parlodel) or its analogues (carbegolin, serocryptin), which, as a rule, result in the restoration of ovulatory menstrual cycles, is recommended.

ALTERNATIVE METHODS OF INFERTILITY TREATMENT

Alternative methods of treating patients with infertility are:

— insemination of the husband's (donor's) sperm;

— extracorporal fertilization and transferring of the embryo;

— intracytoplasmic sperm injection, included in the program of extracorporal fertilization.

Insemination of the husband's (donor's) sperm is artificial fertilization during which the sperm is entered into the sexual path of the woman for a pregnancy.

Indications for insemination of the husband's sperm: anatomic and functional disorders of the reproductive system in a woman (vaginism, deformation of the cervix) and men (premature ejaculation, epispadia); subfertile parameters of the sperm; isolated disorders of the sperm with the normal amount and quality of spermatozoons; retrograde ejaculation with the normal spermogram parameters; immunological and cervical factors of infertility.

Indications for insemination of a donor's sperm: aspermia, necro- and teratozoospermia, hereditary diseases, retrogradation of the ejaculation with the absence of normal spermatozoons. Insemination of the donor's sperm is done only after receiving permission from a married couple.

The sperm is injected mainly into the uterine cavity; the introduction of the sperm into the cervical canal and in the back arch of the vagina with the cervical factor of infertility is ineffective. The sperm (after sexual abstention for 4 days) is taken with a plastic syringe, connected with a special polyethylene catheter, where it enters. Without fixating the cervix the catheter is lead into the cervical canal or in the uterine cavity behind the edge of the internal os, and 0.4 ml of sperm are entered. A disperser hood is put on the cervix to hold the sperm; the patient should be in the laying position for 30 min. The procedure is repeated for 3–5 menstrual cycles.

With a defective lutein phase after insemination chorionic gonadotrophin is prescribed intramuscularly on the 11th, 13th, 15th, 17th, 19th and 21st day of the cycle by 50 U or according to other diagrams. If the follicular phase of the cycle is long, they stimulate the maturing of the follicle and ovulation with clomiphene from the 5th through the 9th day of the cycle with additional introduction of CG intramuscularly on the 12th day (4,500 U) or pregnyl (5,000 U) with ultrasound of the follicle maturing and control of the basal temperature.

Before insemination of a donor's sperm (use native and cryopreserved sperms) tests to reveal local antispermal antibodies (Kremer's test) and tests on the penetration ability of spermatozoons in the cervical mucus are conducted. For three consecutive cycles it is recommended to use the sperm of one donor.

With the decrease in concentration of spermatozoons to less than 500,000 in 1 ml, decrease in mobility and morphological normal forms (less than 20%) intracytoplasmic injections of spermatozoon are conducted.

Extracorporal fertilization and gamete or embryo transfer is recommended to patients in the following cases: infertility after bilateral tubectomy; expressed anatomic changes (occlusion) of the Fallopian tubes; ineffective reconstructive-regenerative operations on the Fallopian tubes; unexplained infertility; absence of pregnancy despite the use of all possible methods of operative and conservative treatment during 2 years of examination concerning infertility.

The method is applied under the following conditions: an ability of the uterus to implant and keeping pregnancy; the absence of contraindications to pregnancy and labour (the method is contraindicated for severe somatic, genetic, mental diseases); the preservation of the ovarian response to endo- and exogenic stimulation of ovulation; the absence of inflammatory diseases, pelvic neoplastic processes. The woman's age should not exceed 40 years.

Before performing extracorporal fertilization exam of sperm, bacteriological analysis, colposcopy, hormonal examinations should be conducted. The method is carried out by stages: 1) superovulation induction; 2) aspiration of the oocyte; 3) fertilization of the oocyte by the spermatozoon; 4) cultivation of the fertilized oocytes; 5) transfer of the embryo to the uterus.

Superovulation is the achievement of the maturing of several dominant follicles — increase the efficiency of getting and fertilization of the ovum (aid function). Stimulation of superovulation is achieved by means of various methods: 1) stimulation of discharge of natural gonadotrophins with the use clomiphene; 2) stimulation of exogenic gonadotrophins, containing lutrophin and follitrophin (pergonal, humegon) or only follitrophin (metrodin); 3) stimulation of exogenic gonadotrophins against a background of blocking natural gonadotrophins with the help of drugs — agonists of gonadoliberin (buserelin, goselerin, decapeptil).

Long and short regimens of gonadoliberin agonists introduction are used. With the application of the long regimen gonadoliberin agonists are entered at the end of the follicular phases of the previous cycle, supervising the decrease in the lutrophin level in the blood; after its stable decrease gonadotrophin is entered. The short regimen provides the introduction of gonadoliberin on the 11th day of the cycle, gonadotrophin on the 5th day. Regardless of the used method, ultrasound control of the growth of the follicles, the thickness of the endometrium, as well as the estradiol level in the blood plasma analysis are conducted.

The eggs are taken by aspiration under the transvaginal ultrasound guidance which is carried out after hormonal stimulation of superovulation of the ovaries with menotrophin and gonadorelin or during the performance of laparoscopy or mini-laparotomy. The ovum (oocyte) is incubated together with the spermatozoon; after fertilization the embryos are transferred to the uterus (approximately 48 h after aspiration). No more than 4 embryos are implanted into the uterus. After this procedure, the woman should

remain in a horizontal position for 2 h. To oppress the immune reaction dexamethasone (0.25 mg) and supporting doses of chorionic gonadotrophin (up to 1,500 U) are prescribed till the stabilization of pregnancy. With the insufficiency of the lutein phase 5,000 U of CG a day are given, while transferring the embryo.

Gametes intra-Fallopian tube transfer is conducted under ultrasound or laparoscopic control. The ovum and spermatozoon are entered into the Fallopian tube with the help of a laparoscopic catheter.

The success rate of the use of extracorporal fertilization methods reaches 50%, consequently spontaneous abortions are observed up to 30% of the time, ectopic pregnancy — up to 6%, multiple gestation pregnancy — up to 12%.

RECOMMENDED READING

18; 21; 24; 48; 75; 79; 90; 92; 93; 94; 95; 101; 103; 108.

Chapter 7

ENDOMETRIOSIS

Endometriosis is a benign disease, characterized by the presence of endometrial glands and stroma outside of the uterus (Fig. 31).

The pathologic changes typical for this disease were described about 1600 B.C. in the Egyptian papyrus. The term "endometriosis" was offered for the first time in 1892 by Blair Bell.

The incidence of endometriosis in women in the reproductive and later periods varies from 7 to 59% and averages 5–15%. Endometriosis is found in every fourth gynaecologic laparotomy and takes place in 50% of the women, who have had an operation concerning infertility. There is data about an increase in this disease prevalence among the patient's relatives in comparison with the general population.

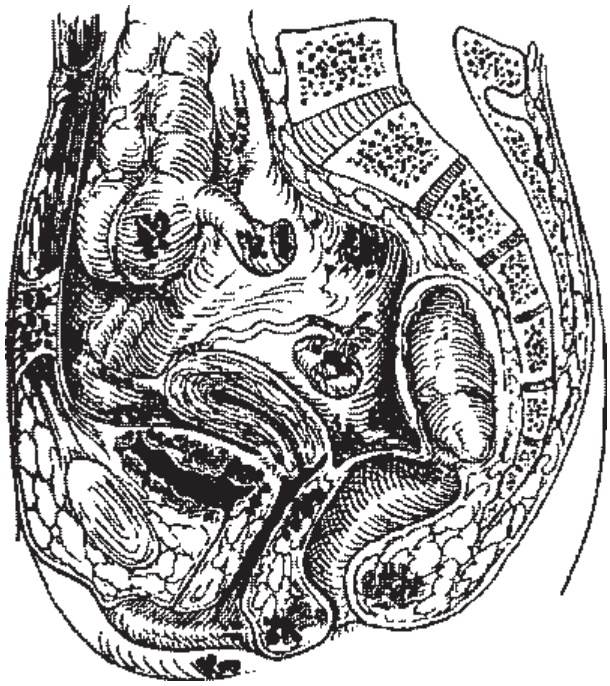


Fig. 31. The most frequent locations for the foci of endometriosis (designated in black):

ovaries, rectal-uterine pouch (Douglas' cul de sac), sacrouterine and broad ligaments, Fallopian tubes, peritoneum, plicae vesicouterina, round ligament, appendix, vagina, rectovaginal septum, sigmoid colon and rectum, caecum and ileal, inguinal canal, abdominal scars (stitches), uterus, bladder, umbilicus, vulva, etc.

The average age of patients suffering from endometriosis averages 28 years (10–83 years) though 75% of the cases are women between 25 and 50 years old irregardless of its location.

The most frequent primary location of endometriosis is the ovaries. Peritoneum, Douglas' cul-de-sac, sacrouterine, round ligament, broad ligament, Fallopian tubes and mesosalpinx, uterine peritoneum, vesicouterine pouch, sigmoid colon and rectum are affected. Less often the endometrial tissue is determined around the caecum, appendix, bladder, vagina, small intestine, in the lymph nodes and omentum. Endometriosis is rarely found around the umbillicus, scars after laparotomy or episiotomy, pleura, lungs, kidneys and heart.

The etiology of endometriosis is not established, though there are some widespread theories of its development.

1. Metaplasia of multipotential coelomic epithelium (peritoneum) *into endometrial tissue.* Under the influence of hormonal disorders, inflammation, mechanical trauma or other influences the mesothelium of the peritoneum and pleura, endothelium of the lymph vessels, epithelium of the renal canalicules and other tissue can be transformed into endometrium-like tissue. This theory has been confirmed experimentally.

2. Disorder of embryogenesis with abnormal remnants of the Muller's duct (in the peritoneum, etc.). It is believed that the endometrial tissue develop from abnormally located embryonal remnants, in particular the Muller's duct. Frequently, endometriosis is combined with congenital anomalies of the sexual system (uterus bicornus, additional uterine horn, etc.). urine system, digestive tract. Thus, congenital malformations, resulting in the difficulty of

normal outflow of menstrual blood from the uterus to the vagina have important value.

3. *Transtubal regurgitation of menstrual blood* — through the Fallopian tubes from the uterine cavity into the peritoneum and *direct implantation of the endometrium.* In 1921, Sampson established that during menstruation the viable cells of the endometrium can move through the Fallopian tubes to the peritoneum and the implants of the endometrium can form endometriosis loci. According to this theory one of the major stages in the development of endometriosis is retrograde menstruation. The existence of this phenomenon is clinically and experimentally confirmed. It is considered, that in women with short menstrual cycles (less than 27 days) and long menstruations (more than 7 days) the risk of endometriosis development is 2 times higher than in women with a longer cycle duration and 5–6 day menstruation duration.

There is an opinion that retrograde menstruation to some extent occurs in each woman during every menstruation. However, implantation of endometrioid heterotopias is possible only under additional conditions, namely: an increased ability to adhesion and implantation of endometrial tissue; a decrease in the protective abilities of the peritoneum due to inflammatory processes, disorder of the immune status, hormonal regulation, as well as genetic predisposition.

4. *Dissimination of the endometrial tissue* from the uterine cavity via the blood and/or the lymph vessels. Hematogenous transportation results in the development of endometriosis of the lungs, skin, muscles (rather rare variants of endometriosis).

5. *Translocation of the endometrium from the uterine cavity* (to the peritoneum, other organs) during surgical operations: for example, during caesarean section, myomectomy (iatrogenic endometriosis). However, it is assumed that the implantation of endometrial tissue in such cases and further development of iatrogenic endometriosis takes place seldom.

6. *The development of endometriosis in connection with disorders in hormonal regulation* in the hypothalamic-hypophyseal-ovarian-target organs axis. The penetration into other organs and the proliferation of endometrial cells are caused by oestrogen overproduction, resulting in an increased allocation of corticosteroids. The earliest cases of endometriosis are found in 10–11-year old girls, when the endocrine system already provides the beginning of menstruation, and full regression of the disease is observed in women after menopause.

7. It is believed that endometriosis can develop due to the *oppression of cellular immune response to endometrial antigenes.*

8. The development of endometriosis as *a genetically caused pathology.* In women, having sick relatives of the I degree of relationship endometriosis has been found in 6.9% of the cases, II degree — in 2% of the cases. Inheritance with family endometriosis is polygenic-multifactorial.

9. *The connection with infertility.* Endometriosis is frequently associated with infertility, though the mechanism of this phenomenon is not completely known. Maybe some role is played by the anatomic disorder of the pelvic organs, adhesions of the Fallopian tubes and ovaries, damage to the ovarian cortex as a result of the development of ovarian endometriomas filled with bloody liquid (chocolate cyst). An increase in the contents of prostaglandin in the peritoneal liquid, which, in turn, prevents conception by damaging the transport of spermatozoons and eggs, the occurrence of luteolysis or disorders of implantation can have some value. An increase in the amount of peritoneal macrophages in women with endometriosis can result in an increased destruction of spermatozoons. The presence of anovulation with endometriosis, defects of the lutein phase of the cycle, luteinization of the non-ruptured follicle, hyperprolactinemia, miscarriage in the early terms has a certain relation to infertility.

Classification. Endometriosis can be *genital* (affection of the genitalia) and *extragenital.* Genital

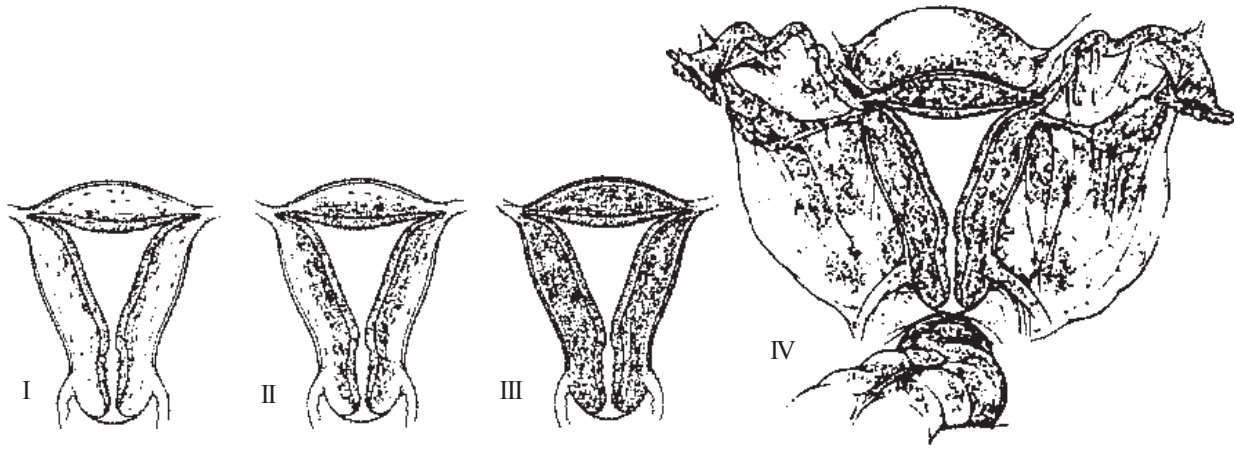


Fig. 32. Classification of internal adenomyosis according to the distribution of the process

Table 5. **Classification of endometriosis**

Location and character of the damage	Evaluation of the damage, points		
Endometriosis	< 1 cm	1–3 cm	> 3 cm
Peritoneum			
Superficial	1	2	4
Deep	2	4	6
Right ovary			
Superficial	1	2	4
Deep	4	16	20
Left ovary			
Superficial	1	2	4
Deep	4	16	20
Posterior cul-de-sac	Partial	Complete	Complete
	4	40	40
Adhesions	1/3 enclosure	1/3–2/3 enclosure	> 2/3 enclosure
Right ovary			
Filmy	1	2	4
Dense	4	8	16
Left ovary			
Filmy	1	2	4
Dense	4	8	16
Left Fallopian tube			
Filmy	1	2	4
Dense	4	8	16
Right Fallopian tube			
Filmy	1	2	4
Dense	4	8	16
The fimbriated end of the Fallopian tubes is enclosed	16	16	16

endometriosis, in turn, is divided into *internal,* or *adenomyosis* (endometriosis of the uterus), *external* (extrauterine locations: endometriosis of the cervix, vagina, perineum, retrocervical, ovaries, Fallopian tubes, peritoneum of the rectouterine pouch). Some experts consider retrocervical endometriosis as a variant of internal endometriosis (adenomyosis).

More than 10 classifications of endometriosis exist. On the basis of the data obtained during laparoscopy, the American Fertility Society (1985) offered a classification for endometriosis depending on the amount of disorders, their location, prevalence, sizes of the endometrial heterotopias and endometriomas. Uni- or bilateral character of the disorder, the presence of adhesions and the degree of its extent are also taken into account. Depending on these parameters, four stages of endometriosis are distinguished: I — minimal; II — mild; III — moderate severe and IV — severe. The stage, as a rule, is determined by the prognosis concerning the restoration of the patient's fertility (Table 5).

Stage I (minimal) is diagnosed, if the score is 1—5; stage II (mild) — 6–15; stage III (moderate severe) — 16–40 and stage IV (severe) — more than 40 points.

According to the clinical classification of internal endometriosis (adenomyosis), also four stages of the process are distinguished (Fig. 32):

I — process is limited to the uterine submucous layer;

II — process extends onto the uterine muscular;

III — process is spread onto the whole myometrium, down to the serous integument;

IV — along with the uterus, the parietal peritoneum of the pelvis and adjacent organs are involved in the process.

Adenomyosis can be diffuse, focal or nodular (Fig. 33).

With ***endometriosis of the ovaries*** four stages are distinguished:

I — small dot-like endometrioid heterotopias on the surface of the ovaries, peritoneum of the cul-de-sac without formation of cystic cavities;

— endometrioid cyst of one ovary with a size up to 5–6 cm with fine endometrioid heterotopias on the peritoneum of the pelvis; insignificant adhesions in the areas of the uterine appendages without spread onto the intestines;

— endometrioid cysts of both ovaries of various sizes (more than 5–6 cm — one ovary and not a large endometrioma of another one); endometrioid heterotopias of small sizes on the serous shell of the uterus, Fallopian tubes and on the parietal peritoneum of the pelvis; expressed adhesions in the areas of the uterine appendages with partial spread to the intestines;

— bilateral endometrioid cysts of the ovaries of large sizes (more than 6 cm) with involving the adjacent organs — the bladder, rectum and sigmoid colon; extensive adhesions.

The severity of the disease is determined also by the presence of accompanying scarring and adhesions, tissue infiltration around the cervix, ureter, intestines, sacrouterine ligament, clinical course of the disease.

Retrocervical endometriosis also has four stages:

— endometrioid foci are located in the limits of the rectovaginal fat;

— disseminating of growing endometrioid tissue onto the cervix and the vaginal wall with the formation of small cysts;

—pathologic process spread onto the sacrouterine ligament and serous integument of the rectum;

— involvement of the rectal mucosa in the pathological process, spreading of the process onto the peritoneum of the cul-de-sac with the adhesions formation in the area of the uterine appendages.

Clinical picture. Endometriosis occurs in women of the reproductive age more often: average age of patients with endometrioid cysts is about 30, with adenomyosis — about 40.

The diagnosis in most cases is established according to the anamnesis and results of objective examination. Many patients have accompanying neuropsychological and vegetovascular disorders, in every third patient endometriosis is combined with uterine myoma and endometrial hyperplasia.

Patients more often complain of a nagging pain in the lower abdomen and back during a month, amplifying at the eve and during menstruation (expressed algodysmenorrhoea). Often patient's complaints are dyspareunia (especially in the case of deep penetration), infertility, pain in the rectum, perineum, premenstrual bloody discharge, and back pain. Pathologic symptoms somewhat depend on the location of the disorder. In the early stages of the disease, the pain can occur periodically, during the III and IV stages — have a steady character, decreasing a working ability. However, correlation between the extent of lesion, duration of the process and the clinical picture of the disease is not always observed. A large ovarian endometrioid cyst can be painless and found casually during routine examination or ultrasound, while a minimal spread of endometriosis onto the peritoneum of the pelvis and sacrouterine ligament and/or onto the rectovaginal septum can cause strong pain, resulting in a woman's disability.

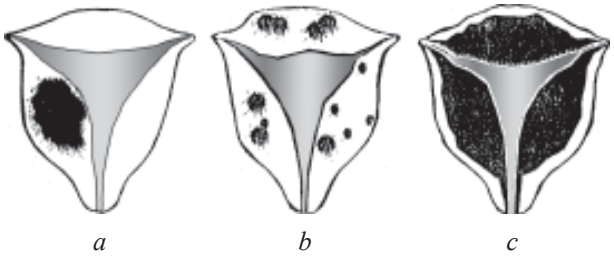


Fig. 33. Variants of adenomyosis:
a — nodular; *b* — focal; *c* — diffusive

Infertility in patients with endometriosis can be a result of tubal occlusion, fimbrias deformation due to adhesions, complete isolation of the ovaries by periovarian adhesions, direct damage to the ovarian tissue by the endometrioid cysts, accompanying endocrine disorders resulting to defective ovulation and/or functional disorder of the corpus luteum, and also as a result of local immunity disorders, the presence of combined hyperplastic processes (myoma, cystoma, etc.).

Diagnosis. An important method of diagnosis is gynaecologic examination, which allows suspecting adnexal masses. The sacrouterine ligament during palpation is tender, their nodularity and induration are found. The uterus is frequently fixed in retroflexio. However, in mild endometriosis the physical findings can not exist.

The dark red punctuated cystic formations are found during examination in patients with endometriosis of the vaginal part of the cervix.

Ultrasound helps specifying the location, size of the endometrioid cysts in various phases of the menstrual cycle.

The most typical ultrasound picture for retrocervical endometriosis is the presence of dense formations (0.7–4.5 cm) located in the rectovaginal fat behind the cervix. Ultrasound criteria of adenomyosis (diagnostic value of ultrasonography is 30–57%) are the occurrence of individual foci of increased echogenity in the myometrium, unevenness of the basal layer of the endometrium, an increase in the anterior-posterior size of the uterus and asymmetric thickening of one of its walls, the presence of round hypoechogenic inclusions with a diameter of 2–5 mm.

The accuracy of adenomyosis diagnosis increases with the use of hysteroscopy, hysterosalpingography; though the exact diagnosis can be established on the basis of the data of hystologic research of the biopsy material or removed uterus. Hysteroscopic criteria of internal endometriosis of the uterus are a change in the relief of the uterine cavity, the presence

of rough rocky figures, which remains unchanged after the removal of the functional layer of the endometrium, scars, and crypt.

The radiological picture of the diffuse form of internal endometriosis of the uterus is characterized by the presence of "extracontour shadows" with a length of 0.2–2 cm. The computer tomography can determine the precise character of the pathologic process, its location, interrelation with adjacent organs, as well as specify the location of the pelvic organs, in particular the retrocervical zones and parametrium. The most informative of the non-invasive methods is nuclear magnetic resonance (NMR), which provides precise visualization of the pelvic organs.

If the pathologic process spread to the intestines and parametrium is suspected, irrigoscopy, proctosigmoidoscopy, and excretory urography are conducted.

One of the most exact methods of endometriosis diagnosis is laparoscopy, expanding the opportunities of verifying the diagnosis. Superficial blue and black or white lesions raised onto the peritoneal surface are visualised as a rule. The prevalence of adhesions is evidence of the lingering of the disorder. The ovaries involved in the process get superficial damage or develop endometriomas ("chocolate cysts"). The accuracy of diagnosis of endometrioid cysts due to laparoscopy reaches 100%.

Laparoscopic characters of *a typical endometrioid cyst* are following: sizes up to 12 cm in diameter (on average 7—8 cm); adhesions with the lateral surface of the pelvis and/or posterior leaf of the broad ligament of the uterus; fine red or dark blue spots on the surface; "chocolate" contents.

The foci of endometriosis during laparoscopy are subject to electrocoagulation, cryo- or laser action, the removal by argon coagulator laser or ultrasonic scalpel after preliminary biopsy. The final confirmation of the diagnosis is the data of hystologic study.

Laboratory screening of endometriosis includes revealing *tumoural markers* in the blood (oncoantigens CA-19-9, CEA and CA-125) by methods of immunoferment analysis (IFA), as well as the use of the Po-test.

It is established, that in the blood serum of healthy women the concentration of oncomarkers CA -19-9 on the average is 13.3 U/ml, in patients with endometriosis — 29.5 U/ml and exceeds the threshold (37.4 U/ml) in patients with adenocarcinoma of the pancreas, cancer of the stomach, rectum, as well as with metastasises in the liver, cancer of the lungs and breast.

The concentration of oncoantigen CA-125 in the blood of healthy women on average is 8.3 U/ml, with endometriosis — 27.2 U/ml and does not exceed 35 U/ml. The contents of CEA (cancer-embryonal antigene) in the blood serum of healthy women averages 1.3 ng/ml and normally does not exceed 2.5 ng/ml. The level of this tumoural (oncomarker) increases with endometriosis, cervical cancer, endometrium, ovaries and vulva. For patients with endometriosis, the average value of the oncomarker is 4.3 ng/ml.

Biopsy with a subsequent hystologic study of the damaged tissue confirms the diagnosis. The identification of endometrial glands and stroma, as well as macrophages with haemosiderin is evidence of the presence of endometriosis. In the future, probably, non-invasive diagnosis of endometriosis will be established with the help of the use of nuclear magnetic resonance and the level of CA-125 in the blood serum (today it is an insufficiently specific test).

Treatment. It is necessary to remember, that patients with endometriosis, as a rule, do not recover till menopause. Medicamental therapy is prescribed with the purpose of suppressing and reducing endometrioid damages.

Young infertile women without expressed symptoms of the disease are recommended the supervision of a doctor and expectant (palliative) management before detailed examination and possible exact establishment of the cause for infertility.

So, with the mild degree of endometriosis, pregnancy is possible in 72% of the patients. A similar occurrence of positive results of conception is achieved due to the use of laser laparoscopy, conservative surgery, laparotomy and medicamental therapy. If pregnancy does not occur in 12–18 months of supervision, surgical intervention is recommended. For patients over the age of 35 hormonal or surgical treatment is conducted.

Hormonal treatment. The main principle of medicamental therapy of patients with endometriosis with the help of the use of any hormonal preparations is the suppression of estradiol secretion in the ovaries. Oestrogen-gestagen drugs (oral contraceptives), progestagen, antigonadotrophin and agonist of gonadotrophin-releasing hormone are prescribed.

Young women with mild or moderate severe endometriosis, those not interested in pregnancy, as well as infertile women are recommended pharmacological suppression of ovulation. The purpose of therapy is to prevent ovulation and the induction of pseudomenopause, which promotes temporary regress of endometriosis and atrophy of the endometriosis foci. After the termination of treatment, a high frequency of relapses of the disease is observed.

Oestrogens and gestagens. The constant use of oral contraceptive preparations with low contents of oestrogen and progesterone or pure gestagen is a method of choice with the mild and moderate severe disease forms in women who are not seeking to conceive. The pregnancy rate after hormone therapy of patients with endometriosis is the same as for palliative therapy. Side-effects of treatment with oral contraceptives are profuse and bloody discharge throughout the menstrual cycle.

Treatment of patients with endometriosis depending on the stage of the disease

Expectant (palliative) (I—II stages)	*Hormonal (I—III stages)*	*Surgical (II—IV stages)*	*Concerning infertility (II—IV stages)*
Supervision Palliative treatment: Analgesics Non-steroid Anti-inflammatory Inhibitors of prostaglandin-synthetase Pregnancy Research the reasons for infertility	Oestrogen-gestagen contraceptives with low hormone doses Progestin Anti-gestagen Danazol Analogues of Gn-RH	Laparoscopic laser or electrocauterization Conservative laparotomy Radical laparotomy (complete hysterectomy with bilateral salpingoovariectomy)	Intrauterine insemination Transfer of sex cells (gamets) into the Fallopian tubes Fertilization *in vitro* and the transfer of the embryo into the uterus

The class of *progestagens* are the following preparations: medroxyprogesterone-acetate (MPA), noretynodrel, norethisteron (dienogest), retroprogesterone (didrogesterone), orgametril (linestrenol).

MPA is prescribed at a dose of 30–50 mg a day for 3–4 months for the moderate and disseminated endometriosis. Side-effects: atherogenous action, increase in body weight, decrease in libido.

Danazol. Before the occurrence of analogues of gonadotrophin-releasing-hormone, danazol had a priority in the medicamentous therapy of patients with endometriosis. This drug is an isoxozol derivative of 17-T-ethinyl-testosterone; it affects many areas of the organism, including the hypothalamus, hypophysis, ovaries and endometrium. Danazol promotes anovulation, reduces oestrogenic influence, atrophy and regress of endometrioid heterotopias. However, it, as a rule, does not influence large endometriomas.

The drawback of danazol that patients experience some side-effects: increase in body weight, hypostases, increase in breasts, acne, hirsutism, oily skin, deepening of the voice. After the termination of treatment some pathologic symptoms can regress. Likewise, menorrhagia, headache, vaginitis, decrease in libido, muscle pain, hot flashes may result from danazol use. Many researchers recommend the use of danazol by 400 mg 2 times a day for 6–9 months. After 1–2 month treatment with this drug, amenorrhoea usually occurs. The menstrual cycle renews in 28–35 days after the termination of treatment.

During the danazol treatment course the patient is recommended to use barrier methods of contraception to prevent pregnancy (masculanization of the female fetus is possible). The majority of patients mark a significant reduction of pain during the given therapy. The use of danazol for 2 months before an operation improves the results of the latter and increases the pregnancy rate. Danazol is possible to prescribe to patients in the postoperative period with severe forms of endometriosis and in case of its incomplete reduction. Due to treatment with danazol women with the mild, moderate and severe forms of endometriosis (II–IV stages) the pregnancy incidence ranges from 15 up to 60% and does not differ from the results of surgical treatment of patients with mild and moderate forms of endometriosis.

Among *antigestagens* miphiprestone and gestrinon (nemestran) are used for endometriosis treatment.

Gestrinon (nemestran) — derivative of 19-norsterone — has not only antiprogestagenic, but also proandrogenic, antigonadotrophic and antioestrogenic properties. The preparation is prescribed orally by 2.5 mg 2 times a week. According to the action mechanism of nemestran against a background of treatment, amenorrhoea and "pseudomenopause" may occur. The terms of the termination of menstruation vary depending on the dosage and initial characteristics of the menstrual cycle. The normal menstrual cycle renews approximately 4 weeks after the termination of treatment. The pain syndrome caused by endometriosis, including algodysmenorrhoea and dyspareunia, subsides or disappears, in most cases, prior to the beginning of the second month of treatment, and after 4 months—almost in all patients. The preparation renders essential involute action on the endometrioid glandular-epithelial cells with the activization of the endocellular lysosomal apparatus. The pregnancy rate after the first month of treatment is 15%, and by the end of the second year of supervision, the incidence of complete pregnancies reaches 60%.

Side-effects include increase in body weight, acne and seborrhoea, hirsutism, sometimes deepening of the voice, reduction of the breasts, hypostases, headache, depression, hot flashes, dyspeptic phenomena, allergic reactions.

At present, the optimum drugs for treatment of patients with endometriosis are considered to be the analogues of gonadoliberin (agonist of Gn-RH), used with this aim at the beginning of the 80-s of the XX century.

Analogues of Gn-RH causes medicamental oophorectomy, promoting thus the regress of endometriosis. In comparison with danazol they have minimal side-effects, can be used as hypodermic, endonasal and depot-injections in patients with mild and moderate forms of endometriosis.

Now the following preparations are the most widely used:

decapeptids — nafarelin, goserelin ("Zoladex"), tryptorelin;

nonapeptides — buserelin, leiprolerin (leiprolid, lupron), historelin.

The medicinal forms of the preparations are introduced intranasally (400 μg a day), as well as hypodermically and intramuscularly as an injection and a depot-implant.

Among the preparations of prolonged action, goserelin ("Zoladex"), which is entered hypodermically by 3.6 mg 1 time every 26 days, and "Deckapeptil-depot" — by 3.75 mg intramuscularly 1 time every 28 days, is widely known.

Endogenic gonadoliberins have an expressed specificity and interact with adenohypophysis receptors which become tolerant to the pulsating release of endogenic peptide. In this connection, after the initial phase of activation of the hypophysis (7–10th day) its desensitization occurs, accompanied by a decrease in the levels of folli- and lutrophin with the termination of the corresponding ovarian stimulations. The level of oestrogen in the blood decreases and is less than 100 pmole/l, i.e. corresponds to the contents of these hormones after castration or during menopause. The production of progesterone and testosterone by the ovaries is reduced also. In conditions of expressed hypoestrogenism, atrophic changes take place in the endometrioid heterotopias. However, treatment with the agonists of Gn-RH, as well as other means, including surgical, does not remove relapses of the disease.

Expressed hypoestrogenism, caused by preparations-agonists of Gn-RH, is accompanied in the majority of patients by such symptoms, as hot flashes (up to 20–30 times a day in 90% of the patients), dryness of the vaginal mucous membrane, decrease in libido, reduction in the breast size, sleeping disorders, emotional lability, irritability, headache, dizziness, as well as an accelerated decline in the mineral density of bone tissue.

For the treatment of patients with *adenomyosis* numerous hormonal modes are offered. However, no one of them is effective enough. The use of oral contraceptives can even worsen the patient's condition. Women, interested in becoming pregnant, as well as patients in the premenopausal period are prescribed analgesics. Hysterectomy is a method of choice when childbearing is completed.

Surgical therapy of patients with genital endometriosis is practically the only method allowing to mechanically remove or destroy with the help of energy (laser, electro-, cryo- or ultrasonic) the morphological substratum of endometriosis. However, during operative intervention only visible lesions are removed, while microscopic heterotopias can be accidentally left, or in connection with the danger of severe complications, or inexpediency of expanding the volume of the operation in young women.

Therefore the modern approach to treatment of patients with endometriosis consists of a combination of the surgical method directed at the maximal removal of endometrioid foci and hormone therapy.

However, even with widespread endometriosis in women interested in pregnancy, it is necessary to adhere to the principles of reconstructive-plastic conservative surgery and to perform radical operations only when all other opportunities have exhausted.

Popularity of laparoscopic surgery, used in treating patients with mild and moderate forms of endometriosis, increases. Laparoscopic operation corresponds to the conditions of minimally invasive surgery, when microcoagulation, exact cuts, aimed destruction, hydraulic preparation are used. One more positive point of the operation is that it is performed in conditions of moisture of tissues with minimal risk of getting in the abdominal cavity of foreign bodies and particles such as talc, tampons, thread, the amount of which decreases as much as possible due to the use of bipolar coagulation, laser vaporization, providing optimum haemostatic effect. The minimal invasiveness and restriction of operational trauma prevent the formation of adhesions in the abdominal cavity.

The extent of the operative intervention is determined depending on the age of the patient, her desire for future fertility, as well as on the prevalence and location of endometrioid foci and the readiness of the surgeon and patient to perform the most optimum (radical) volume of the operation. With endometrioid cysts of the ovaries, the first stage of treatment is operative laparoscopy, resection of the ovaries within the limits of the healthy tissue with the enucleation of the endometrioid cystic capsules and additional processing of the cystic bed by means of bipolar coagulator, laser, ultrasound scalpel for the achievement of haemostasis and ablastic. In women over the age of 35–40 years, not interested in becoming pregnant or having a combination of endometriosis with other defects, the appendages on the damaged side are removed.

Both bipolar, and monopolar technics of electrocauterization of the endometrioid heterotopias are used. Laser vaporization of the endometriosis foci and adhesions with the help of carbonic acid (CO_2), argon (KTP/532) or neodymium (Nd-YAG) laser is a new method, allowing not to preserve healthy tissue. Laser laparoscopy is a method of choice for treatment of patients with the I and II stages of endome-

triosis, in comparison with traditional surgical interventions and long medicamental treatment.

Literature gives data on rise of pregnancy incidence after laser surgery in comparison with electrocauterization and medicamental therapy.

Laparotomy is recommended to patients with space occupying lesions in the uterine appendages which are refractory to hormone therapy; to women with sever forms of endometriosis, with no desire to pregnancy; to patients with disseminated and combined forms of endometriosis and long-lasting diseases, large pelvic adhesions, tubal occlusion or uterine myoma, functional disorders or defects of adjacent organs (intestines, ureter, bladder) by endometriosis; as well as with the combination of endometriosis and other gynaecologic diseases, where surgical treatment with the use of laparotomy is required, or in a situation when the performance of laparoscopy is impossible. The patient's age, her knowledge of laparotomy and the surgeon's skills, who will be conducting the operation, have great value in choosing the given method of treatment.

Vaginal access can be applied separately or together with laparoscopy in the removal of retrocervical endometrioid formations.

The principles and purpose of sparing surgical intervention during the performance of laparotomy provide cautious manipulation with tissue and the use, whenever possible, of microscopic technics. The foci of endometriosis are removed by excision, electrocauterization or laser vaporizations. If it is possible, the ectopic tissue is removed to the maximum *(cytoreduction)*. With damage to the ovaries, they try to leave the maximum of their cortex and prevent bleeding. In case of unilateral severe damage, unilateral ovariectomy is used. If there is damage to the appendix, appendectomy is conducted. For patients with strong pain, pre-sacral neurectomy may be performed. In the III–IV stages of endometriosis and with damage to the ureters, bladder or intestines, after the operation danazol or analogues of Gn-RH (zoladex, decapeptil, luprolid) are prescribed.

Total abdominal hysterectomy with bilateral oophorectomy, as a rule*,* is recommended for depleting symptomic forms of endometriosis and the woman's disinterest in preserving the reproductive function. In most cases, with severe forms of endometriosis, bilateral oophorectomy is conducted. With residual damage (incomplete removal of the endometrioid formations) in the postoperative period, progestin is prescribed permanently for 6–12 months, which helps supervise the vasculomotor symptoms and promotes the regression of endometriosis. After that period, it is possible to use oestrogens; however, the risk of relapses in this case increases. If all the damaged tissue has been removed, combined oestrogen-gestagen therapy is begun immediately after the operation.

Obligatory condition for carrying out an *operation concerning retrocervical endometriosis* is preliminary research of the urinary system (excretory intravenous pyelography, ultrasonic research), irrigoscopy, proctosigmoidoscopy and the preparation of the patient for an operation on the intestines (even if it was not planned), in connection with the high risk of wounding the latter. Cryosurgical (destruction of the endometrioid bed), laser operative technics are used. After the hystologic confirmation of the diagnosis and the reduction in the volume of the endometrioid infiltrate, hormone therapy with agonist of Gn-RH is conducted.

Irregardless of the surgical access it is necessary to apply such means as electrocoagulation, various lasers, cryolysis, argon beam coagulator, radiosurgical or ultrasonic scalpel.

Treatment of patients with *cervical endometriosis* consists of the removal of the damaged area with subsequent cryolysis or evaporation with the help of CO_2-laser, destruction with use of an ultrasonic scalpel.

The results of the treatment depend on the severity of the disease, the extent of the process, the volume and radicality of the operative intervention, full value of hormonal and rehabilitation therapy, the degree of reproductive system disorder before the operation.

During treatment, as well as after its termination, dynamic control over the patient's condition (gynaecologic examination, ultrasonography once every 3 months) is conducted. The dynamic of the levels of the oncomarkers CA-125, CEA and CA-19-9 in the blood serum determine the early diagnosis of relapses of endometriosis and the control of the efficiency of treatment.

The rehabilitation of patients after surgical operations consists of the correction of post-castration syndrome, immune correction (thymalin, T-activin, sandoglobulin), reflexotherapies, physiotherapeutic procedures: electrophoresis with iodine, zinc on the lower abdomen, constant magnetic field, ultrasound in a pulse mode, quantum hematotherapy, sanatorium treatment with the use of radonic waters (general baths, gynaecologic irrigation, microclysters), as well as physiotherapy exercises, diet according to the character of the extragenital diseases.

Conducting patients with infertility. For the treatment of infertility of patients with endometriosis, the use of modern assisted reproductive technologies is recommended. Intrauterine insemination is conducted on patients with the minimal and mild stages of the disease. The transfer of the gamete to the Fallopian tubes is conducted with mild and moderate forms of endometriosis. In the case of extensive damage to the Fallopian tubes, fertilization in

vitro with the subsequent transferring of the embryos is possible.

During pregnancy and after labour, a regression of the foci of endometriosis is observed; a miscarriage worsens the course of the disease.

Prevention of endometriosis consists of the use of oral contraceptives, anatomic performance of surgical interventions on the uterus (caesarian section, etc.).

RECOMMENDED READING

1; 7; 18; 24; 38; 75; 79; 82; 90; 92; 93; 94; 103; 108.

Chapter 8

DEVELOPMENTAL DISORDERS OF THE REPRODUCTIVE SYSTEM

DEVELOPMENT OF THE REPRODUCTIVE SYSTEM

The formation of the reproductive system is a complex, genetically determined multistage process directed towards the achievement of a biological maturity at which the reproductive function is possible. One of the obligatory conditions of an organism's existence is its ability to restore harmony, balance, despite the influence of adverse endo- and exogenic factors.

The control over the development of the reproductive system is carried out by the neurohumoral system of the hypothalamus-hypophysis-sex glands-other endocrine glands (adrenal glands, thyroid gland). The principle of homeostasis maintenance in the endocrine system is in keeping balance between the functional condition of the internal secretion glands and the contents of hormones in the organism. The relation between the "centre" of the endocrine system — hypothalamic-hypophysial axis and the "periphery" — the sex glands, thyroid gland, adrenal glands has the character of inverse relation and is carried out as long (hypophysis-peripheral endocrine glands), and short (hypothalamus-hypophysis) and ultrashort (auto regulation) paths. The interrelation between the endocrine glands explains a high incidence of developmental disorders of the reproductive system, especially during puberty, as a result of the dysfunction of this or that gland, resulting in the change of the homeostasis.

A person's reproductive system is represented as reproductive (sexual glands and organs — the uterus, Fallopian tubes, vagina, external genitalia) and non-reproductive organs (arc-shaped nucleus of the hypothalamus and gonadotrophs of the adenohypophysis).

The embryologic neurons of the hypothalamus develop from the diencephalon on the 8th–12th week of pregnancy, and then migrate to the posterior thalamus. Even in an adult the hypothalamus weighs only 10 g, which is 1/150 part of the whole weight of the brain. Two areas of the hypothalamus — mediobasal and supra decussational — connected with the reproductive system functioning. Luliberin (lutrophin-releasing-hormone, LT-RH) is formed in the hypothalamus. The arc-shaped (*arcuate*) nucleus of the mediobasal hypothalamus generate a specific signal approximately with an hourly interval *(circhoral rhythm),* causing the release of gonadoliberin in the hypophysis portal system. This hypothalamic structure is referred to as the *"arcuate oscillator"*. Impulses of gonadoliberin stimulate the gonadrotrophs of the hypophysis to impulse secretion of lutrophin and follitrophin, which, in turn, promotes the cyclic morphological and secretory changes in the ovaries.

Neuromediators (catecholamin (noradrenaline), dophamin, serotonin and hormone of the epiphysis — melatonin), capable of blocking the secretion of gonadotrophin, take part in the regulation of gonadoliberin secretion; γ-aminobutyric acid (GABA) and acetylcholine cause the opposite effect. Endogenic peptides with morphin-like activity — endorphin, as well as catecholoestrogen play a special role in the regulation of gonadoliberin secretion.

The lobes of the hypophysis develop from different sources: adenohypophysis — from buccal epithelium (somatic ectodermal layer), and neurohypophysis — from the ectodermal neural tube. The posterior lobe of the hypophysis (neurohypophysis) is a derivative of the ectoderm and is directly connected with the median eminence of the hypothalamus by means of axons, going through the pedicle of the hypophysis. The anterior lobe of the hypophysis (adenohypophysis) includes the distal, intermediate and tuberal parts. The adenohypophysis, opposite from the posterior lobe of the hypophysis, has no direct neural connections with the hypothalamus. The anterior lobe of the hypophysis contains cells — gonadotrophs (basophilic cells), which secrete folli- and lutrophin, and lactotrophs (acidophilic cells), secreting prolactin. Except for the trophic hormones connected with the reproductive function (folli- and lutrophin, prolactin), the adenohypophysis produces

somatotrophin, or the growth hormones (somatotrophs), corticotrophin (corticotrophs) and thyrotrophin (thyrotrophs). The posterior lobe of the hypophysis excretes two peptide hormones: vasopressin (antidiuretic hormone) and oxytocin.

For gonadotrophin secretion the pulsating rhythm with intervals between separate "pulses" of about one hour *(circhoral rhythm)* is characteristic. The *circadian* (daily) *rhythm* of secretion can be broken, for example due to a significant increase in the secretion of prolactin during pregnancy or during the development of prolactinoma. The secretion of gonadotrophins by the fetus' hypophysis occurs on the 14th–18th week of its development. In the female fetus' hypothalamus secretion of the releasing hormones and gonadotrophin begins on the 14th–21st week and reaches a maximum on the 25th week of development. Maturing of the gonadotrophin receptors in the fetus' ovaries occurs only after the formation of the ovarian follicles (after the 20th week).

Thus, the hypothalamic-hypophysial-ovarian axis of the fetus starts to function already in the II trimester of the pregnancy; the peak of its activation happens in the middle of the pregnancy with a further decrease in the activity till birth.

The basis typology of the process of physical development is growth and differentiation of the organism. In the various age periods, the growth process and development proceeds non-uniformly. Development of the female organism from a birth till the moment of her maturing can be divided into some periods:

1) prenatal;
2) neonatal (newborn) period;
3) neutral, or the early childhood period (till 7 years);
4) prepubertal, or the childhood period (from 7 years till menarche);
5) pubertal, or the sexual maturing period (from menarche till 15 years);
6) juvenile (from 15 till 18 years);
7) maturity period.

THE PERIOD OF PRENATAL DEVELOPMENT

Throughout prenatal development, the formation of the reproductive system occurs under the influence of both genetic and epigenetic factors (internal and external).

The genetic factors, acting from the moment of conception, have a certain value. The genetic sex of the child is determined at the moment of conception — fertilization of the ovum by the spermatozoon — and is caused by a set of sex chromosomes in the zygote: XX — female, XY — male.

The **epigenetic factors** include internal (enzymes, hormones, genome's inductor) and external (influence of the environment, physical, chemical, infectious, etc.).

The role of internal epigenetic factors is shown by the fact that with the absence of the sex glands (agenesia) in the germ the differentiation of sex ducts occurs by the female type irregardless of the fetus' sex. This basic (female) type of differentiation is preserved with the presence of ovaries in the germ. The development of the genitalia in a genetically male fetus by the male type occurs exclusively with the presence of testicles.

Thus, primary sexual characters (sex determination, the sex glands anlage and their development, some stages of gametogenesis) are determined during fertilization and in the embryonic period, their development proceeds into the fetal period and after birth (the neonatal period). From the beginning of puberty till the end of the maturity period, the secondary sexual characters are being formed.

Primary (germinative) sex cells are formed in the wall of the yolk sac (Fig. 34) approximately till the 25th day of embryonic development and on the 30th day migrate to the sexual crests — germs of the sex glands.

Indifferent germs of the male and female sex glands — sexual crests (gonadal, or urogenital platens) are formed on the 4th week of embryogenesis in the thoracic-lumbar part of the nephrotoma (from the projection on the medial side of the primary kidney) and consist of the medulla and cortex substance, occupied by the primary (germinative) sex cells.

Chromosomal determination of the sex occurs during fertilization. The sex is determined genetically with a Y-chromosome, in particular the gene SRY relating to the family of DNA-regulator of genes S_{OX}; the gene SRY codes the regulator factor TDF, which is one of the inductors of development of the male sex glands. The Y-chromosome provides an increase in the primary gonad of the medulla layer, which further forms the testicle; the X-chromosome is of cortex layer, from which the ovary develops. The future epithelial elements of the sex glands are the derivatives of coelomic epithelium, and connective-tissue and muscular elements of the sex glands — derivatives of the mesenchyma. The interstitial tissue of the sex glands, developing from the mesenchyma, forms in the male embryo interstitial endocrinocytes (Leydig's cells), and in female embryotheca tissue.

The chromosome 17 contains S_{OX}-like gene SRA_1, mutations of which result in *sex reversion* (a genetic male has the female phenotype) and *camptomelic dysplasia* where 2/3 of the patients with a XY genotype have a female phenotype.

The deferent ducts in a male fetus are formed of the conjugate ducts of the primary kidney (Wolff's

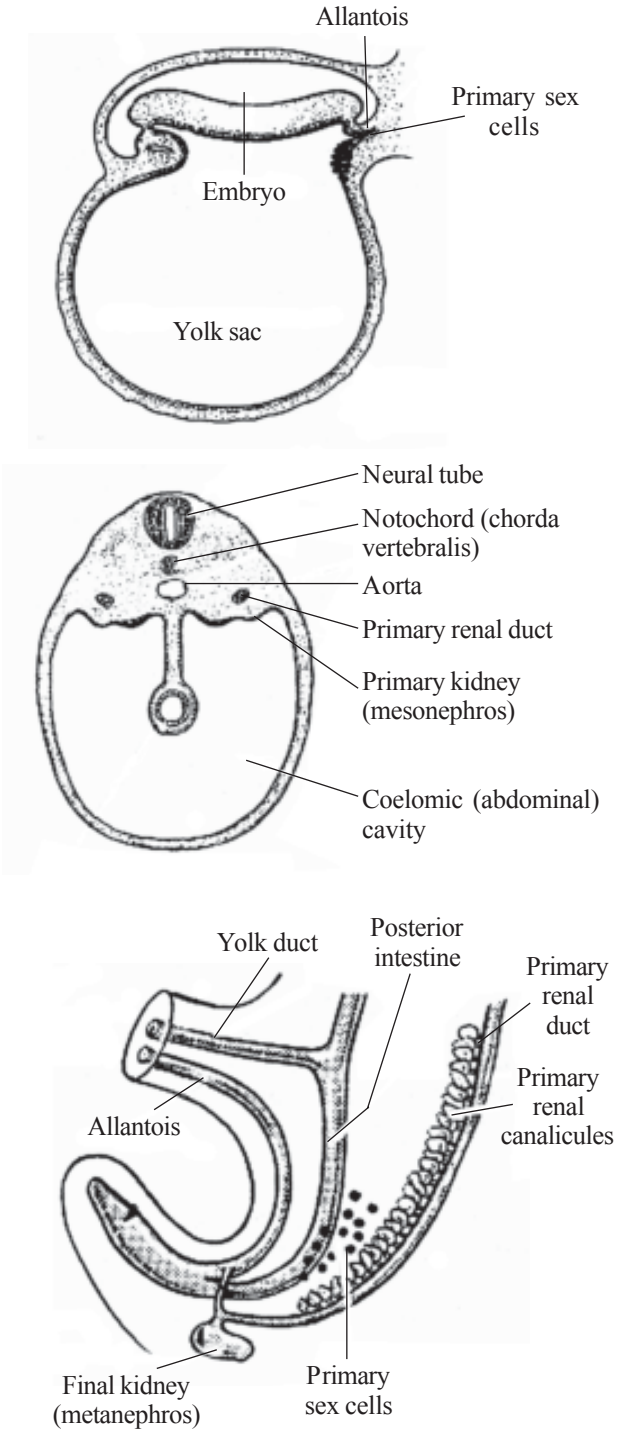


Fig. 34. Formation and migration of the primary sex cells

ducts), while in a female fetus they are obliterated.

Female paramesonephricus ducts (Müllerian ducts) are pulled as tubules along the primary kidney almost in parallel to its ducts and open at the cloaca. The uterus, Fallopian tubes and part of the vagina are formed from them in female fetuses.

Up to the 45th–50th day of embryogenesis the gonadal germs have no sexual differentiation. On the 8th week of prenatal development (the crucial stage of development of non-differentiated sex glands) under the influence of the regulator factor TDF, coded Y-chromosome, as well as genes S_{OX} of chromosome 17 from sexual crests (gonadal elevations) the testicles develop, and with the absence of this factor's influence — ovaries. Nature as if making an additional effort for the development of a male organism. The differentiation of other structures is determined by the male sex hormones and Müllerian inhibiting factor (MIF), produced by the fetus' testicles.

Under the control of the chorionic and hypophysial gonadotrophins, the interstitial endocrinocytes (Leydig's cells) of the fetus's testicles produce testosterone. Under the influence of testosterone, the testicular ducts, testicular appendages, testicular vesicles develop from the primary renal (Wolff's) ducts. Enzyme 5α-reductase catalyzes the transformation of testosterone into dehydrotestosterone (DHT), necessary for embryogenesis completion on the 12th–14th week and the external genitalia (scrotum, penis) differentiation. The supporting endocrinocytes (Sertoli's cells) of the fetus' testicular canaliculi secrete Müllerian inhibiting factor, which causes the regression of the paramesonephric (Müllerian) ducts in the male fetus.

The differentiation by the female type with a 46 XX karyotype occurs under the absence of the factor of the Y-chromosome, testosterone, DHT and MIF, determining the development of the testicles. With the absence of testosterone and DHT the mesonephral Wolff's ducts degenerate. Till puberty, the ovaries do not function, formation by the female phenotype occurs independently, including under the influence of hormones of the mother and placenta. In the female organism in the indifferent sex glands, mainly the cortex develops and the medullar substance atrophies. In the male sex glands, on the contrary, primary development is the medullar substance.

The development of the uterus begins with the merging of the paramesonephric ducts into their lower part, i.e. the formation of the cervix. Differentiation between the cervix and the vagina occurs at the end of the 4th — the beginning of the 5th month. In the beginning, the cervix has a cylindrical, and then gets a conic, form. In a 12-week fetus, the uterus has a bicorn form; from 3.5 till 4.5 months of development, as a result of the merge of the paramesonephric (Müllerian) ducts, it becomes arcuate. The size of the cervix exceeds the sizes of the uterus and by the end of the pregnancy makes up 2/3 of the uterine length.

The Fallopian tubes develop as pair formations from the upper third of the non-merged paramesonephric (Müllerian) ducts during the 2.5 till the 4 months of fetal development. By the birth of a girl the Fallopian tubes completely formed.

The vagina starts to be formed on the 8th week of the prenatal development due to the merge of the caudal ends of the paramesonephric ducts. On the 17th–19th week the vaginal vaults are formed; and

its branching from the uterus takes place, which completes on the 20th–21st weeks. On the 19th, 28th and after the 35th week — periods of amplified growth of the vagina, and by birth, its length reaches 4–5 cm.

The external genitalia under the influence of sex hormones are differentiated from the urinogenital sinus, sexual tubercle, urinogenital folds and sulcus. In a male organism under the influence of testosterone from the urinogenital sinus the prostate glands and bulbourethral glands develop. The sex tubercle under the influence of DHT is differentiated into the penis; the urinogenital folds form the distal part of the urethra, and the urinogenital sulcus develop into the scrotum. With the absence of androgens from the urinogenital sinus the lower part of the vagina develops, from the sex tubercle — clitoris, and from the urinogenital folds and sulcus the large and small pudendal lips are formed accordingly. The differentiation of the extragonadal organs of the female reproductive system promote female sex hormones. However, the genital morphogenesis process of the dependence on the condition of the ovaries is extremely weak in a female fetus. The anlage of the external genitalia occurs on the 5th–7th week of embryogenesis, and the formation of the sex occurs the 12th through the 20th week of prenatal development.

In the fetal period the primary sex cells are differentiated in ovogonium in the developing ovaries or in spermatogonium in the testicles. On the path from ovo- or spermatogonium to the gametes, the sex cells pass through such stages of gametogenesis as duplication, growth and maturing, and for spermatozoon — formation also.

In the differentiated ovaries ovogonium passes through the duplication stage, forming the *primary oocyte.* The duplication stage stops before the 7th month of prenatal development, the oocytes of the first order in the prophase of the first meiotic distribution get shells from the follicular cells *(primordial follicle),* and then their rest period begins, proceeding till sexual maturity. By the 7th month of prenatal development, the amount of primary oocytes reaches 10 million, and by birth about 2 million remains. Spermatogenesis begins with the approach of sexual maturity.

Thus, the process of gonadal embryogenesis is rather complex and covers the period from the 4th–5th till the 20th week of prenatal development. The sex glands up to the 7th–8th weeks of embryogenesis contain all the elements necessary both for the future testicles, and for ovaries. The multiplying of sex cells most actively occurs on the 8th–10th week, even though it continues through all stages of prenatal life. On the 10th–20th week of prenatal development, all the sex cells pass the initial stages of ovogenesis. The first primary (primordial) follicles appear on the 18–20th week of prenatal development in the zone, located on the border between the cortex and medullar substance of the ovaries. Later on this process is distributed to the peripheral ovarian zones. The activity of the steroid-producing cells of the theca shell is shown on about the 30th week of prenatal development, and the maximum of activity is in the last month of the pregnancy. Under the influence of chorionic gonadotrophin, pseudoluteinization of the theca tissue in the ovaries of mature fetus and newborns may occur.

During the whole embryogenesis period, anatomo-morphological right-sided asymmetry of the right ovary (its size is larger, increased innervation and blood supply, more steroidogenic activity) is observed.

Some authors determine two critical periods of prenatal development of the ovaries: the first period is characterized by settling of the primary sex cells into the ovaries (5th–9th week); the second period is connected with the increased development of follicles (28th–33rd week).

Under the influence of endo- and exogenous factors, this process can be broken at any stage, though the clinical displays of these defects can be found only during *puberty* — activization of the function of the reproductive system. Such unfavourable conditions of prenatal development as a complicated pregnancy course, the influence of adverse endogenous (somatic pathology) and exogenous factors (infection, intoxication, physical and chemical influences), can disturb genital development, which further can influence the reproductive system condition. The embryogenesis period (implantation, placentation) and the periods of further morphological and functional transformations of the genitalia are especially sensitive in this respect. The degree of expressiveness of the pathologic process is in direct dependence upon the duration of pathological factor action and time in which it appeared during the organogenesis period. So, for example, the use of progesterone and its analogues in big doses for the threat of a miscarriage can disturb the morphogenesis of the female genitalia and cause masculanization of the female fetus.

The first period of activization of the neural structures of the hypothalamus (activation of neurosecretion) occurs on the 20th–25th week of prenatal development and corresponds to the formation of direct relations between the hypothalamus and hypophysis. The second increase of neurosecretion activity is observed on the 32nd–34th week of prenatal development, which is connected with the decrease in sensitivity to neurohormones of the target organs and to the formation of interstitial connections between nervous cells. During this period, direct and inverse relations between the hypothalamus and internal secretion glands are, probably, formed. It is assumed that the prenatal hypothalamic neurosecretion provides a high level of protective-adaptive reactions of the fetus and promotes its adaptation during birth and immediately after it.

The anlage of the thyroid gland occurs on the 4th–5th week of embryogenesis. Throughout the 12 weeks the fetus receives from the mother hormones of the thyroid gland, providing compensatory-adaptive reactions according to the changes in the conditions of the environment. After the 12th week of pregnancy due to the gradual maturing of the hypothalamic-pituitary structures, the fetus develops its own thyroxin. The relative impermeability of the placentary barrier both for thyrotrophin (TTH), and for thyroid hormones makes the hypophysis-thyroid gland system of the fetus independent. As a result of placentary insufficiency, transitional hypothyroidism, negatively influencing the formation of the central nervous system and causing disorders in the postpartum adaptations, can occur. The final ratio of the thyroid hormones of the child is established during the 1–1.5 months after its birth.

The anlage of the adrenal glands occurs about the 6th week of embryonic development; their increased growth is observed between the 12th–22nd and 36th–40th weeks of pregnancy. The left adrenal gland of the fetus has an advantage concerning growth and development. The development of the cortex of the adrenal glands in the human fetus occurs earlier than the medullar substance. A common character of the embryonic anlage of the cortex of the adrenal glands and sex glands, the identity of enzymes participating in steroidogenesis, give the basis to consider their functional antagonists or agonists.

By the birth of the fetus, the cortex of the adrenal glands has formed the external (definitive) zone, which is differentiated by fascicular and glomerular types, and the internal (fetal). The reticular zone does not appear. By this time, the fetal zone makes up 3/4 of the gland's volume.

The fetal adrenal glands till the end of pregnancy can synthesize about 200 mg of steroid hormones a day, the majority of which are from the C_{19}-steroid group. The majority of these steroids is represented by dehydroepiandrosterone-sulphate (DHEAS), which predecessor is the mother's cholesterol. The synthesis of cholesterol in the mother's liver is stimulated by oestrogens and glycocorticoids, formed in the fetoplacental system. Cortisone is synthesized in the fetal zone of the adrenal glands of the fetus. The growth of the adrenal glands is supervised by corticotrophin, as well as by the insulin-like factor of growth.

The mammary gland is a derivative of the epidermis and is referred to the glands of the skin. However, the development of the glands and their functional activity depends on the hormones of the sexual sphere. So, the anlage of the excretory ducts is supervised by the synergistic action of oestrogen, somatotrophin, prolactin and glycocorticoids, their development — by oestrogens, progesterone, prolactin, chorionic somatomammotrophin. The formation of the secretory departments (during pregnancy) and the secretion of milk depend on the combined actions of glycocorticoids, prolactin, insulin and thyroxin. In embryogenesis, the mammary glands are laid as mammary lines — epidermal mounds, located on both sides of the trunk from the axillary area to the inguinal. In the mesosternum department of the epidermal mounds, the growing of separate epithelial lines into the skin, each of which are further differentiated into complex tubular-alveolar glands. The first secretory departments (alveoli) are formed on the 3rd month of pregnancy.

ANOMALIES OF THE SEX GLANDS DEVELOPMENT AND DEFECT OF SEX DIFFERENTIATION

Anomalies of the ovaries can be agenesia, their decent into the inguinal canal or into the large pudendal lips.

Defective ovarian function with the absence of chromosomal defects can be a result of the speckle mutations resulting in the decrease of hormone synthesis, disorders of tissue reception to hormones or disorder in the production of hormones inhibitors.

Anomalies of sex differentiation. *Genital uncertainty of newborns* is caused by abnormal presence of androgens in utero, i.e. the influence of too much androgen on the embryo, which was intended to be female, or the action of a reduced amount of androgens on an embryo which was intended to be male. In embryos with the programmed male sex, an inadequate secretion of androgen causes a deficiency in the fetal testicular secretions of testosterone or the insufficient sensitivity of the receptors of androgen-sensitive tissue to testosterone and 5T-dehydrotestosterone. On the basis of the above mentioned, all the anomalies of sex differentiation can be divided into three categories:

1) female pseudohermaphroditism;
2) male pseudohermaphroditism;
3) gonadal disgenesis, or true hermaphroditism.

Such attributes are characteristic for ***female pseudohermaphroditism***:

— 46 XX karyotype;
— the presence of ovaries;
— the absence of the production of the Müllerian inhibitor factor (MIF);
— the influence of androgen on the fetus.

Thus, the only anomaly in this case is an increase in the androgen influence on the fetus. In connection with the absence of MIF (the presence of ovaries, instead of testicles) such individuals have a uterus, tubes and the upper part of the vagina. If the embryo was exposed to the influence of a small amount of androgens in late embryonic (early fetal) period of development, the only anomaly can be a

small hypertrophy of the clitoris with the normal female phenotype. The influence of a large amount of androgens in the early embryonic period results in expressed virilism. This virilism process can be accompanied by the development of urinogenital folds, urinogenital sinus and even the male urethra with the formation of the scrotum — the empty scrotum syndrome.

The reason for female pseudohermaphroditism, as already marked, is *excessive androgen influence on the female fetus*. The increase in androgen influences, in most cases, occurs in connection with the increase in secretion of androgen and their predecessors, due to an enzyme defect of the formation of cortisole in the cortex of the adrenal glands, i.e. during congenital adrenal hyperplasia. It is mainly connected with the deficiency of 21-hydroxylase. Due to the inadequate synthesis of cortisole, the secretion of corticotrophin increases. The excessive adrenal stimulation results in an increase in the secretion of the predecessors and metabolites of cortisole, including androgen and androgen prehormones, which are converted into testosterone in the extraglandular tissue.

Another reason for female pseudohermaphroditism can be the *excessive influence of androgen on the fetus due to an increase in the production of androgen by the mother's ovaries* (hyperreactio luteinalis, androgen-producing ovarian tumours). But more often the fetus is protected from the influence of the mother's androgens due to the unique opportunity for trophoblast to aromatize C19-steroids (androgens) into oestrogen.

In addition, some *medical products* (more often synthetics of progestin, used to preserve the pregnancy) can cause virilism of the female fetus.

All patients with female pseudohermaphroditism can be normal fertile women under the conditions of early corresponding treatment.

Such attributes are peculiar for **male pseudohermaphroditism**:

— 46 XY karyotype;
— the presence of testicles or their absence;
— the production of Müllerian inhibiting factor;
— androgen influence on the fetus.

All individuals of this category were genetically intended to be male. Anomalies of sexual differentiations in these cases are connected with incomplete virilism, i.e. inadequate androgen influence.

Incomplete masculanization of the male fetus can be the reason for inadequate testosterone production by the fetus' testicles or a decrease in the sensitivity of the tissue of sexual organs to the normal amount of androgens, including the disorder of local synthesis of 5-dehydrotestosterone in the tissue from which the external sexual organs should be formed. In connection with the production of Müllerian inhibiting factor such patients have no uterus, tubes or the upper part of the vagina.

A decrease in the secretion of testosterone by the fetus' testicles is connected with enzyme defects and results in incomplete masculanization of the male fetus. The phenotype of such newborns varies depending on the degree of expressiveness of the enzyme and androgen deficiency.

The influence of *embryonic testicular regress* on the fetus depends on the embryonic period in which there was the testicular loss. The phenotype of such individuals can change from a normal female, where the uterus, Fallopian tubes and the upper part of the vagina are absent, to the male, but with the absence of the testicles (anorchism).

Tolerance to androgens is connected with the inadequacy or anomalies of androgen receptors in the androgen-dependant tissue or with the disorder of testosterone conversion into 5α-dehydrotestosterone due to the reduction of the activity of the enzyme 5α-reductase.

Testicular feminization is the most extreme degree of disorder connected with androgen tolerance. In this case, the tissue sensitive to androgen, are absent or their amount is not enough. The phenotype is characterized by the presence of a short blind vagina, the absence of a uterus, Fallopian tubes and mesonephral structures. During the prospective time of puberty development, the testosterone level in such women increases to the normal level for men. Besides, virilism does not occur and even the develop of sexual hair does not occur. The increase in the lutrophin level in such women results in an increase in testicular secretion of oestrogen in comparison with those for normal men. An increase in the oestrogen level in a combination to androgen tolerance promotes feminization and the mammary glands development.

In the case of *incomplete testicular feminization,* a weak sensitivity to the action of androgen is shown. In such patients hyperplasia of the clitoris of the medium degree at birth is marked; however, during the prospective pubertal period virilism does not occur, and the mammary glands develop.

The third syndrome associated with androgen tolerance is the *family male pseudohermaphroditism type I,* or the Reifenstein syndrome. The degree of virilism varies from the similar female phenotype, from incomplete testicular feminization, to the male phenotype — with the bifurcation of the scrotum, gynecomastia and infertility. In such persons, the resistance to androgen is shown as a result of the reduced level of 5α-dehydrotestosterone-binding abilities of the fibroblast of sexual tissue.

The fourth form of androgen tolerance is caused by a *deficiency of 5α-reductase in the androgen-sensitive tissue.* The disorder of the external genitalia are female; moderate hypertrophy of the clitoris is observed, accompanied by the presence of well advanced testicular appendages, testicular vessels,

deferent and ejaculatory ducts opening into the vagina.

True hermaphroditism includes the following anomalies:

— usual abnormal karyotype;

— absence of sex glands (with the presence of both ovarian, and testicular tissue);

— absence of the production of the Müllerian inhibiting factor;

— androgen influence on the fetus.

In all patients the testicles or ovaries are absent; however, the uterus, Fallopian tubes and the upper part of the vagina exist.

Gonadal dysgenesis is peculiar to the majority of such patients.

Gonadal dysgenesis manifests itself in several forms: typical (Shereshevsky—Turner's syndrome), obliterate, pure and mixed.

The female phenotype is observed in the *typical gonadal dysgenesis* (Shereshevsky—Turner's syndrome), but during the prospective time of puberty sexual infantilism develops. For the majority of persons with true hermaphroditism, ovarian and testicular tissue is present. Germinative cells of two types (both ovum and spermatozoon) are formed in them.

The Shereshevsky—Turner's syndrome is observed with an incidence of 1 case in 3,000 newborn girls and is caused by a chromosomal anomaly (45X0 karyotype, or mosaicism, — the obliterate form of gonadal dysgenesis), X-chromatin with this is negative. The ovaries are absent; only bilateral lines of connecting tissue, not containing primary (germinative) sex cells, are at their place. The absence of ovarian tissue results in a deficiency of oestrogen, that, in turn, causes sexual infantility, underdevelopment of the mammary glands, the absence of other secondary sexual characters . The reasons for gonadal dysgenesis can be the destruction of primary sex cells at any stage both before and during their migration to the sexual sulcus, and even in later terms of the formation of the sex glands. In case of early destruction of sex cells irregardless of the chromosomal sex, the genitalia always develop by the female type. Due to functional inferiority of the male genitalia, the embryo still can have derivatives both of the mesonephral (Wolff's), and paramesonephric (Müllerian) ducts, and external genitalia will be formed by the female type.

The pure form of gonadal dysgenesis is characterized by the female phenotype, normal or increased growth, underdevelopment of the mammary glands, the presence of secondary sexual hair, hypoplasia of the external and internal genitalia, formation of connective tissue lines at the sex glands' site, negative sex chromatin. 46XX or 46XY karyotype (Swyer's syndrome).

The presence of virilism signs with the absence of somatic anomalies is peculiar for *the mixed form of gonadal dysgenesis*. At the place of the ovaries on one side is a band of connective tissue, on the other one — testicular disgenesis. The sexual chromatin is negative, the karyotype is more often 45X/45Y or mosaicism with obligatory presence of a Y-chromosome or its part. A malignant tumour (dysgerminoma, arenoblastoma), accompanying increased virilism characters, frequently develops in the dysgenesis testicle.

With prenatal sterilization, caused, for example, by the influence of X-ray radiation or chemical preparations, premature proliferation of the granular shell (follicular epithelium) occurs, ovarian sclerosis progresses, the formation of a cavity in the follicles is detained. In case of partial sterilization, alongside with the delayed development of the follicles, their sizes increase, resulting in the formation a follicular cyst. This process is accompanied by an increase in the development of connective tissue, i.e. there are changes in the ovaries, characteristic for the Stein—Leventhal's syndrome.

Diagnosis. The preliminary diagnosis for sexual uncertainty should be established after the child's birth. During physical and ultrasonic examinations, it is possible to find the uterus. With its presence, the diagnosis can be as follows: 1) female pseudohermaphroditism; 2) testicular or gonadal dysgenesis; 3) true hermaphroditism. Having a burdened familial history of congenital adrenal hyperplasia assists to diagnosis. With the absence of the uterus, the diagnosis of male pseudohermaphroditism is established. Androgen tolerance and enzyme defects of testosterone biosynthesis frequently have family character.

Determining the sex is a critical moment. It is considered that all newborns with ambiguous genitalia should be female. This position is explained by the following aspects:

1) persons with female pseudohermaphroditism can be normal women, capable of fertilization;

2) persons with male pseudohermaphroditism do not produce testosterone or are tolerant to it; all of them are infertile;

3) sexual and reproductive functions in patients with androgen tolerance are impossible.

Principles of observing patients. The first step in observing such patients should be the exclusion of the diagnosis of congenital hyperplasia of the adrenal glands which is a life threatening complication. An ultimately sex determination takes place no later than 18 months after the child's birth. For revealing the cause of the defect, the family anamnesis, cases of unexplaned deaths of newborns are investigated; they elucidate whether the mother used medical drugs during the pregnancy (androgens, progesterone, danazol, spironolacton), whether she had virilism attributes during the pregnancy.

Objective examination of the newborns with nondifferentiated genitalia is conducted to rule out oth-

er developmental anomalies (cardiovascular, urinary and digestive systems). The extent of hypospadia is established and the characteristics of erectile tissue, the degree of labial fusion, the presence of the uterus, ovaries are revealed. Palpitation of the newborn's uterus is conducted by rectal examinations or ultrasound, radiography and endoscopy. Laboratory tests and determining the karyotype should be conducted within a week.

Treatment of patients is replacement (sex hormone preparations) and directed at their feminization. Independent menstrual cycle and reproductive function are impossible. Continuous use of oestrogens in puberty (13–14 years) is recommended and the use of them till the breast enlargement and a menstrual-like reaction appearence. Microfollin (etenylestradiol) is prescribed by 0.05 mg (1 tablet) a day for 20 days (1–3 cycles). Cyclic hormone therapy of patients with oestrogen and gestagen is conducted after the first menstral-like reaction. From the gestagen drugs a 1% solution of progesterone by 1 ml intramuscularly; pregnin — by 2 tablets 3 times a day, norcolut — by 5 mg a day the 21st through the 26th day of the menstrual cycle (after the 20 day cycle of oestrogen treatment) are prescribed. Continuous cyclic treatment is recommended for 3–4 months with a subsequent break for 1–2 months. Cyclic hormone therapy reduces the risk of the development of endometrial hyperplasia, atherosclerosis, cardiovascular pathologies and osteoporosis in such patients.

Surgical treatment of patients consists of early reduction of the penis, reconstruction of the vagina and vulva in puberty. Testicular dysgenesis and a rudimentary uterus with the mixed form of gonadal dysgenesis are subject to operative removal in connection with the high risk of their malignancy.

ANOMALIES OF THE FEMALE REPRODUCTIVE TRACT

Anomalies of the female reproductive tract are not frequently observed (about 2.5% of cases). 20% of them are referred to genetic disorders, 5% — to chromosomal aberrations, 10% — to the influence of environmental factors.

A*genesis* (aplasia) means the absence of an organ (part of an organ). *Atresia* (gynatresia) — occlusion of some part of the female reproductive tract. Atresia can be congenital or acquired. *Dysraphia* is nonfusion or open parts of the organ. *Multiplication* — multiple parts or organs. *Hypoplasia* — underdevelopment of the genitalia (the sizes of the organs are less than those for the normal age, functions are reduced) — can occur with general underdevelopment (infantility) or be local.

Two forms of underdevelopment of the uterus are distinguished: *hypoplastic uterus* (uterus hypoplasticus) and infant's (uterus infantilis).

The *hypoplastic uterus* has a normal form, but is considerably reduced in size. Its characteristic attributes are late menarche and hypomenstrual syndrome. The reproductive function is preserved.

The *infant's uterus* is small, dense; the size of the cervix is 2 times larger than the corpus. Women with an infant's uterus suffer from infertility. The presence of both forms of underdevelopment of the uterus is an indication for cyclic hormone therapy.

With the disorder of the merging of the paramsonephral (Müllerian) ducts, for some reason each of them develops independently, resulting in the formation of a *double uterus* and (or) *vagina* (uterus duplex cum vagina duplex (Fig. 35). It occurs on the 8th–10th week of embryogenesis. If the merge of the lower departments of the ducts does not occur, a *double vagina* or *septate vagina* is formed *with the presence of one uterus.* If the merge of the paramesonephric ducts in the upper departments has not taken place, *two uteruses with one vagina* can be formed. Sometimes, only the upper part of the uterus is divided — its fundus *(arcuate uterus,* uterus arcuatus).

After the merge of the paramesonephric ducts a septum can form between them — complete (uterus septus) or partial (uterus subseptus). With the presence of a complete septum a *bicornate,* or *two-cavitary, uterus* (uterus bicornus) is formed. Thus, the

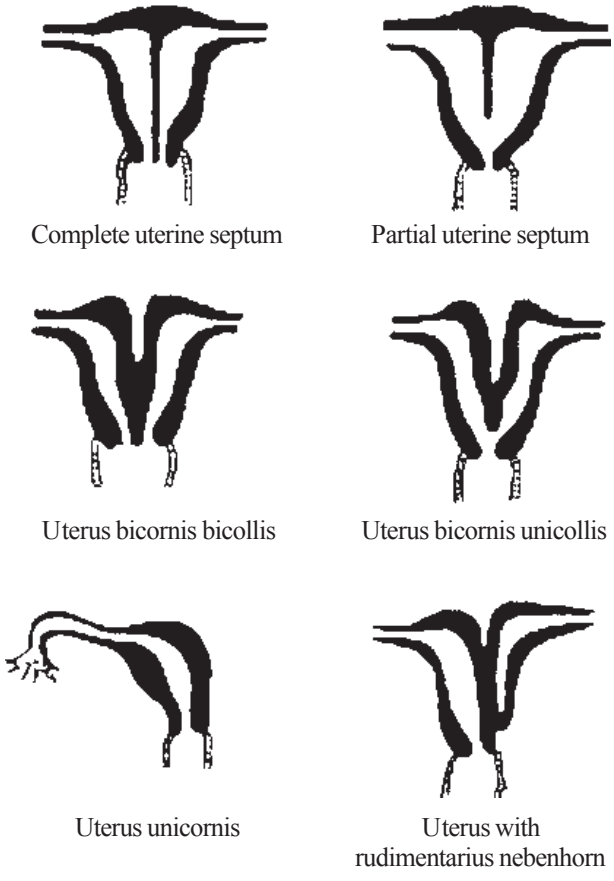


Fig. 35. Most frequent variants of congenital anomalies of the paramesonephral ducts (Müllerian anomalies)

formation of a *uterus with one cervix* (uterus bicornis unicollis), or *two cervices* (uterus bicornis bicollis) is possible.

If one of paramesonephric ducts is less developed, *an asymmetric uterus with a rudimentary horn,* attached with the uterine cavity or not can be formed, or *unicornuate uterus* — due to the agenesis of one of the ducts.

Classification of anomalies of the paramesonephric ducts (Müllerian anomalies):

1. Segmentary agenesis or hypoplasia:
— vaginal;
— cervical;
— fundal;
— tubes;
— combined.
2. Unicornuate uterus with a rudimentary horn:
— with a communicating (non-communicating) endometrial cavity or without a cavity.
3. Uterus didelphis.
4. Bicornuate uterus:
— complete (to the internal os);
— partial;
— arcuate.
5. Septate uterus:
— complete (to the internal os);
— partial.

Thus, *uterine and cervical anomalies* include: complete or partial uterine septa, arcuate, bicorn, unicorn uteruses, a rudimentary horn, duplex uterus, duplex cervix, uterine atresia. The most severe of these anomalies without surgical correction can result in disorder of the reproductive function. An increased risk of spontaneous abortions, ectopic pregnancy, pregnancy in the uterine rudimentary horn, premature birth, delays in the fetal development associated with uterine anomalies. The incidence of a unicornuate uterus among all the anomalies of this organ is 14%. With the presence of a unicornuate uterus with a rudimentary horn in 90% of the cases the latter is not attached to the uterine cavity. The sequelae of pregnancy with a unicornuate uterus are frequently adverse. Due to the pregnancy developing in a rudimentary horn, the uterus can rupture (before the 20 week gestation), leading to profuse bleeding.

The rarest form of uterine anomalies is the *Rokitansky—Küstner—Hauzer syndrome* — aplasia of the uterus with the Fallopian tubes and ovaries present. This defect can be combined with partial or complete aplasia of the vagina, as well as its upper third part.

Anomalies of the Fallopian tubes — aplasia, atresia and douplication — are rarely observed.

Anomalies of the vagina are longitudinal or transverse septa. The transversal septum of the vagina can be formed at any level and be complete or partial. The imperforated transversal septum of the vagina can cause muco- and hematocolpos in girls (cryptomenorrhoea). The longitudinal septum of the vagina is frequently accompanied by uterine and (or) cervical anomalies. A douplex vagina is connected with the douplex cervix. With the absence of pathologic symptoms such conditions do not require treatment.

Total vaginal agenesis can also be observed. As a result of vaginal agenesis or hypoplasia pregnancy is impossible, even if a new vagina was created surgically.

Anomalies of the vulva arise seldom. They are the clitoris cleft (probably, in a combination with extrophy of the bladder), congenital prolapse of the vagina and douplex vulva (often with the duplication of urinary and alimentary tracts). The labia pudendi can be various in sizes. In such cases if necessary surgical treatment is conducted.

Anomalies of the hymen are frequently observed; it is the most variable structure of genitalia. More often the following anomalies are marked: the opening in the hymen is absent (imperforate hymen); different diameters of the opening; more than one opening; thickening of the membrane; medial crest between two openings. The imperforate hymen causes early (muco- and hematocolpos) and late complications (endometriosis).

The clinical picture of congenital malformations of the genitalia:
— primary amenorrhoea;
— irregular vaginal bleedings;
— dysmenorrhoea;
— cyclic pelvic pain;
— impossibility of sexual intercourse;
— dyspareunia;
— infertility;
— spontaneous abortions;
— premature birth;
— postpartum bleedings;
— hematocolpos, mucocolpos;
— cyst of the Gartner's duct;
— hematometer, hematosalpinx;
— absence of the uterus, cervix, vagina, short vagina;
— ambiguous genitalia;
— absence of sexual hair;
— malpresentation of the fetus;
— retained parts of the fetus in the uterus.

The genital malformations are *diagnosed* during gynaecologic bimanual examination, with the help of ultrasonography, hysteroscopy, hysterography, laparoscopy, during caesarian section, bimanual examination of the uterine cavity after birth.

Observing and treating patients. With atresia of hymen a cruciform cut of the hymen is conducted, the edges are sewn up in separate catgut ligatures.

The patients with vaginal atresia require surgical treatment. Results of such treatment are most adverse with aplasia of the upper third of the vagina. Various types of vaginal septums are removed

surgically. During the surgical treatment of patients with vaginal aplasia, an artificial vagina is created from the sigmoid or small pelvic peritoneum.

Various forms of douplex uterus and vagina do not require treatment if they are not accompanied by menstrual blood outflow disorders. With uterine anomalies and burdened obstetric anamnesis (miscarriage, premature birth) metroplastics is possible. If pregnancy develops in the uterine rudimentary horn, it is removed. With a bicornuate uterus transabdominal metroplastics is conducted (resection of the septum and restoration of the uterine fundus). With the presence of a uterine septum the method of choice is its transcervical-prenatal resection under hysteroscopic control.

THE NEONATAL PERIOD

The reproductive tract of a newborn girl is under the influence of long transplacental stimulation by the mother's hormones. After cutting the umbilical cord, the level of mother's hormones in the child decreases, and within the first month of his life their effect gradually restors. In the newborn as a result of the absence of the mother's oestrogen influence the levels of folli- and lutrophin increase. In some newborns within the first 2 weeks after birth, a sexual or hormonal crisis can occur: hypostasis of external genitalia, increase in mucous production, hypostasis of the mammary glands and discharge from the papilla, vaginal bleeding, even the formation of follicular ovarian cysts is possible. During such transitory conditions special medical intervention is not required.

Maturing of the reproductive system in the postpartum period is influenced by the hormones of the thyroid gland (stimulation of protein synthesis, growth and differentiation of tissue, metabolic processes). After the child's birth, the weight of the adrenal glands decreases because of involution of the fetal zones; the process comes to an end by the 2nd year of life.

Soon after birth, the low levels of folli- and lutrophin secretion are established. Within the first month of life, an increase in the gonadotrophin concentration with an increase in the estradiol level is observed.

Throughout the first 20 months of a newborn's life, the peripheral blood contains a large amount of prolactin.

At birth, a girl has external and internal genitalia by the female type. The large pudendal lips do not completely cover the labium minora; some swelling and hyperaemia are possible. The clitoris is well seen and has a larger size than during the subsequent periods of the girl's life. The clitoral index (length of the clitoris × thickness of the clitoris) ≥ 0.6 cm^2. The vestibular glands do not function. The bright red hymen is well visible. The vagina has length of about 4 cm, is located parallel to the vertical axis of the body; its folds are well expressed. In the vaginal smear of a newborn girl high eosinophilic and karyopyknotic indices that testify to a significant oestrogen influence are found. In the vagina there are Lactobacilli (Dederlane's), contributing to acidic reaction of the vaginal contents. In 6–8 weeks the oestrogen level is reduced, involute changes occur in the vagina: the epithelial layer considerably decreases, parabasal and basal cells, cocci microflora start to prevail in the smears.

The newborn girl's uterus is in the abdominal cavity, it can be enlarged (up to 4 cm in length). The uterus has a lenticular form with an "arcuate" fundus. The ratio between the size of the uterus and the cervix is 3 : 1; the angle between the cervix and uterus is not determined. The internal os is not yet developed; the uterine opening has a slit-like form. In the area of the external os it is possible to reveal ectopia of the cylindrical epithelium. The cervical canal is filled with mucous excreted into the vagina. After birth the secretory endometrium undergoes desquamation, which can be accompanied by menstrual-like vaginal discharge. This discharge stops by the 10th day of a girl's life.

The Fallopian tubes in a newborn are long (on average 3.5 cm), convoluted, with a developed muscular layer; the right tube can be a little longer.

The ovaries in a newborn are located in the abdominal cavity at the level of the corpus of the I lumbar vertebra, have a little elongated form, their sizes on average are 19×0.6×25 mm. The ovarian surface is smooth; the mass is 0.3–0.5 g. The ovarian stroma is very poorly developed; the primary (primordial) follicles are very close to each other. Each ovary of a newborn girl contains 500–700 thousand of oocytes. Atresia of the follicles in all stages of their development occurs in the ovaries. In newborns the ovaries are not yet descended into the small pelvis and are not palpated.

Thus, features of the reproductive system condition during the newborn period testify, on one hand, to an ability of the organs to react to hormonal influence due to high differentiation by the moment of birth, and on the other hand — to the presence of enough hormones, influencing the reproductive organs before birth.

THE EARLY CHILDHOOD PERIOD (NEUTRAL PERIOD)

The early childhood period (1 to 7 years), or the neutral period, is characterized by changes in the hypothalamic-hypophyseal-ovarian axis, connected with the development of a negative inverse relation and the central oppression of GN-RH release. The

level of sexual steroids is reduced, and the sexual tract in this period is tolerant to the influence of endogenic hormones.

In the childhood period the external and internal genitalia due to low oestrogen stimulation are exposed to some involution in comparison with their condition at birth. The labia pudendi are thin and do not completely close the opening to the vagina. The clitoris does not stick out any more, although the clitoral index remains increased. The mucous membranes are pink and slightly moist.

The vagina increases slowly: by 6–7 years its length reaches only 5 cm. The vaginal fornices do not develop till puberty. The vaginal mucous membrane has a light pink colour, thin; the epithelium consists of 4–5 layers mainly parabasal and basal cells. The reaction of the vaginal contents becomes neutral or alkaline, which is the reason for the high incidence of vulvovaginitis in this period. Diplococci, streptococci, staphylococci, E. coli are found in the vaginal micro flora.

The uterus is reduced in comparison with the newborn period. The ratio between the size of the uterus and cervix decreases to (1.5–2) : 1. By the age of 3, the girl's uterine fundus lowers down to the level of the entrance plane to the small pelvis.

The amount of primary (primordial) follicles decreases twice in comparison with the newborn period. The further decrease in the amount of follicles continues till menarche. The maturing of the follicles has no cyclic character. A slight ovarian enlargment occurs at 4–6 years of age. During this period, the ovaries start descending to the small pelvis.

The pubis and inguinal hair, breasts do not develop during childhood.

Thus, during childhood the reproductive organs develop slowly. The hypothalamic-hypophysial-ovarian axis is characterized by immaturity and poor function. The gonadotrophin-releasing-hormone is formed in the hypothalamus in very small number. The folli- and lutrophin form and release in the hypophysis; the inverse relations are creating. The immaturity of the system manifests itself by high sensitivity of the anterior lobe of the hypophysis and the mediobasal hypothalamus' neurosecretory nuclei to estradiol (as high as 5–10 times than in adults). Low doses of estradiol inhibit the gonadotrophin release by the adenohypophysis.

The level of follitrophin at the age of 4–5 is higher in girls than in boys. At the neonatal period, the lutrophin concentration is higher in boys and increases till the middle of the neutral period reducing by the age of 6. The level of prolactin in the neutral period nears to the low norm limit for the reproductive age women.

During the newborn period and neutral period a decrease in the concentration of oestrogen, DHEAS, progesterone and other steroid hormones are observed in the blood.

By the age of 8 in the girl all five levels of the hypothalamic-hypophyseal-ovarian axis, the activity of which is regulated only by negative inverse relations mechanisms are formed. Estradiol is synthesized in a small amount; the follicles seldom mature. The Gn-RH releases incidentally; synaptic relations between the adrenergic and dophaminenergic neurons are not developed; the secretion of neurotransmitters is low. The release of folli- and lutrophin by the hypophysis has no cyclic character.

If during embryogenesis the pathologic influences result in a defect of the formation of gonads, ovarian morphofunctional disorders, for example at acute infectious diseases take place during childhood and puberty.

The **late childhood** (8–11 years) is characterized by a gradual "awakening" of the hypothalamic-hypophysial-ovarian axis.

THE PERIOD OF SEXUAL MATURATION

Sexual maturation is a gradual physical, emotional and sexual transition of an organism from the childhood period to the adult state. It is a chain of smooth sequential events; delay or premature development is evidence of pathology of the reproductive system. The knowledge of the features of the neuroendocrine mechanisms of this period is important for understanding the reproduction process as a whole.

The period of sexual maturation consists of the following periods:

1) prepuberty (late childhood — from 8 years to menarche);

2) puberty (from menarche to 15 years);

3) juvenile (16–18 years).

The given transitional period is characterized by the activation of the hypothalamic-hypophysial-ovarian axis that promote the rapid development of a girl and reaching the maturity of the reproductive system, i.e. readiness for performing the generative function.

During prepuberty *a great advance in growth* happens, *secondary sexual characters* appear, further development of the reproductive organs and the first menstruation — *menarche* occur. During puberty and the juvenile periods, the formation of secondary sexual characters comes to an end, the first ovulatory menstruation cycles occur, growth slows down. By the end of the juvenile period, sexual and somatic development of an organism comes to an end, i.e. transition to a state of sexual maturity. During this period the stimulated secretion of folli- and lutrophin by the sexual steroids results in the development of secondary sexual characters and the reproductive ability. Synthesis and secretion of sex

hormones are regulated by a hormonal chain: gonadoliberin of the hypothalamus — gonadotrophin of the hypophysis.

A possible initial phase for the onset of puberty is considered the increase in the synthesis of dehydroepiandrosterone in the reticular zone of the cortex of the adrenal glands, which is shown in girls at the age of 8. Further increase in the secretion of testosterone and oestrogens is observed, which is also connected with the increase of function of the cortex of the adrenal glands. It is the *adrenarche* stage, or the first phase of puberty. Gradual liberation of the hypothalamic-hypophysial system suppression is accompanied by the growth in amplitude and frequency of the Gn-RH pulsating release, first only at night, and then — day and night. Soon after that, the secretion of follitrophin, the production of gonadoliberin increase, the sensitivity of the hypophysis to liberins and of the sexual glands to gonadotrophin increases. With an increase in the level of gonadotrophin, the secretion of the sexual steroid hormones increases and the positive and negative inverse reactions occur.

In the prepuberty (I stage of puberty) the maturing process of the hypothalamic-hypophysial-ovarian axis (HHOA) occurs, s strong synaptic connection between the cells, secreting liberins (gonado-, somato-, cortico-, thyroliberin) and neurotransmitters are formed. The circadian (daily) rhythm of the gonadoliberin secretion is stabilized; the release of gonadotrophins, which has rhythmic character, increases. The release of lu- and follitrophin increases, activating the synthesis of oestrogens by the ovaries. The amount of receptors increases and their sensitivity to sexual steroid hormones in all of the organs of the reproductive system increases. Achieving a high level of estradiol in the blood stimulates the release of gonadotrophin which, in turn, finishes the maturing processes of the follicle and ovulation. Under the influence of an increased follitrophin concentration, mitosis of granulose cells amplifies; the growth of follicles is accelerated. Secondary follicles, secreting oestrogen, are formed. The latter promotes the development of secondary sexual characters. This period comes to an end with the appearing of the first menstruation — menarche. Lutrophin secretion increases a little bit later and approximates the adults level at 15–16 years.

The external genitalia enlarge, mainly due to the development of adipose tissue. By the end of the prepubertal period, the hymen is located more superficially than in the childhood period; the greater vestibular glands (Bartholin's) start to function. At the juvenile period the external genitalia are already the same as for adult women. The vagina enlarges and reaches the length of 10.5–11 cm; its vaults are formed; the folds increase; the epithelial layer gets thicker. Directly before menarche, the secretion of the cervical glands and the greater vestibular glands increases (pubertal leucorrhoea, at which a special treatment is not required). In the vaginal discharge, Döderlein's bacilli are revealed again; the vaginal reaction shifts to the acidic side. In puberty, the colpocytogram can already reflect the cyclic changes in the vaginal epithelium.

The volume of the uterus during puberty quickly increases; the ratio between the length of its corpus and cervix in the prepuberty is 1 : 1, in puberty — 2 : 1, and the angle between the corpus and cervix is more expressed. The weight of the uterus increases from 4.2 g in girls of the age of 10 up to 7 g — in 11–12 year olds; at 16 it is 23 g and comes nearer 50 g by the end of puberty. The especially fast growth of the internal genitalia occurs after menarche. In menstruating girls during a ultrasonography, the medial structure of the uterus (M-echo) is determined.

At the prepubertal period the ovaries have a smooth surface, a fibrous capsule, looking like polycystic. The process of development and atresia of the follicles proceeds and amplifies in them. During the prepubertal period the ovaries increase in size, the vessels become more coiled, the amount of arterial anastimosis increases, providing much greater blood flow to the ovaries. The innervation of the sex glands increases; paravasal and paraneural plexus are formed; primary receptors develop in the walls of the follicles, interstitial tissue. At 10–11 years the ovaries move to the small pelvic cavity; their volume increases, in comparison with 8–9 years about 2.5 cm^3 up to 3–4 cm^3; at 12–13 years their volume reaches over 5 cm^3. For girls after the beginning of menstruation, the ovaries are located near the uterine corners. In puberty and the juvenile periods, the volume of the ovaries is 6.88 and 8.81 cm^3 accordingly. The cyclic changes similar to those in the reproductive period occur in the ovaries and endometrium.

The maturing of the hypothalamus-pituitary-ovarian system comes to an end at the II stage of puberty (1.5–2 years after menarche). The hourly (circhoral) rhythm of gonadoliberin secretion is stabilized; the release of gonadotrophin by the hypophysis and synthesis of estradiol by the ovaries increase. The mechanism of the positive inverse relation is formed. Throughout first years after menarche, anovulatory cycles prevail, the amount of which gradually decreases due to the increase in ovulatory cycles.

Some authors allocate also at III stage of puberty — the formation of ovulatory cycles.

Directly before ovulation, the follicle contains a high concentration of folli- and lutrophin, progesterone and a decrease in the contents of androstendion, prolactin, and estradiol. For the high-grade growth and development of the follicle, providing for ovulation, the formations and functioning of the corpus luteum, a strict sequence of endocrine influences is necessary. With change in this sequence, the process of normal development of the follicle can be broken. So, without the influence of follitrophin

inside the follicle, the follicular endocrinocytes (granulosa cells) cannot produce enough oestrogen. With the absence of oestrogen, the amount of granulose cells does not increase; the increased lutrophin level blocks mitosis of the granulous cells, despite the presence of oestrogen. The sequence of endocrine processes inside the dominant follicle causes secretory activity of the corpus luteum after ovulation. Hormones of the follicular liquid influence the ability of the granulous cells to produce progesterone. The functional activity and life expectancy of the corpus luteum depend on the adequate pre- and postovulatory stimulations, as well as on the specific inhibitor, binding lutrophin inside the corpus luteum.

Together with the changes in the reproductive system, there are somatic changes, characteristic for puberty. These changes are caused by the influence of oestrogen and androgen, which are released from the ovaries, and, to a lesser degree, the adrenal glands. Under the influence of oestrogen, the breasts, uterus enlarge; there is fatty tissue distribution by the female type. Androgen and oestrogen in girls promote the development of pubis and axilary hair. The joint action of these hormones causes acceleration in bone growth, increase in external genitalia. The progesterone promotes the proliferation of alveoli of the mammary glands.

Among secondary sexual characters the earliest one is the formation of breast *(telarche)* (Table 6) which, as a rule, precedes the development of pubis hair *(pubarche)*.

The domestic literature use a classification of the age parameters of sexual development (Table 7), offered by L. M. Ulanov and co-authors (1981).

The development of mammary glands *(telarche)* in the initial stages concerns only the peripapillary circle (areola) which "swells" a little, becomes pigmented. Further, the formation of the glandular tissue begins. In the beginning it looks like subareolar eminences ("buds"), later it is distributed beyond the borders of the areola, and further the mammary glands are formed, equivalent to the contours of the glands of an adult woman. The development of the breasts can be asymmetric. With *galactorrhoea* (discharge from the papilla not during lactation) it is necessary to exclude a tumour of the hypophysis and hypothyroidism.

For girls **hair** comes earlier than for boys. Hair of the axillary area in children of both sexes begins at 1.5–2 years after pubic hair and reaches the maximal development by the age of 20. The character and intensity of hair are determined by the sex and hereditary factors. So, the female type of pubic hair is characterized by the presence of a transversal border of hair (a triangle with the bottom point), the male one by hair growth along the white abdominal line as a triangle with the top point.

Physical changes, characteristic for puberty occur in boys about 6–12 months later than in girls.

Table 6. **Development of secondary sexual characters (by Marchall and Tanner, 1970)**

Secondary sexual characters	Girl's age, years
The beginning of the formation of breasts ("buds")	9.8
The beginning of pubic hair	10.5–11
Maximum growth	11.4
Menarche	12.8
Adult pubic hair	13.7
Adult breasts	14.6

Table 7. **Age parameters of sexual development**

Sexual formula	Average age, years	Age limits, years
$P_0Ax_0Ma_1$	10.3	8.7–11.9
$P_1Ax_0Ma_1$	11.7	9.9–13.5
$P_2Ax_2Ma_2$	11.9	10.3–13.5
$P_3Ax_{2-3}Ma_3$	12.8	11.2–14.4
$P_2Ax_{1-2}Ma_3Me+$	12.8	11.2–14.4
$P_2Ax_2Ma_3Me+$	13.8	12.2–15.4
$P_3Ax_2Ma_3Me+$	14.2	12.8–15.6
$P_3Ax_3Ma_{3-4}Me+$	15.2	13.6–16.8

Note: P — pubic hair, Ax — axillary hair, Ma — development of breasts, Me — menarche.

Characteristic changes start to occur during the period between 9.5 and 13.5 years and proceed for 3 years.

Menarche (first menstruation) occurs later — from 12 to 14 years.

The concept "gynaecologic age" is estimated at years past after the occurrence of menarche. In the month, previous to the approach of menarche, the girls can have short pains in the abdomen; vaginal discharge increase. The approach of menarche before the age of 9 and after 15 is an indication for additional examination of the girl. The period for the approach of menarche depends on exo- and endogenic factors (climate, geographical width, light exposure, race, nationality, heredity, constitution, state of health, material life conditions and stressful situations, physical and mental loads).

Menstrual bleedings last, as a rule, 4–5 days; within the first two years, the menstrual cycle can be irregular. 20% of girls have anovulatory cycles by 17–18 years.

The body weight matters for the duly beginning and correct course of puberty. Menarche occurs after the girl's body weight reaches 44–47.8 kg. Due to the reduction of the fatty layer of up to 10–15% of

body weight, the menstrual function stops. With insufficient or extra body weight, disorders of menstrual functions in teenagers are observed 2–4 times more often.

Deviations in sexual development should be considered as the display of secondary sexual characters at the age of 8; the absence of the development of the mammary glands and hair by the age of 13–14 years and the approach of menarche after the age of 15.

Pubertal growth spurt. The highest rate of growth of the bone skeleton occurs at the end of the prenatal period, then the growth rate slows down; the second growth spurt is marked before puberty. The hormonal control of the acceleration of growth in girls is carried out due to the influence of estradiol, growth hormone, and, probably, ovarian and adrenal androgens. Boys have the growth spurt 2 years later than girls have; it is caused by the action of testosterone and the growth hormone and has an advanced manifestation.

Growth acceleration in teenagers occurs in three stages: 1) the period of minimal growth rate in the beginning of puberty; 2) the period of maximal growth rate; 3) reduction of speed and the termination of growth, the epiphyses adhesion.

During puberty, the girl's growth exceeds the growth of boys. The earlier the first menstruation occurs, the more intensive the growth spurt in girls. The maximal increase in growth (about 8 cm) is observed at 10–11 years mainly due to the length of the legs; and after 14 years — due to length of the trunk. The increased growth of the pelvic bones occurs at 10-14 years, the transversal size of the pelvis increases to the maximum at 13-15 years.

The age changes of the bones are so specific *(biological, or bone, age),* that they allow to estimate the maturity of an organism. This is an important condition for revealing pathology of the pubertal period (premature sexual development or its delay, hyperandrogenism with the advancing of the bone age). The biological (bone) age should correspond with the calendar one (±1 year). For diagnosis, the radiological characteristic of the bones of the hands and radiocarpal joints are used. So, the occurrence of sesame-like bones of the I finger coincides with the onset of pubic hair, enlargement of brest and precedes menarche by 1.5–2 years. The fusion of the hand ossification nuclei corresponds to 16–20 years.

The period of permanent teeth eruption depends on the processes of both somatic and sexual developments. The first phase of accelerated development of permanent teeth in girls is observed between the ages of 5 and 6 (the first molars and central incisors — in the maxilla and lateral incisors in the mandibular); the second phase takes place at 10–11 years.

The course of puberty in modern conditions is characterized by the acceleration of development rates *(acceleration)*. This process is shown by an increase in the initial level of development (weight and growth at birth), speeding up of its rates, earlier menarche, and rise in the physical development parameters. Sexual maturity — a wider concept including not only the ability to reproduce viable sex cells and conception, but also the opportunity to bear, give birth, feed and bring up a healthy child. Sexual maturity comes on the average at 17–18 years.

On the other hand, there are data that acceleration, observed in the beginning of our century, is starting to abate, and there is even stagnation, delay of sexual development together with the reduction of the absolute age dimensional attributes in teenagers of large industrial centres.

Thus, the period of sexual maturity is a critical period in the life of a girl, her postnatal development. The functioning of the reproductive system of a mature organism depends on it.

Dynamic processes in the endocrine system of a girl during the period of sexual maturing are characterized by the increased sensitivity to harmful factors, resulting in the occurrence of disorders of consecutive mechanisms of formation of a mature organism, especially during the critical periods corresponding to the three stages of puberty.

DISORDERS OF SEXUAL MATURATION

Disorders of sexual maturing are represented by premature sexual development, incomplete sexual development, delay and absence of sexual development (Table 8). With the presence of such disorders it is necessary to examine the hypthalamic-hypophysial-ovarian axis and the lower departments of the reproductive system. The initial examination should include the determining of the levels of pituitary gonadotrophin (folli- and lutrophin), allowing to distinguish hypothalamic-hypophysial reasons for the disorders from the ovarian ones.

Premature Sexual Development

Premature sexual development (PSD) is diagnosed if any of the secondary sexual characters appear in girls before 7.5 years, and in boys — before 9 years. The incidence of this complication is about 2–2.5% of gynaecologic pathologies in girls. PSD can be isosexual (by the female type) and heterosexual (by the male type). The true one is connected with the increased secretion of gonadotrophin; premature sexual maturity is observed in girls more often.

The classification of disorders of sexual development in girls, used in domestic literature, is submitted in Table 8.

Premature isosexual sexual development can be gonadotrophin-dependent and gonadotrophin-in-

Table 8. **Disorders of sexual development in girls**

Disorder of sexual development	Pathological process	
	Location	Type
Premature sexual development	Central nervous system	Organic and functional disorders
	Adrenal cortex	Hormone-active tumou
	Ovaries	Follicular cyst
		Congenital adrenogenital syndrome
Disorder of sexual development during puberty ("obliterate" virilism type)	Central nervous system	Functional diencephalic disorders
	Ovaries	Hyperandrogenism
	Adrenal glands	Pubertal (acquired) adrenogenital syndrome
		Organic and functional insufficiency
Delay in sexual development	Central nervous system	Anatomic and functional insufficiency
	Ovaries	

dependent and is characterized by the premature occurrence of sexual characters corresponding to a genetic sex of the child. The reason for such condition is the activation of the hypothalamic-hypophysial axis too early. The increase in the level of gonadotrophins due to the discharge of gonadoliberins, does not differ from those during normal pubertal development.

Premature isosexual sexual development can be complete (true), partial (pseudopuberty) and isolated.

Complete (true) ***premature sexual development*** is characterized by early disorder in the sequence of female sexual development. Premature maturing of the hypothalamic-hypophysial sistem causes cyclic menstruation, ovulatory cycles. The bone age progresses, then there is a growth spurt, and pubic hair develops. The reason for such conditions is not determined in 90% of the cases, and the cases like that are classified as constitutional or idiopathic. 10% of the patients have organic brain pathologies, mainly of tumoural character (hamartoma, hemangioma, neurofibroma, cranyopharyngioma), other diseases of the central nervous system (trauma, asphyxia at birth, encephalitis, meningitis) can be found. In such cases neurologic examination, electroencephalography (EEG), computer tomography and nuclear magnetic resonance are conducted on the girls.

Partial (pseudopuberty) ***premature sexual development*** is observed in girls under the influence of endo- and exogenic oestrogen. The premature reaction to the action of gonadoliberins is observed in them; there are feminising attributes. However, the hypothalamic structures and the hypophysis remain immature, the levels of folli- and lutrophin are lower than in adults, ovulation is absent. The most often reason for this complication is oestrogen-producing cysts or ovarian tumours (granulosa- or thecacellular). This condition received the name *ovarian forms of premature sexual development.* Less often the reason for such a condition can be teratoblastoma and chorionepithelioma with elements of teratoblastoma. The first symptom of the erroneous diagnosis of PSD in these cases can be menstrual-like vaginal discharge against a background of insufficient secondary sexual cheracters development, i.e. disorder in the sequence of sexual maturity signs is observed. The development of external and internal genitalia corresponds to those in girls at the end of the first phase of puberty. A thickening of the hymen, vaginal mucous membrane, accumulation of cervical mucus in the uterine opening are found; the angle between the corpus and cervix is formed, while the length, body weight, bone age of the girls with hormonal-active ovarian tumours do not exceed the specifications of the calendar age.

The diagnosis can be established during gynaecologic examination and is confirmed with the help of ultrasonography or computer tomography.

Hormonal-active tumours of the adrenal glands (adenoma, carcinoma) can also result in isosexual premature sexual development.

Treatment is surgical; the volume of the intervention is determined by the character of the tumour.

The McCune—Albright—Braitsev syndrome is referred to very rare forms of premature sexual development of the central genesis. The following triad of signs is typical:

— asymmetric pigmentation of the skin ("coffee spots", as a rule, on the breast or back);

— polyostotic fibrous dysplasia of the bones, accompanied by the development of bone pathology (fractures, dysplasia, colliquation of bone tissue);

— premature pubertal development.

This pathology is connected with an increase in the level of oestrogens, probably, due to autonomous functioning of ovarian cysts and occurs only in girls. There is an accelerated physical development, first of all, growth acceleration. The growth rate of tubular bones and ossification of the epiphyses coincide, therefore girls with the partial form of PSD, having

reached the reproductive age, do not differ by growth and constitution from their age-girls with duly sexual development. If with the complete form of PSD, the rate of sexual maturity is accelerated, with a partial one it is longer in comparison with the physiological.

In some cases, premature sexual development can be accompanied by hypothyroidism, galactorrhoea. An increase in the level of thyrotrophin, gonadotrophin, oestrogen and prolactin is established.

The constitutional form of true PSD has a hereditary character. The rate and sequence of the sexual maturity process is not disturbed; neurologic and other organic pathologies are absent.

The isolated forms of partial premature sexual development are *premature breast development* (premature thelarche), connected with the transitory release of oestrogen by the ovaries in the prepubertal period or in connection with the increased sensitivity of organs and tissue to low doses of oestrogen and the *premature occurrence of pubic and inguinal hair,* or premature pubarche (in girls — till 8 years, in boys — till 9 years), which is connected with an early increase in androgen secretion by the adrenal glands (premature adrenarche), has a benign course, spontaneously regresses, and sexual development comes to an end in due time.

Treatment. The correction of premature sexual development represents a challenge and has two aspects: 1) treatment of the pathologic process caused by PSD, and 2) treatment of PSD itself. With the benign course of PSD (constitutional, cerebral, partial, isolated forms) and the favourable prognosis concerning further reproductive functions, vitamin therapy, dehydrational therapy, physical methods of influence, psychotherapy are prescribed.

Hormone-producing ovarian tumours and adrenal glands are subject to removal. Follicular ovarian cysts (up to 4 cm in diameter by ultrasonography data) in 2–3 months, as a rule, are subject to inverse development. The treatment of girls with PSD, caused by organic pathology (neuroinfection, trauma at birth, asphyxia) is an extremely difficult challenge and is connected with the blocking action of hormones on the target organs. With this purpose, medroxyprogesterone acetate (100–200 mg 2 times every 2 weeks for 6 months), danazol (9–17 mg/kg long-term), cyproterone acetate (by 50 mg a day long-term), synthetic agonists of gonadoliberin (analogues of gonadoliberin), the action of which is based on the blocking of periodic gonadoliberin secretion, as well as receptors of folli- and lutrophin resulting in a reduction of their release from the anterior lobe of the hypophysis (pituitary desensitization), which promote the termination of premature hormonal ovarian activity, are prescribed. Buselerin (intranasally daily by 400–600 mg) is referred to such preparations.

In order to prevent premature sexual development oestrogen containing drugs and products (oral contraceptives, meat and other products with an increased content of oestrogen) should be prescribed for the girls.

Premature sexual development of the heterosexual type can be caused by hyperplasia of the adrenal cortex (simple form of congenital adrenogenital syndrome — AGS), virilising tumour of the adrenal glands or ovaries, resulting in virilism and masculinization in girls.

The simple virilising form of AGS (1:3500–1:5000 newborns) is a genetically caused congenital disease connected with the insufficiency of the fermental system of 21-hydroxylase in the cortex of the adrenal glands. It results in the reduction of cortisole production and an increase in the release of corticotrophin, that, in turn, causes an increase in the synthesis of androgen and bilateral hyperplasia of the adrenal cortex.

After birth, hypertrophy of the clitoris, the presence of a urinogenital sinus, excavation of the vaginal vestibule, high perineum, underdevelopment of labia pudendi down to difficulty in determining the child's sex, are found. The growth rate is sharply accelerated during the first 10 years of life and slows down by 12 years, which is connected with the fast completion of ossificating processes. The constitution is dysplastic (wide shoulders, narrow pelvis, short extremities, and long trunk). Puberty begins at 4–6 years and develops by the male type; breasts and menstruation are absent, the uterine sizes are less than the normal for that age. An increase in the level of testosterone and its predecessors in blood serum is determined in the patients: dehydroepiandrosterone (DHEA), predecessor of cortisole — 17-hydroxyprogesterone, an increase in the release of 17-ketosteroids.

Differential diagnosis is conducted with virilising tumour of the adrenal glands. The difference between AGS from other forms of disorders of sexual differentiation (hermaphroditism) is the presence of ovaries, uterus and vagina, which open into the urinogenital sinus, positive sexual chromatin, 46 XX karyotype.

Treatment is with glycocorticoids: prednisolon or dexamethason under the control of the hormonal parameters. The earlier the treatment is started (first ten years of life), the better the prognosis. Correction of external genitalia is conducted surgically.

Disorder of Sexual Development by the "Obliterate" Virilization

Disorder of sexual development by the "obliterate" virilization type in clinical practice is observed the most frequent and can be caused by central disorders at the level of the hypothalamus, ovaries and adrenal glands. The disorders appear as a rule after menarche, and connected with the activation of the hypothalamic-hypophyseal-ovarian axis.

Hyperandrogenism of the central genesis received the name neuroendocrine syndrome of puberty. As a result of the defect in the synchronous maturing of nuclei of the hypothalamus, an extensive and spasmodic stimulation of the anterior lobe of the hypophysis with an increase in lutrophin release takes place. The extensive increase in the levels of lutrophin and corticotrophin causes hyperstimulation of the ovaries (increase in oestrogen and androgen secretion) and cortex of the adrenal glands (increase in androgen and glycocorticoid excretion). Early menarche, irregular menstrual cycles, obesity, stretch marks on the skin, hirsutism can be observed in the girls; vegetovascular disorders are possible: arterial hypertension, sleeping disorders, thermoregulation disorders.

For differential diagnosis of the origin of hyperandrogenism the tests with synthetic progestins and dexamethasone are used: decrease in the level of testosterone and discharge of 17-KS by 40–50% is evidence of the central genesis of hyperandrogenism.

Treatment consists of the girls' keeping a diet, carrying out vitamin and physiotherapy with the further use of synthetic progestins (three-four 21-day courses).

Ovarian hyperandrogenism can be shown at the age of 12–16. It is associated with an increase in the formation of testosterone by the ovaries, which can be caused by congenital deficiency of enzymes and other reasons. The classical form is the polycystic ovarian syndrome (PCOS), or Stein—Leventhal's syndrome, for which oligomenorrhoea, obesity, hirsutism, bilateral ovarian enlargement are typical. In the clinic, more often the obliterate forms of the syndrome prevail, which are characterised by an increase in the contents of lutrophin with a normal or reduced level of follitrophin (ratio > 2–3), an increase in the levels of testosterone and androstendion, decrease in the level of oestrogens in the blood. The discharge of 17-KS is a bit increased or normal. Anovulatory cycles, enlarged ovaries, multiple follicular cysts are determined. Laparoscopy improves the results of diagnosis.

The treatment of girls-teenagers is directed on the restoration of regular menstrual cycles, in the reproductive period — on the achievement of ovulation (see "Neuroendocrine syndromes" p. 67).

Adrenal hyperandrogenism (pubertal form of AGS) is the result of less expressed insufficiency of 21-hydroxylase enzyme in the cortex of the adrenal glands. Oligo- or amenorrhoea, virilism, hypertrophy of the clitoris are marked. In the blood — an increased level of testosterone, DHEA, which are reduced by more than 70% after the test with dexamethasone. The zones of bone growth are prematurely closed. A reduction of the uterus with normal sizes of the ovaries is characteristic.

Differential diagnosis is conducted with virilising ovarian tumours and adrenal glands.

Treatment is with supporting doses of glycocorticoids (dexamethasone).

Sexual Development Delay

Sexual development delay (SDD) — the absence of secondary sexual characters before the age of 14 in children of both sexes; the absence of menarche in girls before the age of 16 with the presence of secondary sexual characters (primary amenorrhoea). Reasons for a delay in sexual development:

— premature depletion of the ovaries;
— Turner's syndrome;
— deletion of the long shoulder of the X-chromosome;
— influence of chemotherapy;
— inadequate gonadoliberin secretion;
— Kallmann's syndrome;
— constitutional delay in sexual development;
— cranyopharyngioma;
— hypothalamic hamartoma;
— the use of marihuana;
— inadequate gonadotrophin secretion;
— isolated gonadotrophin deficiency;
— prolactin-secreting adenoma of the hypophysis:
— obesity;
— neural anorexia;
— hypothalamic dysfunction, caused by physical exercises;
— anomalies of the genitalia;
— agenesis of the vagina and uterus (Rokitansky—Küstner—Hauser's syndrome).

Constitutional form of SDD is connected with the family anamnesis and occurs only in 0.6% of the cases. Such teenagers have shorter height; the bone age is slowed, but while girls reach the age 11–14 years and boys — 12–14 years the sexual development renews.

SDD of the central genesis (hypogonadotrophic hypogonadism) can develop as a result of previous infections, intoxications during childhood. The deficiency of gonadotrophin can be connected with tumours of the hypothalamus, defects of the hypophysis. Isolated gonadotrophins deficiency can occur as the result of the Kallmann's syndrome, connected with the hypoplasia of the olfactory tract and the disorder of gonadoliberin secretion by the arcuate nucleus of the hypothalamus. Menstruation is absent, growth is high, trunk is short, and the bone age equals the calendar one or delays. Underdevelopment of the secondary sexual characters is observed; hypoplasia of the external and internal genitalia is present. The gonadotrophins level in the urine and blood is reduced.

Diagnosis. Functional tests with gonadotrophins, clomiphene and gonadoliberin are conducted.

Treatment. Gonadotrophins, cyclic therapy with oestrogens and gestagens for 3–4 months is prescribed. Oral contraceptives as a replacement therapy are recommended.

SDD of the ovarian genesis (hypergonadotrophic hypogonadism) is connected with the decrease in the hormone-producing functions of the ovaries, as a result of a defect to their follicular device (probably, infectious genesis) or insufficiency of fermental systems of the ovaries, participating in the synthesis of oestrogens with a sensitivity disorder to gonadotrophins.

The constitution of such patients is intersexual or eunuch-like; menstruation is absent; secondary sexual characters are underdeveloped. The bone age lags behind the chronological. The genitalia are hypoplastic. The contents of gonadotrophins in blood is acutely increased, and oestrogens — decreased.

Treatment. The replacement therapy with sex hormones is prescribed. The use of gonadotrophic preparations and clomiphene is ineffective.

Sexual infantilism is a concept which is used to determine various conditions, accompanying the underdevelopment of sexual organs and ovarian hypofunction in girls over the age of 15. If sexual infantilism is combined with the general one (delay in the development of secondary sexual characters, anthropometrical parameters, by 1–3 years from the normal for that age), the diagnosing is possible already at 13–14 years.

The reasons for sexual infantilism can be genetic anomalies, eating disorders, hypovitaminosis, diseases (rheumatism, tonsillitis), and previous operations on the ovaries.

Two variants of sexual infantilism are distinguished: 1) with the ovarian hypofunction (occurs more often); 2) without the ovarian hypofunction.

Ovarian hypofunction is revealed by incomplete secretory changes in the endometrium; probably in combination with hypofunction of the thyroid gland.

With infantilism there is a decrease in the sensitivity of the ovaries to gonadotrophins, and target organs — to steroid hormones. Quite often there is an increase in the production of follitrophin against a background of an insufficient lutrophin secretion.

Girls with infantilism, as a rule, are shorter (or a little bit above average). The pelvis is contracted. Later menarche, hypomenstrual syndrome, algodysmenorrhoea are observed. With genital infantilism, there is a discrepancy between proportionality of the constitution and the underdeveloped genitalia.

The size of the uterus plays a big role in determining the extend of sexual infantilism. Three degrees of uterine underdevelopment are distinguished: rudimentary (feotal), infantile and hypoplastic uterus.

The rudimentary uterus (uterus fetalis) has the length of 1–3 cm; the cervix makes up the most part. Hypoestrogenia and stable amenorrhoea are characteristic. The prognosis concerning the restoration of specific functions of the female organism is unfavourable.

The length *of an infantile uterus* (uterus infantilis) exceeds 3 cm; the ratio between the cervix and corpus is 3:1 (as for girls in the prepubertal period). During bimanual examination, hyperantefixal uterus, the vaginal vaults inadequately marked are found. The ovaries are located higher up; the Fallopian tubes are long, twisting. Oligomenorrhoea, algodysmenorrhoea are marked. Menstrual and reproductive functions are possible under the condition of adequate treatment.

Hypoplastic uterus (uterus hypoplasticus) has the cavity length of less than 7 cm and a correct ratio between the cervix and corpus. The prognosis concerning the reproductive function is favorable.

Diagnosis is based on the history, examination results, gynaecologic examination, uterine intubation, hysterosalpingography, hysteroscopy, laparoscopy, determining the bone age. A decrease in the level of steroid hormones is found in the blood. The contents of sexual chromatin and karyotype of patients are normal.

Differential diagnosis is conducted with the pure form of gonadal dysgenesis, hypogonadotrophic hypogonadism, and polycystic ovarian syndrome.

Treatment. The cyclic hormone replacement therapy with oestrogens and gestagens, combined oral contraceptives are prescribed. Physiotherapeutic treatment: electrophoresis with copper ions (the 5th through the 13th day of the cycle) and zinc (the 14th through the 24th day of the cycle), acupuncture, electropuncture, electrostimulation of the cervix, medical gymnastics, gynaecologic massage, balneotherapy, the use of paraffin, ozokerite, sulphidic water.

RECOMMENDED READING

7; 17; 21; 24; 54; 63; 65; 67; 75; 79; 90; 93; 94; 108.

Chapter 9

ANOMALIES OF POSITION OF THE FEMALE GENITALIA

The genitalia of a healthy woman are characterized by physiological mobility caused by the general tone, changes in body position, physical loads, the filling of adjacent organs, pregnancy, age, anatomic protection of muscular and connective tissue elements of the pelvic fundus, the condition of suspending and supporting apparatus of the uterus.

Normally, if a woman is in the vertical position with an emptied bladder and rectum, the uterus is located in the centre of the small pelvis at an identical distance from the pubic symphysis, sacrum and lateral walls of the pelvis (Fig. 36). The uterine fundus does not go beyond the limits of the pelvic inlet plane. The vaginal part of the cervix and the uterine aperture are located in one plane, going through the interspinal line.

The uterine fundus is tilted upward and forward *(anteversion),* the vaginal part of the cervix — down and backwards, the uterine aperture is located near the vaginal wall, near its posterior vault. Between the corpus and cervix, an obtuse angle is formed, opened to the forward *(anteflex)*. The vagina is located in the cavity of the small pelvis bending in the direction upwards and backwards.

A complex of factors provides the normal position for the internal female genitalia, namely:

— tone of the sexual organs;

— the suspending apparatus of the uterus (round,

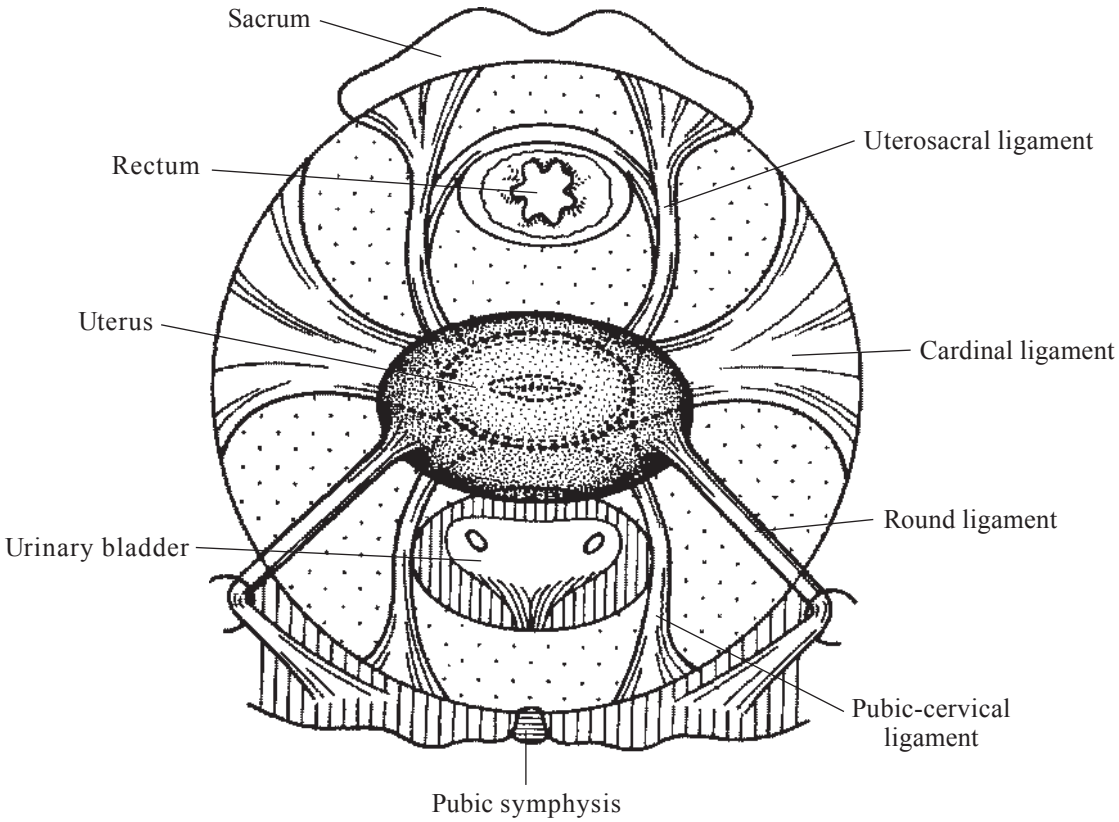


Fig. 36. Normal topography of the uterus

broad ligaments of the uterus, ovarian ligament; the round ligament promotes the bending of the uterus to forward);

— the fixating apparatus of the uterus (sacrouterine, cardinal (basic), uterovesical and vesico-pubic ligaments; areas of thickening in the pelvic fat provide the basis for the ligamentous apparatus);

— the supporting device of the genitalia (three layers of muscles and fascia of the pelvic fundus);

— the coordinated activity of the diaphragm, abdominal wall and pelvic fundus.

The term positional anomalies of the genitalia means their steady deviations from the normal (anatomic) location, which can be accompanied by pathologic symptoms. The wrong position of the genitalia can be caused by their abnormal development, inflammatory processes, tumours, traumas, etc.

Some types of positional anomalies of the genitalia are distinguished:

1) Pathologic inclination (versio) and inflections (flexio).

2) Shift in the transversal plane — to the front, back and side.

3) Turn (rotatio) and twist (torsio) of the uterus.

4) Shift in the vertical plane — the descending and prolapse of the vagina and uterus, descending of the ovaries and Fallopian tubes; inversion of the uterus and the uterine elevation (elevacio).

Pathologic version (versio) — the shift of the uterus to one side, and the cervix — to the other one. Such a condition can occur due to inflammatory processes in the pelvic fat and ligamentous apparatus of the internal genitalia. The following pathologic inclinations of the uterus are distinguished:

Anteversion **—** forward inclination of the uterus and the cervix is tilted backwards (Fig. 37, *b*).

Retroversion **—** the uterus is inclined backwards, and the cervix has forward inclination; the vertical axis of the uterus is directed to the backwards (Fig. 37, *c*).

Dextroversion **—** the uterus is inclined to the right, the cervix — to the left.

Sinistroversion **—** the uterus is inclined to the left, the cervix — to the right.

The **wrong positions** of the uterus (shift in the transversal plane) include anteposition, retroposition and lateroposition of the uterus, according to its forward shift, backwards, right and left.

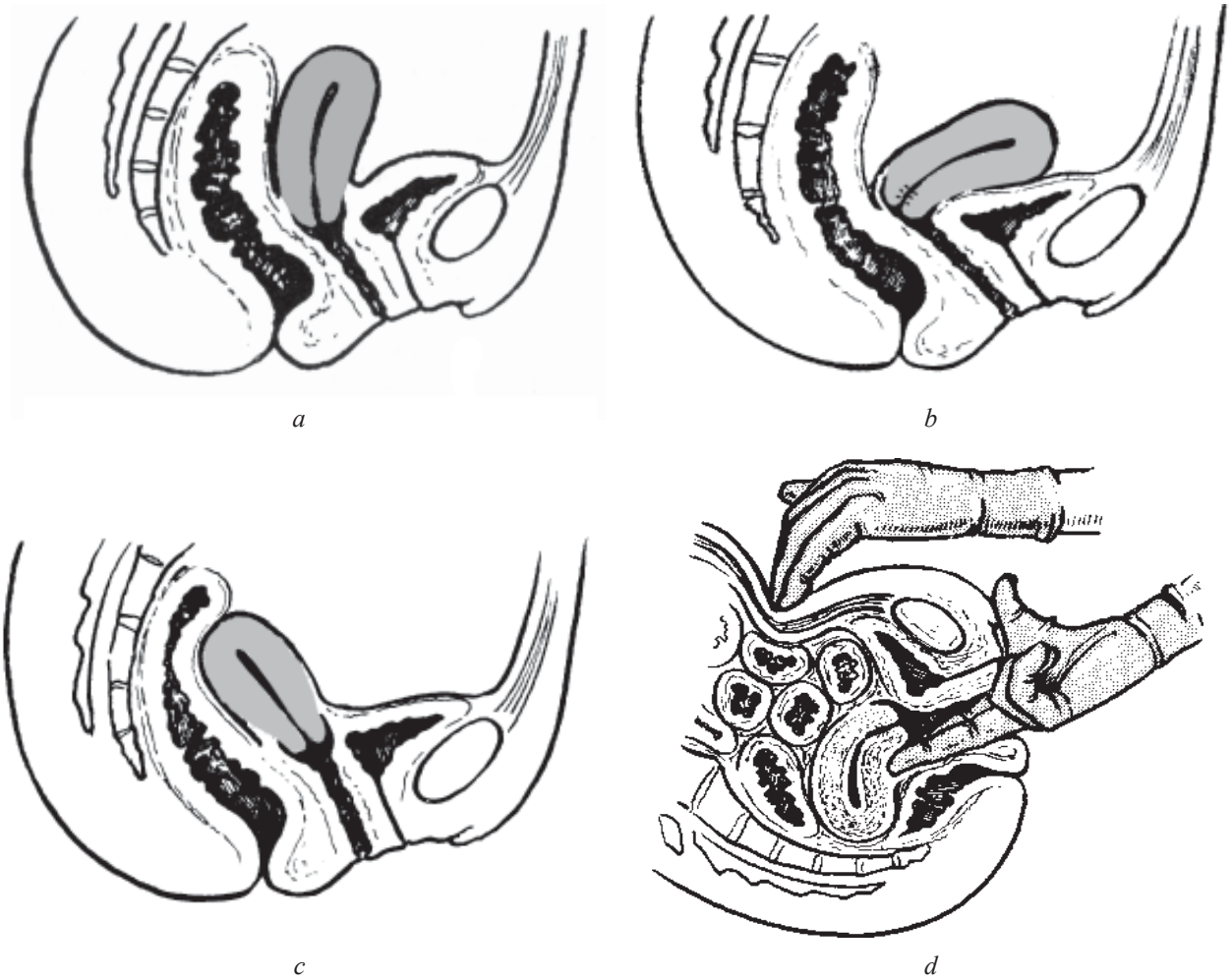


Fig. 37. Wrong positions of the uterus:
a — retroposition; *b* — anteversion; *c* — retroversion; *d* — retroflexion

Anteposition (forward shift of the uterus) as a physiological phenomenon is observed due to overfilling of the rectum; can be caused also by a tumour in the rectal-uterine space or the presence of exudate in it.

Retroposition (Fig. 37, *a*) a shift of the uterus backwards while maintaining the correct direction of the uterine axis (forward); can occur due to overfilling the bladder, space occupying lesions in the pelvic organs, located in front of the uterus.

Lateroposition (lateral shift of the uterus) can be caused by tumours of the pelvic organs (for example, uterine appendages), parametritis.

The following conditions are referred to **inflexion of the corpus in relation to the cervix**.

Hyperanteflexion — a forward pathologic inflexion of the uterus, when an acute angle is formed between the corpus and cervix. Such a uterine position is quite often congenital, can be connected with general and sexual infantilism, constitutional features; it is sometimes caused by the development of inflammatory processes in the pelvic organs, sacrouterine ligaments.

Clinical picture. Patients complain of hypomenorrhoea, oligomenorrhoea, algodysmenorrhoea, chronic pelvic pain, dyspareunia, infertility.

The *diagnosis* is established on the basis of the anamnesis (later menarche, hypomenstrual syndrome, infertility or spontaneous abortions), typical complaints of the patients, as well as the results from the general and gynaecologic examinations. In this case, the sizes of the uterus are reduced, its sharp forward deviation is observed, the cervix can have a long, conic form; the vagina is narrow, its vaults are thickened.

Treatment consists of eliminating the reasons for the occurrence of the pathologic inflexion of the uterus (infantilism, inflammatory process). For painful menstruations, 2–3 days prior to the onset of the next menstruation the patients are prescribed inhibitors of prostaglandin synthesis and non-narcotic analgesics.

Retroflexion — arc-like inflexion of the uterus backwards with the formation of an angle, opened backwards, between the corpus and cervix. The cervix, as a rule, remains in the normal position (Fig. 37, *d*).

Retrodeviation of the uterus is a combination of retroflexion and retroversion. Mobile and fixated retrodeviation are distinguished. If during bimanual examination, it is possible to put the uterus in the correct position such a condition is called *mobile retrodeviation*. Mobile retrodeviation can be the manifestation of anatomic-physiological disorders (decrease in the tone of the supporting, suspending and fixating apparatuses of the genitalia) and occurs in girls and young women with an asthenic constitution, as well as as a result of infantilism. The similar disorders can occur after giving birth as a result of a severe reduction of the body weight. *Fixated retrodeviation* of the uterus is more often the result of inflammatory processes, tumours of the pelvic organs, endometriosis.

With retroflexion, the bladder is not covered by the uterus, and the loops of the intestines put pressure upon the anterior surfaces of the uterus and bladder, causing the falling of the genitalia.

Clinical picture. Mobile retrodeviation of the uterus can be not accompanied by pathologic symptoms and is found only during gynaecologic examination.

Fixated retrodeviation is accompanied by chronic painful syndrome (the pain is located in the bottom of the stomach and sacrum), disorders of menstrual functions (hyperpolymenorrhoea, algodysmenorrhoea), function of the adjacent pelvic organs — rectum (constipation), bladder, as well as miscarriages. During gynaecologic examination, putting the fixated uterus into the normal position is not possible.

Differential diagnosis is conducted with the help of laparoscopy to eliminate the diagnosis of retrocervical endometriosis. In some cases, retroflexion is necessary to differentiate with tumours of the uterus, ovaries or tubal pregnancy. Additional methods of examination allow to specify the diagnosis.

Treatment. With the presence mobile retrodeviation, not causing the above-mentioned complaints the patients require no treatment: after conception the uterus starts to increase and gradually obtains the correct position. With promoted symptoms, treatment is conducted, directed on the elimination of the principal cause of the disease. With fixated retrodeviation of the uterus, treatment consists of eliminating the inflammatory process and its results. Physiotherapeutic procedures, sanatorium treatment, medical gymnastics, gynaecologic massages are widely used.

Surgical treatment of patients with retroflexion of the uterus is seldom; in most cases it is used only as an accompanying intervention (after the removal of a tumour) — shortening the round ligament with their fixation to the back wall of the uterus.

Rotation of the uterus (rotatio) around the vertical axis occurs as a result of inflammation of the sacrouterine ligament, its shortening, as well as with the presence of a tumour of the pelvic organs, located behind and to the side of the uterus.

Treatment consists of eliminating the reasons for the uterine rotation.

Tortion of the uterus (torsio) — turning of the uterus with a fixated cervix. The reasons can be unilateral space occupying lesions of the uterine appendages, large subserous myomatous nodes on the uterus.

Shifting of the uterus upwards (elevatio) occurs with space occupying lesions in the pelvic organs: ovarian tumours, the presence of extrauterine

exudate, infiltrate or hematomas, etc. Physiological reasons for the shifting of the uterus can be overfilling of the bladder and rectum.

Treatment consists of the removal of the pathologic formations, elimination of inflammatory processes in the pelvic cavity.

Ectropion of the uterus can occur while giving birth, due to incorrect conducting the afterbirth period (excessive traction for the umbilical cord with the underdetached placenta).

Treatment consists of replacement of the uterus under general anaesthesia (inhalation or intravenous narcosis).

Descent and prolapse of the internal genitalia. The descent and prolapse of the internal genitalia (shift of the uterus and vagina downwards, or genital prolapse) are observed most frequently. Despite the numerous methods of treatment, there are often relapses of the disease, connected both with the inferiority of muscles of the pelvic fundus, and with imperfection of operative methods of treatment.

Etiology. The descent and prolapse of the genitalia occur due to disorders of the integrity of the pelvic fundus and a decrease in the muscle tone of the pelvic diaphragm (relaxation). In women who have not yet given birth, this pathology is observed extremely seldom. The reason for such a condition may be congenital weakness of the supporting tissues, especially muscles of the pelvic diaphragm, and cardinal ligaments of the uterus; however, in most cases the etiological factor is its trauma during delivery. Therefore such complications more often occur in women of the advanced age who have given multiple births.

The reason of relaxation can be connected also to operations on the pelvic organs. Muscles of the pelvic fundus are frequently injured during traumatic, especially operative deliveries (applying obstetric forceps, extraction of the fetus by the pelvic end, vacuum-extraction of the fetus), due to long and, on the contrary, rapid deliveries, giving birth to a large fetus, multiple gestation pregnancy.

The descent and prolapse of sexual and other organs (Fig. 38) are possible in the case of long-term increase in intraabdominal pressure due to heavy physical work, chronic constipation. The risk factors for this complication are also physical work in the early postpartum period, frequent deliveries with short intergenetical intervals, retroversion of the uterus, severe body weight loss, infantilism, atrophy of tissue in the climacteric period and elderly age.

In case of the descent and prolapse of the internal genitalia cysto-, recto- and enterocele are frequently observed as well.

Cystocele (Fig. 38, *a*) — vaginal prolapse during which together with the anterior vaginal wall, as a rule, the urinary bladder lowers and falls out (cystocele). The dropping out of the urethra is also possible — urethrocele.

The support of the urethra and bladder is with the help of the pubic-vesico-cervical fascia. Primary cystocele occurs as a hernia of the anterior vaginal wall; secondary — in connection with the weakening or defect of the fascia. The frequency of symptomatic cystocele is not precisely established. However, the majority of women who have given birth have some descent of the anterior vaginal wall.

Clinical picture. The majority of cases of cystocele are asymptomatic and are diagnosed during gynaecologic examination. The disease develops gradually. With symptomatic cystocele, patients complain of a feeling of heaviness, pressure in the pelvis or vagina, presence of a foreign body in the vagina, pain in the lower abdomen, the occurrence of bulging in the vagina. Cystocele, except for the advanced cases, seldom causes urine delay or difficulty during urination.

Traditionally, cystocele is classified into three degrees depending on its position concerning the entrance to the vagina (with the III degree the bladder drops out through the entrance of the vagina).

Treatment of patients with cystocele is necessary only with the presence of pathologic symptoms. Cystocele of the III degree requires surgical treatment. Operations are conducted mainly through vaginal access, especially with large sizes of cystocele. The first stage of operation is the anterior colporrhaphy (Fig. 39, *a*), i.e. restoration of the anterior vaginal wall (surgical creation of a fold of the anterior vaginal fascia, supporting the bladder). In cases where the uterus drops out, this procedure, as a rule, is conducted together with vaginal hysterectomy (see "Operative gynaecology").

Cystocele of the I–II degree can be corrected abdominally, removing a small V-shaped wedge from the anterior vaginal wall. The removal of a large wedge can result in the reduction of the uretrovesicular angle and promote urine incontinence. As a result during restoration of cystocele, a fold of the uretrovesicular angle is created.

If there are contraindications to the operation, patients can use vaginal pessaries, which, unfortunately, are not always effective. In women of the advanced age who are not leading an active sexual life, sometimes partial (Le Fort) or complete obliteration of the vagina (colpocleisis) can be conducted.

The descent and prolapse of the posterior vaginal wall is accompanied by the descent and prolapse of the anterior rectal wall (rectocele).

Rectocele (Fig. 38, *b*) is a hernia of the posterior vaginal wall due to the weakening or defect of the rectovaginal septum (fascia) and the muscle lifting the anus *(m. levatores ani)*. The reason of this complication more often is trauma during delivery.

Clinical picture. The majority of cases of rectocele are asymptomatic and are found, as well as cystocele, during the usual gynaecologic examination. The prolapse of the rectal wall is frequently accom-

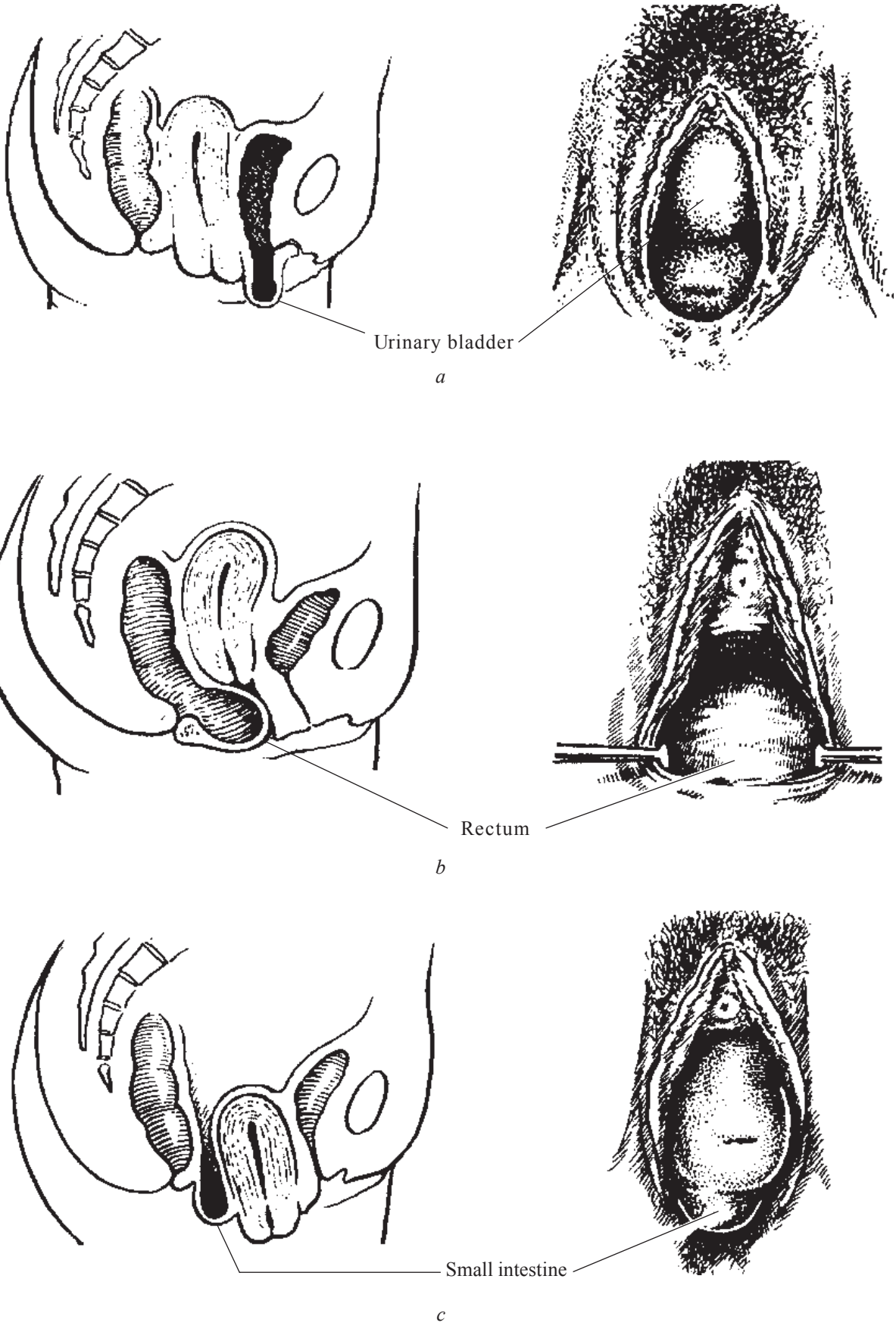
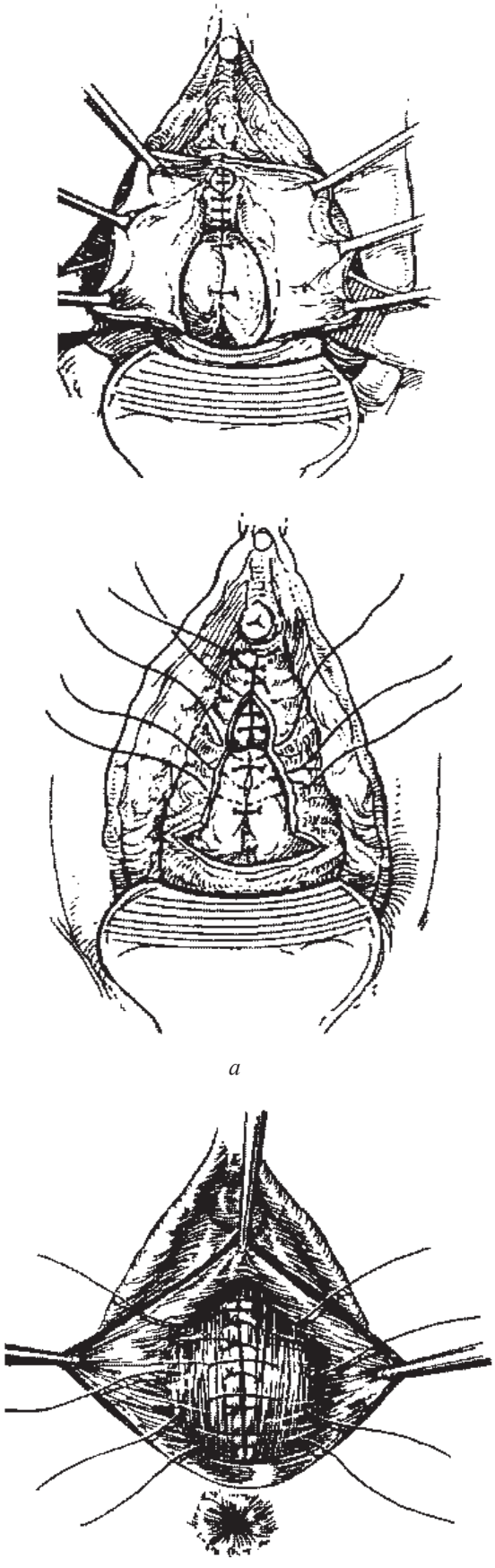


Fig. 38. The descent and prolapse of internal genitalia and other organs:
a — cystocele; *b* — rectocele; *c* — enterocele



a

b

Fig. 39. Surgical method of treatment of III degree of cystocele — anterior colporrhaphy *(a)* and rectocele — colpoperineorrhaphy *(b)*

panied by constipation, incontinence of urine and gases during cough and sneezing. In case of expressed rectocele (large sizes) complaints of difficulty in passing stool, the presence of space occupying lesions, "fullness" sensation in the vagina can be observed. Rectovaginal examination helps to determine the size of the hernial defect.

The *diagnosis* is established on the history data, examination and palpation of the dropped out organs. Bimanual and rectal examinations are conducted. The condition of muscles of the pelvic fundus, ligament device, uterine appendages are evaluated; the presence of other pathologies is ruled out.

Treatment of patients with insignificant asymptomatic rectocele is not necessary. In the case where the rectum protruding through the vaginal entrance, as well as with the presence of pathologic symptoms, patients are subject to surgical treatment, as a rule, posterior colporrhaphy method. This operation includes the opening of the posterior vaginal wall above the hernial defect and the creation of folds in the rectovaginal fascia. The muscle lifting the anus (levator) is moved to the middle line (Fig. 39, *b*), the remainder of the vaginal mucous membrane is removed.

With the presence of contraindications for the operation, symptomatic treatment is prescribed: laxative means preventing constipation. The use of vaginal pessary for rectocele is ineffective.

Enterocele (Fig. 38, *c*) — hernia of the Douglas' cul-de-sac in the rectovaginal septum (fascia). The reason for the occurrence of enterocele in most cases is also connected with birth trauma.

Clinical picture. The majority of patients with enterocele have no complaints. A typical symptom is the "fullness" sensation and pressure in the pelvic area. Patients can find space occupying lesions in the vagina. During objective examination, enterocele is differentiated with rectocele (the bulge of the posterior vaginal wall is determined, first its upper departments, then the lower ones).

The *diagnosis* of enterocele proves to be true by rectovaginal examination, palpation of foreign mass.

Posterior enterocele of large sizes is frequently accompanied by uterine prolapse, cysto- and rectocele. Sometimes anterior enterocele can be established as cystocele. For differential diagnosis the Folea catheter is entered into the bladder and palpation is repeated.

Treatment, as well as in the previous cases, is surgical. It can be conducted with both abdominal and vaginal access. If there is no accompanying recto- or cystocele, the best results are achieved with the abdominal access. The operation consists of tying off of the hernial bag with the obliteration of the rectouterine cul-de-sac. With a combination of enterocele with recto- and cystocele, the vaginal access is preferable. The operation includes a high ligation of the hernial bag and the coming together of

the sacrouterine ligaments, correction of accompanying prolapses and, as a rule, hysterectomy.

Descent and falling (prolapse) of the uterus. The descent of the uterus — such a position of the organ during which the uterine cervix is located below the interspinal line, but do not go beyond the limits of the sexual rima. The uterus is supported by the internal pelvic fascia, cardinal and sacrouterine ligaments. Prolapse of the uterus, as a rule, is connected with the weakening of these supporting structures. The reasons for this complication, as well as vaginal prolapse, are trauma received during vaginal delivery in most cases. Other adverse factors are an increase in abdominal pressure during to ascites or tumours.

Three degrees of uterine prolapse are distinguished (Fig. 40, *a*, *b*): I — cervix remains inside the vagina; II *(partial prolapse)* — the cervix comes out of the sexual rima (outside of the vagina), but the uterus remains in the pelvic cavity; III *(complete prolapse)* — the whole uterus (cervix and corpus) fall outside the limits of the sexual rima together with the vaginal walls.

Clinical picture. The majority of women, who have given birth, have prolapse or descent of the uterus of some degree, which, as a rule, does not cause any feeling of discomfort. The symptoms occur with significant descent when the uterus bulges out from the vaginal opening and is palpated as "a foreign firm body". The patients thus can complain of sensation of pelvic pressure and vaginal bulge.

Uterine prolapse is frequently combined with the vaginal one. The diagnosis is established during gynaecologic examination.

With partial uterine prolapse and fixated retrodeviation, the cervix can be elongate and appear from the sexual rima during physical strain (due to an increase in the intra-abdominal pressure).

In the case of complete genital prolapse decubitus develops quite often on the cervix and vaginal walls, the vaginal walls become rough, non-elastic, swollen; cracks and excoriation occur in them easily. The presence of decubitus results in the development of secondary infection, which quite often spreads to the urinary tract. The prolapsed uterus, as a rule, is swollen, cyanotic due to disorder of the lymph and venous flow and blood stasis. It is repositioned when the patient is in the transversal position. The decubital ulcer on the vaginal walls and vaginal part of the cervix is differentiated with malignant neoplasm (colposcopy, cytologic diagnosis, biopsy).

Treatment. In the case of insignificant uterine and vaginal prolapse, medical gymnastics is carried out to strengthen the muscles of the pelvic fundus, and it is recommended avoiding heavy physical work.

With significant descent or uterine prolapse treatment should be operative. Preoperative preparation includes: obligatory consultations with the urologist, therapist, endocrinologist, cytologic examination of

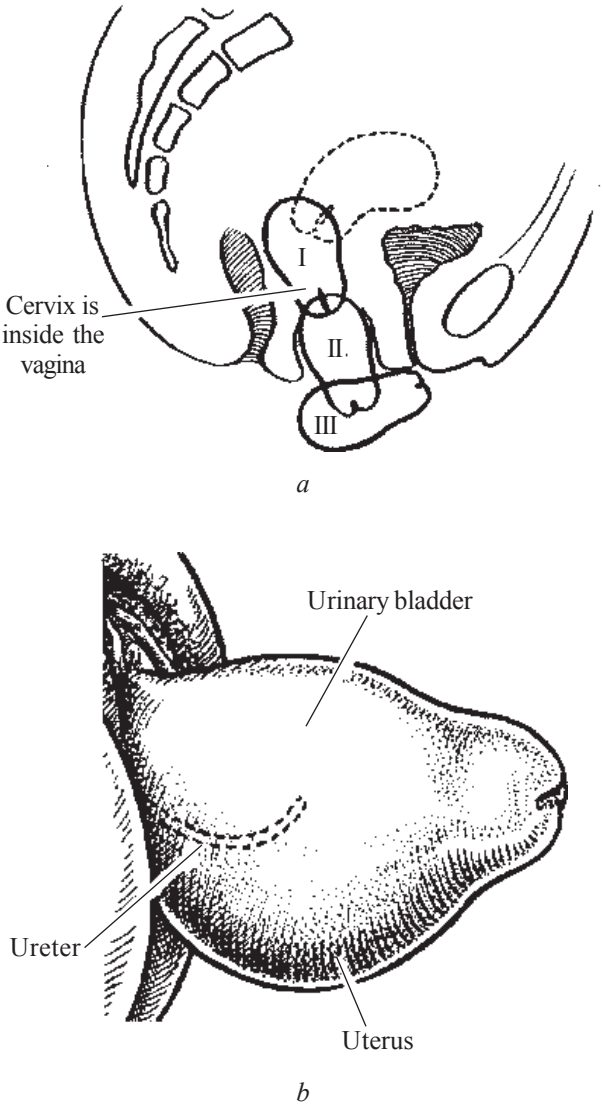


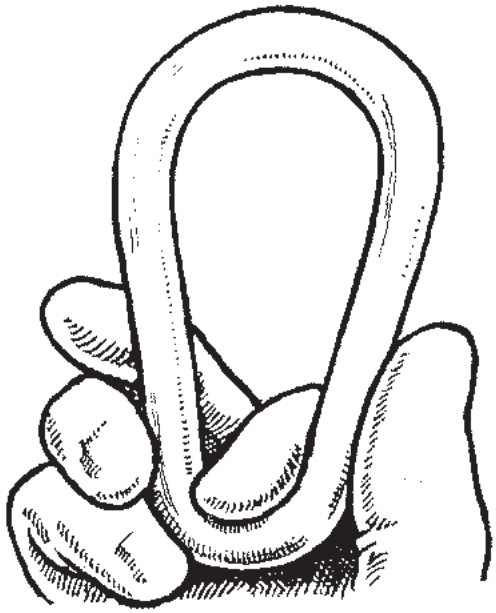
Fig. 40. Uterine prolapse:
a — I–II degree; *b* — complete (III degree)

smears, taken from the cervical canal, colposcopy; bacteriological examination of smears from the cervix, ureter and vagina; blood and urine study.

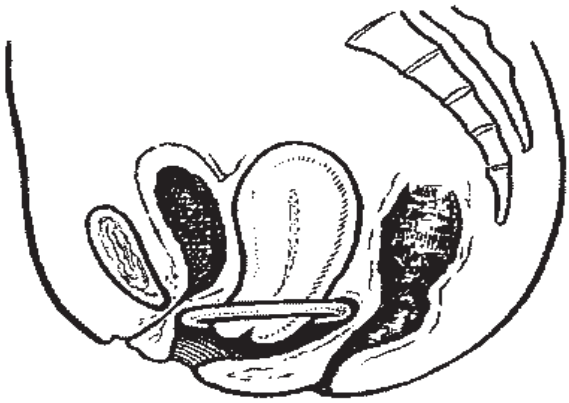
While choosing the operation method, the patient's age, general health condition, features of menstrual function, interest in preserving the reproductive function, degree of prolapse of the vaginal walls and uterine prolapse, the presence of cysto- or rectocele, the condition of the cervix, as well as the condition of the sphincters of the bladder and rectum are taken into account.

The operation consists of the abdominal or vaginal hysterectomy depending on the degree of prolapse and presence of accompanying genital hernias. With the absence of pelvic adhesions as a result of previous operative interventions, inflammatory diseases, the vaginal hysterectomy is preferrable. In other cases the abdominal approach is used.

In patients with descent of the uterus, the vaginal top loses a necessary support, which demands the



a



b

Fig. 41. General view *(a)* and arrangement *(b)* of the pessary

performance of vaginal or abdominal sling of the vaginal stump after the hysterectomy.

All types of operations for genital prolapses include the plastic of the muscles of the pelvic floor. In the postoperative period rehabilitation therapy is recommended.

Orthopaedic treatment. With contraindication to surgery orthopaedic treatment (vaginal pessaries) or oestrogen-therapy with the absence of contra-indications are conducted. Round pessaries are usually used. The pessary is entered in the inclined direction in relation to the vulva, further by pressings on the perineum it is put in the correct position in the vagina. It should be placed with inclination, closer to the transversal position, leaning on the pelvic floor on one side and the pubic arch — on the other one (Fig. 41, *a*, *b*). While using a pessary it is necessary to conduct vaginal syringing, ointment tampons application; it is necessary to wash a pessary monthly and change its model. The use of pessaries can be complicated by the occurrence of decubitus; therefore such patients are subject to medical examination every 2 months.

Prevention of the descent and prolapse of the internal genitalia consists of rational conducting of deliveries, afterbirth and postpartum periods, the exclusion of unnecessary operative vaginal interventions, anatomic stitching of the ruptures along the maternal passages, especially the perineum, elimination of excessive physical loads, the performance of special physical exercises directed on strengthening of the muscle tone of the pelvic floor, especially in the postpartum period.

For women in the postmenopausal period, treatment with low doses of oestrogen is recommended, especially with atrophy of the vagina (estriol, ovestin), which promotes an increase in the tone of the tissue of the genitalia, prevention of urogenital infection.

RECOMMENDED READING

7; 16; 21; 24; 38; 57; 78; 90; 92; 93; 94; 95; 103; 108.

Chapter 10

BACKGROUND AND PRECANCER DISEASES OF THE FEMALE GENITALIA

DISEASES OF THE VULVA

Neoplastic (tumour) and non-neoplastic (background, or pretumour) defects of the external genitalia are distinguished. Background defects of the external genitalia also received the name **dystrophy of the vulva.** This term unites three basic groups of diseases:

1. Kraurosis (lichen sclerosis).
2. Leukoplakia (planocellular hyperplasia).
3. Other dermatoses.

Now the majority of obstetrician-gynaecologists of the world consider these lesions of the vulva as background (non-neoplastic). The malignancy potential of vulvar dystrophy is approximately 5% and can be realized only after a long period.

Dystrophic epithelial lesions of the vulva occur in women after menopause (5th–6th decade of life) more often, but may take place in the reproductive age too. The etiology and pathogenesis of these diseases are not elucidated.

Kraurosis of the vulvas (lichen sclerosis; fig. 42, *a*) — the most widespread dystrophic disease of the vulva; develops mainly after menopause though sometimes occurs at a younger age and even in children. The disease can involve the large and small pudendal lips, perineum.

It is characterized by a severe reduction of the fatty tissue of the large pudendal lips, atrophy of the sebaceous and sudoriferous glands, cracks, synechias, especially promoted in the posterior 2/3 area of the labium minora, narrowing of the vaginal entrance, resulting in disorders of normal anatomic proportions. The injured skin becomes thin, white or pale yellow and looks like parchment. Patients frequently complain of dryness, irritation of the skin, itching and burning feeling resulting in scratching, secondary inflammation (vulvitis).

Leukoplakia of the vulva (planocellular hyperplasia) is characterized by the occurrence of white spots, representing a thickening of the keratinising epithelium on the external genitalia. The spots are located mainly on the labia pudendi, folds between them, on the posterior fusion (Fig. 42, *b*). The spots, nodes on the vulva can be grey, brown, red with excoriation.

Depending on the expressiveness of hyperkeratosis *flat, hypertrophic* (elevated above the surface of the skin) and *warty* (verrucous) leukoplakia are distinguished.

The basic clinical signs are white spots or nodes on the skin, itching, at times very intensive.

Sometimes the combination of leukoplakia and kraurosis of the vulva can be observed, receiving the name *mixed dystrophy.* Hence, more often cellular atypia takes place, as a result it is necessary conducting histological examination of the biopsy material.

For the diagnosis of kraurosis and leukoplakia of the vulvar colposcopy (vulvoscopy), and cytologic examination of smears are used. However, the exact diagnosis can be established extremely on the basis of the biopsy of the defective areas with the subsequent histological examination (hyperkeratosis, acantolysis, parakeratosis, inflammated cells in the derma). The cellular atypia is diagnosed in 1–2% of the patients; in these cases the defect of the vulva is considered neoplastic, which demands the establishment of the degree of dysplasia or cancer. The exam of the glucose level in the blood is obligatory to rule out diabetes.

Treatment of patients with vulvar dystrophic processes should begin after histological confirmation of the clinical diagnosis. Conservative treatment includes desensitizing, vitamin therapy, local application of ointments, creams with corticosteroids, testosterone propionate, and progesterone. Among the non-medicamentous methods novocaine block of the pudendal nerve is recommended too. For minimally invasive surgical treatment for leukoplakia carbon dioxide laser (CO_2-laser), cryoablation are applied.

Surgical treatment is conducted in the case of inefficient conservative therapy with expressed

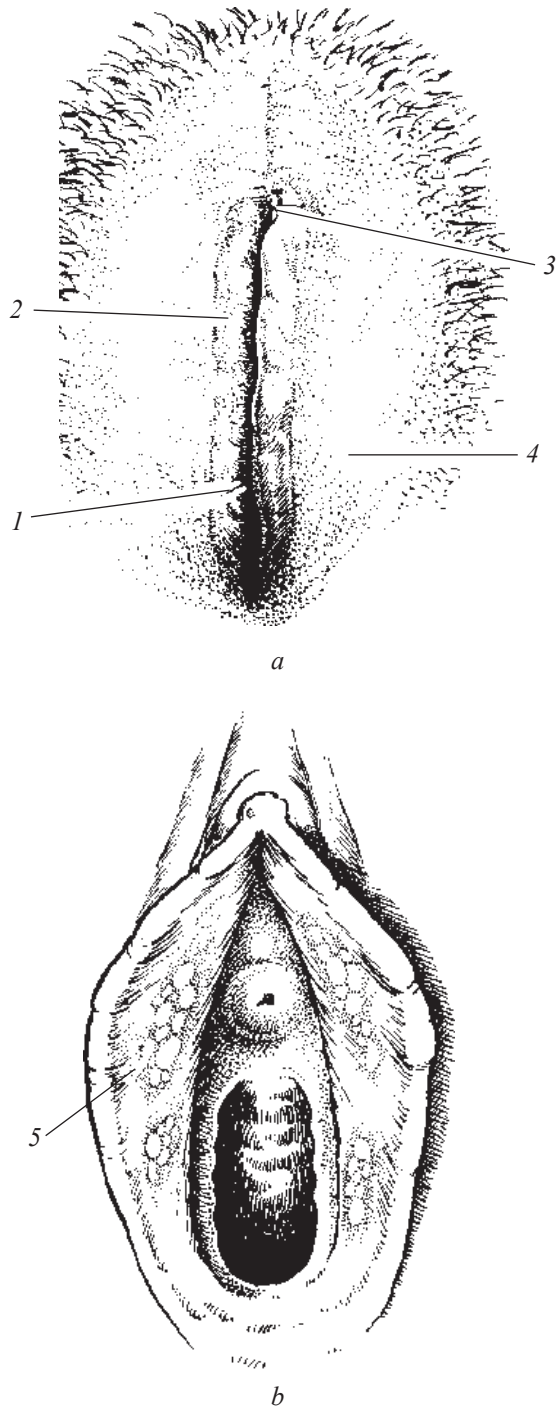


Fig. 42. Diseases of the vulva:

a — kraurosis (*1* — narrowing of the vaginal entrance; *2* — thin red skin; *3* — corrugated clitoris; *4* — loss of the hypodermic fat); *b* — leukoplakia (*5* — spots, nodes on the sexual labia)

symptomatic forms of the disease. It consists of the removal of the defective part of the external genitalia within the limits of healthy tissue or complete vulvectomy depending on the prevalence of the process.

Other dermatoses — flat herpes, psoriasis, etc. are the general diseases of the skin; patients with such pathologies require consultation and treatment by dermatologists.

Acuminate condyloma is also referred to the group of background diseases (see "Viral diseases" p. 34).

Precancerous conditions of the external genitalia are represented by **epithelial dysplasia** of various degree of expressiveness which has no pathognomonic attributes. Clinically epithelial dysplasia is possible to suspect in patients with background dystrophic processes. The diagnosis is established exclusively after histological examination of the removed tissue.

Epithelial dysplasia is morphologically characterized by expressed proliferation of cells, damage to the arrangement of the epithelial layers, occurrence of attributes of atypia of various levels of the epithelial layer, except for its top part.

Treatment of patients with epithelial dysplasia of the vulva consists of the removal of the defective areas by excision, CO_2-laser surgery. Vulvectomy is performed with significant distribution of the process.

CERVICAL DISEASES

Non-neoplastic (nonmalignant) pathologic processes of the cervix can also be conditionally divided into background (benign) and precancerous (epithelial dysplasia).

Background processes include erosion, pseudoerosion (ectopia of the cylindric epithelium, ectropion), metaplasia of the plane epithelium and the formation of retention cysts, endocervicitis, leukoplakia (without attributes of cellular atypia), polyps, condylomata lata, endocervicitis, cicatricial changes of the cervix. Hyperplasia of the epithelial cells, resulting in the formation of new glandular and papillary structures is typical for background processes.

Benign (background) processes make up 80–85% of the total pathologic processes in the cervix.

Erosion. Normally the plane epithelium covers the cervix up to the level of its external os. Any process resulting in the destruction of the plane epithelium of the ectocervix is referred to as erosion of the cervix. Erosion, as a rule, is painless, bright red colour, with inflammatory changes. From the erosion cultures of bacteria are excreted. The basic symptoms of erosion can be mucopurulent scanty or insignificant bloody postcoital discharge.

Treatment consists of anti-inflammatory therapy. Biopsy is conducted in order to eliminate the diagnosis of carcinoma.

Pseudoerosion (ectopia) (Fig. 43, *a*) — replacement of plane epithelium of the ectocervix with cylindrical endocervical one. Posttraumatic ectopia of

the cylindrical cervical epithelium (due to rupture of the cervix while giving birth, as well as traumas during abortions) are referred to as ***ectropion*** (a rolling outward of the cervical mucus membrane).

Ectopia (pseudoerosion) of the cervix is a benign polyetiological disease occurring in 40–50% of gynaecologic patients, and in more than half of cases in patients before the age of 25.

There are some theories of the pathogenesis of cervical ectopia:

— *the mechanical theory* (the stratified squamous epithelium shelling off due to the mechanical influence with the subsequent joining of inflammatory process);

— *the theory of inflammatory origin* of ectopia, which does not explain the origin of congenital pseudoerosion, its disappearance in connection with pregnancy;

— *the hormonal theory* which finds more and more supporters worldwide.

According to V. M. Prilepsky and co-authors (1993), in women with disorders of the menstrual cycle, the frequency of background cervical lesions 5–6 times exceeds those in population. The shift of the transitive zone on the ectocervix during the intrauterine period is a stage of development of the cervix and is explained by the hormonal, in particular, oestrogen influence of the mother's organism. The so-called congenital erosion (ectopia), occurring during prenatal development, can be kept till puberty and even more advanced ages (till 25 years).

There is also a theory of the *autoimmune component* of the pathogenesis of the cervical pathology. The close interrelation between the parameters local and humoral immunity and the degree of morphological changes in the cervix, which is evidence of the possibility of the influence of antibodies of various classes on the occurrence and progressing of background diseases, is established.

Cervical ectopia is a benign disease with very low malignancy potential. Reparative processes in the pseudoerosion zone, promoting the differentiation of reserve cells in the stratified squamous epithelium, are controlled by many factors: age, presence of inflammation, infection, the level of sex hormones, and the condition of local immunity. Ectopia can exist in two forms: non-complicated and complicated.

Prominent features of ectopia of the cylindrical epithelium are the presence of precise borders, the absence of pathologic secretion and inflammatory changes. Opposite to ectopia, in the case of true cervical erosion, the true erosive process is observed, occurring due to various reasons (radionuclide, surgical, chemical influence, etc.).

The term "pseudoerosion" is more often used with the presence of a site of cervical tissue, covered with the cylindric epithelium, with a transformation zone in various relations. As is known, the transition place for stratified squamous epithelium into the cylindric one has a complex histoarchitectonic. Dysplasias with subsequent malignancy of the cervix occurs most frequently there.

With congenital ectopia the colposcopic picture is characterized by a shift in the cylindric epithelium beyond the limits of the external os. This occurs even during prenatal development, and, as a rule, the transformation zone is not shown.

In the case of acquired ectopia, or pseudoerosion (non-complicated, complicated), the colposcopic picture is characterized by the presence of ectopia with a transformation zone. A combination of ectopia with inflammatory process of the cervix or vagina of any etiology is typical for the complicated form.

The *transformation zone* is understood as the place where the cylindric epithelium is overlapped by the stratified squamous one due to exogenic or endogenic influences. The overlapping process occurs two ways: 1) from the cells of ectopia; 2) from the reserve cells. According to the last researches (by M. I. Kondrikov and co-authors, 1993), the process of planocellular metaplasia in this case can be regarded as physiological *(physiological transformation zone)*.

The atypical transformation zone is characterized by the presence of atypical vascular figures, sites of iodine-negative epithelium, zones of hyperkeratosis, thickening of the gland ducts. With expanded colposcopy, changes are observed, which cause the suspicion of dysplastic processes. To confirm the diagnosis, biopsy of the pathologic changed area of the cervix is conducted for histological verification of the diagnosis.

After examining with the specula, it is possible to suspect a pseudoerosion, which is located usually around of the external os; more often it looks like a spot with incorrect outlines and a colour from bright red to light pink.

With expanded colposcopy, ectopia is possible to find in various combinations with transformation zones. The sites of ectopia represent clustering accumulations of round or oblong papilla with a bright red colour, caused by the exposure of blood vessels through the simple cylindric epithelium. The transformation zone against a background of a bright red surface of ectopia looks like placid pale and grey uvula of the stratified squamous epithelium, thus open and closed glands, as well as a vascular network, especially on the surface of the closed glands, can be observed. For more detailed research of the cervical lesions, colpomicroscopy, which allows investigating the cervical epithelium with magnification of 90 times and more is conducted.

Cytological exam of cervical smears is a very important method used in a complex of diagnostic actions, which supplements the data from the colposcopy and promotes the specification of the diagnosis.

The pathology revealed during the cytological exam is confirmed by data from the histological exam in 92.2% of the cases.

The cytological exam of the smears in the case of ectopia reveals cells of superficial and intermediate types, basal and parabasal cells of the squamous epithelium, as well as cells of the cylindric epithelium are mainly found.

The smears are taken from the vaginal part of the cervix, transformation zone, directly from the surface of the ectopia and the lower third of the cervical canal.

The cytological method should be considered as a screening one, anticipating colposcopy and cervical biopsy.

The basic method of diagnosis of background processes of the cervix is its histological study of the tissue sampling after the performance of cervical biopsy under the control of colposcopy.

During histological study two forms of pseudoerosion are distinguished: 1) glandular; 2) papillary.

Metaplasia of squamous epithelium (planocellular (squamous) metaplasia) and the formation of ***retention (nabothian) cysts.*** Epidermization is a normal physiological process occurring in the cervix. The squamous epithelium moves and "overlaps" the glandular cylindric epithelium of the endocervix (transformation zone). Metaplasia of the squamous epithelium is diagnosed with the help of colposcopy; biopsy is not necessary in this case. The process of planocellular metaplasia results in the overlapping of the ducts of the endocervical glands resulting in the formation of retention (nabothian) cysts. One retention cyst (or more) usually exists on the ectocervix in reproductive age women. Retention cysts vary in size, from 1 mm up to 6 cm; can have a white, yellow, blue or pink colour. They are filled with mucoid secret from the endocervical glands, which is always secreted during a puncture. Vascularization of the cysts quickly increases, which sometimes demands differential diagnosis with cervical cancer. In some cases it is necessary to differentiate nabothian cysts with mesonephral cysts (remnants of the wolffian canals) and cervical endometriosis.

The mesonephral cysts can reach 2.5 cm in diameter, contain the cubic epithelium and are located deeply in the stroma, frequently near the external os. Treatment, as a rule, is not required. Revealing the zones of atypical epithelium with the help of colposcopic examination of the cervix (atypical transformation) demands the conduction of biopsy.

Endocervicitis (cervicitis fig. 43, *e*) is a frequent cervical lesions. The main etiological factors of its development are ectopia of the cylindric epithelium of the endocervix (due to trauma or infection) and postpartum damages to the cervix.

Cervicitis is caused mostly by staphylococci, streptococci and chlamydia. The symptoms of cervicitis can be leucorrhoea (serous-purulent discharge, frequently with an odour), irritation of the vulva and vagina (itching, burning). Pain in the back and the lower abdomen, dyspareunia, dysmenorrhoea, dysuria, postcoital bloody discharge can be observed.

During the acute stage of cervicitis (till 2 days) the cervix is hyperaemic, tender during palpation and excursion, there may be discharge. Mucopurulent discharge, friability and fragility of tissues, increased vascularization, infected glands, and hypertrophy of the cervix are observed at the chronic stage. In doubtful cases, the cervical biopsy is conducted.

Differential diagnosis is conducted with an early stage of neoplastic process, chancre, chancroid, tuberculosis, granuloma.

Etiotrophic therapy is prescribed if pathogenic micro organisms are revealed.

Leukoplakia — dystrophic changes of the mucous membrane in the form of white spots with a nacreous shine, smooth or fine-grained contour (Fig. 43, *b*). With the occurrence of planocellular metaplasia, the red colour of the endocervical tissue turns to white. Any white "spots" on the cervix, visualized by the naked eye without the use of chemical materials (acetic acid), are considered leukoplakia and can be an attribute of serious diseases. With any abnormal picture of the cervix it is necessary to conduct colposcopic and cytological (cervical biopsy) examination of its epithelium. The zone of leukoplakia is subject to biopsy under the control of colposcopy. Histologically, hyperplasia, proliferation of the cells of the basal and intermediate layers of the epithelium, and hyperkeratosis of cells of the superficial layer are revealed. The smears defect keratosic squamous epithelium, and the scrapes taken from the deep sites reveal epithelium with signs of moderate dysplasia.

Leukoplakia is necessary to distinguish from flat condylomas (venereal warts), intraepithelial defects of the cervix — cervical intraepithelial neoplasia (CIN).

Polyp (Fig. 43, *f*). Proliferation of the endocervical tissue can result in the formation of cervical polyps. The primary complaint of patients with cervical polyps are inter-menstrual or postcoital bleeding. The formation of such polyps can be caused by the use of oral contraceptives and pregnancy. Cervical polyps, as a rule, have a small size and seldom reach a diameter of 1–2 cm. A polyp's pedicle has usually a small length; therefore it can be removed easily by cutting or twisting. Histological study of polyps is obligatory.

Cicatricial changes. Damages to the cervix frequently take place while giving birth; can cause strong bleedings and demand stitches immediately after delivery. Invisible submucous separation of the fibrous connective tissue of the cervical stroma at the level of the internal os can result in cervical insufficiency. This condition sometimes is the result of a trauma to the cervix during an abortion, curettage of the uterine cavity. Perforations, circular abruption

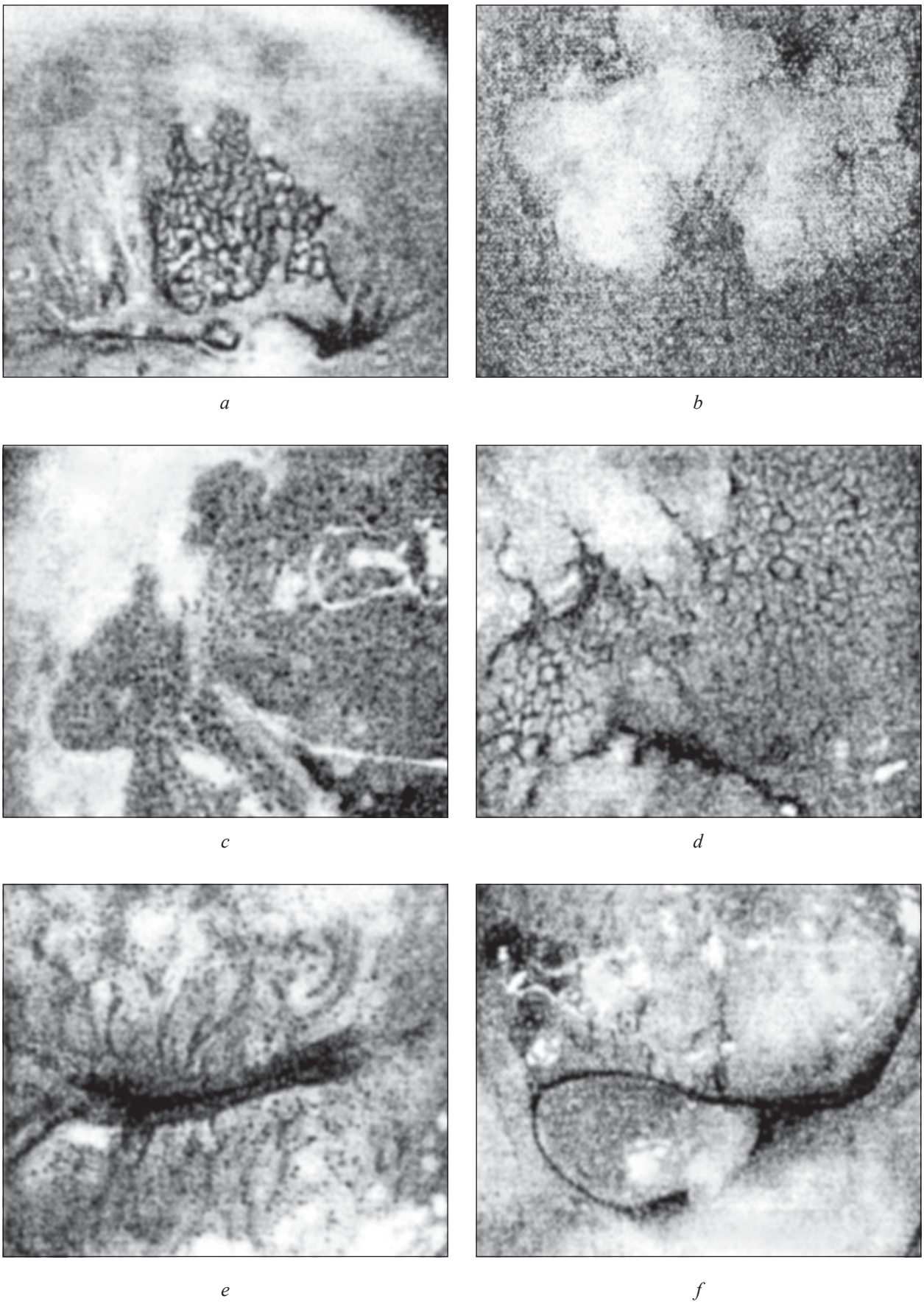


Fig. 43. Colposcopic picture of cervical diseases:
a — ectopia with the transformation zone; *b* — leukoplakia; *c* — stippling of the cervix ("base" of leukoplakia); *d* — mosaic ("field") of the cervix; *e* — colpitis and endocervicitis; *f* — polyp

of the cervix due to severe dystocia also represent damages to the cervix.

Cervical stenosis can have hereditary, inflammatory, neoplastic or, more often, iatrogenic (postoperative) origin (due to conization, electrocoagulation of the cervix; very seldom — laser vaporization or cryocoagulation). Its display can be dysmenorrhoea; in the case of complete occlusion — hematometry. Treatment consists of gentle dilation of the cervix.

Precancerous processes of the cervix are epithelial dysplasias of various degree, leukoplakia with displays of epithelial atypia and adenomatosis. Epithelial dysplasia is 15–18% of the total pathologic processes of the cervix.

Epithelial dysplasia of mild, moderate and severe (expressed) degrees are distinguished depending on the course of the pathologic process. Cytological examination of the smears is conducted by the Papanicolaou's method. For all the types of dysplasia (precancer), proliferation of the epithelial cells at various levels, however, without invasion into the stroma is typical. The absence of invasion and therefore metastatic potential enables conservative treatment to be conducted opposite to invasion defects.

In modern literature for the classification of epithelial defects of the cervix the term "cervical intraepithelial neoplasia" (CIN) is used to determine the pathologic changes of the stratified squamous epithelium depending on the expressiveness of microscopic changes.

Mild dysplasia corresponds to CIN I, moderate — CIN II, severe dysplasia and preinvasive cancer (carcinoma *in situ*) — CIN III.

The distribution of CIN (or dysplasia) into degrees is based on the frequency of their progressing into invasive cancer (with the absence of treatment). The frequency of progressing into invasive carcinoma for CIN I is 10%, for CIN III — 30%.

Pathohystology. *Mild dysplasia (CIN I)* is characterized by moderate proliferation of epithelial cells of the basal and parabasal layers, while the cells of the top epithelial layer have no attributes of atypia, remain mature and differentiated. 1/3 of the cervical epithelium is affected.

Moderate dysplasia (CIN II) is accompanied by defects of the lower half of the epithelial layer (1/2 to 2/3 of the epithelium).

Severe dysplasia (CIN III, carcinoma in situ) is characterized by significant proliferation of cells of the basal and parabasal layers, occurrence of hyperchromatic cells in epithelium, disorder of the nuclei- cytoplasmic ratio to an increase of the nucleus of cells. The whole epithelial layer is affected.

The cytopathic effect of viruses, in particular human papilloma virus, — coilocytic atypia, differs from cytological changes with CIN, though they are frequently combined.

The basal membrane with all the variants of CIN remains intact, i.e. invasion of the underlying stroma is absent.

Clinical picture and diagnosis. Patients with epithelial dysplasia, as a rule, do not have complaints. Bloody discharge from the genital tract, leucorrhoea, pain in the lower abdomen and lumbar area are occasionally possible. During visual examination of the cervix, attributes of ectopia, ectropion, hypertrophies or leukoplakia can be found. The patients are asked about previous gynaecologic diseases, their duration, especially with the cervical affection, as well as about the previous examinations, conservative and surgical treatment and its results, relapses of the disease.

The complex of examination includes expanded colposcopy, cytological, histological studyes, as well as the study concerning the basic kinds of sexually transmitted diseases, and also determining the condition of the endocrine (ovarian function) and immune systems.

The most exact *screening-diagnosis* of preinvasive and early invasive cervical lesions is achieved by cytological research of Papanicolaou's smears (accuracy of diagnosis — 85%). The smears are taken separately from the ecto- and endocervix with the help of special spattles, making an 360° arch, and fixating in an alcoholic solution. Erroneous negative results of cytological research are possible in 10–20% of the cases in connection with poor-quality taking of the smear or mistakes during cytological research. During research of the Pap smears atypia can be found, but not dysplasia (in case of accompanying vaginitis, cervicitis, and papilloma virus infection). With the absence of clinically expressed inflammation the patients are subject to further examination (colposcopy, biopsy).

Cytological research of the Pap smears is only screening, the final diagnosis is established during histological evaluation of the sample material. With the presence of visual cervical defects, a biopsy is necessary in all instances, irregardless of the cytological picture of the smear.

Complex examination of the cervix with abnormal cellular morphology of the Pap smears provides the use of such methods:

1) Simple and expanded colposcopy.

2) Cervical biopsy.

3) Curettage of the mucous membrane of the cervical canal (endocervical curettage).

4) A cone-shaped cervical biopsy.

Expanded colposcopy (cervicoscopy) with the use of the Schiller's test (determining the iodine-negative zones on the cervix by rubbing its vaginal part with Lugol's iodine solution) and tests with acetic acid have great value in revealing pathological changes on the cervix. Colposcopy gives an opportunity to identify the zones of changed epithelium, determine the sizes of the injury, to perform a target

multifocal biopsy if necessary. Colposcopy is recommended in all cases of doubtful concerning CIN cytological picture or with the detection of atypical non-inflammatory changes in the cervical epithelium.

Till now our country uses the classifications of pathological conditions of the cervix, suggested by L. M. Vasilevska, I. A. Yakovleva, B. G. Kukute and other authors more than 20 years ago, the terminology of which differs a little bit from generally accepted ones in the majority of the countries of the world. In the opinion of leading experts (V. M. Prilepska and co-authors, 1998, E. V. Kokhanevich and co-authors, 1998), the creation of a uniform information space in modern conditions induces to the necessity of transition to the unified international colposcopic terminology accepted in 1990 at the VII World Congress on Cervical Pathology and Colposcopy in Rome.

According to the international colposcopic terminology, the **normal colposcopic pictures** has the following signs:

1) Original squamous epithelium.

2) Cylindric epithelium.

3) Normal transformation zone.

The following changes are associated with the **pathologic colposcopic picture** both in the transformation zone, and outside its limits (vagina, exocervix):

1) *White (acetowhite) epithelium:* a) squamous; b) micropapillary.

2) *Punctate* (placid and coarse).

3) *Mosaicism* (placid and coarse).

4) *Leukoplakia* (fine and dense).

5) Iodine-*negative zone.*

6) Atypical *vessels.*

Other kinds of colposcopic picture are allocated separately:

1) *Suspicion for invasive carcinoma.*

2) *Unsatisfactory colposcopy* (the border of different types of epithelium is not visualized, expressed inflammation or atrophy).

3) *Mixed picture* (not white micropapillary surface, exophytic condyloma, inflammation, atrophy, ulcer, etc.).

Original squamous epithelium (squamous — flake, i.e. shelling off epithelium) corresponds to the term "stratified squamous epithelium" (SSE) — fine, practically colourless, without vessels, consists of four lines of cells, covers the vagina and vaginal part of the cervix. As a result of processing with acetic acid the whole mucous membrane becomes evenly pale, and the Lugol's iodine solution makes it even dark brown. Vascular figure of the stroma normally is placid, with lengthened branches like a net, trees with branches, brushes.

The test with a 3% solution of acetic acid. The acetic acid removes the superficial mucous and reveals the atypical sites on the epithelial surface. Due to temporary coagulation of fibres and intercellular dehydration, cellular hypostasis, reduction of subepithelial vessels, anaemization of tissue, changes in colour occur. This test is an important key stage of expanded colposcopy because it ensues maximum information on the condition of the epithelium. It assists in precise differentiation of SSE and cylindric epithelium (CE). The effect lasts from 1 up to 5 min, if needed additional application is conducted.

The Lugol's iodine solution test (iodine — 1 g, iodide potassium — 2–4 g, distilled water — 300 g). Under the action of the solution, the cells of the superficial layer of the epithelium, containing lots of glycogen which binds with iodine, are coloured, turning dark brown. The changed tissue is coloured by the Lugol's iodine solution with various intensity, depending on the type of damage, extent of tissue keratinisation.

Cylindric epithelium (CE) normally covers the surface of the endocervix, consists of one line of high cylindric cells, secreting mucous. During colposcopy, CE looks like a reddish papillary surface, it is more precisely shown after processing with the acetic acid, and it is not practically coloured with the Lugol's iodine solution.

The normal transformation zone (NTZ), or transformation zone (TZ), occurs during the overlapping of the CE zone by the squamous epithelium and is located in the joint area (area of junction) of different types of epithelium and the natural SSE. In women of the reproductive age normally this joint is located in the area of the external os. The transformation zone is characterized by the presence of metaplastic epithelium, open and closed (retention, or nabothian, cysts) endocervical glands, island of CE, has indistinct contours (see fig. 43, *a*).

Squamous metaplasia is a normal physiological process during which the CE is overlapped by the SSE, which depends on a number of factors (hormonal stimulation, vaginal pH, infections, etc.). Metaplastic epithelium is histologically immature (partial differentiated) squamous epithelium, covered by CE, cells of which gradually degenerate. Colposcopically in the limits of the TZ, filmy epithelium, having sometimes open and closed glands, indistinct contours and poorly coloured with the Lugol's iodine solution (depending on the degree of a maturity) is found. Squamous metaplasia can cause the presence of different types of epithelium, therefore cervical neoplasia develops in the TZ in 90% of the cases.

Open glands (OG). Cylindric epithelium of the cervical canal has no true glands, its basic elements are cracks and excavations (crypts) — pseudoglands; their cells secrete mucus. Due to the regeneration of tissue there is an overlapping of the pseudoglands and for some time they remain open. During colposcopy the open glands look like dotted oval apertures with precise contours.

Closed glands (CG), or retention (nabothian) cysts, are formed with another type of metaplasia: the external aperture of the pseudogland is closed, secret starts to accumulate, which stretches the glands, causing vessels dilation and perifocal inflammation.

Keratinous glands. Endocervical crypts can be replaced by metaplastic immature, atypical or mature SSE, thus at times fillet of keratinisation are formed, located around the aperture of the excreting duct of the gland. During morphological research of such zones quite often dysplasia, intraepithelial carcinoma or invasive cancer are found.

Atypical vessels. Malignant processes, as a rule, are accompanied by the proliferation of blood vessels and change in their structure. The short vessels in the form of various formations (pin, corkscrew, comma, etc.), different density, with sharp gradation, which does not disappear after processing with acetic acid are considered atypical.

White (acetowhite) epithelium are zones of whitening after the use of vinegar, they should not be confused with leukoplakia. The epithelium with a defective structure, that quite often is associated with dysplasia, can become white.

Iodine-negative epithelium. Quite often, only the Lugol's iodine solution test can reveal pathologically changed epithelium, which is not raised above the surface of the underlying tissues, has precise edges — so-called mute iodine-negative zones (as a rule, zones of epithelial keratinisation).

Leukoplakia (see fig. 43, *b*) — colposcopically it is a white spot with clear contours on the cervical epithelium, quite often visible with the naked eye before conducting expanded colposcopy; it can be raised above the surface of SSE or be on the same level with it. The condition of the tissue under the keratous layer of superficial cells is impossible to determine, therefore, a biopsy is obligatory for revealing leukoplakia.

Stippling corresponds to the former term "basis of leukoplakia"; the "basis" is a show of atypical vascularization of the epithelium (see fig. 43, *a*). During colposcopy, numerous reddish dots on a limited area of the epithelium are found. Fine, evenly located, identical (light stippling), testify to the mild degree of dysplasia; and the relief, large, non-uniformly located dots, becoming clear after being processed by acetic acid (stippling) correspond to the expressed degree of dysplasia.

Mosaicism (see fig. 43, *d*) corresponds to an earlier accepted term of "field", "pagonization". During colposcopy before acetic acid applications, it is possible to reveal a non-specific picture, resembling one of the vascularization zones in the TZ, on which open and closed glands are absent. After the test with acetic acid, the picture and borders of the mosaicism become more precise, look like a grid consisting of pale and red lines. The coarse mosaicism is characterized by unequal in size and form islands, more raised sulci of red colour. After the application of acetic acid, sometimes the course mosaicism sharply transforms to the side of displaying the formations, as opposed to the mild forms of stippling and mosaicism which don't undergo such changes.

Atypical transformation zone (ATZ) allows the presence of typical (normal) TZ as the basic component, as well as such signs, as atypical vessels, keratous glands, acetowhite epithelium, leukoplakia, mosaicism, stippling, iodine-negative epithelium, testifying that the epithelium has obtained an atypical character. In connection with this it is considered that cervical intraepithelial neoplasia always develops in the zone of ATZ during the metaplasia process. However, the occurrence of foci of dyskeratosis can occur and against a background of normal SSE. It is established also that viruses can damage the natural SSE, thus the changes in the epithelium are shown as leukoplakia, mosaicism and stippling. Therefore, a majority of researchers now believe that in the case of revealing the classical picture of acetowhite epithelium, leukoplakia, stippling and mosaicisms it is more expedient to include them in the colposcopic conclusion as the diagnosis with separate attributes as in the modern classification of colposcopic pictures the term ATZ is not used though practically it is widely applied.

The colposcopic picture of ATZ looks like and is described differently depending on the presence of CE, thin metaplastic epithelium, iodine-negative changes in the zones of keratinising surface, mosaicism, stippling, open, closed and keratous glands, vascular figures and their combinations. The above-listed attributes can be mild or promoted. The histological basis of ATZ depends on the presence, character and sizes of atypia of the epithelium. CIN of different degrees, cellular and nuclear atypia, differentiation and maturing disorders of cells, attributes of proliferation, etc. can be found. The proliferated cells can occupy 1/3, 2/3 and more volume of SSE, that accordingly is determined as CIN of the I, II, III degrees.

Colposcopic suspicion for invasive carcinoma allows the presence of signs of AZT with plus-tissue, ulcers, etc.

Mixed colposcopic picture includes various displays, which quite often are difficult to precisely classify and treat. The following ones are most often observed.

Exophytic condyloma serves as a display of papillomavirus infection, as a rule, projecting above the surface of the mucous membrane, has a thin leg, less often — wide light pink or red basis. A condyloma can be thin, high, single or like a cauliflower or crests. On the cervix, fine condylomata can obtain a nacreous shine after the test with acetic acid that allows differentiating them with CE.

Inflammation (diffuse and local) can effectively complicate the management of colposcopic pictures.

Having removed the discharge, it is possible to see fuzzy indistinct dots, reddish spots due to the dilation of capillaries, which after the tests with acetic acid turn white. After processing with the Lugol's iodine solution the picture becomes dotted, indistinct contours of the inflammation foci (see fig. 43, *b*) are observed.

Atrophy, as a rule, is the result of oestrogen insufficiency. It frequently occurs after menopause *(atrophic vaginitis)*. The epithelium is thin, easily injured, unevenly coloured by the Lugol's iodine solution.

Ulcer (true erosion) is a local defect of the epithelium. Typical attributes of erosion — intensive red colour, "unfolded" edges. The fundus of the ulcer is the stromal layer of the epithelium. Stroma is iodine-negative. The surface of the erosion is flat, but it can be granular, covered with fibrinous exudate. The ulcer frequently occurs against a background of epithelial atrophy and has a traumatic character. True erosion is not observed in women in the reproductive period; it should be differentiated with cervical carcinoma by taking a biopsy.

Endometriosis. Endometriodal heterotopias colposcopically can look like a blue cyst, linear and dotted bleeding zones.

Polyp of the cervix — outgrowth of stroma, covered with cylindric epithelium with focal proliferation of the endocervix. Polyps can be single or multiple, project into the canal or beyond the limits of the external os (see fig. 43, *f*). During colposcopy, the condition of the polyp surface is evaluated. It can be covered only by CE and have a typical aciniform surface, as well as stratified squamous epithelium, including immature or atypical.

The term *adenosis* means the presence of CE sites on vaginal epithelium.

If full visualization of the transformation zone (the transformation zone between squamous and cylindric epithelium) is impossible, the results of colposcopy are considered unsatisfactory. With the presence of abnormal cytology data, cone-shaped biopsy (diagnostic conization) of the cervix is necessary for patients.

Curettage of the mucous membrane of the cervical canal (endocervical curettage) is conducted to exam the epithelium of the cervical canal not visible during colposcopy or in case of defects revealed visually. The cone-shaped cervical biopsy is recommended with the revealing of abnormal cytological picture.

Cone-shaped biopsy (conization) consists of the surgical removal of the area of the cervix containing the transformation zone ("risk zone"). This procedure can be conducted with diagnostic and medical purposes. Indications to cone-shaped cervical biopsy are the following:

1) the absence of visualization of the defective zone during colposcopy with the presence of abnormal cytological data;

2) unsatisfactory results of the colposcopy with suspicious data from the colposcopy or cytological study in relation to CIN;

3) revealing of CIN during exam of the material received as a result of curettage of the mucous membrane of the cervical canal;

4) disagreement in the data of the cytological and histological studies of the material taken during biopsy;

5) suspicion of invasive, microinvasive or adenocarcinoma *"in situ"* in the material taken during biopsy.

With abnormal data from the cytological exam of the cervical material in pregnant women it is necessary to conduct a complete examination in minimal modification. The performance of colposcopy during pregnancy is simplified due to the physiological ectropion of the transformation zone between the squamous and cylindric epithelium. Bleeding during biopsy is stopped by using tampon or, as a last resort, stitches. Endocervical curettage is not conducted because of the risk of bleeding. The cone-shaped biopsy of pregnant women is conducted only in case when there is suspicion of invasive cancer in connection with the large (15–30%) risk of bleeding, spontaneous abortion or premature birth.

Natural delivery is contraindicated for pregnant women with a histological confirmed diagnosis of CIN. Treatment begins after the delivery (in connection with the slow progressing of intraepithelial defects of the cervix immediate intervention during pregnancy is not required).

While conducting bimanual vaginal and rectovaginal examination, the form and consistence of the cervix and uterus, ovaries, their interrelation with other pelvic organs are determined.

Histological study plays an important role in establishing the diagnosis of cervical precancer.

Treatment. There are various methods of therapy of patients with background and precancer cervical lesions: medicamentous, electrosurgical, cryogenic and laser influence, surgical treatment.

The era of diagnosis and treatment of cervical pathologies began in 1924 when Hinselmann invented the first colposcope. During the past period, the notions about pathological processes developing in the cervical epithelium repeatedly change, and new ways of treatment were offered. Now, lots of experience have accumulated and remote results of application of various ways of treatment of cervical diseases are investigated.

So, today it is considered that medical actions amid background processes of the cervix should be directed on the liquidation of accompanying inflammatory processes in the cervix and vagina, stimulation of regeneration of stratified squamous epithelium and the removal of pathologically changed tissue in the cervix.

Accompanying diseases — vaginitis and cervicitis play an important role in the persistence of pseudoero-

sion, because the cytological picture changes and high-class examination and treatment can not be conducted.

With the complicated pseudoerosion and accompanying inflammatory changes in the cervix, it is necessary to reveal the activators of the disease, and then conduct etiopathogenic therapy.

In the complex treatment of patients with inflammatory processes of the cervix and vagina, the use of *biological preparations* containing lactobacillin (tampons with bifidumbacterium — 5 doses, lactobacterium — 6 doses, "Narine", vaginal suppositories "Vagilak", etc.) to normalize the local micro flora is recommended. The tampon is entered into the vagina and left for 2 h 3–4 times a day, the suppositories — for the night.

Preparations with coagulative action, especially vagotil, earlier were widely used. However, they have no specificity to the pathologically changed epithelium, and during coagulation also damage the normal stratified squamous epithelium of the vagina. Coagulation with vagotil is very superficial, requires multiple applications (up to 8–12), which promotes damage to the vaginal epithelium, and cuticularization of the coagulative zones takes a long time. All this results in the development of secondary complications (leukoplakia at the place of coagulation, multiple cysts).

The advantages of *medicamentous means* of treatment of patients with background processes of the cervix are the simplicity of their application, absence of need in usage of expensive equipment. One of the new effective preparations for local treatment of patients with benign processes of the cervix by chemical coagulation is solcovagin, or solcogin (mixture of acids, having tropism to cylindric epithelium) which has no side-effects and does not cause complications. The depth of the coagulative action of the preparation reaches 2.5 mm, therefore it is expedient to use for pseudoerosion, retention (nabothian) cysts after their opening, postoperative granuloma, small polyps in the cervical canal. Contraindications to the use of the preparation are CIN and malignant transformation of the cervix.

Before using solcovagin, the cervix is cleared of mucous with a tampon, with the help of the test with acetic acid, the defective borders are determined. As a result of the use of solcovagin a white or yellow scab is immediately formed in the area of the lesion. In 2–3 min to increase the depth of penetration of the preparation into the pathological zone, the solcovagin application on the scab is repeated. Bloodless and painless tearing away of the scab takes place on the 3rd–5th day. The cuticularization of "young" stratified squamous epithelium lasts till the 9th day after coagulation. If during the control colposcopy on the 9th–10th day after coagulation, partial cuticularization is found, repeated application is conducted on the uncuticularizated sites. 14 days after that the patient is examined again and with the absence of cuticularization a 3rd and 4th application is conducted. However, if there is no effect from treatment after the 3rd application, the 4th application is useless.

The presence of inflammation in the stroma of the exo- and endocervix can interfere with the effective treatment of patients with solcovagin. In this case, for the regeneration of the stratified squamous epithelium while using solcovagin locally, the use of low-intensity helium-neon laser (7–10 sessions), high-frequency ultrasound, is recommended.

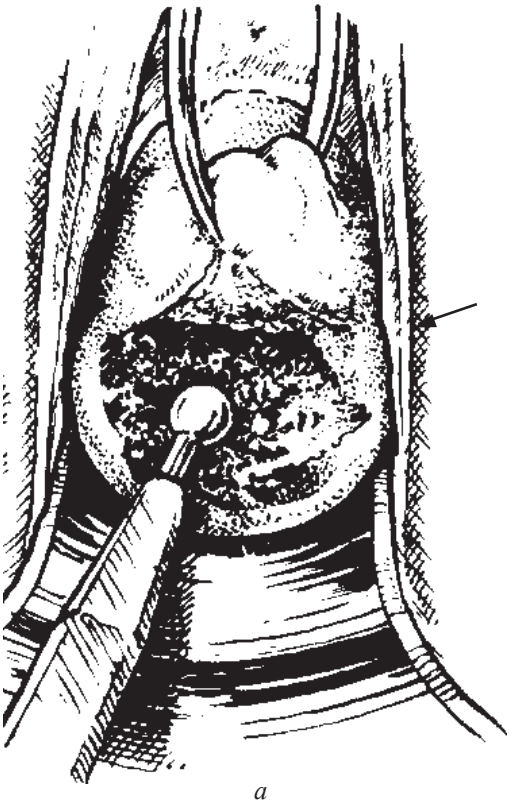
Today, the point of view that with uncomplicated pseudoerosion in young women who have not given birth the use of local therapy is not essential is controversal. Such patients should only be under constant medical supervision with colposcopy and cytological exam every 6 months. The cuticularization of pseudoerosion in young women is promoted by the use of three-phase oral contraceptives.

The basis for *diathermocoagulation,* offered for the first time in 1926, is the use of high-frequency current, causing thermal fusion of tissue, thus, the electric circuit includes a person's organism and heat generation occurs in the tissue of the cervix.

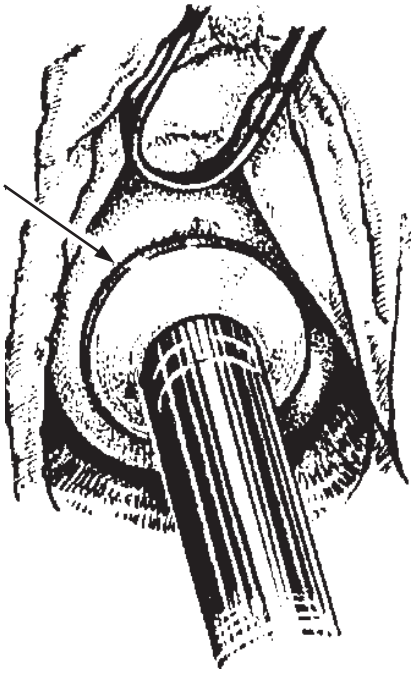
Complications during diathermocoagulation, including the tearing away of the scab, can be bleeding which demands surgical intervention. Late complications can be stricture, stenoses of the cervical canal, implantation endometriosis, infertility (due to the disorder of the anatomic-functional integrity of the cervix), isthmic-cervical insufficiency, spontaneous abortion, premature birth, dystocia of the cervix during delivery. In connection with this the given method can be considered inacceptable for the treatment of young women who have not given birth yet. While treating women of the reproductive age, it is also necessary to consider the possibility of the development of complications. Diathermocoagulation is basically used to treat patients with CIN (Fig. 44, *a*).

To prevent complications after diathermocoagulation on the cervix (endometriosis, bleeding, stricture of the cervical canal) it is necessary to conduct treatment in the I phase of the menstrual cycle and only after the liquidation of inflammatory processes. For this purpose syringing with decoction of camomile, sage, eucalyptus leaves with subsequent introduction of antiseptic suppositories into the vagina are recommended. Diathermocoagulation of benign processes on the cervix is better to conduct with the help of bio-active electrodes. Diathermosurgical intervention is recommended with the use of the electroknife EK-57 or EK-57a.

The effectiveness of treatment in many respects depends on its adequacy after diathermocoagulation. Immediately after electromanipulation it is necessary to put a gauze tampon moistened with an antiseptic cream on the cervix for some time. In 3 weeks it is possible to recommend syringing with the subsequent use of vaginal suppositories. Repeated examination



a



b

Fig. 44. Diathermocoagulation *(a)* and cryolysis *(b)* during cervical diseases

of the patient is conducted in 4–5 weeks. Sexual contact is not recommended until complete cuticularization of the cervix.

Today, the most acceptable method of treatment of patients with background and precancerous cervical lesions is *cryotherapy* (cryolysis), with the help of low temperatures achieving a high therapeutic effect.

Liquid gases are used as cold agents: nitrogen (boiling temperature –196°C), nitrogen oxide (–89°C) and carbon dioxide (–78°C). Cryoprobes of various forms, selected according to the sizes of the pathological area, are used to process the surface of the vaginal part of the cervix. The cryoprobe is selected so that it blocks the whole pathological area on the cervix (Fig. 44, *b*). Freezing is carried out until a fillet of hoarfrost with a width of 2–2.5 mm is formed around the tip, consequently a part of the cervical canal is exposed to the processing.

Advantages of this method are the painlessness of intervention, which is explained by the fast destruction of nerve endings under the action of cooling, the manipulation does not cause bleeding and an opportunity to use it in out-patient conditions, as well as immune-modulating action. Cryotherapy does not cause sclerosis of the connective tissue, does not deform the cervix, and does not negatively influence the process of cervical dilation during birth.

Disadvantages of the method are the small depth of influence, impossibility of local removal of the pathological area with minimal trauma to the underlying tissue, rather high rate of relapses (up to 20%); 13% of the patients are very likely to develop the coagulated cervical syndrome. Cryosurgical therapy is not always effective in patients with leukoplakia, therefore *laser-coagulation* is preferable in such cases.

One of the most effective methods of treatment of patients with cervical pathologies is *laser vaporization* with the help of CO_2-lasers (Fig. 45), which provide the evaporation of the defective tissue at the right depth under the control of colposcopy, and thus, without damaging the underlying tissue. Therefore, practically no scab is formed and the healing process further occurs without the formation of cicatricial tissue.

Laser vaporization can be effectively used for all cervical diseases. However, a drawback of this method is the frequent development of postcoagulation endometriosis. To decrease the risk of endometriosis development, laser vaporization against a background of monophase oral contraceptives for 3 months, which sharply reduces the occurrence of endometriosis, is recommended. Besides, the given method demands the presence of expensive equipment, specially equipped cabinets and highly skilled personnel.

With the presence of pseudoerosion in patients with menstrual disorders, its correction is initially conducted with gestagen preparations (norcolut, primolut-nor, dufastone, utrojestan), which patients should take the 16th through the 25th day of the cycle by 1 tablet a day for 3–4 months under dynamic colposcopic control; afterwards cryosurgical treatment or laser vaporization is conducted.

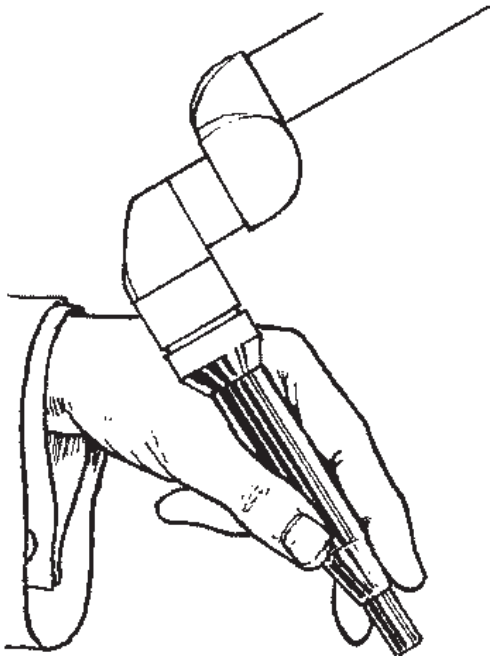


Fig. 45. CO_2-laser

In case of disorder of the cervical architectonics (e.g. its deformation in combination with pseudoerosion) cryolysis, diathermocoagulation, laser coagulation, surgical treatment are conducted. Posttraumatic ectopia of the cylindric epithelium and benign transformation zone are subject to diathermocoagulation, and with the presence of large ectropion, scars and ruptures — diathermic excision, diathermoconization, corrected diathermopuncture or plastic operations on the cervix (Sturmdorf's or Emmet's operation).

Monotherapy of patients with benign cervical diseases with antibacterial preparations improving regeneration (methyl-uracil ointment, oil of sea-buckthorn berries or dogrose), and such coagulative means as silver nitrate, Gordeyev's liquid and vagotil, are considered inexpedient today due to its low efficiency and danger of development of numerous complications. The most effective methods of treatment, causing a small amount of complications, are cryolysis, laser vaporization and the use of solcovagin.

Diathermosurgical methods, conization (Fig. 46), knife amputation of an organ, cryolysis of the defective areas, the influence of laser (CO_2-laser) radiation are used for the treatment of patients with epithelial dysplasia and preinvasive carcinomas of the cervix.

Clinical management of patients after treatment concerning background processes is recommended for 1 year, and with their combination with dysplasia — for 2 years with control cytological and colposcopic studies every 3 months.

Prevention of cervical diseases consists of duly treatment of inflammatory diseases of the genitalia, correction of menstrual disorders, rational conducting of birth, prevention of abortions, use of oral contraceptives, with correct tactics of conducting patients with the use of screening technologies.

ENDOMETRIAL HYPERPLASIA

Endometrial hyperplasia are hyperplasia and polyps.

In domestic literature the classification according to which the following endometrial hyperplasia are distinguished is frequently used:

a) glandular hyperplasia;
b) glandular-cystic hyperplasia;
c) atypical hyperplasia (adenomatosis);
d) polyp.

The classification of endometrial hyperplasia, accepted by the World Health Organization (WHO), differs a bit from the domestic one. So, according to the international classification of endometrial hyperplasia, the following kinds are distinguished:

a) cystic (simple);
b) adenomatous (complex);
c) atypical (simple and complex).

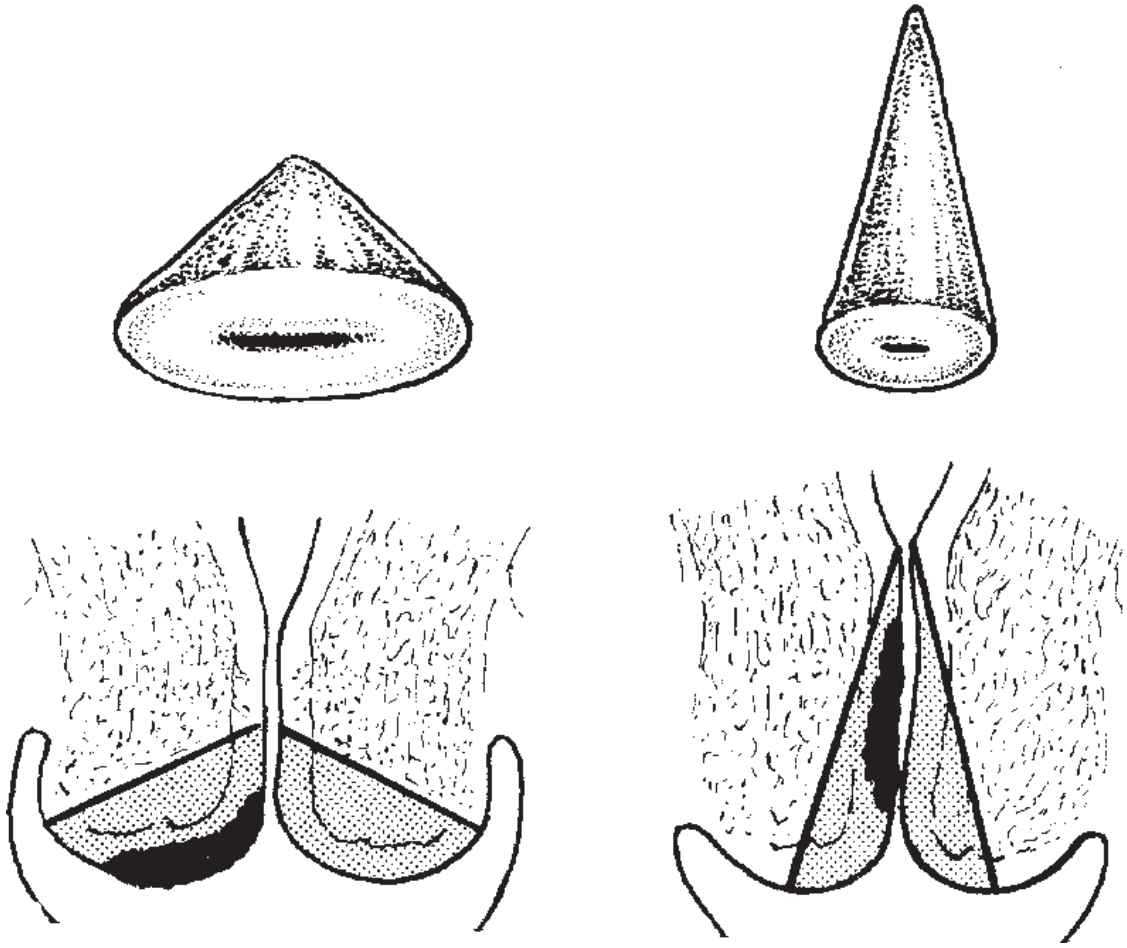
Endometrial hyperplasia can be revealed in different extent and have a character of a precancerous disease.

Background processes of the endometrium are glandular, glandular-cystic endometrial hyperplasia (cystic and adenomatous, by the classification of the WHO) and polyp (Ya. V. Bokhman, 1989).

Precancerous process is atypical endometrial hyperplasia.

Polyp (Fig. 47) is the second most frequent (after hyperplasia) benign formation of the endometrium. Polyps frequently occur in women between the ages of 29–59, with a peak of morbidity after 50 years. The frequency of asymptomatic polyps in women after menopause is about 10%. The genesis of these structures is unknown. The diagnosis of a polyp is more "architectural" than histological. The polyp grows by the stretching of tissue and forms a pedicle. Histologically, the endometrial polyp has a central stromal element and is supplied with blood from the peripheral sections of the endometrium. A polyp's pedicle can be thick and short or long and thin, which sometimes results in a prolapse of the polyps through the external os of the cervix, like the prolapse of the submucous leiomyoma. Polyps can have a spheroid or cylindric form, single or multiple. A small polyp, as a rule, is asymptomatic while a large one can cause abnormal bleedings, squeezing of the adjoining endometrium. A small polyp can be subject to ulcerization and degeneration.

The polyp's tissue can react to hormonal stimulation exactly like the normal endometrium. Moreover, the endometrial component of some polyps reacts only to oestrogen, resulting in their hyperplasia,



a *b*

Fig. 46. Cone-shaped biopsy (conization of the cervix):
a — at the reproductive period; *b* — at the premenopausal period

opposite of the adjoining normal endometrium. The polyp inadequately reacts to hormonal influences (endocrine autonomy), which is frequently connected with the occurrence of bleedings in different days and phases of the menstrual cycle (intermenstrual bleedings), similar to anovulatory menstruations. However, unlike the latter, the menstrual cycles with the presence of a polyp and leiomyoma, as a rule, are ovulatory.

Hormone therapy is not recommended, because it does not solve the problem. Surgical treatment is conducted to correct the symptoms of the disease. The method (V. M. Zaporozhan, A. V. Hait) of cryosurgical processings of the polyp's bed, the use of which results in the normalization of the oestrogen-receptor device of the endometrium and prevents relapses of the polyp in 90% of cases, was offered.

Endometrial hyperplasia, more often than the endometrial polyp, can with time progress till the formation of adenocarcinoma of the endometrium.

Etiology, pathogenesis, pathomorphology. Endometrial hyperplasia morphologically is characterized by the proliferative endometrial response to

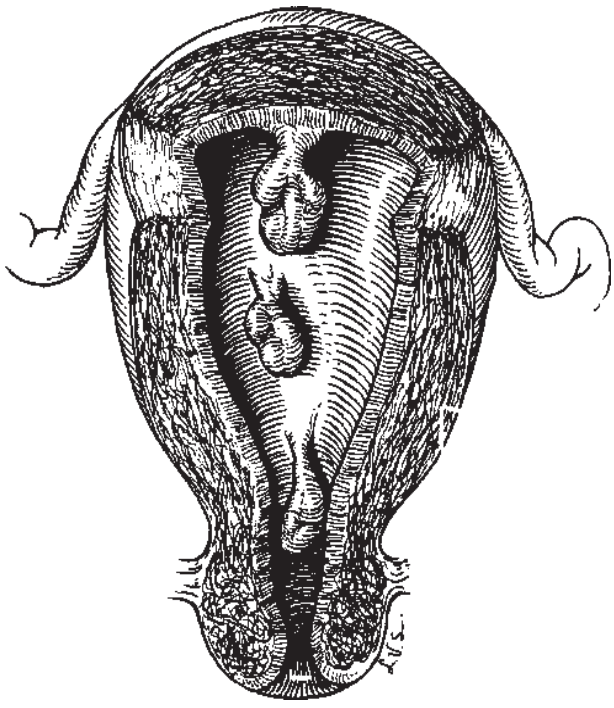


Fig. 47. Endometrial polyps

the stimulation by endogenic and exogenic oestrogens.

The concentration of receptors to oestrogen and progesterone in the normal endometrium varies during the menstrual cycle, which corresponds to the changes in the levels of these hormones in blood plasma. Due to endometrial hyperplasia, the amount of receptors to oestrogen and progesterone, as a rule, increases, while with the development of endometrial carcinoma the amount of receptors decreases. So, according to the literature data, the oestrogen receptors have been revealed in 93% of cases with endometrial hyperplasia and in 79% — with endometrial adenocarcinoma; progesterone receptors were found in 73% and 56% of cases accordingly.

Glandular and glandular-cystic endometrial hyperplasia, in fact, are uniform processes with a various degree of expressiveness. The difference between these kinds of hyperplasia consists of the presence of cystic expanded glands with the glandular-cystic form of pathology and the absence of cysts with the simple glandular hyperplasia. In connection with this, it is considered, that the basic differences between glandular and glandular-cystic hyperplasia do not exist.

Simple and complex endometrial hyperplasia occurs frequently enough and is connected with physiological anovulation before menarche and in the premenopause period when the production of progesterone is reduced or is absent. Endometrial hyperplasia can also be connected with the presence of oestrogen-producing ovarian tumours (thecoma, granulose-thecacellular tumour), polycystic ovarian syndrome and hyperplasia of the cortex of the adrenal glands. Simple and complex endometrial hyperplasia has no atypical attributes, and their differentiation is based only on structural features. Therefore, such kinds of endometrial hyperplasia are not precancerous diseases. The risk for potential malignancy of simple and complex endometrial hyperplasia varies from 1 up to 4%. The cyclic introduction of progestin is effective in patients with such conditions as a rule.

However, with the presence of atypical cytological attributes (atypical hyperplasia) the malignancy potential of endometrial hyperplasia in women in the postmenstrual period, if treatment is not conducted, increases up to 23% (Table 9).

Because the process of malignant transformation can last some years, some pathologists classify sever atypical hyperplasia as carcinoma of the endometrium *in situ*.

Metaplasia of the endometrium is observed in several histological variants:

1) planocellular;
2) ciliocellular;
3) mucinous;
4) eosinophilic;
5) lightcellular;
6) papillary.

Endometrial metaplasia is a benign change in the tissue and, as a rule, does not demand treatment. With the occurrence of atypical attributes endometrial metaplasia is classified as atypical with the definition of its type.

Clinical picture and diagnosis. The main symptom for endometrial hyperplasia is dysfunctional uterine bleedings; the exact diagnosis is established on the basis of the results from the histological study of the endometrium after fractional curettage of the mucous membrane of the uterus and cervical canal. For biopsy and control over the complete removal of the changed endometrium the method of choice is *hysteroscopy,* conducted before and after curettage. Hysteroscopy is the optimum method of dynamic supervision of the patient and determining the efficiency of the therapy. If during biopsy of the endometrium hyperplasia with atypical attributes is revealed, it is necessary to conduct fractional curettage of the cervical canal and uterine cavity with subsequent histological study to exclude the possible diagnosis of invasive carcinoma.

A *transvaginal ultrasonography* serves as a supplementary method for determining the location of changes in the endometrium. Typical ultrasonographic attributes of endometrial hyperplasia are the nonuniformity of the structure, the presence of hypo- and hyperexogenic inclusions, increase in the thickness of the endometrium up to 15 mm and more.

Observing and treatment of patients depends on their age and histological features of the endometrial hyperplasia. The presence or absence of cytological atypia of the hyperplastic endometrium is a major criterion in choosing the method of treatment, which should be individualized and depends on the patient's age and her desire to keep the reproductive function. Endometrial hyperplasia is frequently combined with anovulatory cycles. It is considered, that voluntary regression can occur in almost 80% of cases of hyperplasia without atypia and up to 60% of cases with the presence of atypical hyperplasia (Hustin, 1976; Lucas, Yen, 1979).

Endometrial hyperplasia without atypical changes found in teenagers and women in the premenopausal period easely reacts to cyclic hormonal suppression with progestin, but such patients should have a control serial biopsy of the endometrium. Repeating episodes of uterine bleedings in women over 40 years of age, their tolerance to hormone therapy can cause a necessity of hysterectomy.

Treatment of women of the age of 40–50 with atypical endometrial hyperplasia can begin with suppression with progestin under the control of the repeated biopsy down to the liquidation of the process. In case of tolerance to hormone therapy hysterectomy is recommended. In women with

Table 9. **Malignancy potential of endometrial hyperplasia**

Hyperplastic process	Features	Malignancy risk
Metaplasia	Replacement of usual glandular cells for ciliary; eosinophilia of the cytoplasm, squamous metaplasia or mucinous differentiation	Insignificant or absent
Cystic (simple) hyperplasia	Unequal degree of increase of glandular cells	1–3% in 15 years
Adenomatous (complex) hyperplasia	Glandular cells are compactly arranged, increased, with pappilary growths, small stratification; some of the cells are dilated (structural atypia)	3–4% in 13 years
Atypical hyperplasia	Cellular atypia, dilated nuclei and nucleoli, hyperchromatism, stratification, dyspolarity	23% in 11 years

atypical hyperplasia, having contraindications to hormone therapy, hysterectomy can be an alternative first stage of treatment. For patients over the age of 50 hysterectomy is the method of choice.

Women with atypical hyperplasia require more aggressive treatment, especially in the perimenopausal period. The method of choice in this case will be hysterectomy with bilateral salpingo-oophorectomy. Patients, wishing to keep the reproductive function, are given treatment with progesterone or ovulation induction. As a rule, women before the age of 40 are given preparations of progesterone, after 40 hysterectomy is performed.

Serial histological studies of the endometrium are performed for the control of the efficiency of treatment.

Agonists of gonadoliberin (zoladex, decapeptil), causing "medicamentous oophorectomy" are also applied. It is also possible to use hestrinon — 2 times a week by 2.5 mg or danazol — by 400–800 mg a day for 6 months with subsequent control curettage of the endometrium.

With relapsing of the glandular-cystic endometrial hyperplasia 17-oxyprogesterone capronate (17-OPC) is prescribed on the 14th, 17th and 21st day of the cycle for 3 months; then — on the 17th and 21st day of the cycle for 3 months.

Patients in the reproductive period with endometrial hyperplasia without atypical changes can be prescribed oestrogen-gestagen drugs by the usual scheme. The duration of treatment — 8–12 months. Oestrogen-gestagen drugs are prescribed only under the condition of excluding the chance of malignant changes in the endometrium.

In the premenopausal period 17-OPC is recommended to use continuously by 250 mg 2–3 times a week.

With atypical endometrial hyperplasia the use of oestrogen-gestagen preparations is not recommended. At the first stage of treatment 17-OPC is prescribed intramuscularly by 500 mg: the first 2 months — 3 times a week, 3rd and 4th months of treatment — 2 times a week; 5th and 6th months — once a week. Norcolut is prescribed the 5th through the 25th day of the cycle by 5–10 mg for 6–8 months, further — the 16th through the 25th day of the cycle for 3 months, under the control of hysteroscopy and histological study of the endometrium.

Preparations stimulating ovulation are recommended at the second stage of treatment to young women for whom pregnancy is desirable, — clomiphene, clostilbegit by 50 mg a day the 5th through the 9th day after occurrence of bloody discharge.

Effective modern method of treatment is the use of gestagen with prolonged action, "Depot-Provera" — by 400–600 mg intramuscularly once a week for 3–4 months or orally by 5–10 mg a day. The advantages of these preparations are the prevention of complications caused by the introduction of injections of abundant 17-OPC oil solution. The duration of treatment — 8–12 months. For prevention of the influence of preparations on the liver it is necessary to appoint allochol, nospan, methionine, carcil at the usual doses.

Resection of the endometrium with the help of hysteroresectoscope, that allows to delete the uterine mucosa under visual control, has been successfully used for the last few years.

The personnel of the gynaecologic clinic of the Odessa State Medical University developed the methods of cryosurgical and cryoultrasonic treatment of patients with endometrial hyperplasia, as well as with hormonal and immunomodulating therapy that allows to combine radical treatment with the stimulation of the regenerative ability of tissue. Our experience of endoscopic surgery covers more than 5,000 operative hysteroscopies, performed concerning endometrial hyperplasia, including in a combination with minimally invasive surgery (laser vaporization, electro- and laser resection, cryolysis).

In case of relapse of the hyperplastic process, the method of choice is panhysterectomy. In the menopausal period extirpation of the uterus with appendages is recommended for atypical changes in the endometrium, glandular-cystic relapsing endometrial hyperplasia, especially in combination with such dis-

eases, as diabetes, hypertension, and obesity. With the presence of contraindications to operative treatment (severe extragenital pathology) agonists of gonadoliberin are applied.

When choosing the method of treatment they consider the contraindications of hormonal preparations (thrombophlebites, diseases of hepato-biliary system, diabetes, hypertension, otosclerosis). The risk of side-effects of the hormonal preparations is increased by smoking and alcohol use.

RECOMMENDED READING

9; 24; 30; 49; 59; 67; 68; 75; 79; 92; 93; 94; 95; 103; 108.

Chapter 11

BENIGN TUMOURS AND TUMOUR-LIKE CONDITIONS OF THE FEMALE GENITALIA

UTERINE TUMOURS

Benign diseases of the uterus are the most widespread pathology in the practice of the doctor-gynaecologist.

Myoma (leiomyoma, fibromyoma, fibroma, fibroid) — develops from smooth muscular tissue of the uterus and is at the first place in the incidence among tumours of the female reproductive system. Every second gynaecologic laparotomy is conducted concerning a myoma of the uterus. From autopsy data 20% of women over the age of 30 have uterine leiomyoma of various sizes. The tumour, as a rule, does not occur before puberty, develops only during the reproductive age and regresses after menopause. The myoma varies in sizes (from microscopic nodules to huge tumours) and tends to grow in multiple nodes though individual nodes are also observed.

Etiology, pathogenesis, histopathology. Factors for the occurrence of a uterine myoma are precisely unknown. However, it is established that a tumour can develop from a smooth-muscle cell and grow under the influence of oestrogens. In the beginning of the development of a tumour, the concentration of cytosol receptors for oestrogens and progesterone in tissue of the myometrium is not broken, which corresponds to the normal contents of these hormones in the blood and is accompanied by biphase menstrual cycles. In some patients with uterine myoma the contents of progesterone in the blood is on the lower limit of the norm, which is accompanied by a defective II phase of the cycle. It is established that the amount and activity of the total progesterone receptors on a cell with uterine myoma is lower than for healthy women, and the oestrogen receptors — is higher. Depending on the sizes of the myoma the level of progesterone reception in a tumour of the myometrium changes.

With age, and also due to accompanying ovarian dysfunction, the role of absolute or relative (against a background of hyperoestrogenism) the deficiency of progesterone increases. Functional disorders of the ovaries are observed in patients with bleedings, connected to the direct development of a tumour, and to anovulation (anovulatory uterine bleeding) or an insufficiency of function of the corpus luteum, as a result absolute or relative hyperoestrogenia with a deficiency of progesterone occurs. These hormonal disorders can result in hyperplastic processes of the endometrium, cystic changes in the ovaries, frequently developing in patients with uterine myoma.

The term “fibroma”, or “fibromyoma”, is not precise, because the initial element of this tumour is the smooth muscle cell with an extended nucleus. A fascicle of such cells goes in various directions. However, it tends to form folds. These cells are similar by form and sizes and are placed in one projection. Mitoses are absent as a rule.

A large leiomyoma is usually firm, with a characteristic trabecula or twirled arrangement of fibres on a cross-section. It can have a pseudocapsule, that allows in some cases enucleating the tumours from the myometrium (myomectomy).

Under the influence of hormonal stimulation during pregnancy the myoma can enlarge, soften, which complicates its diagnosis during palpation. After birth, the sizes of the tumour, as a rule, decrease.

Classification. Approximately in 95% of cases the myoma develops in the corpus uteri, in 5% — in the cervix. 80% of the women have multiple nodes of myoma.

Depending on the site concerning the uterine wall the following fibroids are distinguished: subserous, intraligamentous, intramural, submucousal or cervical myoma (leiomyoma).

Subserous leiomyoma is located under the peritoneal (serous) surface of the uterus, it can be small or large, and in some cases has a pedicle. The subserous myoma can receive additional blood supply from the omentum due to a fusion formed with it (parasitic tumour).

Intraligamentous leiomyoma is characterized by a lateral growth or primary development between the leaves of the broad ligament of the uterus.

Intramural (interstinal) leiomyoma develops in the uterine wall. With the small sizes it can not cause changes in the contours of the uterus. Increasing, such a uterine myoma gets a nodular asymmetric form. With the large sizes the myoma is distributed up to the serous and mucous membrane of the uterus.

The subserous and intramural uterine myoma before reaching large sizes, as a rule, is asymptomatic.

The submucous myoma is rare (5–10% of cases), but a dangerous type of benign uterine tumour (strong bleedings can be observed, infected nodes with distribution of the infection onto the uterus).

The cervical myoma occurs most frequently on the posterior surface of the cervix and quite often is asymptomatic. The anterior cervical leiomyoma is accompanied by symptoms of compression of the bladder.

A large cervical myoma is observed rather seldom, but it is characterized by significant technical difficulties during its surgical removal and a high probability of damage to the adjacent organs (intestines, ureter, bladder).

Rare types of myoma. Rather seldom myoma spreads to the pelvic veins. Despite the benign character, dessimination is possible to the lungs and other organs. Myomatous cells can implant also into the omentum and on the peritoneum; such a condition is referred to as disseminated peritoneal leiomyomatosis. Treatment consists in extirpation of the uterus with its appendages and subsequent hormonal therapy.

Such conditions are considered ***degenerative changes*** of myoma:

1) hyalinosis;
2) cystic and carneous (red) degeneration;
3) calcification (calcination);
4) myxomatosis.

Hyalinosis is the most widespread (65% of cases) degenerate change of myoma. The latter gets a more homogeneous appearance, has a yellow colour, and softens.

Cystic degeneration, as a rule, occurs after hyalinization due to the reduction of the blood supply. The uterus becomes soft during palpation, which sometimes results in the erroneous diagnosis of uterine pregnancy.

Calcification is observed in 10% of cases, more often occurs in asymptomatic leiomyoma in the postmenopausal period and is characterized by the deposit of calcium carbonate and calcium phosphate in muscular tissue. Calcification zones can form concentric circles that can be accidentally revealed during radiological study.

Carneous (red) degeneration. Necrosis can be observed in any type of myoma due to disorder of its blood supply. The subserous pedicled myoma can be twisted with subsequent necrotization and even separating from the uterus. Necrosis occurs in the centre of a tumour more often, however it can be located in its various sites. In places of necrosis, the usual trabeculous or twisted structure of the muscular cells is absent; the tissues are soft, yellow. The factor promoting necrosis can be carneous degeneration of a node during pregnancy, connected with infarctions in its tissue.

During pregnancy carneous degeneration of myoma can be accompanied by a slight increase in the body temperature and moderate leukocytosis. With an acute development this process is characterized by pain, morbidity of a tumour during palpation, which can lead to the erroneous diagnosis of detachment of the placenta (an often symptom is bleeding, opposite to infarction of myoma) or chorioamnionitis, which always causes the development of fetal tachycardia.

Myxomatosis (15% of cases) develops after hyalinization and can be accompanied by necrosis.

Leiomyosarcoma is found in 0.1–0.5% of the patients with leiomyoma; however its development from leiomyoma is not established.

Clinical picture, diagnosis. Clinical manifestations depend on the duration of the disease, the patients age, the sizes of the myoma and site of the myomatous nodes, previous and accompanying genital and somatic pathologies. Therefore concerning the symptomatology of myoma there are opposite points of view: in the opinion of some experts, the asymptomatic myoma does not exist; others support, that in 2/3 cases the myoma has no pathognomonic symptoms and is accidentally found during bimanual gynaecologic and abdominal exams (with enlarged uterus) or ultrasonography.

Patient's most often complaints are:

1) pain, including secondary algodysmenorrhoea;
2) uterine bleedings (with an increase in their duration and degree of blood loss);
3) symptoms of compressing adjacent organs due to the large myoma or multiple nodes.

Common laboratory symptom of myoma is anaemia due to uterine bleedings. Leukocytosis and elevated ESR are marked with the presence of accompanying endometritis or carneous or septic degeneration of myoma.

The **submucous myoma** is found in women over the age of 40. Thus, in the anamnesis there can be data of frequent abortions, intrauterine interventions, which can result in the disorder of the receptor device of the myometrium. A small submucous myoma frequently causes uterine bleedings connected to damage or compressing of vessels in adjoining sites of the endometrium. Strong bleeding due to twisting of the endometrium, dilation of the uterus with a submucous myoma quite often are indications for hysterectomy. In some cases submucous myoma can form a pedicle and project through the cervix, which is accompanied by spasmodic pain in

the lower abdomen and bleeding (hypermenorrhoea). With a prolapse of such a tumour through the cervix, it can become infected or covered with ulcers, also promoting the development of bleeding. In the thinned mucous membrane above the myomatous nodes, inflammatory changes occur. For differential diagnosis of endometrial cancer a biopsy is performed.

Due to the infected submucous myoma, the infection can be distributed to the uterus and upper-located departments of the reproductive tract, which demands parenteral antibacterial therapy.

Anterior cervical myoma can cause compressing symptoms of the bladder (polyuria, urine incontience with pressure, with large tumours — urine retention). The cervical myoma can cause excessive production of mucus resulting in an increase of vaginal discharge (mucorrhoea). In case of obstruction of the cervical canal and the reduction of its diameter patients suffer from algodysmenorrhoea. With the mass of conglomerates in the small pelvis, dyspareunia and infertility are possible.

Fast growth of myoma for some patients (0.7—3%) is connected to the development of hypostasis due to disorder of blood supply to the myomatous node. Fast growth is considered an increase in the sizes of the tumour within one year (or less) till the sizes equivalent to 5-week pregnancy. Patients in such cases most frequently complain of pain, feeling of heaviness in the small pelvis. If the sizes of the tumour exceed the sizes of the uterus equivalent to a 12-week pregnancy, leucorrhoea, urination disorders, constipation are observed.

The uterine myoma can cause nausea, vomiting (during obstruction of the intestines), pain and feeling of heaviness in the stomach (small pelvis), mass of conglomerates, increase of vaginal discharge, algodysmenorrhoea, abnormal uterine bleedings, urination disorders (frequent, compelled, retention), constipation, fatigue (with the development of anaemia), dyspareunia, leucorrhoea (mucorrhoea) and pain. Uneven contours, firmness of the uterus, and also the ultrasound data allow to exclude the diagnosis of pregnancy.

Ultrasonography, including transvaginal, plays an important role in the diagnosis of the uterine myoma, apart from clinical (bimanual gynaecologic and abdominal studies). Ultrasound allows to precisely determine the sizes, site of myomatous nodes, the presence of deformity of the uterine cavity in case of submucous nodes, to conduct differential diagnosis with ovarian tumour, adenomyosis, and also to reveal disorders of the blood supply and necrosis of the myomatous nodes.

Submucous myoma can be diagnosed with the help of hysterosalpingography (during examination concerning infertility) and hysteroscopy (during examination concerning uterine bleedings). The advantage of hysteroscopy is an opportunity of conducted endometrial biopsy, which is important for diagnosis of accompanying hyperplastic processes (hyperplasia, polyps, adenomatosis). Laparoscopy is used in the complex examination of patients with infertility, and also in case of the necessity for differential diagnosis, with the combined defects of the uterus and its appendages, suspicion of degenerate changes of the myoma (haemorrhage, necrosis). Computer tomography and nuclear magnetic resonance can be useful in conducting differential diagnosis of myoma with tumours of the intestines and ovaries.

The uterine myoma is accompanied by the growth of risk of spontaneous abortions, complications during vaginal delivery (dystocia, abnormal position of the foetus, detachment of the placenta, postpartum bleeding) due to an inefficiency in the uterine contractions or mechanical obstruction of the birth path. A large tumour can mask the presence of other serious diseases of the ovaries or intestines, and during pregnancy result in nonconformity between the size of the uterus and the gestation age of the fetus.

Observing and treatment of patients. The concept of domestic scientists (K. M. Vikhlyayev et al., 1996) concerning uterine myoma as a system disease of the female organism consists of refusing the position of "non-interference" for the given category of gynaecologic patients during the period from the moment of occurrence of the tumour till the occurrence of indications to surgical treatment. However, foreign experts consider that with the presence of one or more myomas no treatment is necessary.

Patients with a uterine myoma are subject of clinical follow up. The first step in conducting patients with a uterine myoma is specification of the form and growth rate of the tumour. Patients with intramural nodes, as a rule, are sensitive to conservative therapy while patients with a submucous myoma are subject to operative treatment.

In connection with the introduction of new diagnostic technologies (ultrasonograpy, computer tomography) and the opportunity for dynamic control of the myoma development, aggressive surgical tactics sometimes does not prove its value.

The presence of myoma does not always influence the histological structure of the endometrium. However, in some cases due to the reduction of the blood supply to the endometrium atrophic changes can take place and histological attributes of chronic endometritis with lymphocytic and plasmatic infiltration appear. Inflammatory reaction occurs secondary after a reduction in the blood flow. The decision on the methods of treatment of patients with myoma should be individual and depend on the severity of the symptoms, sizes and site of the myoma, as well as on the age, parity, general state of health of the patient and her desire to become pregnant.

Medicamentous treatment. All patients with uterine myoma, irregardless of the selected medical tactics, are recommended a rational diet (fresh fruits, vegetables, restriction of carbohydrates and animal fats); medicamentous correction of metabolic disorders — B vitamins (thiamin, pyridoxine, cyanocobalamin) and ascorbic acid (influences the steroidogenesis in the ovaries and adrenal glands), tocopherol acetate (to normalize the functions of the hypothalamus-pituitary systems). Among non-medicamentous means especially with the presence of accompanying salpingo-oophoritis, electrophoresis with copper, zinc, potassium iodide, proteolytic enzymes, ultrasound therapy are applied.

The basic component of conservative treatment is hormonal therapy with progestagen (norcolut, dufastone, orgametril, primolut-nor, medroxyprogesterone acetate — "Depot-Provera"), antigonadotropic means (danazol, danol), antiprogestin (gestrinon — nemestran, RU-486), agonists of gonadoliberin (zoladex, decapeptil). The antitumoural action of gestagen consists of the reduction of mitotic activity of tumour cells that promotes the oppression of its growth.

Norcolut (dufastone, orgametril) is prescribed by 10 mg a day to patients with a regular menstrual rhythm, the 16th through the 25th day of the cycle or by 5 mg a day the 5th through the 25th day of the cycle for 4–6 months. In the premenopausal period norcolut is prescribed by 5–10 mg a day continuously. 17-OPC is prescribed intramuscularly on the 14th, 17th and 21st day of the cycle at a dose of 125–250 mg for 6 months. Danazol is prescribed by 400 mg a day for 4–6 months continuously; gestrinon — by 2.5 mg 2 times a week for 4–6 months.

Women with symptomatic myoma when an operation is undesirable for any reason are prescribed analogues or agonists of gonadotrophin-releasing-hormone (zoladex, decapeptil) can be prescribed. These preparations oppress the ovarian hormones secretion and promote the reduction of the tumour's size. Treatment should be done with alternating courses, because long therapy of such patients results in a significant loss of bone density and (in some cases) osteoporosis. According to literature data, a reduction in the sizes of myoma is observed already 3 months after beginning the use of gonadoliberin agonists, but 6 months after the termination of treatment the myoma quickly comes back to the initial size. In case of infertility, miscarriages, due to uterine myoma, preoperative suppression of the growth of the myoma with analogues of gonadoliberin creates the conditions for organ-preserving laparoscopic myomectomy.

Conservative treatment is recommended to women with intramural and subserous nodes with the size of the uterus equivalent to a 12 week pregnancy and the absence of meno- and metrorrhagia. Hormonal treatment is conducted in the reproductive and premenopausal periods if there are contraindications to surgical intervention, as well as preparation for conservative myomectomy and postoperative prevention of relapses of the tumour.

Non-operative treatment allows deferring surgery concerning a uterine myoma untill menopause when it isn't often necessary in connection with age involution of the myometrium.

Hormonal treatment is contraindicated, if the sizes of the myoma are more than those equivalent to a 12-week pregnancy, with submucous sites of the nodes, the presence of intramural nodes with centripetal growth and the suspicion of necrosis, degeneration of the node, as well as with the tendency to fast growth of the tumour (suspicion of the development of sarcoma), combinations of uterine myoma and pregnancy, uterine myoma and adenomyosis, ovarian tumours, etc. General contraindications to hormonal therapy are diseases of the gastro-intestinal-hepatic complex, hypertension, diabetes, obesity, thrombophlebitis and varix dilation.

Surgical treatment. Indications for surgical treatment, as a rule, are the following:

1) the size of the tumour exceeds the size of the uterus equivalent to 12–14 weeks of gestation;

2) the presence of severe anaemia, resistant to therapy, symptoms of degeneration and necrosis in patients with submucous myoma;

3) compression or obstruction of the adjacent organs, caused by myoma.

With an increase in the uterus up to the level of the navel (equivalent to 20 weeks of gestation) partial obstruction of the ureter can occur.

Conservative and radical operations, each of which have indications and contraindications (see "Surgery in gynaecology" p. 191), are performed for patients with a uterine myoma.

After conservative myomectomy fibroids recur in 15–45% of cases. When a node of myoma is impossible to remove, accompanied by severe symptoms, hysterectomy is performed. This operation is preferred, if the tumour is of a large size and quickly grows, especially in premenopause.

The operation of removing a uterine myoma can present significant technical difficulties, especially in case of a low lateral position of the nodes. With the lateral site of the tumour there is always a disposition of the ureter and the anatomic ratio between it and the uterine artery (it passes under *a. uterinae*, at the place of its entrance into the uterus) is broken. To eliminate a possible intersection of the ureter together with the uterine vessels, it is necessary to determine its position prior to tissue removal. With a large myoma the ureter can move in the anterosuperior direction and settle down at the level of the round uterine ligaments.

A small submucous tumour can be deleted during hysteroresectomy or while performing a curettage of the uterine cavity. A large myoma, being the reason

for infertility, sometimes can be removed during laparotomy or laparoscopy without entering the uterine cavity (in order to prevent a rupture of the uterus at the spot of the scar during future gestations).

Surgical treatment should be postponed for 3–6 months after birth in connection with the possibility of spontaneous involution of the uterine myoma.

TUMOURS AND TUMOUR-LIKE CONDITIONS OF THE OVARIES AND FALLOPIAN TUBES

The ovary is a usual place of volumetric masses location in the small pelvis, and its increase, as a rule, is connected to physiological cyst or a tumour development.

Ovarian tumours represent a serious gynaecologic problem for all age groups of patients. Any organ of the human body hasn't such a histological variety of tumours as ovaries have. Benign defects of the ovaries are classified into non-neoplasitic (tumour-like) and neoplactic (tumours). Some authors, apart from benign and malignant tumours of the ovaries, allocate a group of borderline tumours.

Classification. In 1973 the WHO offered a histological classification of tumours and tumour-like conditions of the ovaries. According to this classification, they are divided into 9 groups, 32 subgroups and 66 forms. A list of these groups is the following:

I. Epithelial tumours.
II. Sex cor-stromal tomours.
III. Lipidocellular tumours.
IV. Germ-cell (germinogenic) tumours.
V. Gonadoblastoma.
VI. Tumours of soft tissue, nonspecific for the ovaries.
VII. Non-classified tumours.
VIII. Secondary (metastatic) tumours.
IX. Tumour-like changes of the ovaries.

Diagnosis. In case of detection of any volumetric masses in the area of the ovaries, careful examination of the patient should be conducted to rule out possible neoplastic processes. Tumours of the Fallopian tubes occur extremely seldom and frequently are asymptomatic.

The area between the lateral walls of the pelvis and the corners of the uterus are called the zone of the appendages. This includes the ovaries, Fallopian tubes, an upper part of the broad uterine ligament and the remainder of the embryonic paramesonephral (müllerian) ducts. The ovaries and Fallopian tubes are affected most frequently in this area.

Besides of the reproductive organs, there are also some sections of the urinary and gastro-intestinal tract in the area of the appendages. The most widespread urological pathologies, which is necessary to differentiate with defects of the uterine appendages, are *infections of the upper and lower sections of the urinary tract* and (less often) *calculi in the kidneys and ureter.* Very seldom *a falling of kidney, or pelvic kidney* (which can be single), may resemble an adnexal mass. Symptoms in the right half of the stomach can be connected with *appendicitis*. Sometimes defects of the appendages are necessary to differentiate with *inflammatory diseases of the intestines* in the ileocecal zone. Diseases of the rectum and sigmoid intestine (sigmoid diverticular disease, acute or chronic diverticulitis, rectosigmoidal cancer) more often develop in elderly women. Therefore, in such patients pain in the left half of the stomach eliminates the diagnosis of damage of the uterine appendages.

Bimanual gynaecologic examination is the basic when examining the uterine appendages. Clinical displays can occur due to both physiological, and pathological processes in the ovaries. Bimanual examination allows to reveal asymptomatic defects of the uterine appendages also. A large tumour of the appendages is located between the uterus and sacrum, more often. A medium tumour with a pedicle (from the ligaments of the uterus and ovaries), normally easily moves from one side to the other one (Fig. 48). However, existing pelvic adhesions can cause significant difficulties while diagnosing a tumour by palpation. Interpretation of the data received during bimanual gynaecologic examination demands knowledge of the physical characteristics of the ovaries during the stages of the life cycle.

So, the ovaries of girls *before menarche* should not be palpated. Otherwise, a detailed examination

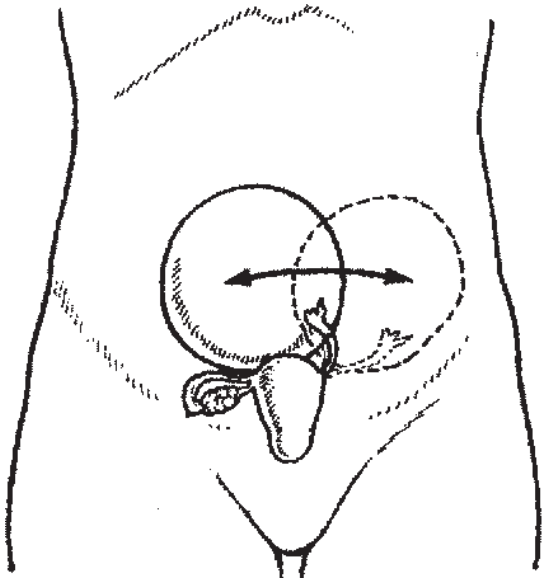


Fig. 48. Mobility of an ovarian tumour during palpation as a result of the formation of a pedicle

to eliminate the diagnosis of an ovarian tumour is necessary.

In *the reproductive period* normal ovaries are palpated in every second case. The important characteristics which can be received during palpation are the size, consistence (firm or cystic) and mobility of the ovaries. In women of reproductive age taking oral contraceptives, the ovaries can be smaller, more symmetric and are palpated less often than in patients who do not use them.

During *the postmenopausal period* the ovaries are in a condition of functional rest, except for an insignificant production of androgens. Such ovaries are already tolerant to gonadotrophic secretion, and their follicular activity gradually decreases, disappearing approximately 3 years after the termination of menstrual function. During this period, residual functional cysts can be formed. In general, the revealing of enlarged ovaries during palpation in women after menopause should be evaluated more critically than in young patients, in connection with an increase in the risk of neoplasm in this age group. Approximately 1/4 of the ovarian tumours in postmenopause are malignant, while in the reproductive period — only 10%. Enlarged ovaries in postmenopause — *postmenopausal palpated ovary syndrome* is an indication for surgical intervention.

Additional methods of examination of the uterine appendages are ultrosonography (abdominal and transvaginal), laparoscopy. If during a transvaginal ultrosonography of woman in the postmenopause, a single-chamber cystic adnexal mass with a diameter of less than 5 cm found, treatment of the patient should include dynamic follow up while conducting a series of gynaecologic and ultrosonographic examinations. The mass with a diameter of more than 5 cm is subject to surgical removal. Lately, laparoscopy plays a leading part in the differential diagnosis and treatment of patients with ovarian tumours.

Ovarian cysts are not true tumours because with their presence blastomatous growth of tissue is not observed. The majority of ovarian cysts are in the group of retention masses (*retentio* — delay). They are formed due to a delay or accumulation of various contents, glandular secret in the pre-mass cavities. The cysts can develop in connection with the softening of tissue due to haemorrhage, necrosis. Besides of the ovaries, such cysts can be formed on the external genitalia (cysts of the great vestibular glands, paraurethral, sebaceous and sudoriferous glands), in the vagina (cysts of the remainders of the embryonal epithelium of the vertical duct of the ovarian appendage, producing a transparent mucous secret).

A physiological ovarian cyst varies in size, depending on the phase of the menstrual cycle and is frequently accompanied by such symptoms, as disorder in the rhythm of menstruation and pain in the lower abdomen. It is not a true tumour and represents the anatomic variant occurring due to the normal function of the ovaries. Ovarian tumours have a constant size or enlarge, can be benign or malignant, solid, cystic or combined.

Differential diagnosis of adnexal masses in many respects depends on the age of the patients.

Types of ovarian tumours and rate of their malignancy depending on the age of the patients

Prepubertal period	*Reproductive period*	*Menopausal period*
Germ-cell — 80%	Functional cysts — 70%	Malignant — 50%
Malignant — 10%	Endometrioma — 10%	
	Neoplastic — 20% a) benign — 85% b) malignant — 15%	

Observing patients with ovarian masses always represents a challenge for the gynaecologist. The method of choice for treatment of patients with functional cysts is conservative therapy; benign ovarian tumours quite often demand operative intervention.

Functional cysts (tumour-like conditions, non-neoplastic defects) of the ovaries. ***Follicular cyst.*** The follicle becomes cystic in reply to stimulation by the gonadotrophic hormones. If ovulation does not occur, the follicle, as a rule, is subject to atresia. During persistent anovulation numerous cystic follicles can be formed. If the follicle does not take place, reaching maturity, ovulation does not occur; as a result a follicular cyst also can be formed. Such a condition slows the follicular phase of the cycle and results in oligomenorrhoea and secondary amenorrhoea.

Follicular cyst is a frequent complication and very much varies in size. If a thin-walled mass in the ovary exceeds 2 cm in diameter, it is called a follicular cyst, if less than 2 cm — cystic follicle. Follicular cysts seldom reach the size more than 6–8 cm in diameter. Histologically, one or more layers of normal granular cells and strongly protruding internal and external theca membranes of the ovaries are found in it. The cyst is unicameral and contains a liquid with high oestrogen contents.

Follicular cysts become clinically significant in case of its enlargment or the development of the pain syndrome persisting more than one menstrual cycle. Granular cells, covering the follicular cyst remain during ovulation and throughout the II phase of the cycle. The cyst can enlarge in size and exceed 5 cm in diameter, cause moderate pain in the abdomen and disrupt the menstrual cycle. The following ovulation does not occur, resulting in bleeding due to hyperstimulation by oestrogens. The high oestrogen level, absence of ovulation again promote hyperstimulation of the endometrium and become the reason for irregular bleedings.

During bimanual gynaecologic examination, mobile cystic adnexal masses (more often — to the side and in front of the uterus), tender during palpation, are found. To specify the site of the tumour ultrasonic examination is performed. Ultrasonographically a follicular cyst is unicameral, the absence of blood elements, soft tissue and external outgrowths. Repeated gynaecologic examination and ultrasound study are conducted in 6–8 weeks. In the majority of cases the follicular cyst spontaneously disappears or remains unrecognised.

A rupture of the follicular cyst can be accompanied by sharp pain in the abdomen, hemoperitoneum, which demands surgical intervention.

Cyst of the corpus luteum (lutein cyst) occurs after ovulation if the follicle has not regressed during the lutein phases of the cycle. In case of pregnancy and an increase in the production of human chorionic gonadotrophin (HCG), the corpus luteum will be transformed into the corpus luteum of pregnancy and continues to secrete progesterone. If pregnancy does not occur, the corpus luteum normally regresses and is transformed into the corpus albicans.

The cyst of the corpus luteum is covered with layers of lutein granular cells and theca endocrinocytes. The typical cyst of the corpus luteum has a bright yellow wrinkled edge, hemorrhagia in the centre of the cyst or the cavity, filled with fibrin. The lutein cyst, as a rule, has a larger size than a follicular one, can be firm during palpation and look solid during ultrasonic examination.

Two variants are possible for the clinical course of the lutein cyst. With the first variant the slightly increased corpus luteum can continue to develop progesterone longer than the usual 14 days. The delay in menstruation is from several days to several weeks, although, as a rule, it occurs after a 2-week delay. Pain in the lower abdomen and the absence of the expected menstruation are characteristic attributes of a persistent corpus luteum. A delay in menstruation after small vaginal bloody discharge ("spotting") and pain in the lower abdomen demand the differentiation of a cyst of the corpus luteum with an ectopic pregnancy. To eliminate the diagnosis of pregnancy the β-subunit of CG is studied. With the help of bimanual examinations an increase and sensitivity of the ovaries, which can be solid or cystic, are found.

With the second clinical variant of cysts of the corpus luteum, its fast increase with spontaneous bleeding in it is observed. Such a haemorhagic cyst (corpus haemorrhagicum) can rupture at the end of the lutein phase of the cycle. It is characterized by pain in the lower abdomen in the late lutein phase, is more often in patients with regular menstrual cycles, not using oral contraceptives.

Observing and treatment of patients. Functional cysts (follicular or lutein), as a rule, are subject to inverse development. In the reproductive period, the cyst should regress within 2 months. If during this period regression of the cyst does not occur, additional examinations are performed — ultrasonography, laparoscopy, removal of the cyst within the limits of the healthy ovarian tissue (in the reproductive period).

Regression of functional ovarian cysts occurs in 80% of patients in case of using combined oestrogen-gestagen preparations (such as oral contraceptives) daily for 4–8 weeks. Functional cysts are seldom formed in women taking oral contraceptives. Therefore in case of mass of cysts while using hormonal contraceptives, as well as in the prepubertal or postmenopausal periods its ultrasonographic examination and surgical removal by laparoscopy or laparotomy are necessary.

Indications for surgical intervention are:

1) cystic masses of the ovaries with the size exceeding 8 cm in diameter;

2) ovarian cyst with the diameter of more than 5 cm after 8 weeks of supervision or taking oral contraceptives;

3) any volumetric masses of the ovaries before menarche;

4) any ovarian masses after menopause;

5) solid ovarian masses in women of any age.

In case of cyst rupture, the development of intraabdominal bleeding (hemoperitoneum) and oligemia are possible, which demands immediate surgical intervention. In nonsevere cases, the pain gradually decreases and bleeding stops.

Polycystic ovaries, as a rule, are bilaterally enlarged due to the presence of small follicular cysts and cystic follicles without attributes of ovulation. This disease is more often diagnosed in women at the age of 15–30 (see "Neuroendocrine syndromes" p. 67). The superficial membrane of the polycystic ovaries can be thickened and has a pearl-white colour. Besides of cystic follicles, follicular and stromal hyperthecosis are observed. Follicular hyperthecosis occurs when luteinization of the internal membrane (teca interna) of the cystic follicles occurs. Stromal hyperthecosis consists of isolated islets and sites of luteinized thecal endocrinocytes (theca cells) in the ovarian stroma. Hyperthecosis zones secrete androstendion and testosterone, which quite often results in the development of hirsutism, anovulation and oligomenorrhoea in such women. Obesity and anovulatory infertility are frequently observed. The serum level of follitrophin is normal, while the level of lutrophin is essentially increased but has no ovulatory wave (lutrophin/follitrophin ratio — > 2). The levels of 17-ketosteroids (17-KS) and testosterone can be a little increased. Persistent anovulation promotes the development of hyperplasia of the endometrium, which increases the risk of carcinoma of the endometrium in such patients.

Treatment consists of the induction of ovulation, conducted in the beginning by cyclic use of clomi-

phenecitrat, and in case of inefficiency — menstrual gonadotrophin (pergonal) and human chorionic gonadotrophin (prophase). Clomiphene-resistant patients require operative treatment (electrocoagulation, laser vaporization of the cyst, clinoid resection of the polycystic ovaries). The development of postoperative adhesions or ovarian insufficiency worsens the results of surgical treatment, especially in the remote (more than 6 months after the operation) period.

Theca lutein cyst and luteoma *(hyperreactio luteinalis)* are functional ovarian cysts, which is connected with pregnancy and an increase in the HCG level (or sensitivity to HCG). Theca lutein cyst can be formed in patients with vesicular moles and ovarian choroicarcinoma, as well as as a reaction to the induction of ovulation with the help of menotrophins (pergonal) and HCG. Theca lutein cyst is formed most frequently in teca interna and is connected with the luteinization of several follicles. Trophoblastic disease can result in the mass of large bilateral theca lutein cysts.

Theca lutein cyst can occur during pregnancy. The luteinization of the theca membrane is the source of massive production of androstendion. Therefore, a characteristic symptom for such patients can be the start of virilism during pregnancy. The female fetus, as a rule, is protected from the mother's androgens due to their aromatization into oestrogens in the placenta. This condition regresses after birth, however, can recur during subsequent pregnancies.

Luteoma of pregnancy usually is solid and bilateral, has a typical cloudy look (multifocal and multinodular fusion masses from luteinization cells). The exact reason for their occurrence remains unknown. In the zones surrounding the parenchyma of the ovaries. Stromal hyperthecosis is found. These benign masses regress after a childbirth.

Paraovarian cyst is a retention benign tumour-like mass, located between the leaves of the broad uterine ligament and the developing from the supraovarian appendages (paraoophoron). The morbidity rate is 8–16% of all the ovarian masses. Paraovarian cyst is more often formed in patients between the ages of 20–40. Sometimes malignancy is possible.

The paraovarian cyst in most cases is unicameral, with transparent liquid contents; the average diameter is 8–10 cm. On the superior pole of the cyst a deformed Fallopian tube is located; the ovary is located near the posterior inferior pole of the cyst. The paraovarian cyst has a small size, as a rule, has no pedicle. However, with its growth towards the abdominal wall, the protruding of one of the leaves of the broad ligament and a pedicle is formed, consisting of leaves of the mesosalpinx, the Fallopian tube itself and ovarian ligament. Histologically, the cystic wall is formed from connective tissue, its internal surface is covered with cylindrical, cubic or plane epithelium, and sometimes papillary nodes are available.

The *clinical picture* is characterized by pain in the lower abdomen, in case of large cystic sizes — symptoms of the adjacent organs compression, rarely — disorders of the menstrual cycle, infertility. With the twisting of the cystic pedicle, the picture of an acute abdomen may develop, which demands immediate surgical intervention (see "States of emergency in gynaecology" p. 179). Diagnostic opportunities considerably expand due to the use of ultrasonography, and especially, laparoscopy.

Treatment is surgical. The organ-preserving operation consists of the cyst enucliation from the intraligamentous space with subsequent stitching of the leaf of the broad uterine ligament.

Dermoid cyst is considered at below (see "Germ-cell (germinogenic) tumours of the ovaries" p. 147).

Ovarian tumours (neoplastic defects).

According to the classification suggested by FIGO, three basic groups of ovarian tumours are distinguished:

1) Epithelial (from the superficial ovarian epithelium).

2) Stromal (from the stromal elements).

3) Germ-cell, or germinogenic (from germinal cells).

The most widespread ovarian tumours are dermoid tumours (cysts), developing from germinal cells, and the tumours, formed from superficial ovarian epithelium (benign epithelial).

Epithelial tumours of the ovaries (cystomas) are formed in 60–80% of cases of all ovarian neoplasia. The paramesonephric (müllarian) ducts develop from the superficial epithelium, descending from coelomic coverings. These tumours differentiate depending on the type of cells from which they develop into the following types:

1) Serous
2) Mucinous
3) Endometrioid
4) Brenner's tumour
5) Light-cellular (mesonephroid)
6) Non-differentiated

Serous tumours (cystomas) are covered with vibrating epithelium, similar to the epithelium of the fallopian tubes. Benign serous cystomas make 70% of all cases of serous ovarian tumours. Borderline (potentially malignant) tumours (10% of cases) are characterized by proliferation of the epithelium, contain atypical cancerous cells and can spread to the omentum and peritoneum. However, the invasion of stroma does not occur and the prognosis concerning life is rather favourable (the survival rate within 5 years is 100%, 10 years — 75%).

Serous cystomas can be smooth-wall and papillary. *The smooth-wall serous cystoma* (serous cystadenoma, cylioepithelial cystoma), as a rule, is unicameral, with a smooth shiny surface, contains a pure

yellow liquid. *Papillary serous cystoma* (papillary serous cystadenoma) is characterized by the mass of a small amount of internal or external papillary growths. The tumour seldom reaches large sizes as opposed to the mucinous cystoma. One of the identifying attributes of a papillary serous tumour is the deposit of calcium in them (psammoma corpuscles). However, such corpuscles can be present also for malignant and potentially malignant tumours. Benign serous tumours are bilateral in 10% of the patients; tumours on the border of malignancy — in 25%; serous cystadenocarcinoma — in 2/3 cases.

In most cases serous tumours are asymptomatic and are accidentally diagnosed during bimanual gynaecologic examination (smooth-wall mobile mass on the side or behind the uterus) for patients at the age of 30–50. The basic complaint of such patients can be pain in the lower abdomen. The diagnosis is specified with the help of ultrasonic examination and laparoscopy.

Treatment is surgical. The volume of the operation depends on the patient's age, accompanying complications. Any solid or papillary zones, which have been found in serous tumours (papillary cystoma), should be histologically studied to determine the malignancy zones.

Mucinous tumours (cystomas). *Pseudomucinous cecernizing cystoma* is covered with cylindrical mucinous epithelium, similar to endocervical. Sometimes such tumours reach large sizes. The tumour can have an ovoid form, frequently with a rough surface due to its multilocularity. The tumour's capsule is smooth, shiny, silver-white. Its epithelium can be similar to the intestinal one, at times contains goblet cells.

Mucinous tumours, as a rule, are multilocular; in 5% of cases — bilateral. About 85% of mucinous tumours are benign and occur in women over 40 years old. Disorders of the menstrual function occur less often in comparison with other variants of cystomas.

Sometimes together with a mucinous tumour there is a condition which received the name peritoneal pseudomyxoma *(pseudomyxoma of the ovaries and peritoneum)* and is characterized by mucin getting in the abdominal cavity. If malignant regeneration does not occur, such a long-term complication can result in the delay of mucin in the abdominal cavity and the development of mucinous ascites.

Mucinous tumour can be combined with a uterine myoma. In case of *papillary mucinous cystomas* there is a growth of papilla.

The *clinical picture* depends on the sizes of the tumour. With a large tumour, pain, feeling of heaviness in the lower abdomen, in the lumbar and sacral areas, constipation is possible. During bimanual examination to the side and behind the uterus a volumetric mass with a rough surface is palpated. With the presence of an ovarian pseudomyxoma and the development of mucinous ascites, an enlargement of the abdomen is observed; "colloid crackling" is found during its palpation. The development of peritonitis with large fibrous fusions in this case is possible.

Treatment is surgical. Palliative operations are conducted in young women with a preserved reproductive potential. Abdominal hysterectomy with bilateral salpingo-oophoriectomy and careful examination of the abdominal cavity are preferable. In the case of pseudomyxoma immediate radical operation is recommended including the removal of internal genitalia, resection of the omentum and clearing of abdominal cavity from mucinous masses.

Endometrioid tumours have a high potential of malignancy (endometrioid carcinoma). Benign endometrioid tumours of the ovaries are most frequently represented by endometrioma and, in other words, is not a true superficial tumour of the endometrium. Endometriosis is not considered a condition preceding the development of endometrial tumours.

The Brenner's tumour consists of a layer of the epithelium, similar to the transitive epithelium of the urinary bladder, containing mucinous cells inside. The malignant Brenner's tumour is observed very seldom. In the majority of cases the tumour is accidentally found in women over 40 as a fibrous mass. The development of ascites and Meigs' syndrome (ascites, hydrothorax and anaemia), establish on the basis of the patients complaints, can be connected with the Brenner's tumour.

Sex cord-stromal tumours (tumours from the ovarian stromal cells, gonadal stromal tumours) develop from the ovarian stroma and can be endocrine-active. As a result of an ability of stromal cells to produce androstendion, estron and estradiol, these tumours can be masculanizing or feminizing. Stromal tumours of the ovaries are differentiated, depending on the cells covering them, into granular—thecacellular (covered by ovarian epithelium) and androblastoma (a tumour from the Sertoli's cells, covered by testicular epithelium). A more complete classification on the basis of the stromal cells of the ovaries includes such tumours:

1) granulocellular;
2) thecoma (fibrothecoma);
3) androblastoma (Sertoli—Leydig's tumour);
4) Leydig's tumour;
5) gynandroblastoma.

Granulocellular tumour is feminizing and can cause premature sexual development in children and blood flow due to hyperplasia or carcinoma of the endometrium in women after menopause. The tumour cells have morphological attributes of granular cells and are characterized by the presence of so-called Call—Exner corpuscles as pseudosockets around the central hyaline zone, probably, residual nuclear degenerations.

The ovarian stroma contains lutein theca endocrinocytes which can be transformed into a *granulocellular tumour*. Probably, the majority of granulocellular tumours are secondary induced by luteinizing stroma. One of the characteristic histological attributes — the presence of nuclear grooves, similar to those at coffee beans. It is considered that granular cells have a low malignancy potential. However, they can persistent or recur.

Treatment consists of the surgical removal of the tumour. Salpingo-oophorectomy is performed in young women; hysterectomy and bilateral salpingo-oophorectomy are performed in older patients.

The *fibroma (fibrothecoma)* is in the category of gonadal stromal tumours. It is observed in 6–9% of the patients with adnexal tumours over the age of 40. Before puberty a fibroma is not formed. On one hand, actually the fibroma is not connected to the abnormal production of steroids and is frequently found in elderly women. The tumour is dense at palpation, smooth, white, frequently is similar to the form of the ovaries. It can reach large sizes and be subject to cystic degeneration (thus, the consistence of the tumour becomes non-uniform). Sometimes the fibroma is accompanied by the development of ascites, hydrothorax and anaemia (Meigs' syndrome).

On the other hand, the tumour in most cases includes rich lipid luteinized theca endocrinocytes, as a rule, with oestrogen function, i.e. includes components of fibroma and thecoma. Mature fibrothecoma is formed most frequently and seldom is malignant.

Fibromas, as well as other tumours, are diagnosed in case of revealing volumetric masses on the side and behind the uterus. Fibrothecoma can be combined with a uterine myoma, adenomyosis, cyst or cystoma of the second ovary; bilateral fibrothecoma is formed seldom. The growth of a tumour is slow, acceleration of its growth can be observed in case of the tumour degeneration. Complications, as well as for other ovarian tumours, can be twisting of the pedicle, necrosis, and purulent fusion of the tissue of the tumour.

Differential diagnosis is conducted with subserous myomatous node on a pedicle, other tumours. The development of ascites in such patients demands differentiation with ovarian cancer.

Androblastoma (tumour from Sertoli—Leydig's cells) is covered with testicular cells, virilism is frequently observed (hirsutism, baldness, clitoromegaly, increase in muscular mass). The incidence of androblastomas is about 0.2% of all ovarian tumours; the tumour forms mainly in patients between the age of 20–40. More often androblastoma is a combined tumour developing from two types of cells — Sertoli's and Leydig's. However, cases of pure Sertoli-cell tumours are observed. A highly differentiated Sertoli-cell tumour can be oestrogen-active while the mixed (combined) tumour is androgen-active, producing testosterone. Irregardless of the differentiation of the Sertoli cells, the combined tumour can be highly differentiated (Pick's tubular adenoma), low differentiated or have intermediate histological attributes. The less the extent of differentiation of the tumour, the more its malignant potential. The Leydig-cell component in all these tumours is similar and contains polygonal cells with dense eosinophilic cytoplasm and Raynke's crystals.

Hiluscellular tumour is similar to Leydig-cell and is differentiated depending on its anatomic site in the ovary. Such tumours include a uniformed population of Leydig's cells with Reinke's crystals. With the absence of Reinke's crystals it is considered that the tumour has the other origin (lipidocellular tumour). The presence of Reinke's crystals — a characteristic attribute of the benign nature of the tumour.

Gynandroblastoma is observed very seldom; it is differentiated both in the ovarian and testicular directions.

Arrhenoblastoma (hypernephroma) — a tumour developing from the tissue of the cortex of the adrenal glands which can be formed in the ovaries. It develops more often in young women (before the age of 30); has a dense capsule, small size, by form it is similar to the ovary. The frequency of the tumour is 1.5–2% of cases, and in 20–25% of the patients malignancy of the tumour is observed.

Lipidocellular tumours develop very seldom (more often in the premenopausal period) and consist of cellular elements, relating to the cellular type of the adrenal cortex and the cells looking like the Leydig's cells.

The clinical displays of the lipidocellular tumours are connected to the development of hyperandogenia and defeminization (the termination of menstruation, depending of the breasts, decrease in the hypodermic fatty layer or, on the contrary, obesity, deepening of the voice, clitoromegaly, hirsutism or baldness); the pain syndrome can appear.

With the purpose of diagnosis, apart from gynaecologic examination, ultrasound, laparoscopy, determining the levels of androgens in the blood (testosterone, cortisole, dehydroepiandrosterone sulphate), 17-ketosteroid and 17-oxyketosteroids in the urine are used. The character and prognosis of lipidocellular tumours are determined by their size; the tumours with the size less than 9 cm in diameter, as a rule, have no aggressive attributes.

Treatment is surgical.

Germ-cell (germinogenic) ovarian tumours, developing from germinative cells, should be studied as potentially malignant, except, maybe for teratoma. In the absolute majority of cases teratoma (dermoid cyst) is benign and the most widespread ovarian tumour. However, malignant forms of teratoma also are possible.

According to the classification of germ-cell tumours of the ovaries such groups are distinguished:

1) teratoma;
2) dysgerminoma;
3) embryonal carcinoma;
4) tumours of the yolk sac and endodermic sinus;
5) polyembryoma;
6) choriocarcinoma (chorionepithelioma);
7) gonadoblastoma.

The histogenesis and interrelations of the germ-cell tumours are shown in fig. 49.

Teratoma can be mature or immature. Mature teratomas of the ovaries, as a rule, are cystic. However, can be a solid tumour.

Mature teratoma (dermoid cyst) — the most widespread germ-cell tumour (10–20% of cases of all volumetric masses of the ovaries), formed in women mainly of the age of 30. Mature teratoma can develop from all three germinal leafs: exto-, meso- and endoderm. Such tumours contain hair, fats, keratin tissue, sometimes even bones and fully formed teeth in the central zone (Rokitansky's tubercles). More often dermoid cysts are associated with tissue, corresponding to the head end of the embryo. The cyst's form is round with a smooth surface and white and yellow colour. The cystic wall is formed from the connective tissue, and the cavity is covered with flat multilayered or cubic epithelium. Malignant transformation can occur in any component of the teratoma, but more often — in the planocellular (planocellular cancer). Sometimes in the teratoma proliferation of the active thyroid tissue (ovarian stroma) takes place.

Clinically the cystic teratoma has a diameter of no more than 12–15 cm, mobile (freely "floats" in the abdomen), the ovarian pedicle can increase and be located *above* and *anterior to the uterus* (Küstner's sign). In this way it differs from other ovarian tumours which, as a rule, are located behind the uterus. Dermoid cysts develop in the right ovary more often, but can be bilateral, grow slowly. Symptoms are similar to those of other ovarian tumours (feeling of heaviness and pain in the lower abdomen, dysuria).

The dermoid cyst with the inclusion of the bone tissue can be found on the general roentgenogram of the organs of the abdominal cavity, as well as during ultrasound (heterogeneity of the exostructure).

The mature teratoma, as a rule, is removed by a simple ovariectomy, if the patient wishes to keep the reproductive function. Bilateral teratoma is formed in 15% of cases; therefore visualization of the second ovary during the operation is necessary.

An immature teratoma is considered malignant with various degrees of aggression. Immature teratoma is determined by the presence of fetal tissue, especially neuroepidermal. In most cases immature teratomas are solid. However, can sometimes have a cystic component. The size of the tumour, clinical stage and degree of malignancy determine the prognosis of the disease.

Dysgerminoma and embryonal carcinoma develop from nondifferentiated germinal cells. Dysgerminoma is not differentiated, while embryonal carcinoma is multipotential and is differentiated into two directions: 1) embryonal (somatic) as a result teratoma is formed, and 2) extraembrional with the mass of choriocarcinoma (chorioepithelioma) and tumours of the endodermic sinus. The place of development of the *polyembrioma* is not completely established (in world literature only 8 cases of this tumour are described).

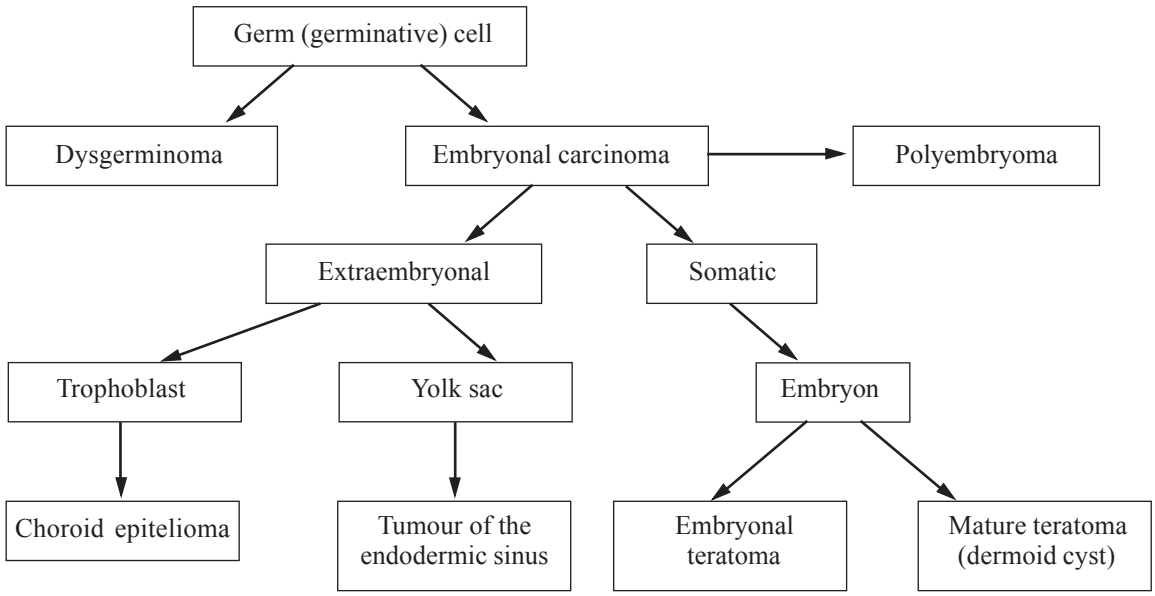


Fig. 49. Histogenesis of germ-cell (germinogenic) ovarian tumours

Dysgerminoma is the least differentiated among all germ-cell tumours, is considered universally malignant. It frequently develops in women about 30 years old or in patients with gonadal dysgenesis in the mosaic karyotype which has a Y-chromosome or its part. Such tumours are characterized by homogeneous cellular population of primitive germinative cells with relief nucleolus, as well as fibrosis and lymphocytic infiltration. There can be a benign differentiation of the syntrophoblast with its production of low level CG. In most cases dysgerminoma is unilateral, solid, with a smooth surface.

Treatment consists of removing the tumours as well as the second nondifferentiated ovary (for Turner's syndrome).

Tumours of the yolk sac and endodermic sinus are considered germ-cell and are characterized by the development of that, similar to the embryonic, in the yolk sac. Tumours of the endodermic sinus are observed extremely seldom. However, they occupy the second place in the malignancy rate after ovarian tumours. More often they develop in children and teenagers and rarely in women over 40 years of age. Patients frequently complain of abdominal pain and the enlargement of the abdomen due to the tumour. In most cases such tumours reach 15 cm in diameter. The external surface is mainly smooth, with sites of ruptures. With the development of haemorrhagia and necrosis the tumour becomes soft and pliable. The presence of cystic zones gives the tumours a honeycomb look (on the surface of the cut). As a rule, this tumour is unilateral; a bilateral one forms secondary.

In every second case, a tumour of the yolk sac contains so-called Schiller—Duval's corpuscles. Clinically a tumour of the yolk sac is considered malignant. The marker of efficiency of treatment of patients with such tumours is the level of α-fetoprotein in the blood serum.

Gonadoblastoma is a mixed tumour consisting of germinal, immature Sertoli's, Leydig's and granular cells, as well as dysgerminoma cells. The tumour is solid, on the cut has pink and orange colour and frequently develops as dysgerminoma, in dysgenetic gonads. Growth of the tumour can be accompanied by the development of virilism (hirsutism, clitoromegaly, and decrease in the timbre of the voice) on the background of the absence of female secondary sexual characters.

Treatment consists of removing the tumour and second dysgenetic gonad, as for dysgerminoma.

Complications of benign ovarian tumours are the following:

1) malignancy (more often cilioepithelial papillary cystoma, rarely mucinous cystoma and dermoid cysts);

2) twisting of the uterine appendages (tumour pedicle's);

3) infection, haemorrhages, degenerative changes (purulent fusion, infarction and necrosis of the tumour);

4) rupture of the cyst's (cystoma) capsules;

5) intestinal obstruction.

Twisting of the uterine appendages (tumour pedicle's) is the reason for more than 3% of cases of all urgent gynaecologic operations, occurs more often in children. The fallopian tube and the ovary, as a rule, twist; an ovary can be twisted twice (at 360°). In adults (mainly of the age of 20–30 years) in 50–60% of cases the volumetric masses of the ovaries, which usually have sizes of 8–12 cm in diameter, twist. Most frequently the benign cystic teratoma (dermoid cyst) twists, although there are cases where serous, solid and paraovarian tumours twist (Fig. 50). The right ovary is twisted more often, but women with one episode of such twisting have a risk of the recurrence of this complication in the second ovary (10% of cases).

Anatomically the tumour's pedicle consists of stretched infundibulopelvic and ovarian ligament, parts of the posterior leaf of the broad uterine ligament, Fallopian tubes and contains vessels (ovarian, uterine arteries), nerves.

The twisting of the tumour's pedicle can be caused by sharp movements (running, sports), physical exercises, and change in the size of the uterus during pregnancy, in the postnatal period.

The *clinical picture* is caused by the nutrition disorder of the tumour. A symptom of the twisting of the ovarian cyst is acute pain in one side of the abdomen, accompanied by nausea and vomiting in 2/3 patients. The pain can decrease and increase depending on the patient's position. During palpation, the woman feels pain; however, symptoms of peritoneum irritation in such cases are not characteristic. With the progressing of infarction and necrosis of the appendages, leukocytosis and a slight increase in the body temperature can be observed. In most cases the appendages are swollen, cyanostic, sometimes even get black. During the histological examination, haemorhagic infarctions are found. The twisted pedicle cannot be untwisted in connection with the danger of thrombus and embolism. A delay in

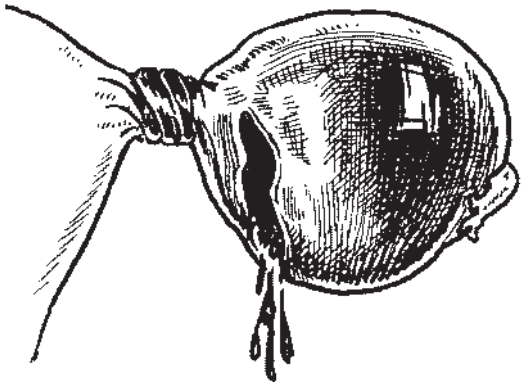


Fig. 50. Twisting of the pedicle and rupture of the capsule of the ovarian cystoma with bleeding

performing the operation can lead to the development of secondary infection, peritonitis.

Degenerative changes of the tumour (purulent fusion, necrosis, disorder of the blood supply) are accompanied by pain, leukocytosis, symptoms of peritoneum irritation due to a rupture of the purulent mass. The abscess can rupture into the rectum, bladder with the mass of fistulas.

A rupture of the cystic (cystoma) capsules can be provoked by a trauma, be combined with the twisting of the tumour's pedicle and be accompanied by bleeding (see fig. 50), development of shock, implantation of tumour elements into the peritoneum (especially pseudomyxomas).

Intestinal obstruction can develop due to the large sizes of the tumour, accompanying adhesions which disorders the normal function of the intestines and narrows their opening.

Thus, the benign ovarian tumours are characterized by the following main positions:

1) they are observed more frequently than malignant ones in all age groups;

2) the malignant transformation rate increases with the increase of the patient's age;

3) ovarian tumours demand surgical treatment in connection with the malignancy risk;

4) before surgical intervention it is necessary to conduct an ultrasonographic exam of the ovaries, laparoscopy;

5) surgical treatment can be sparing (organ-preserving), especially in patients wishing to keep the reproductive function.

Benign tumours of the Fallopian tubes. These tumours are frequently asymptomatic and are found during surgical operations performed for other reasons. Tumours of the Fallopian tubes are myoma, fibroma, hemangioma. The most widespread disease of the Fallopian tubes is inflammation: hydrosalpinx, pyosalpinx.

More often a benign tumour of the Fallopian tubes is mesotelioma (adenomatous tumour). It develops by the proliferation of serous mesothelial covering of the Fallopian tubes (mass of firm nodes). The large tumour can narrow the opening of the Fallopian tubes. Epithelial papilloma and polyp are sometimes formed.

Paratubular cysts can develop from the remainders of the mesonephral (wolffian) and paramesonephral (müllerian) ducts or from mesothelium (morgagnian hydatid cysts). Cysts developing from the paramesonephral ducts are covered with ciliary epithelium, containing intraplasmatic mucin.

RECOMMENDED READING

7; 16; 24; 49; 51; 57; 67; 75; 79; 90; 92; 93; 94; 103; 108.

Chapter 12

MALIGNANT TUMOURS OF THE FEMALE GENITALIA

The female reproductive system is most sensitive to aggressive influence of the environment, which promotes the development of neoplastic process in it more often.

According to modern view *cancer is a genetic disease,* therefore its occurrence and development is connected to certain consecutive mutations occurring mainly in somatic cells. However, hereditary predisposition does not determine the rigid determinacy of the development of the tumour. By the data of the WHO, 75–80% of cases of development of oncologic diseases are connected with the adverse influence of environmental factors, which can be prevented. These factors are smoking, the use of alcohol, malnutrition, disorders of the reproductive function and sexual behaviour, increased professional loads and stressful situations, technogenic environmental contamination and adverse geographical features. Only in rare cases it is possible to speak about the hereditary predisposition to cancer, caused by germinal mutations (mutations in sex cells), — so-called members of the "cancer family" in which the risk of the disease increases tens and hundreds of times.

In the structure of oncological diseases of organs of the reproductive system 93.3% of cases are *hormone-dependant tumours* (oestrogen-dependant cancer of the endometrium, mammary glands). There are two possible mechanisms of participation of hormones in the realization of tumour growth. The first one is physiological, or promotor, mechanism at which the hormone promotes growth in the amount of already initiated cells, and second one genotoxic, connected to damage to the membrane and the influence of their products of metabolism (catecholoestrogen) on DNA.

The development of a neoplastic process depends on the *condition of the immune system* of the organism. It is established, that the excess of oestrogen oppresses the immune system by inhibiting cytotoxic T-lymphocytes and natural killers, serves as the reason for the disorder of the supervising function of the immune system, promotes the reduction of expression of molecules of adhesion on the lymphocytes and tumour tissue, responsible for preserving the integrity of the tissue, migration of leukocytes and interaction of immune—competent cells during the immune reaction. Recently, the role of separate cytokines, natural antagonists of cytokine, as well as mutations of the genes participating in the control of apoptosis (programmed destruction of cells), in the realization of neoplastic process is convincingly proved.

Features of cancer of the genitalia consist of *screening* the disease at the early stage in many respects determines the efficiency of the treatment. Practically all kinds of cancer of the reproductive system are accessible to treatment if revealed at the stage of precancer or intraepithelial cancer. About 85% of malignant neoplasms are easily found when using screening methods, and only 15% of cases cannot be recognized in due time due to the latent disease course.

CANCER OF THE VULVA

Cancer of the vulva makes up 3–4% of all gynaecologic malignancies and by its prevailence takes the fourth place among malignant neoplasms of the female genitalia. Seldom it is observed in young patients, the average age of patients is about 60 years. Despite the low incidence of cancer of the vulva, severe clinical course, insufficient efficiency and traumatic methods of treatment of such patients cause special importance of this problem.

Etiology. The reason for cancer of the external genitalia is not completely established. The risk factors for the development of cancer of the vulva are the sexually transmitted diseases, and, in particular, infection of the human papillomavirus (the letter revealed in 84% of patients with intraepithelial neoplasm and in 58% — with invasive carcinoma of the vulva). The increased risk of development of vulvar cancer is observed in women with preinvasive and invasive cervical carcinomas.

In the opinion of some experts, among the factors causing the development of vulvar cancer, hypooestrogenia plays an important role. Prolonged ovarian hypofunction results in hypotrophy of the vulvar tissue, kraurosis, leukoplakia, on the background of which cancer can develop.

Pathomorphology. The most widespread histological type of cancer of the vulva — squamous, or epidermoid (90% of cases). With less incidence melanoma (5%), sarcoma (2%), adenocarcinoma (1%), and basocellular carcinoma (1%) are observed.

Intraepithelial carcinoma of the vulva (carcinoma *in situ*) is distinguished by histological criteria of epithelial structure disorder, occurrence of cellular atypia and extent of distribution of the tumour in the epithelial layers and is classified into *mild, moderate and severe.* A characteristic attribute of intraepithelial defects is the *absence of invasion into the stroma,* the basal membrane thus remains intact. Opposite to invasive cancer of the vulva, intraepithelial carcinoma develops in women of the younger age (average age about 35). However in 75% of cases the severe stage of intraepithelial neoplasia of the vulva happens in the premenopausal period.

Carcinoma *in situ* is considered a preinvasive disease; the incidence of its progression into invasive carcinoma is not precisely established. A rare form of intraepithelial carcinoma of the vulva is ***Paget's disease***. Even though the invasive potential of Paget's disease is insignificant, it can be accompanied by primary cancer of the genitalia of other site.

Clinical picture and diagnosis. When gathering the anamnesis about 2/3 of the patients specify long presence of itching at the area of the external genitalia and defect of the vulva, in other patients the illness proceeds asymptomatically. The pain occurs later during invasion of the tumour into other tissue.

To identify small defects of the vulva it is necessary to examine it with corresponding illumination. During objective examination it is possible to find single or multiple changes of the vulva: precisely outlined spots or papule, which can be white (leukoplakia), red (erythroplakia), hyperpegmentated or warty. Cytological exam of the smears-prints is conducted. However, the exact diagnosis is established on the basis of the data from the histological biopsy material.

Biopsy of the defective area is performed under local anaesthesia, desirably with the help of colposcope (vulvoscope) or a magnifying glass, after preliminary applying a 3% solution of acetic acid. The colouring of the vulva with methyl aniline is recommended with the presence of pathological symptoms without visual attributes of the defect.

Treatment of patients consists of removing a zone of defect, reducing the frequency of relapses while preserving, whenever possible, the anatomic integrity and physiological function of the vulva. The method of treatment should be chosen depending on the patient's age, severity of the condition, amount of defects and their site.

Local excision is conducted under local anaesthesia in case of single defects. The method enables to carry out histological research while determining the border of surgical intervention which is very important in preventing relapses.

Laser therapy (CO_2-laser vaporization) is recommended in cases of single and multiple defects (two or more courses) and is conducted under general anaesthesia.

Vulvectomy with skin transplantation has been replaced by laser surgery in many surgical centres today, which has a better cosmetic effect. It is applied only in individual cases with the presence of extensive or relapsing defects (Fig. 51).

Chemotherapy consists of the use of a 5 % fluorouracil cream (efficiency — 50%). A disadvantage of the method is its necrotizing influence on the epithelium, in connection to which chemotherapy is a resort mainly with relapsing of the disease.

Invasive cancer, as a rule, is diagnosed at the age of 60–70. A background for the development of cancer can be previous epithelial defects of the vulva.

Clinical picture and diagnosis. Invasive cancer (carcinoma) of the vulva develops more often from large and small pudendal lips (Fig. 51, *a*), clitoris and (seldom) skin of the perineum. The majority of patients take notice to an increase in the vulvar tissue, in their anamnesis there are data of long-term itching, burning and chronic irritation of the skin of the vulva. Bloody discharge and pain in the perineum are late symptoms and connected to the great volume of the tumour. A very rare symptom can be secondary dysuria due to defect of the ureter.

By the character of growth ulcerous (subsequently-endophytic), papillary (exophytic) and nodulous (warty) tumours are distinguished. Most frequently such a tumour develops from the large or small pudendal lips, clitoris, vaginal os, as well as multicentral and may be distributed onto the vagina, the skin of the perineum, the anus, the urethra.

At the early stage of development of invasive vulvar cancer an infiltrate or an ulcer with dense edges and necrotic fundus is formed and in due time cracks, ulcers, excoriation appear; the inguinal lymph nodes increase.

Invasive cancer of the vulva is characterized by tendency to fast growth and early malignancy, which occurs mainly lymphogenously, due to significant lymph vascularization of the external genitalia. Lymph vessels from both sides carry the lymph to the regional lymph nodes and simultaneously form anastomosis among themselves. Therefore in patients with unilateral tumour, bilateral metastases can be formed. In some cases lymphedema of one or both of the lower extremities can occur.

The biopsy of the affected zones is performed in out-patient conditions under local anaesthesia. The

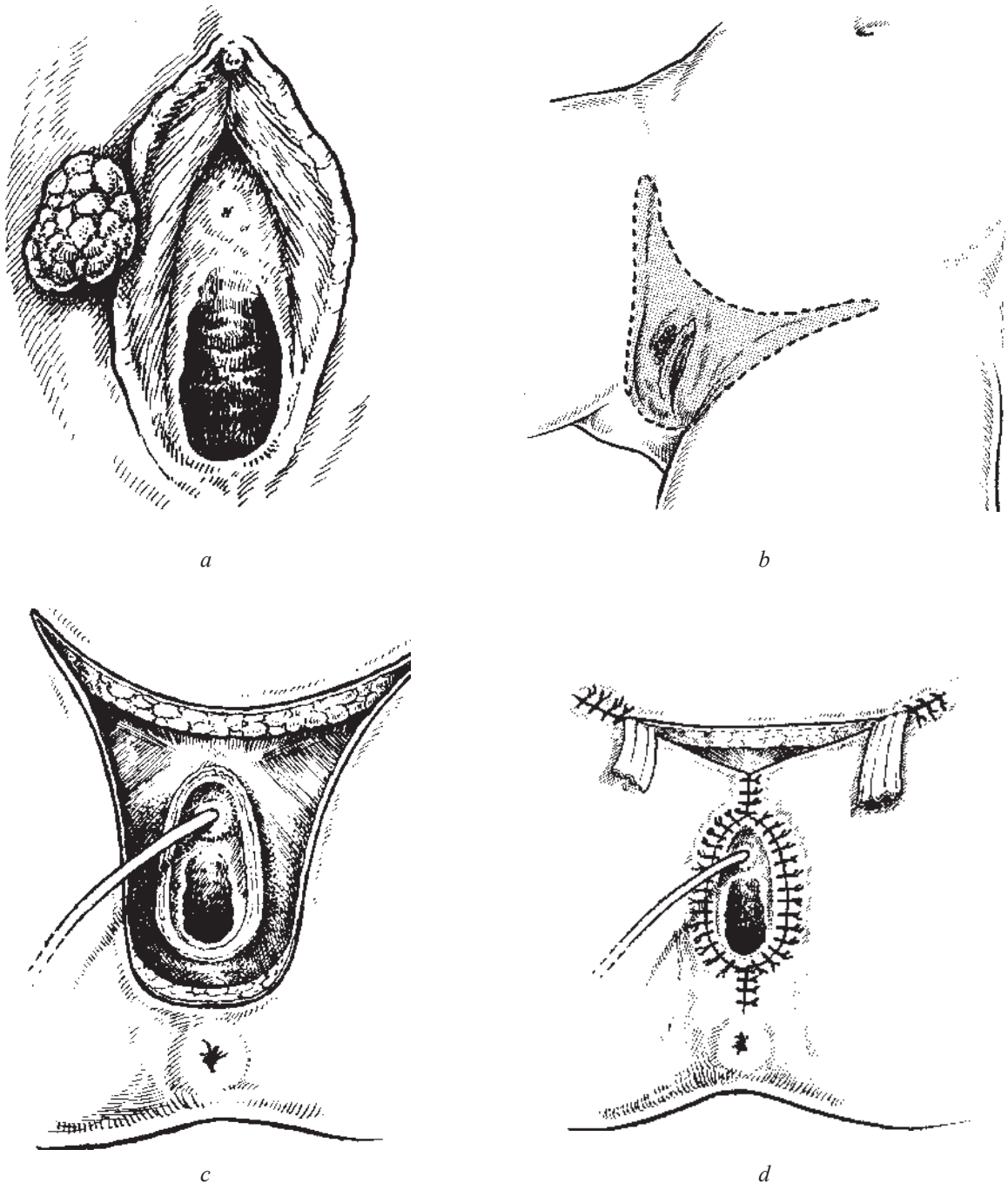


Fig. 51. Vulvar cancer:
a — location of the primary cancer; *b*, *c*, *d* — stages of radical vulvectomy

regional lymph nodes include the femoral, inguinal, external and internal ileal. The condition of the femoral, inguinal lymph nodes is revealed during objective examination by palpation for the diagnosis of regional metastases. "Suspicious" lymph nodes are subject to aspiration biopsy. Additional methods of determining the stage of the disease include roentgenography, excretory urography, cystoscopy, lymphography, irrigoscopy, proctosigmoidoscopy. More than 50% of cases of invasive vulvar cancer are diagnosed during the I or II stages.

Ways of spreading. Squamous carcinoma of the anus, urethra, bladder and rectum is distributed by germination into the adjacent organs, in particular, into the vagina, the skin of the perineum. Superficial and deep inguinal and femoral, and then pelvic lymph nodes are affected by the lymphatic way. The contralateral inguinal lymph nodes in most cases are intact.

Classification. The stage of the disease is established by studying the primary tumour and the degree of its spread onto adjacent organs and inguinal lymph nodes. The determination of the stage of vulvar carcinoma, by the recommendations of the International Federation of Gynaecologists and Obstetricians (FIGO), is based on the TNM classi-

Table 10. **Characteristics of the stages of invasive caner (carcinoma) of the vulva (by FIGO, 1988)**

Stage	Characteristic
0 Tis	Intraepithelial carcinoma (carcinoma *in situ*)
I T1N0M0	The tumour is limited to the vulva and (or) perineum; its largest sizes ≤ 2 cm. Metastases into the lymph nodes is not present (lymph nodes are not palpated)
II T2N0M0	The tumour limited to the vulva and (or) perineum; its largest sizes > 2 cm. The lymph nodes are not involved.
III T3N0M0 T3N1M0 T1N1M0 T2N1M0	The tumour of any size with 1) spread the lower part of the urethra and (or) vagina or onto the anus and (or) 2) spread to the regional lymph nodes on one side
IV A T1N2M0 T2N2M0 T3N3M0 T4, any N, M0	The tumours involves the upper part of the urethra, mucous membrane of the bladder, rectum, pelvic bones and (or) there are metastases in the regional lymph nodes
IV B Any T, N, M1	The presence of any metastases in distant organs, including pelvic lymph nodes

fication (T-tumour, N-node, M-metastasis) (Table 10).

The *prognosis* concerning recovery and survival rate of patients is dependent upon the clinical stage of the disease. The chances of treatment decrease, if the tumour spreads to adjacent organs and the regional lymph nodes.

The lesion of the lymph nodes depends on the extent of differentiation of the tumour, its size (> 3 cm), depth of invasion (if it exceeds > 3 mm, metastases in the lymph nodes occur almost in 30% of cases). The involvement of the bilateral lymph nodes in the process, their amount, as well as the tumour spread to the vessels are signs serving as the basis for an adverse prognosis concerning recovery.

Treatment. Three basic methods of treatment are used: 1) surgical; 2) combined; 3) radiation. Chemotherapy has a certain value.

Adequate *surgical treatment* of patients with microinvasive carcinoma consists of its local resection while capturing the healthy tissue at a distance of 1 cm outside the tumour to prevent local relapses. Depending on the size of the tumour, the wound is closed with the help of primary or secondary skin transplantation.

Combined methods of treatment may be used for patients with I stage invasive carcinoma*:* radical vulvectomy with bilateral lymphadenectomy of the inguinal and ileal lymph nodes and subsequent radiation therapy or preoperative radiation therapy on the area of the tumour and regional zones involved with subsequent vulvectomy, or radiation therapy. Vulvectomy is a wide resection of the external genitalia while preserving the external aperture of the urethra.

Patients with vulvar cancer of the II–III stage are subject to combined treatment, which provides a wide local resection or radical vulvectomy of the basic tumour with the use of radiation therapy of the inguinal lymph nodes (instead of lymphadenectomy). Thus, it is necessary to take into account the size of the tumour and the depth of invasion. So, with the presence of a small tumour with invasion < 3 mm, the incidence of involving the lymph nodes is no more than 3%, it is possible to be limited to local resection or partial vulvectomy with subsequent biopsy of the lymph nodes. If the depth of invasion exceeds 3 mm, as well as with the II, III and IV stages of the disease the method of choice is radical vulvectomy with bilateral inguinocoxofemoral lymphadenectomy. For patients with IV stage, sometimes it is necessary to perform additional excision of the pelvis or symptomatic treatment. In case of the inoperable affected lymph nodes, it is possible to use radiation therapy.

Radical surgical treatment more than in half of cases is accompanied by complications (separation of the sutures, infection of the wound, prolonged healing). Remote consequences of the operation include lymphedema of the lower extremities, recurrent cellulitis, psychosexual disorders.

Radiation therapy of the inguinal and pelvic zones is used as additional methods of treatment, with the lesion of inguinal and coxofemoral lymph nodes. Primary radiation of the tumour of the vulva is performed to reduce the volume of the tumour before surgical treatment.

Chemotherapy is recommended to patients with remote metastases, regional and local relapses, where surgical and radiation treatment are ineffective. The

sensitivity of squamous carcinoma to chemotherapy is low (25%) as a result a substantial increase in the survival rate of such patients is not observed. The majority of regimes of chemotherapy include a combination of platinum preparations.

Survival rate. With all stages of the disease, the frequency of relapses after therapy reaches 30–40%. The prognosis for patients with I and II stages of the disease without lymph nodes involvement is favourable enough — within 5 years 85–90% of patients survive. With the affection of the inguinal and coxofemoral lymph nodes the survival rate within 5 years decreases to 50%, with pelvic metastases — to 20%.

Other tumours of the vulva. ***Melanoma*** takes the second place in the incidence of development among all cancerous tumours of the vulva (5%) and is in most cases characterized by pigmentation of the defect. The depth of invasion of melanoma has a great prognostic value.

Treatment depends on the size of the tumour, its site and depth of invasion. Radical surgical intervention has no advantages over broad local excision of the tumour.

CANCER OF THE VAGINA

Vaginal cancer is observed very seldom (1–2% among malignant neoplasm of the female genitalia). About 90% of cases — squamous cancer, 10% — adenocarcinoma, sarcoma and melanoma. The tumour is mainly located in the upper third of the vagina and on its posterior wall. Spread of the tumour occurs by contact, hemato- and lymphogenous way. Symptoms can be vaginal bleedings or other discharge from the reproductive tract. A biopsy of the material from all suspicious areas is performed.

Treatment includes surgical intervention, radiation therapy and can be combined. The survival rate within 5 years does not exceed 40%.

CANCER OF THE CERVIX UTERI

Cervical cancer is one of the most widespread gynaecologic malignancies in the world. The average age of patients is 45–55 years. In Ukraine cervical cancer is at the third place by frequency among malignant neoplasms of the female genitalia (17.1 in 100 thousand of women in 1996) after endometrial cancer (21.4 in 100 thousand of women) and ovarian cancer (17.6 in 100 thousand of women of the female population). In the past years due to the improvement of early diagnosis there is some decrease in the morbidity of invasive cervical cancer, although there is a dangerous tendency to the development of this disease in younger women. So, intraepithelial (preinvasive) defects of the cervix already occur in patients after the age of 20. In Ukraine, every fifth patient with first time diagnosed cervical carcinoma dies, which is inadmissible for a visual form of cancer and testifies to a poor-quality diagnosis of the early stages of the disease.

Etiology of cervical cancer is not established; however, the majority of risk factors for the development of this disease are external, connected to the sexual behaviour of the women. It is believed that cervical cancer can be associated with the human papilloma virus, type 2 simple herpes virus, early beginning of sexual life, frequent change of sexual partners, low social and economic status, smoking, deficiency of retinol (vit. A), ascorbic and folic acid.

According to the widespread hypothesis, the agents transmitted sexually can influence the more sensitive zones of the cervix-transformation zones. Cylindrical epithelium in these zones is constantly replaced with multilayered plane epithelium by way of metaplasia. The majority of forms of cervical cancer develop on the *border of cylindrical* and *squamous epithelium.*

According to other hypothesis, the oncogenous transformation is a result of integration of viral genetic information into the DNA of epithelial cells.

The presence of background processes in the cervix is not obligatory for the occurrence of cervical cancer. Cancer can develop in unchanged epithelium.

Cervical intraepithelial neoplasia. The given term in modern literature replaced the one used earlier: dysplasia, precancer, carcinoma *in situ*, preinvasive cancer, although the latter also are used. All these terms exist to determine the proliferation of neoplastic defects on different levels of the epithelium, but without invasion into the stroma. The absence of invasion, i.e. the absence of metastatic potential, and in connection with this an opportunity for conservative treatment, distinguishes this group of diseases from invasive cancer.

Screening-diagnosis is carried out by cytological research of Pap smears. Complete analysis in addition includes colposcopy, biopsy of the cervix, and curettage of the cervical canal, cone biopsy of the cervix (see "Background and precancer diseases of the female genitalia p. 122"). The place to take the biopsy material for histological examination should be chosen in view of the fact that the site of the border (joint) between two kinds is different depending on the age of the woman (in the reproductive period — on the level of the external os, and in the menopausal one — on the level of the internal os).

Microinvasive carcinoma. Invasive squamous carcinoma of the cervix is the last disease developing from the cervical intraepithelial neoplasm (CIN). The term microinvasion means an early stage of invasion into the stroma (at a depth up to 3 mm) without af-

fecting the lymph nodes and vessels. Treatment in case of microinvasion can be less radical than for to invasive stage of the disease.

Invasive cancer (carcinoma). The following histological types of cervical cancer are distinguished:

1. *Squamous cancer (epidermoid):* a) macrocellular keratosic; b) macrocellular nonkeratosic; c) microcellular.

2. *Adenocarcinoma:* a) pure endocervical; b) endometrioid; c) light cell cancer; d) malignant adenoma; e) papillary cancer.

3. *Mixed carcinoma (glandular-squamous cancer).*

4. *Sarcoma.*

5. *Lymphoma.*

6. *Melanoma.*

7. *Carcinoid.*

8. *Secondary tumours.*

Invasive cervical cancer (carcinoma) is squamous histologically in 90% of cases. The precise correlation of the histological type and extent of differentiation of cervical cancer with the prognosis of the outcome of the disease is not established.

About 10% of cases of invasive cervical cancer is adenocarcinoma or mixed (combined) adenosquamous carcinoma (glandular-squamous cancer). Adenocarcinoma of the cervix develops from endocervical glands. Cervical adenocarcinoma should be distinguished from primary endometrial adenocarcinoma, because the prognosis and methods of treatment depend on it.

Exophytic, endophytic, ulcer and mixed growth forms of the clinically expressed cervical cancer are distinguished.

The exophytic form of cancer is observed more often, formed from the exocervix and develops in the vagina; in most cases it is squamous. In the beginning of the development the tumour can look like a little protrusion, missing the smooth surface, which in due time looks like cauliflower and with significant growth can fill the whole vaginal opening. Sometimes on the vaginal wall, at the place where it comes in contact with the tumour, isolated contact implants are formed. At the late stages it spreads to the muscular layer of the cervix and parametrium. With the exophytic form of tumour growth metastases into the lymph nodes and remote organs are observed later.

The endophytic form of cancer develops from the endocervix and more often is adenocarcinoma, stretching the cervix and cervical canal, although a shortening or thickening of the organ can take place. The endophytic form of cancer is characterized by early metastases in the lymph nodes.

The ulcerous form of cancer develops from the cervix and upper third of the vagina, is characterized by the mass of craters with necrotic fundus which can bleed. Sometimes the process looks like a "pig snout". During menopause cancer can be located in the cervical canal, spread through the thickness of the cervix, parametrium and to the bladder and rectum.

Clinical picture and diagnosis. Early stages of invasive cervical carcinoma are as a rule asymptomatic. A progressing of the disease is accompanied by a characteristic triad of gynaecologic symptoms: pain, bloody discharge and leucorrhoea ("death symptoms"). When the tumour reaches large sizes, there are vaginal discharge with an unpleasant odour, containing admixture of blood. Vaginal bleedings, which frequently occur after sexual intercourse (postcoital), are possible. However, pathological menstrual and intermenstrual bleedings can be observed. Other possible symptoms are pelvic pain and edema of the legs. With the spread of the tumour to the pelvic walls, the pain syndrome increases; edema of the legs can appear.

Late disease manifestations include urine or feces incontience due to the mass of vesicovaginal or rectovaginal fistulas.

The regional lymph nodes include the parametric (paracervical), obturator, external and internal ileal and sacral.

During objective examination it is necessary to examine carefully the inguinal and supraclavicular lymph nodes, pay attention to the presence of exudate in the pleura, volumetric masses in the small pelvic cavity. During bimanual examination, which has crucial importance in determining the stage of the disease, is necessary to establish:

1) the size of the cervical tumour;

2) tumour spread to the vaginal mucous membrane;

3) thickness or nodularity of the parametrium;

4) the size of the uterus;

5) adnexal enlargement.

Rectovaginal examination which enables to estimate the condition of the lateral and posterior sections of the parametrium is also performed to increase the accuracy of diagnosis. With the presence of II–III stage cervical cancer infiltrates are palpated in the parametrium and/or invasion of the tumour into the rectum is found.

While examining the cervix with the specula the form and sizes of the vaginal parts, anatomic conditions are determined. Intraepithelial and microinvasive cervical cancer can proceed as pseudoerosion type with an atypical transformation zone. The colposcopic picture of the initial forms of cancer is characterized by the presence of acetowhite epithelium, iodine-negative zones, mosaic, stippling, atypical vessels. An important symptom is bleeding, occurring with the touch of a tampon to the cervix or as a result of manipulations with the specula, although such a condition can be shown also with inflammatory and atrophic processes in the cervix and vagina.

Diagnosis is carried out by performing a biopsy from one or several characteristic zones of the tumour with subsequent histological examination. In

some cases biopsy of the parametrium and lymph nodes is conducted by transvaginal or punch biopsy is applied.

Selective lymphadenectomy of the pelvic and periaortic lymph nodes is carried out to reveal microscopic defects.

The *classification* of cervical cancer is based on the clinical, endoscopic and histological data (Table 11).

Gynaecologic examination, assisting in the establishment of the limits of invasion of the carcinoma to the vagina and parametrium (Fig. 52), plays the basic role in determining the stage of the disease. Additional data are possible to receive with rectovaginal examination. Among the applied diagnostic procedures, the greatest importance is colposcopy, excretory urography, cytoscopy, colonoscopy, proctosigmoidoscopy, radiography. Modern methods of examination are computer tomography, nuclear magnetic resonance, lymphoangiography.

Spread of the tumour occurs by the continual (in the vagina, corpus uteri, parametrium) and lymphogenous ways (external and internal ileal and obturatory lymph nodes). Further the process seizes the general ileal, periaortic and pericaval lymph nodes. Hematogenous metastases, as well as intraabdominal spread of the tumour, are observed seldom. Even for patients in the agonal stages of the disease, the metastases, spread to distant organs, are observed in 25–40% of cases.

The prognosis concerning the survival rate of such patients depends on the stage of the disease and considerably worsens with the invasion of growth beyond the cervix. *The size of the tumour* is an independent prognostic factor. Potential opportunities for the tumour to spread to lymph nodes increase with an increase in the size of the tumour. *The depth of the invasion* into the stroma correlates with the potential lesion of the lymph nodes. The presence of metastases in the lymph nodes, especially pelvic and periaortic, is an important parameter in the prognosis of the outcome of the disease. Vascular defects are connected to an increase in the risk of development of metastases in the pelvic lymph nodes. The question on how the extent of cellular differentiation of a tumour influences the prognosis of the disease remains debatable.

Treatment. For patients with preinvasive and microinvasive cervical cancer conization or amputation of the cervix are applied. In case of accompanying complications (uterine myoma, ovarian cystoma), as well as because of technical difficulties (with cervical atrophy), conization is performed with extirpation of the uterus together with the affected appendages.

Patients with early stromal invasion *(microinvasive carcinoma),* is characterized by the spread into the stroma to a depth of more than 3 mm from the basal membrane and the absence of defects of the vascular spaces, are subject to treatment by carrying out the usual hysterectomy. Conization within the limits of the healthy tissue can be performed in young patients with non-realized reproductive function, then they should be under constant supervision of the doctor. However, this method cannot be standard. Radical surgical treatment can be conduct-

Table 11. **Characteristics of staging for carcinoma of the cervix uteri (by FIGO, 1986)**

Stage	Characteristic
0	Intraepithelial carcinoma (carcinoma *in situ*)
I	The carcinoma is strictly confined to the cervix
IA	Preclinical cervical carcinoma (identified microscopically): IA_1 — minimal microscopic stromal invasion IA_2 — microscopic invasion, depth < 5mm, no wider than 7mm
IB	Lesion greater than at the IA_2 stage
II	The carcinoma extends beyond the cervix, but has not extended the pelvic wall; the carcinoma involves the vagina, but only to its lower third
IIA	Parametrium is free. Invasion into the vagina, but no as far as the lower third
IIB	Invasion of the parametrium
III	The carcinoma involves the pelvic wall, affects the lower third of the vagina; hydronephrosis, nonfunctioning kidney
IIIA	No extension to the pelvic wall, but the lower third of the vagina is affected
IIIB	Spread onto the pelvic wall and/or hydronephrosis or nonfunctioning kidney
IV	The carcinoma spreads beyond the true pelvis or has clinically involved mucous membrane of the bladder or rectum
IVA	Spread of the growth to the adjacent organs (rectum, urinary bladder), which is confirmed by the biopsy results
IVB	Spread to distant organs

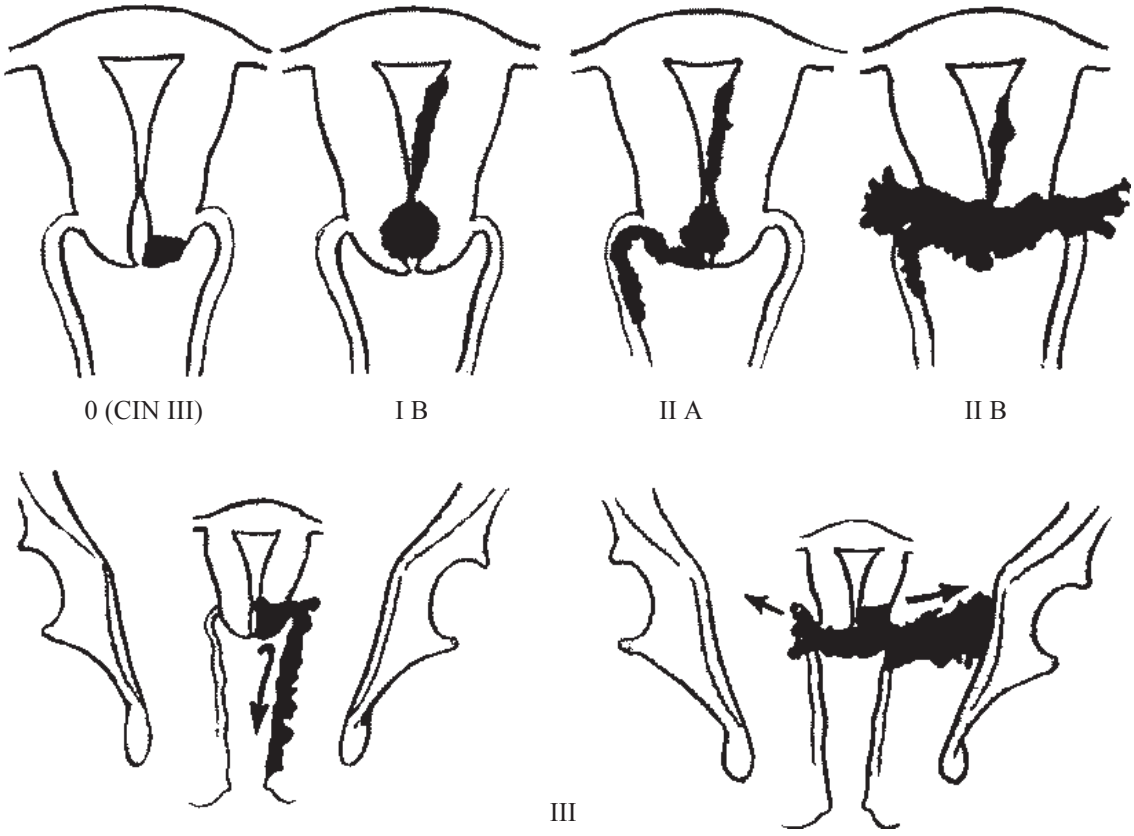


Fig. 52. Cervical cancer: stage 0 (CIN III)–III

ed in patients with I stage of the invasive cervical carcinoma. If the depth of invasion into the stroma exceeds 3 mm, the method of choice is radical abdominal hysterectomy, removal of the uterus with the appendages, the upper third of the vagina and pelvic fat, as well as bilateral pelvic lymphadenectomy (Wertheim's operation). In case of metastases in the pelvic lymph nodes, postoperative radiation therapy is performed.

Complications of surgical treatment can be postoperative dysfunction of the bladder, ureterovaginal fistula.

Radiation therapy is conducted as the standard procedure for patients with invasive IIB–IVA stage cervical cancer. It provides various combinations of external (applicational) radiation of the pelvis, intracavitary close-focal, or brachytherapy and the use of radionuclides. Gamma-therapeutic device, betatron and linear accelerator are used. The corresponding dose of energy is usually directed on the zones of parametrium and regional lymph nodes from 2–4 fields. The sessions of distant and application radiation therapy are alternated. External pelvic radiation is used to influence the central affected focus and the sites of possible pelvic dissimination (parametrium, pelvic lymph nodes). Caesium, radium or cobalt are used for intracavitary treatment (on the central site of the tumour). The total course dose of radiation should not exceed the total tolerant dose of adjacent organs (about 60 Gr).

The palliative course of distant radiation, symptomatic therapy are conducted in patients with IV stage of the disease.

Complications of radiation therapy can be radiation injuries to the adjacent organs, in particular the bladder and rectum (radiation proctitis and cystitis), reactivation of inflammatory diseases of the small pelvic organs, down to the development of pelviperitonitis and peritonitis. Radiation therapy together with extrafascial hysterectomy is recommended to patients with IB stage, barrel endophytic growth, which promotes the reduction of the incidence of central relapses. Radiation of the periaortic lymph nodes is performed in some patients with microscopic defects of the lymph nodes and potentially curable pelvic tumours.

Recurring cancer. Approximately in 40–50% of patients after primary surgical treatment or radiation therapy, relapses of cervical cancer develop; in most cases they are diagnosed within the first 2 years after treatment and demand further therapy.

Clinical picture and diagnosis. For recurring cervical carcinoma decrease in body weight, vaginal discharge or bleeding, pain in the pelvis, back, hips, knees, edema of the legs are characteristic. During gynaecological examination, central necrosis of the cervix and vagina, thickening or volumetric masses in the small pelvis, increase in lymph nodes can be observed. With the help of excretory urography obstruction of the ureter can be revealed.

Central relapse can result in the lesion of the cervix, vaginal vaults, the basis of the bladder, anterior wall of the rectum and, as a rule, is accompanied by bleeding or vaginal discharge. Recurring affection can be asymptomatic with central exophytic or infiltrative tumours.

Regional relapse is characterized by involvement of the pelvic wall with displays of pain in it or in the legs, as well as edemas of the legs, obstruction of the ureter.

Remote relapse is accompanied by the symptoms connected to the site of metastases. It is desirable to conduct histological documentation of the recurring tumours. For diagnosis, aspiration biopsy and cytological exam are used.

Treatment. *Radiation therapy* for pelvic relapse is a method of choice for patients who have had primary surgical treatment. Repeated radiation treatment is not recommended in connection with the low incidence of positive results. Radiation of the remote metastases (in bones) is conducted for some patients.

Surgical treatment. Patients with isolated central relapses, who first had radiation therapy, are recommended pelvic exenteration. The operation includes the removal of the affected pelvic organs (uterus, vagina), bladder (anterior exenteration), rectosigmoid section of the intestines (posterior exenteration) or their combination (total exenteration). In some patients, the efficiency of such treatment can reach 50%. Pelvic exenteration is accompanied by significant early and late morbidity; therefore it is conducted only for radical, instead of palliative, purposes. Total pelvic exenteration demands the removal of the urinary system by implantation of the ureter in an isolated segment of the intestines (ileal, colonic intestine) with the creation of a constant colostoma.

Chemotherapy is recommended with the presence of metastases in distant organs, as well as in case of absence of reaction of the local or regional metastases to surgical treatment and radiation therapy. The reaction of squamous epithelium to chemotherapy is observed in 25% of cases; however, precise proofs of an increase in the life expectancy of such patients are not present. Cisplatin and its combinations are used in many chemotherapeutic modes.

The *prognosis* concerning treatment of recurring cervical cancer depends on the site of relapse and the type of primary treatment.

The survival rate of patients depends mainly on the stage of the disease, volume of the tumour and lymphogenous distribution. A high (100%) survival rate can be guaranteed only with well-timed diagnosis of microinvasive carcinoma. Patients with stage IB in 85% of cases can recover due to the use of combined surgical and radiation therapy; with IIB stage the survival rate is 65%; IIIB — 35%; IVA — 16%; IVB — 0%. The worst prognosis is connected to metastases in the pelvis and paraaortal lymph nodes in the late stages of the disease.

Cervical cancer in pregnant women is observed with a frequency of 1:2,000. The most often symptom of this disease — vaginal bleeding. In 20% of cases there is an asymptomatic disease course, which is diagnosed during gynaecologic examination. Diagnostic procedures, including biopsy, are conducted in the same volume as for non-pregnant women, except for curettage of the cervical canal. Determining the stage of the disease by means of gynaecologic examination can be difficult, especially at the second half of pregnancy. In such cases, nuclear magnetic resonance tomography, which is not accompanied by a radiation load, is recommended.

The influence of the carcinoma on the delivery is not precisely established because a majority of patients give birth by caesarean section.

Treatment. The methods of choice for young women with early stage carcinoma are radical hysterectomy and pelvic lymphadenectomy. In other cases it is recommended to perform pelvic radiation with intrauterine and intravaginal introduction of caesium. When the fetus reaches vitality, birth is necessary as soon as possible. Treatment begins 7–10 days after birth, i.e. after the involution of the uterus.

The cancer of the cervical stump has no essential differences in diagnosis, stages and principles of treatment from intact cervical cancer. With the use of radiation therapy, the difficulties can be connected to the impossibility of intracavitary radiation because of the absence of the uterine cavity. In this case, the greatest doses of external pelvic or transperitoneal radiation are used. The survival rate for patients within 5 years does not differ from that of intact cervical cancer.

Invasive cervical cancer with the removal of the uterus concerning benign processes is in most cases characterized by a significant extent of invasion. Such patients are subject to treatment by external pelvic or local vaginal radiations. The survival rate of patients within 5 years changes from 96 to 37% depending on the adequacy of removal of the tumour and the condition of its borders with healthy tissue.

Adenocarcinoma is observed in 10% of cases of cervical cancer, develops from endocervical glandular elements, producing mucous, and has the same risk factors as squamous cancer. The age of patients, spread of the tumour and clinical symptoms are similar to those for squamous tumours, therefore treatment is conducted by the same principles. In connection with the high frequency of endophytic growth after hysterectomy, radiation therapy is applied.

Adenosquamous carcinoma contains squamous and glandular malignant elements and makes up 5–25% of all cases of adenocarcinomas. The prognosis in case of a low degree of differentiation of cellular elements of the tumour is bad.

Light cell cancer (light cell adenocarcinoma) is formed (but not necessarily) in patients who were subject to the influence of diethylstulbestrole *in utero*. Treatment is combined (surgical intervention and radiation therapy).

Adenoid cystic carcinoma occurs more often in the respiratory tract, salivary and mammary glands than in the cervix uteri. Histologically it is characterized by the presence of hyperchrome nuclei with the minimal contents of cytoplasm. The prognosis is adverse due to early metastases.

Verruciform(warty) carcinoma is a variant of squamous cancer and is characterized by exophytic growth similar to that for acuminate condyloma. During cytological and histological study malignancy of tumours can be not revealed in connection with a high degree of its differentiation. The given tumour is locally invasive and will not penetrate deeply into the stroma; metastases in the lymph nodes are observed seldom. Surgical treatment is conducted at the I stage of the disease, in later stages — radiation therapy.

Small cell carcinoma was traditionally considered as a histological subtype of squamous cancer. However, data from the latest researches, conducted by means of electronic microscopy, testify to the neuroendocrine character of the cellular elements of the given tumour (presence of neurosecretory granules). This cancer has a tendency to forming early and disseminated metastases.

Treatment is combined (radiation and chemotherapy). The rarest variant of this tumour is cervical carcinoid, developing from argyrophilic cells.

Oat cell carcinoma of the cervix is observed seldom, is similar to bronchogenic and has very adverse prognosis.

Other tumours. The cervical sarcoma is observed seldom; leiomyosarcoma, stromal cell sarcoma, embryonal rhabdomyosarcoma, adenosarcoma and mixed müllerian sarcoma are distinguished. The prognosis is very adverse, irregardless of the method of treatment.

Lymphoma is also a rather rare cervical tumour; is subject to radiation therapy.

Melanoma forms seldom; treatment is surgical, the prognosis, as a rule, is adverse.

Secondary cervical carcinoma occurs due to the involvement of cancer to the endometrium. Metastases in the cervix from zones outside the pelvic limits are extremely seldom; they are observed with breast cancer, cancer of the abdomen, intestinal, urinary tract and lungs. Metastases can sometimes develop from clinically unidentified primary tumours.

CANCER OF THE CORPUS UTERI

Cancer of the corpus uteri (endometrial cancer, endometrial carcinoma) is one of the most widespread malignant diseases of the female reproductive system and recently in Ukraine, as well as in many other countries of the world, it takes first place in incidence among all gynaecologic malignancies. About 80% of cases of endometrial carcinoma are observed in women in the postmenopausal period, as a rule, at the age of 55–69.5% — before the age of 40.

Etiology, pathogenesis. The reason for endometrial cancer remains unknown, though its connection with increased exo- and endogenous oestrogen stimulation of the endometrium is established. Risk factors for endometrial cancer are conditions connected with hyperoestrogenism (obesity, chronic anovulation, oestrogen-producing ovarian tumours, therapy with oestrogen without progesterone modification), diabetes, arterial hypertension, liver dysfunction, late menopause, burdened familial history (family polyneoplasia).

The morbidity growth of endometrial cancer is explained by the ageing of the population, increased amount of fats in the diet and energetically valuable (high-calorie) diets. Endometrial cancer more often occurs in industrial advanced regions, occurs in women with high social and economic status, the presence of disorders of the menstrual cycle in the anamnesis, bleeding in menopause.

Obesity is observed almost in every second woman suffering from endometrial cancer. It is established that in fatty tissue there is a peripheral conversion of weak androgens (which normally are synthesized in the adrenal glands) in oestrogens (estrone). Constant endogenous stimulations of the endometrium by oestrogens of the fatty tissue promotes proliferative changes and the development of cancer. It is believed that diabetes and arterial hypertension are connected to endometrial cancer due to frequent accompanying obesity.

Chronic anovulation in women, who have not given birth, with polycystic ovarian syndrome can result in the development of endometrial cancer even before the age of 35. The monthly absence of the corpus luteum and production of progesterone results in oestrogenous stimulation of a constant and spontaneous character.

Oestrogen-producing ovarian tumours (thecoma, granular-theca cell tumour) can be associated with endometrial cancer.

The risk factors for the development of endometrial cancer can be oestrogen replacement therapy, which depends on the doses and duration of treatment, in women after menopause. The protective ef-

fect consists of additional cyclic use of progesterone with oestrogen replacement therapy.

There are data that the use of combined oral contraceptives promotes a 50% decrease in the risk of endometrial cancer.

Pathomorphology. According to the histological classification, the following types of endometrial cancer are distinguished:

1. Endometrioid: a) cellular; b) secretory; c) papillary; d) adenoacanthoma; e) adenosquamous carcinoma.
2. Papillary-serous carcinoma.
3. Mucinous carcinoma.
4. Light cell carcinoma.
5. Squamous carcinoma.
6. Mixed carcinoma.

The most widespread histological type of endometrial cancer (95% of cases) is adenocarcinoma with the differentiation by the type of uterine glands (endometrioid); sometimes — in combination with the histological attributes of similar benign (adenoacanthoma) or malignant squamous elements (adenosquamous carcinoma).

The prognostic value of various histological variants of endometrial cancer differs just a little. So, in the opinion of some authors, adenoacanthoma is less malignant, adenosquamous carcinoma — more. In the opinion of others, the dicisive factor in determining the consequences of the disease is the degree of differentiation of the carcinoma. So, adenosquamous carcinoma more often is high differentiated. According to the classification of the International Federation of Gynaecologists and Obstetricians — FIGO, three degrees of differentiation of adenocarcinoma are distinguished:

Degree 1: < 5% nonsquamous or nonmorulous samples of solid growth.

Degree 2: 6–50% nonsquamous and nonmorulous samples of solid growth.

Degree 3: > 50% nonsquamous and nonmorulous samples of solid growth.

The *screening* of the general population to reveal endometrial cancer is not popularized in connection with the difficulties occurring with the dilation of atrophic and frequently narrowed (stenosed) cervical canal and the penetration into the cavity of the endometrium in the postmenopausal period. Besides, histological analysis of a smear from the endometrium with the absence of clinical displays of the disease ethically is not justified. Despite this, some methods of screening diagnosis is offered:

1) endometrial lavage;
2) biopsy;
3) irrigation with an isotonic solution of sodium chloride;
4) vacuum-aspiration;
5) endometrial biopsy.

Sensitivity of these methods to determine endometrial cancer is 60–90%.

Clinical picture and diagnosis. Vaginal bleedings are the basic symptoms for endometrial cancer in 90% of women. In the pre- or perimenopause menometrorrhagia is observed. Obesity and anovulatory cycles promote the development of endometrial cancer in young women. The colour of the bloody discharge in postmenopause may change from bright red or dirty-brown to pale-pink. Differential diagnosis is based on the data from the histological study of the biopsy material. Negative results from the endometrial biopsy with vaginal bleedings do not exclude the diagnosis of carcinoma. In this case fractional curettage of the uterine cavity and cervical canal is performed, under the control of hysteroscopy.

All patients with vaginal bleedings in the postmenopausal period are subject to careful examination to exclude the diagnosis of carcinoma of the endometrium (in 20% of such patients). The risk of development of endometrial cancer grows from 15% in the early postmenopausal period to 50% — over the age of 80.

The data from gynaecologic examination not always helps in diagnosis. The uterus can have a normal size; it enlarges at the II–IV stages of cancer. With the absence of obesity of the patient, sometimes it is possible to reveal heterogeneity of the uterine consistence, its softening, and deformity. During examination of the vagina the presence of dilation of the uterus, vagina, parametrium is paid attention to. The condition of the parametrium is examined more precisely through the rectum. Metastases in the vagina develop in the late stages of the disease.

With spread to the cervix, differential diagnosis of endometrial cancer is conducted with primary cervical carcinoma. The symptoms of the disease can be an increase in the lymph nodes, the presence of liquid in the pleural cavity, space-occuping masses and ascites.

For diagnosis and differential diagnosis of endometrial cancer with ovarian lesions, ultrasound study is conducted. Hysterosalpingography has a potential risk of the cellular dissimination development, in connection with this its application is limited. Metastatic spread to the regional lymph nodes is revealed with the help of lymphography. Computer tomography helps determine the site of other intra- and retroperitoneal structures. It is expedient to use nuclear magnetic resonance before an operation to reveal the invasion into the myometrium and its distribution onto the lower uterine segment.

The classification of endometrial cancer according to the stages (by FIGO, 1988) is submitted in table 12.

More than 75% of cases of the revealed endometrial cancer are at the I stage of development of the disease (Fig. 53). The distinction between I and II stages is based on the data from the histological study of the affected endocervix. To determine the stage of cancer, besides of already specified procedures, roent-

Table 12. **Characteristics of the stages of endometrial cancer (by FIGO, 1988)**

Stage	Degree	Characteristic
I A	1, 2, 3	Tumour is limited to the endometrium
I B	—«—	Invasion < 1/2 of the myometrium
I C	—«—	Invasion > 1/2 of the myometrium
II A	—«—	Only the endocervical glands are affected
II B	—«—	Invasion into the cervical stroma
III A	—«—	Invasion into the serous membrane and (or) ovaries and (or) positive peritonial cytology
III B	—«—	Vaginal metastases
III C	—«—	Metastases to the pelvis and (or) periaortic lymph nodes
IV A	—«—	Tumour invasion to the urinary bladder and (or) bowel mucosa
IV B	—«—	Metastases to distant organs, including intraabdominal and (or) inguinal lymph nodes

genography, excretory urography, cytoscopy, radiopaque study (irrigoscopy), proctosigmoidoscopy can be used.

Metastases. Endometrial cancer spreads to various directions. However, most often — to the cervix, vagina, myometrium; by the lymph vessels it disseminates to the pelvis and periaortic lymph nodes; transluminal (through the Fallopian tubes) can reach the abdominal cavity. Hematogenously — to the distant organs, more often — to the lungs, liver and bones. The most widespread is lymphatic dissemination into the deep layers of the myometrium.

Ways of spread of endometrial cancer

Direct	*Lymphogenous*	*Hematogenous*
Surface of the endometrium	Pelvic lymph nodes	Lungs
Myometrium	Paraaortic lymph nodes	Bones
Endocervix		Liver
Fallopian tubes		

The *prognosis* of the disease depends on the time of diagnosis and stage of cancer, depth of invasion of the myometrium, prevalence in lymph nodes and presence of metastases in distant organs. Highly differentiated tumours (degree 1) have more favourable prognosis than low differentiated ones (degree 3).

The depth of invasion of the myometrium — an important prognostic attribute. With the tumour spread to the endometrium and internal third of the myometrium the incidence of metastases development is very low while with the tumour spread the external third of the endometrium it reaches 30%.

The revealing of microscopic metastases in the pelvic and periaortic lymph nodes has great value for the choice of tactics of treatment. Selective lymphadenectomy is necessary for all patients with a high risk of development of central metastases, i.e. in cases of low differentiated tumours and invasion of the deep layers of the myometrium.

Ablations from the peritoneum *(peritoneal cytology)* are more often positive with the presence of more extensive stages of endometrial cancer.

The level of cytosole receptors to progesterone correlates with the degree of differentiation of the tumour, as well as with its sensitivity to hormonal therapy. A higher level is observed with highly differentiated carcinoma, lower — with low differentiated. The metastases incidence in the lymph nodes depends on the sizes of the tumour as well.

Treatment. The basic method of treatment is surgical because tumours of the corpus uteri are insensitive to radiation therapy. If the tumour is located in the uterine fundus and has a highly differentiated (mature) structure, extirpation of the uterus with its appendages is performed in older patients with obesity and the absence of tumoural changes in other organs.

For patients with *I stage* cancer with the absence of contraindications to surgical intervention, the method of choice in any case is an operation. Its efficiency depends on the precise definition of the limits of the tumour spread and a rational plan of treatment. Methods of choice are abdominal extrafascial hysterectomy and bilateral salpingo-oophorectomy. With insemination of the peritoneum it is washed, the subdiafragmatic surface, liver, omentum, pelvis, retroperitoneal space are examined and palpated. Material for a biopsy is taken from suspicious places. A biopsy of the pelvic and periaortic lymph nodes is performed in all cases. If the tumour is impossible to remove completely, its maximal reduction is conducted. With all cases of affected lymph nodes, postoperative external radiation of the pelvis or aortal area is recommended.

More and more supporters are found for organ-sparing hormonal therapy with progestin ("Provera", "Depostat") of patients with highly differentiated endometrial cancer I A stage, especially women of the reproductive age, as well as laparoscopic hysterectomy with the presence of I stage endometrial cancer.

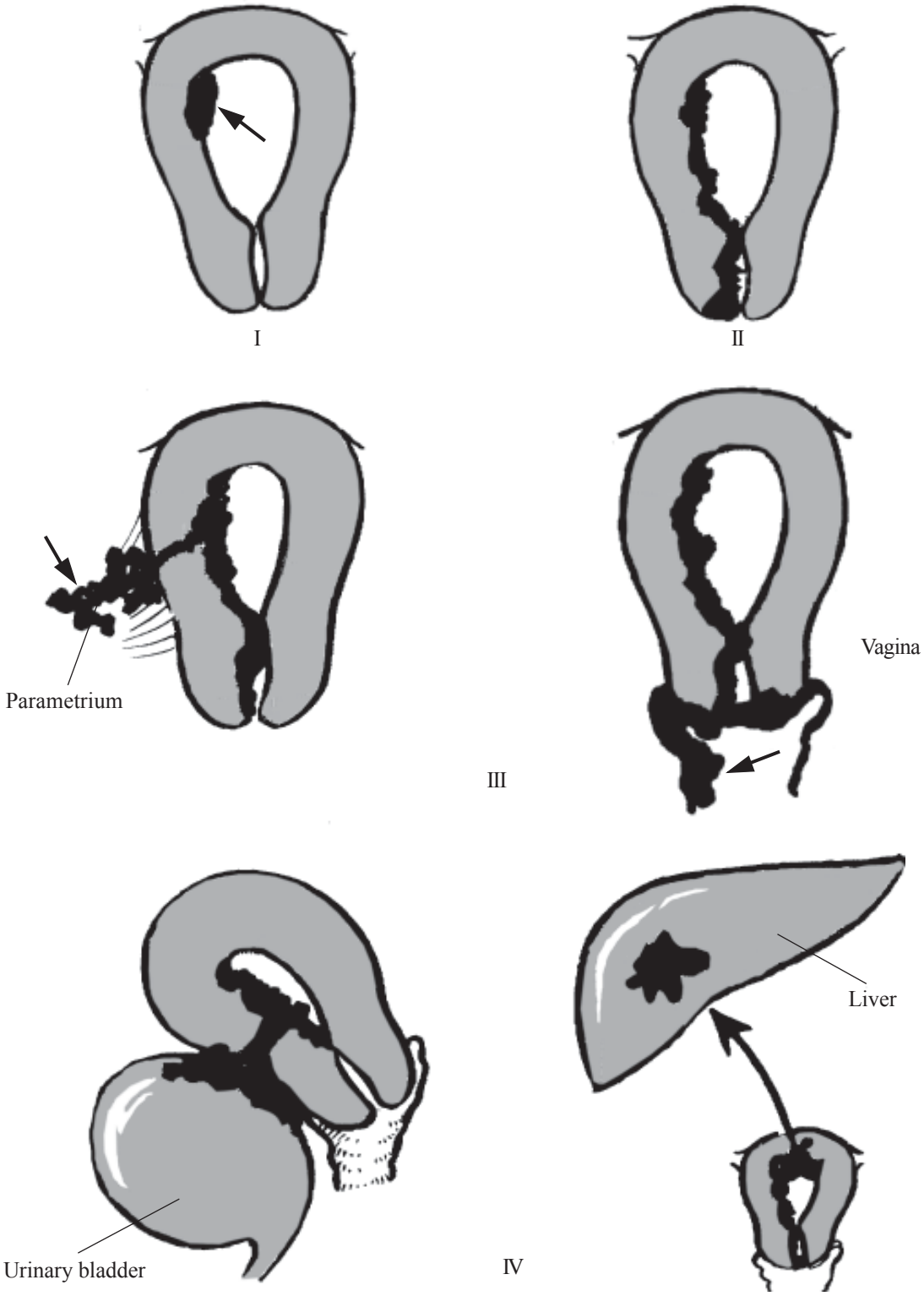


Fig. 53. Cancer of the endometrium: stages I–IV

Patients with *II stage* endometrial cancer, as a rule, are subject to surgical treatment in combination with pelvic radiation. With extensive cervical lesion, preoperative pelvic radiation with subsequent performance of extended hysterectomy is recommended. In the postoperative period it is necessary to continue radiation therapy. Radical hysterectomy and pelvic lymphadenectomy are performed in some patients with cervical injury. However, the majority of such patients cannot endue a radical surgical intervention because of the age, obesity, accompanying extragenital pathologies.

III stage of endometrial cancer is observed in a small amount of women, as a rule, causes suspicion in connection with tumour spread to the vagina and parametrium. The most effective method of treatment in this case is primary external radiation therapy, conducted after surgical reduction of the tumour,

which is possible in some cases. With the absence of defects of the ovaries and lymph nodes, therapy is performed in the intraperitoneal and retroperitoneal spaces. With the revealing of microscopic ovarian invasion, additional radiation therapy is recommended. Affected retroperitoneal lymph nodes demand the use of radiation therapy of the pelvis and paraaortic areas. In case of positive peritoneal cytology, the majority of oncologists do not recommend aggressive therapy, which is accompanied by significant morbidity.

For patients with *IV stage* cancer in case of dissimination of the carcinoma to the bladder and rectum, external radiation therapy of the pelvis with subsequent intracavitary introduction of caesium or radium is necessary. If the tumour did not spread to pelvic walls, pelvic exenteration can be performed. Patients with IV stage or relapse of a tumour need chemo- and hormone therapy. Medroxyprogesterone acetate (”Provera”) is used as additional or palliative treatment of patients with relapses of endometrial cancer or metastases at a dose of 200–600 mg a day till the achievement of the therapeutic effect.

The data on the amount of progesterone receptors help determine the mode of treatment. Parenteral introduction of medroxyprogesterone acetate (”Provera”) or oral use of megestrol acetate can be the first stage of treatment of patients with the presence of progesterone receptors. For patients with no progesterone receptors, as well as in case of the tumour progressing after therapy with progestin, chemotherapy is necessary. In 30% of patients a positive effect from the use of cisplatin or its combinations with doxorubicin is observed. With the presence of isolated relapses, radiation therapy is possible.

The survival rate of patients and prognosis of the disease depends on the stage and duly diagnosis and treatment. The survival rate within 5 years is observed in 60 to 90% of women with I and II stages of the disease and from 0 to 30% — with III and IV stages.

SARCOMA OF THE UTERUS

Sarcoma of the uterus is a rather rare (< 4% of all cases of endometrial cancer). However, one of the most malignant and lethal kinds of gynaecologic cancer. The reason for this disease is not established. A combination of sarcoma of the uterus with obesity and arterial hypertension is not as regular as with endometrial cancer. An increase in uterine sarcoma incidence is observed in patients exposed to radiation therapy concerning other kinds of malignant tumours of the pelvic organs. Malignancy of uterine myoma is only in 1% of cases.

The most precise is the histological classification of sarcoma types offered by Oberg (Table 13). “Pure” types of sarcoma differ from the mixed ones in that they consist only of one kind of cells. Homologous sarcoma consists of malignant elements, developing from the tissue of the uterus (smooth muscles, endometrial stroma). Heterologous tumour develops from tissue which normally is not present in the uterus (bones, fat). A simplified classification of sarcoma of the uterus includes four of the most widespread types of tumours:

1) leiomyosarcoma;
2) sarcoma of the endometrial stroma;
3) mixed mesodermal (Müllerian) sarcoma;
4) adenosarcoma.

According to this classification carcinosarcoma is included under the type of mixed mesodermal tumours. Other variants of sarcoma are observed very seldom.

Leiomyosarcoma is more often intramural. However, cases of subserous and submucous tumours have been observed. The parameters of the prognosis of the outcome of the disease are the amount of mitosis in 10 fields of vision and the presence of cellular atypia. Premenopausal age of the patient, the development of a tumour from a uterine myoma and the absence of necrosis are considered as favourable prognostic attributes.

Sarcoma of the endometrial stroma is divided into sarcoma with a high degree of malignancy (> 10 mitosis in 10 fields of vision) and a low degree of malignancy (< 10 mitoses).

Mixed mesodermal sarcoma, as a rule, develops from polypoid masses, stretching the uterine cavity. The depth of invasion into the myometrium correlates with the incidence of metastases in lymph nodes. It is considered, that patients with homologous tumours have the best prognosis of treatment, rather than patients with heterogenous tumours.

Table 13. **The Oberg’s classification of uterine sarcoma**

Kind of tumour	Type of tumour	
	Pure	Mixed
Homologous	Leiomyosarcoma Sarcoma of the endometrial stroma	Adenosarcoma Carcinosarcoma
Heterologous	Rhabdomyosarcoma Chondrosarcoma Osteosarcoma Liposarcoma	Mixed mesodermal tumour (Müller’s)

Clinical picture and diagnosis. The average age of patients with leiomyosarcoma is about 55 years and, as a rule, about 10 years less than the age of patients with mixed mesodermal sarcoma and sarcoma of the endometrial stroma. Most frequently such patients complain of uterine bleedings and pelvic pain. During bimanual examination an increase in the uterus and the presence of polypoid masses in the cervical canal are found.

An endometrial biopsy, fractional diagnostic curettage of the uterine cavity help to establish the diagnosis less than in 50% of cases, because such tumours are frequently intramural, without invasion to the endometrium. With cervical injury it is necessary to perform biopsy. In most cases the tumour is accidentally found during hysterectomy when leiomyosarcoma happens by accident.

The stages of uterine sarcoma development are similar to the stages of endometrial cancer. More than in half of cases the sarcoma is diagnosed at the I stage.

Metastatic sptead of uterine sarcoma occurs in the following ways: 1) haematogenous (in most cases); 2) lymphogenous, 3) continual. More than in 90% of cases metastases in distant organs are observed, more often — in the lungs.

Treatment and prognosis. The most effective method of treatment is abdominal hysterectomy with bilateral salpingo-oophorectomy. All intraperitoneal and retroperitoneal organs are carefully examined; material for biopsy is taken from all suspicious sites. Unexpected detection of metastases in lymph nodes is observed in 35% of patients with I stage of the disease. Negative data during an operation for the presence of metastases do not give full confidence that they will not form.

Primary radiation therapy is not recommended except for cases when surgical treatment is contraindicated. In some situations after operative intervention concerning I stage sarcoma, as well as with the presence of other pelvic tumours, auxiliary (adjuvant) radiation therapy may be prescribed.

Chemotherapy (doxorubicin, cisplatin, dacarbacin, etc.) is used with palliative purpose in patients with metastases in distant organs or with relapses of a tumour. The use of adjuvant chemotherapy at the I and II stages of the disease to prevent metastatic spread or relapses does not bring benefit. Large doses of progesterone can be prescribed in cases of endolymphatic stromal miosis.

For patients with I stage sarcoma of the uterus, the survival rate within 5 years is about 50% and sharply decreases — from 10 to 0 % — for patients with III and IV stages, without precise dependence on the histological type of the tumour.

Prevention of endometrial cancer consists of duly diagnosis and adequate treatment of patients with hyperplastic processes (hyperplasia, polyps) of the endometrium and precancer conditions (atypical hyperplasia of the endometrium, polyps of the endometrium with adenomatosis). Endoscope technologies play an important role: hysteroscopy with biopsy, cryolysis, electric and laser resection, high-frequency coagulation, laser ablation of the endometrium.

The new methodological approach is based on conducting clinic-genealogic examination of patients, studying of the degree of hereditary predisposition to endometrial cancer, revealing of members of the family with premorbidal conditions and their duly treatment.

OVARIAN CANCER

Ovarian cancer is one of the most widespread gynaecologic malignant diseases. The death rate from this disease both in Ukraine and in other countries of the world, for example the USA, is the highest among all gynaecologic malignancies, which is connected to the absence of effective screening at the early stages of the disease. As a result, ovarian cancer is extremely seldom diagnosed in the early stage; even the most advanced methods of treatment do not render essential influence on the survival rate of patients. In 70–75% of patients symptoms of the disease appear only after the development of metastases beyond the ovaries and pelvis (i.e. at III–IV stages of cancer).

Ovarian cancer is a disease developing mainly in the 5th–6th decade of a woman's life. The risk of formation of ovarian carcinoma is about 1% and increases by 70 years of age.

The *etiology* of ovarian cancer is not established. According to one hypothesis, cancer can be caused by trauma to the ovarian superficial epithelium due to monthly ovulation on the background of low parity of the woman. This theory is proven by clinical supervision, testifying of rare cases of development of ovarian cancer in children, in women with gonadal dysgenesis, in those using oral contraceptives which oppress ovulation, as well as about an increase of its incidence in women who have not given birth.

The groups of risk of ovarian cancer development are not precisely determined. The risk factors include hormonal, genetic (familial ovarian cancer), viral infections, ionizing radiation, obesity, diseases of the gallbladder. The probability of the development of a tumour increases with an increase in the amount of ovulation, in case of early pregnancy, development of early menopause. Ovarian cancer is observed in women in advanced countries of the world more often.

Familial ovarian cancer (including more remote degree of relationship than the first one) can develop in young women and is notable for a high death rate. In connection with this, patients with familial cancer in the anamnesis are recommended preventive

oophorectomy after 35 years of age. The presence in the family anamnesis of cases of breast cancer, endometrial cancer or intestines (polyneoplasm) also increases the risk of ovarian carcinoma. A preventive effect concerning ovarian cancer is achieved under the condition of long use of combined oral contraceptives (induction of anovulation).

Pathomorphology and classification. **Epithelial tumours** develop in a prevailing majority (85%) of cases of primary ovarian cancer. **Germinogenic (germ cell) tumours** make about 8–10%, **stromal** — 4 % of cases of ovarian cancer.

The **metastatic ovarian cancer** occurs in 15% of cases (more often metastases from cancer of the breast, endometrium, intestines and abdomen).

Every second case, epithelial ovarian tumours are *papillary, serous* tumours, which after their detection already have, as a rule, metastases in the upper sections of the abdominal cavity. So, the serous type of ovarian cancer is observed in 50% of cases; mucinous, endometrioid and undifferentiated — in 15% of cases; clear cell — in 5% of cases.

Mucinous tumours, making up 15% of all epithelial neoplasms, have histological attributes similar to those of adenocarcinoma of the intestines and endocervix. Such tumours, as a rule, are limited to the pelvic cavity and by size are the largest among primary epithelial carcinomas.

Endometrioid ovarian cancer histologically is similar to endometrial cancer. A combination of primary endometrial cancer with ovarian cancer is observed in 20% of cases in patients with endometrial carcinoma. Sometimes the development of endometrioid ovarian carcinoma can be connected with endometriosis of the ovaries.

Clear cell (mesonephroid) tumours also are connected with endometriosis of the ovaries and make up 5% of all epithelial neoplasm. They, as a rule, are bilateral and are connected with primary endometrial adenocarcinoma.

Metastases of ovarian cancer have similar histological morphology and biological characteristics (growth rate, resistance to chemotherapy, survival rate of patients).

Classification. The stages of ovarian cancer, according to the classification of the International Federation of Gynaecologists and Obstetricians (FIGO, 1985), opposite to other gynaecologic malignancies, are determined only by the surgical data (Table 14).

The cancer staging remains the most important prognostic attribute for all cellular types of cancer (Fig. 54). Some researchers select a special group of ovarian carcinomas with low malignancy potential (12% of cases of ovarian malignancy).

Visual defects of the ovaries with the tumour spread to the upper sections of the abdominal cavity are observed only at the stage III of the disease. The presence of retroperitoneal cancer — more adverse prognostic attribute in comparison with intraabdominal one. In 70% of cases ovarian cancer when diagnosed is already at the stage III.

The second important prognostic factor after determining the stage of the disease is the degree of differentiation of the tumour (I — highy differentiated; II — moderately differentiated; III — low differentiated).

Ways of spreading. Ovarian cancer spreads by metastases in all possible ways: *continual* (with intergrowth into adjacent organs); *implantation* (transcoelomic — through the peritoneum into the intestinal mesentery, right part of the diaphragm, omentum); *lympho- and haematogenous* (typical places of metastases — lungs and liver). *Retroperitoneal* ovarian cancer spreads to the paraaortic and pelvic lymph nodes.

More often dissemination of the process occurs in the peritoneum. The occurrence of growths on the surface of an ovarian tumour or breach of its integrity are considered factors promoting the dissemination of cancer cells. Lymphogenously the way process spreads to the Fallopian tubes and uterus, pelvic and paraaortic lymph nodes. Haematogenous metastasing is less widespread and, as a rule, is later.

Regional lymph nodes include the inguinal, obturator, and external ileal, sacral and paraaortic lymph nodes.

Clinical picture and diagnosis. In most cases ovarian cancer has a latent beginning and in connection with this represents the greatest difficulties in diagnosis among all kinds of gynaecologic cancer. Stage I ovarian cancer is diagnosed only in 15% of cases. Late diagnosis of ovarian cancer is caused mainly by its aggressive clinical course. Even with the presence of visual defects of one or both ovaries, the upper part of the abdomen and retroperitoneum are involved in every third patient.

Till now there were no reliable methods of preclinical diagnosis of ovarian cancer, because at the early stages of the disease, cancer is microscopic masses the sizes of which are outside the sensitivity of available modern instrumental methods.

The first clinical symptom may only be irregular menstruation; the pain syndrome is characteristic for the late stages of the disease (III stage). Patients can feel a discomfort in the stomach and intestines (nausea, loss of appetite, swelling of the abdomen). Compression symptoms of adjacent organs (frequent urination, constipation or diarrhoea, oliguria) are observed less often.

Due to anatomical-topographical features of the ovaries, the detection of their malignant neoplasm is complicated both during objective examination, and during ultrasonic and radiological examinations. Unqualified gynaecologic examination (without draining the bladder and intestines, without rectovaginal examination) do not reveal infiltrates in the rectouterine excavation (Douglas' cul-de-sac), rectovaginal fat. The atypical arrangement of a tumour (conglomerate with

Table 14. **Staging of ovarian cancer** (by FIGO, 1985)

Stage	Characteristics
I	Growth is limited to the ovaries
A	Growth is limited to one ovary; ascites is not present; the capsule is intact, cancer has not spread to the external surface
B	Growth is limited to both ovaries; ascites is not present; the capsule is intact, cancer has not spread to the external surface
C	The same as for stage I A and I B. The tumour spreads to the surface of one (both) ovaries, or rupture of the capsule, or ascites with the presence of malignant cells, or positive peritoneal cytology
II	One (both) of the ovaries are affected with the pelvis involved
A	The tumour spread or metastases to the uterus and (or) Fallopian tubes
B	Extention to other pelvic tissue
C	The same as for stage III A and III B. Extention to the surface of the ovaries, or rupture of the capsule, or ascites with malignant cells, or positive peritoneal cytology
III	Tumour affects one or both ovaries with spread to the abdominal cavity, beyond the limits of the pelvis and (or) into retroperitoneal or inguinal lymph nodes. Superficial metastases in the liver
A	Tumour is limited to the pelvis, but histologically has spread to the small intestine or omentum
B	Tumour is limited to the pelvis, lymph nodes are intact; microscopic defects of the peritoneal surface are visible
C	Tumour of one or both ovaries with histological implantation into the peritoneum no < 2 cm Abdominal tumour implantation > 2 cm in diameter and (or) involement of the retroperitoneal or inguinal lymph nodes
IV	One (both) of the ovaries are injured with metastases in distant organs (pleura, parenchyma of the liver). Cancer cells are found in the pleural liquid

the uterus) promotes erroneous diagnosis of fibromyoma. Frequently the most adverse form of cancer is not diagnosed — microdefects of the ovaries with extensive metastases to the abdominal and chest cavities.

The spread of cancer to the upper parts of the abdominal cavity occurs faster because of ascites (in 80% of cases). The amount of ascitic liquid can vary from several millilitres to several litres. With serous cancer, the ascitic liquid has a straw-yellow colour, transparent; with mucinous-muddy, viscous (peritoneal pseudomyxoma); in the terminal stages of ovarian cancer ascites has a haemorhagic character.

Late symptoms of ovarian cancer are weight loss, subfebrile condition, symptoms of abdomen and intestinal obstruction. Superficial breathing is a symptom confirming the spread of cancer beyond the limits of the abdominal cavity. IV stage cancer is accompanied by the outpouring of the ascitic liquid into the pleura.

With the revealing of ascites and adnexal mass during gynaecologic examination, it is necessary to exclude the diagnosis of ovarian carcinoma. In the small pelvis, bilaterally enlarged ovaries, located on both sides or behind the uterus, are found. Their consistence is non-uniform; the surface is tuberous.

Sometimes with normal ovarian size ascites is observed. The diagnosis is based on the patient's age and symptoms connected to it. Any enlargement in the ovaries demands examination.

Menstruating women, having enlarged appendages > 7–8 cm in diameter, should have an ultrasonographic examination to determine the functional character of the found masses (physiological cysts). Such patients are subject to constant supervision or suppression (oppression) of the ovarian function by taking combined oral contraceptives for 2 months; after that, surgical examination is necessary (laparoscopy, laparotomy). The role of laparoscopy in diagnosis and treatment of patients with early stages of ovarian cancer has recently increased, especially in groups with a high risk (opportunity for conducting a target biopsy), repeated ("second-look") laparoscopies are conducted to determine the efficiency of cytoreduction during the postoperative course of chemotherapy, which helps in the decision of the necessity of a repeated operation. In patients with clinical displays of a tumour, laparoscopy enables to determine the features of its extention, examine the organs of the abdominal cavity to reveal metastases. The factor of reduction of tumour growth after laparoscopy in comparison with laparotomy is considered, although the use of pneumoperitoneum can give adverse effects.

In the periods before and after menarche, a cystic ovarian enlargement can occur due to damage to the pituitary-ovarian ratio. Chronic anovulation can result in the mass of multiple cystic structures in both ovaries. With the regulation of ovulation, the cystic ovaries regress.

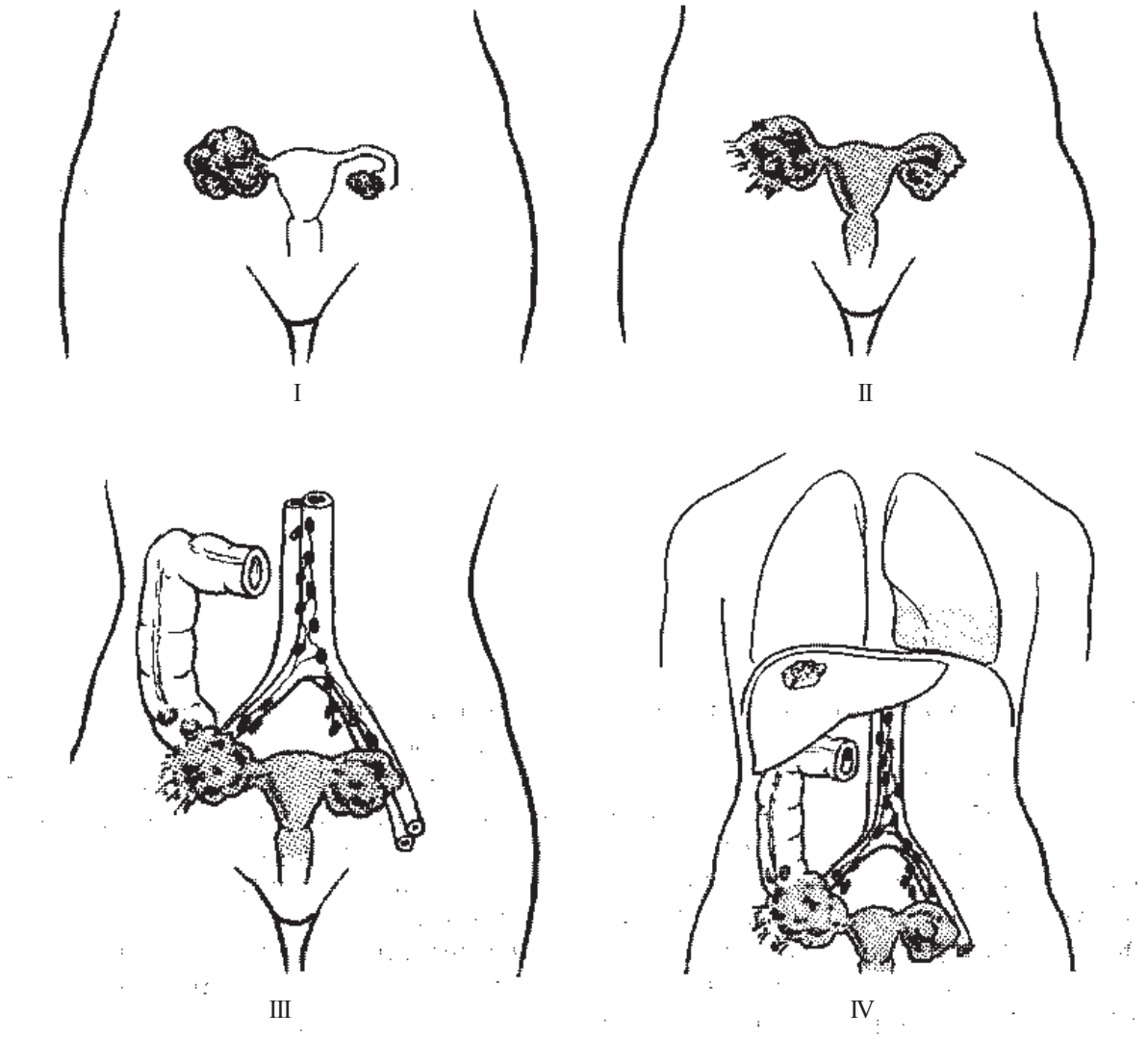


Fig. 54. Ovarian cancer: stages I–IV

Markers of a tumour. In connection with the high incidence of malignant germ cell tumours, which can form before menarche, in teenagers and girls between the age of 19–20, the level of their markers is determined (α-fetoprotein, β-CG, lactate dehydrogenase). The level of CA-125 in blood plasma is an antigenic determinant of ovarian carcinoma. However, unfortunately, it is nonspecific and insufficiently sensitive. This test is also conducted as a screening one in case of patients' relative tolerance to chemotherapy. For differential diagnosis of endometriosis and ovarian cancer, the complex exam of the levels of CA-125, CA-19-2 and CEA is more expedient. The disappearance of CA-125 during therapy is not proof of the tumour's regression, which is connected to the presence of this antigen in very small quantities, which can not be determined by the available methods.

Additional methods of inspection include colonoscopy in women over the age of 50, as well as with symptoms of colon obstruction (to eliminate the diagnosis of intestinal cancer as the reason for the pelvic masses). In the latter case, contrast roentgenograms of the upper segments of the abdomen and intestines should be performed.

With the presence of symptoms of urinary tract disorders, excretory urography should be performed, especially if retroperitoneal operative intervention to remove the tumour is provided. Routine mammography is obligatory, because breast cancer has a significant tendency to ovarian involvement. Such metastases are frequently bilateral and seldom reach sizes more than 10 cm.

Treatment. Surgical and medicamentous methods of treatment (chemotherapy) are applied. Radiation therapy is used seldom in connection with its low efficiency.

The basic method of treatment for ovarian cancer is *surgical,* i.e. the presence of an ovarian tumour is an absolute indication for operative intervention. If the patient's condition is operable (I, II stages of cancer), radical interventions (removal of the ovaries, extirpation of the uterus, removal of the big omentum) are done; with late stages of the disease — maximal cytoreduction whith taking material for a bio-

psy. A reduction in the volume of the tumour increases the efficiency of chemotherapy, as a result the duration of remissions increases.

In case of highly differentiated cancer (I degree) with the injury of one ovary, even organ-sparing operations can be performed in young women: unilateral oophorectomy with clinoid biopsy of the second (intact) ovary. With the desire of the patient to terminate the reproductive function, as well as at stages > I C, degrees 2 or 3, the method of choice is total abdominal hysterectomy and bilateral salpingo-oophorectomy (adnexectomy).

With the preserved second ovary in patients with I stage cancer, an adjuvant therapy is needed. Treatment for stage I, degrees 2 and 3 consists in the use of melphalan or combinations of cisplatin and cyclophosphamid; stage I C demands intraperitoneal treatment with radioactive phosphorus, intraabdominal radiation or combined chemotherapy. All patients should have serial analysis of the serum level of CA-125 — an antigenic determinant, if it is high at the beginning of treatment.

Considering that tumours with low malignancy potential, as a rule, are at the stage I A, conservative treatment is prescribed to women, wishing to keep the reproductive potential. If a woman wishes to terminate the reproductive function, radical abdominal hysterectomy with bilateral salpingo-oophorectomy (adnexectomy) is performed. Adjuvant therapy in this case is not done. Within 5 years 90 % of the patients with stage I of the disease survive.

For patients with II–III stage ovarian carcinoma, surgical treatment consists of removing the greatest possible mass of the tumour *(cytoreduction)*. The preference is radical abdominal hysterectomy with bilateral salpingo-oophorectomy (adnexectomy), omentectomy, the removal of peritoneal and retroperitoneal implants and as much as possible resection of the intestines.

Reducing the mass (cytoreduction) of the tumours with the impossibility of its full removal is justified from the point of view of preventing intestinal and urinary obstruction. Theoretically, cytoreduction causes an activation of growth and replication of cells, making them more sensitive to chemo- and radiotheraphy, as well as helps to reduce the amount of chemotherapy courses.

Chemotherapy is conducted after operative treatment. The most effective agents are considered cisplatin and carboplatin. The given preparations are frequently prescribed in combination with cyclophosphamid or doxorubicin for 6–8 courses with satisfactory cytoreduction. With unsuccessful cytoreduction three initial courses of PAC are prescribed: platinum (cisplatin or carboplatin), adriamicin (doxorubicin) and cyclophosphamid or PC (platinum and cyclophosphamid). After these courses, a second attempt with cytoreduction is conducted. For patients with metastases in the liver and lungs, cytoreduction is conducted only with the palliative purpose for intestinal obstruction.

Unsatisfactory results of chemotherapy are possible with old processes, the development of resistance of the tumour to chemopreparations. The problem is complicated with the necessity of complex influence on all three components of tumour growth for ovarian cancer: 1) primary tumour; 2) metastases to the peritoneum and omentum; 3) cancer cells contained in the ascitic liquid.

Radiation therapy should be very limited and as primary treatment can be applied at the stages I C, II C, and, maybe, III A.

Repeated operation is conducted after the termination of the course of chemotherapy for patients, not having clinical displays of progressing of the disease: with the level of CA-125 < 35 IU (international units); with negative data from the roentgenography of the thorax and computer tomography of the organs of the abdomen and pelvis; with negative data from bimanual examinations.

The purpose of repeated operation is to determine the opportunity of restriction or termination of further chemotherapy with the absence of displays of the disease or continuation of supporting therapy. Unfortunately, repeated operation does not guarantee 5 year survival rate for patients with epithelial ovarian cancer. With the performance of repeated operation, the limits of cancer dissemination are carefully investigated — in the pelvis, peritoneum, upper abdomen, retroperitoneal space, as well as multifocal biopsy is done (omentum, diaphragm, intestines). With the absence of remains of cancer tissue further treatment is not conducted.

The remained tissue of the cancerous tumour during a repeated operation can appear macroscopic and microscopic. In most cases the presence of large residual masses of the tumour, which are found during a computer tomography, physical examination or CA-125-screening, is adverse in the prognosis. On the contrary, the patients with microscopic or macroscopic (< 0.5 cm) remains of cancer tissue have a more favourable prognosis with supporting therapy. Possible variants of such therapy are as follows:

1) intraperitoneal chemotherapy;

2) complete abdominal radiation therapy;

3) intensified doses of chemopreparations (double doses: 100 mg/m^2 of cisplatin);

4) system chemotherapy of the second series;

5) immune-modulating therapy (interferon, BCG, *Corynebacterium parvum*, interleukin-2 with natural killer cells);

6) new preparations having experimental confirmation.

The prognosis improves in case of using massive chemotherapy.

Germ cell (germinogenic) tumours make up about 10% of primary ovarian cancer and when diagnosed frequently hase only stage I.

Dysgerminoma develops in 50% of cases of germ cell tumours and can be bilateral in 15% of the patients. This tumour is characterized by the ability to spread to the retroperitoneal lymph nodes (in 30% of cases), therefore the latter should be closely investigated during the operation.

The peak of dysgerminoma is in the teenage period and after 20 years of age. Specific markers of dysgerminoma do not exist. However, there can be some increase in the levels of α-CG and lactate dehydrogenase in the blood serum.

Treatment is conservative, includes unilateral salpingo-oophorectomy (adnexectomy) with a clinoid biopsy of the second ovary, retroperitoneal research of the pelvic and paraaortic lymph nodes. If the lymph nodes are affected, the method of choice is radiation therapy. Additionally chemotherapy VAC is prescribed: vincristin, actinomycin (dactinomycin) and cyclophosphamid. If the tumour don't spread beyond the ovaries, adjuvant therapy is not done.

Tumour of the endodermic sinus — the most malignant among all germ cell tumours. Even with stage I of the disease, the death rate reaches 60% of cases. This cancer, as a rule, is unilateral and involves a single ovary in 70% of cases. The tumour of the endodermic sinus is radioresistant. A distinctive feature of such tumour is the level of α-fetoprotein; this tumoural marker is also used to determine chemotherapy sensitivity.

Treatment consists of adjuvant chemotherapy with the use of bleomycin, ethoposid, cisplatin, carboplatin.

Immature teratoma in most cases develops in one ovary. However, metastases in the upper segments of the abdomen can be observed in 20% of the patients. The degree of immaturity of the teratoma is determined according to the immaturity of the germinative cellular elements of the ovary.

Treatment. Immature teratoma is very sensitive to combined chemotherapy with the use of vincristin, dactinomycin and cyclophosphamid. Repeated courses of treatment are conducted with a III stage tumour. With the inefficiency of the specified preparations, bleomycin, ethoposid and platinum are prescribed.

Mixed germ cell tumour is formed due to a combination of several germivative cellular elements — dysgerminoma, endodermic sinus, immature teratoma. Treatment is determined by the most malignant type of tumour: so, if there are cells of the endodermic sinus, the primary chemotherapeutic mode will include bleomycin, ethoposid and cisplatin or carboplatin.

Stromal tumours, as a rule, when diagnosed are unilateral. They can be oestrogen and androgen-producing and frequently tend to rupture. These tumours have an insignificant malignancy potential, and in most cases chemotherapy or radiation therapy is necessary.

Granulosa-theca tumour occurs more often in women in their 4th–5th decade, and in 85% of cases it is limited to one ovary. This hormone-active tumour causes symptoms connected to oestrogen hyperproduction (feminizing tumours). So, in the postmenopausal period vaginal bleedings can develop; in women of the reproductive age irregular bleedings can be the only symptom. In 25% of cases in patients with granulosa theca cell tumour of the ovaries, adenocarcinoma or hyperplasia of the endometrium also develops. Juvenile granulosa theca cell tumour develops in the pre-pubertal period. The prognosis is the same as for women with a more advanced age.

Treatment includes radical abdominal hysterectomy with bilateral salpingo-oophorectomy. Conservative operations are done for very young patients. In rare cases with intraabdominal tumour spread with a high amount of mitoses, additional chemotherapy is conducted with the preparations used for treating germ cell tumours.

Sertoli—Leydig's cell tumour causes virilism; more often it is formed in women at the age of 20–30. Virilism symptoms include acne, clitoromegaly, the presence of a rough voice, frontal baldness. In 95% of cases the tumour is unilateral.

Treatment with the absence of intraperitoneal spread of low differentiated tumours (in 50% of cases) is limited to the removal of the ovary. Patients with a low differentiated tumour are prescribed chemotherapy similar to those with germ cell tumours.

Secondary (metastatic) ovarian cancer with primary genital sites is observed extremely seldom (1–2%) and more often spreads by direct invasion through the broad uterine ligament rather than by true metastasing.

Metastases in the ovaries are observed with extragenital site of the primary cancer of the breasts or in the abdomen and intestines (1% of all ovarian neoplasm). The metastatic cancer, as a rule, is bilateral (75%) and may be massive. The cellular type depends on the primary site of cancer.

The Krukenberg's tumour is characterized by its massiveness, sometimes hypostasis of the stroma with islets of moderately dilated epithelial cells, vacuolate and mucin-filled cytoplasm, a little hyperchromasia of the nucleus. The primary tumour, in this case, as a rule, is formed in the abdomen, but can be located in the intestines, breast or thyroid gland. The tumour may produce oestrogens.

Treatment is surgical, consists of removing the maximal possible volume of the tumour with subsequent chemotherapy.

Prognosis is adverse.

Prevention. The detection of premalignant conditions and early forms of ovarian cancer is promoted by clinical-genetic monitoring. Improvement of instrumental methods of examination play an important role in the improvement of diagnosis (emission

and transformation contrast echography, minilaparoscopy, laparoscopy, computer tomography, nuclear magnetic resonance).

CANCER OF THE FALLOPIAN TUBES

Primary adenocarcinoma of the Fallopian tubes is found in 0.3% of cases of all gynaecologic malignancies, mainly in women between the ages of 40–60, although significant variations are possible. In every second case cancer of the Fallopian tubes takes place in women who have not yet given birth. The tumour develops from cylindrical epithelium of the Fallopian tubes, more often in its ampullar part. Metastatic spread occurs by lympho- and haematogenous metastases.

Clinical picture and diagnosis. Patients complain of the presence of serous-bloody vaginal discharge. Late symptoms can be spasmodic or constant pain in the lower abdomen, serous-bloody leucorrhoea, intestinal obstruction. The pathological results for cytological examination of the vaginal smears are sometimes observed. During bimanual examination adnexal sensitivity or morbidity is marked. Ultrasonography can help in revealing cystic or solid pelvic masses separated from the uterus and ovaries. Hysterosalpingography is not performed because of the possibility of tumour cells entering the abdominal cavity. To a certain extent laparoscopy increases the opportunities of diagnosis.

The majority of cases (95%) of primary cancer of the Fallopian tubes is papillary adenocarcinoma, bilateral in 40–50% of women. Tumour's spread beyond the limits of the Fallopian tubes is not always a bad prognostic attribute.

Treatment consists of hysterectomy and bilateral salpingo-oophorectomy or cytoreduction. In the postoperative period chemotherapy is performed (cisplatin and cyclophosphamid), in some cases — radiation therapy.

The *prognosis* is more favourable if the tumour has not spread beyond the limits of the Fallopian tubes. The survival rate of patients within 5 years is 30–40%.

RECOMMENDED READING

7; 16; 21; 24; 49; 50; 51; 57; 79; 90; 92; 93; 94; 96; 98; 104; 108.

Chapter 13

TROPHOBLASTIC DISEASE

Trophoblastic, or gestational trophoblastic, disease is understoodas a group of benign and malignant tumours developing from the trophoblast and appearing during pregnancy or after it. Trophoblastic tumours are not widespread (1:20,000 pregnancies). However, last years in Ukraine an increase (1.5–1.76 times) in the morbidity of choriocarcinoma is observed.

Classification. Such histological forms of trophoblastic diseases are distinguished: hydatidiform moles, invasive mole and choriocarcinoma (chorioepithelioma). According to the clinical classification the following are distinguished:

I. Hydatidiform mole:

a) complete, or classical;

b) incomplete, or partial.

II. Gestational trophoblastic neoplasm:

1. Invasive mole.

2. Choriocarcinoma: a) metastatic; b) non-metastatic.

The system of evaluating the risk factors for the development of gestational trophoblastic disease offered by WHO is submitted in table 15.

Hydatidiform mole histologically is characterized by a various degree of proliferation of villi, their hydropic transformation and hypostasis of the chorion stroma. The latter, as a rule, is in the uterine cavity. However, can sometimes develop in the Fallopian tubes and ovaries. The presence of fetal tissue determines the kind of hydatidiform mole (Table 16). With complete hydatidiform mole, the chorion villi are transformed into a mass of transparent alveoli (Fig. 55) which vary in size from hardly visible to centimetres in diameter, frequently incorporate thin small stalks (”pedicle”) and can stretch the uterus in to various extent.

Table 15. **Evaluation of the risk factors for gestational trophoblastic disease** (by WHO)

Prognostic factors	Evaluation, score*			
	0	1	2	4
Age	< 39 years	> 39 years		
Antecedent pregnancy	Hydatidiform mole	Abortion, ectopic pregnancy	Full-term pregnancy	
Interval between pregnancy and the beginning of chemotherapy, months	< 4	4–6	7–12	> 12
Human chorionic gonadotrophin, IU/l	< 1000	1,000–10,000	10,000–100,000	> 100,000
AB0 blood groups (male-female)		0–A A–0	B AB	
Size of the largest tumour, cm	< 3	3–5	> 5	
Site of metastases	—	Spleen, kidney	Abdomen, intestines, liver	Brain
Amount of metastases	—	1–3	4–8	> 8
Prior chemotherapy	—	—	Single drug	Two or more

* > 4 points — low risk; 5–7 points — moderate risk; > 8 points — high risk.

Table 16. **Characteristics of complete and partial hydatidiform mole**

Attributes	Kind of hydatidiform mole	
	Complete (classical)	Incomplete (partial)
Embryonal or fetal tissue	Absent	Present
Hydatidiform transformation of the villi	Diffuse	Local
Hyperplasia of the trophoblast	The same	The same
Affection of stroma	Absent	Present
Festoon villi	The same	The same
Karyotype	46XX (96%) or 46XY (4%)	Triploidy: 69XXY or 69XYY
Risk of developing trophoblastic tumour	About 20%	About 5%, choriocarcinoma — rare

The risk of the development of trophoblastic tumour after hydatidiform mole is about 20%.

Local hydatidiform changes of the chorion with the presence of a fetus or amniotic sac is referred to as *partial hydatidiform mole*. This hydatidiform transformation of the part of usually avascular villi progresses slowly, while the other part of vascular villi takes part in fetoplacental circulation. With a partial hydatidiform mole the risk of developing choriocarcinoma is low.

In 25–60% of cases of hydatidiform mole thecalutein cysts are found in the ovaries, and can vary in size from microscopic to large (over 10 cm in diameter). Such cysts have a smooth surface, yellow colour and are covered with lutein cells. Ovarian thecalutein cysts is the result of hyperstimulation of lutein elements by a large amount of chorionic gonadotrophin, secreted by the proliferated trophoblast. After normalizing the level of chorionic gonadotrophin they usually regress.

Fig. 55. Complete hydatidiform mole

The large size of the cyst is connected to the large hydatidiform mole and long period of stimulation of chorionic gonadotrophin. However, such cysts are not necessarily connected with hydatidiform mole, they can also occur with multiple pregnancies, stimulation of ovulation, and hypertrophy of the placenta.

Incidence. Hydatidiform mole occurs in the beginning or at the end of the reproductive period more often. So, in women after the age of 45 the frequency is 10 times higher than for women between the ages of 20–40.

Classification of trophoblastic disease (by FIGO) is submitted in table 17.

Clinical picture and diagnosis. In the anamnesis patients mark a delay in menstruation, nausea, vomiting, whining or spasmodic pain in the lower abdomen, bloody discharge from the sexual path, sometimes (with the presence of metastases in the lungs) — dyspnea, general weakness. Bloody discharge can vary from poor ("spotting") to profuse bleedings. Sometimes they begin directly before an abortion. However, as a rule, occur with small intervals for weeks and even months. Iron deficiency anaemia frequently develops.

During gynaecologic examination cyanosis and hypostasis of the vaginal mucosa and vaginal part of the cervix are found. Distinctive symptoms are repeating uterine bleedings, enlarged uterus, which can have a spherical form, homogeneous consistence, be mobile, painless. Palpation of the uterus causes a weak contracting reaction. On occasion, the uterus is soft, its wall is thin. The uterus frequently (but not always) enlarges faster than usual. In every second case the size of the uterus corresponds with the prospective pregnancy term. Palpation of the uter-

Table 17. **Characteristics of the stages of trophoblastic diseases (by FIGO)**

Stage	Characteristics
I	The disease is confined to the uterus
A	Risk factors are absent
B	One risk factor is present
C	Two risk factors are present
II	The disease spreads beyond the uterus, but is confined to the genitalia
A	Risk factors are absent
B	One risk factor is present
C	Two risk factors are present
III	The disease spreads to the lungs with detected or undetected affected genitalia
A	Risk factors are absent
B	One risk factor is present
C	Two risk factors are present
IV	Distant metastases
A	Risk factors are absent
B	One risk factor is present
C	Two risk factors are present

us can be complicated in connection with its softening, especially with women giving birth for the first time, having a hard abdominal wall. Differential diagnosis of hydatidiform mole is done with uterine myoma, hydramnion, multiple pregnancy, erroneous increase of the gestational age. To distinguish hydatidiform mole from true pregnancy in the early stages of the disease is especially difficult.

Enlarged ovaries in every second case can be connected to the development of retention theca-lutein cysts (Fig. 56), which can fill the whole abdominal cavity and reach the diaphragm. With pressure to the capsule, a rupture of the cyst is possible.

The most exact method of diagnosis — *determining the level of chorionic gonadotrophin* in the blood serum. Tumours of the trophoblast, as well as normal trophoblast, release a hormone — CG, which can be revealed in the blood or urine by various methods. The most exact is the radioimmune method of determining the level of CG β-subunits in the blood. The titre of a hormone with the presence of trophoblastic tumours is much higher than during a normal pregnancy. After removing the hydatidiform mole from the uterus the titre of CG is reduced and in a few weeks (in most cases) does not appear. However, in some cases, CG excretes for a long time, which testifies to the presence of persisting trophoblastic tumour.

Ultrasound study allows to visualize precisely the contours of the uterus, its size, thickness and condition of the myometrium, to reveal the character of the contents (tumours), the size of the ovaries, with the presence of cystic masses — their size, thickness of the wall, number of camers, arrangement of the

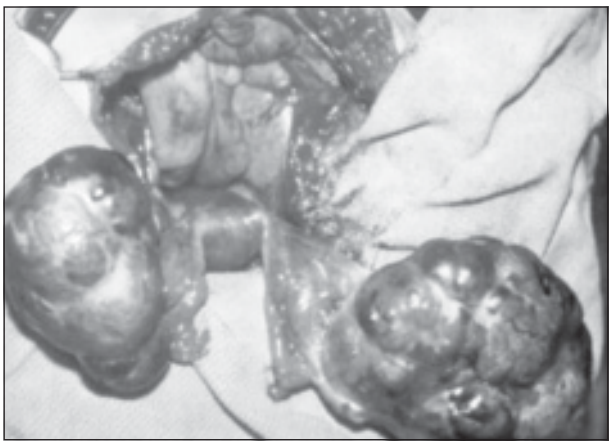


Fig. 56. Bilateral theca-lutein cysts with trophoblastic disease

cysts in the pelvic cavity, condition of the bladder. A characteristic ultrasonographic symptom of hydatidiform mole is a "snow storm" (Fig. 57).

During *hysterosalpingography* after removing the hydatidiform mole, the deformity and displacement of the uterine cavity are visualized.

While carrying out *histological study* the type of hydatidiform mole is ultimately determined.

Due to hydatidiform mole the incidence of late gestosis increases, especially with their early beginning (before the 24th week of pregnancy). The level of thyroxine in the plasma elevates, though symptoms of hyperthyroidism are observed only in 2% of cases.

Differential diagnosis of hydatidiform mole is conducted with an incomplete abortion, placentar polyp, and submucous uterine myoma.

The following symptoms are poor prognostic attributes of hydatidiform mole:

1) the size of the uterus is more than 16-week pregnancy;

2) the presence of ovarian theca-lutein cysts;

3) significant degree of proliferation and (or) anaplasia of the trophoblast;

4) hyperthyroidism.

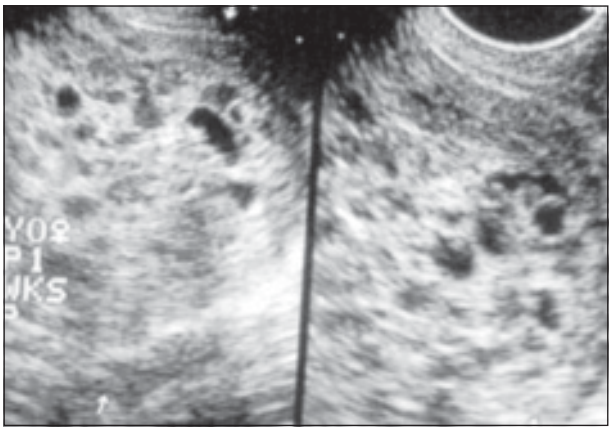


Fig. 57. Ultrasonogram of a woman with hydatidiform mole at 19-week pregnancy (a "snow storm")

Treatment of patients with hydatidiform mole provides, first of all, the removal of the hydatidiform mass. Spontaneous expulsion of the hydatidiform mole is possible before 16 weeks and is seldom observed after 28 weeks of pregnancy.

Before removing the hydatidiform mole, roentgenography of the thorax to reveal metastatic defects of the lungs is recommended.

There are different methods of evacuation of hydatidiform mole:

1) medicamentous, conducted with the help of the introduction of oxytocin and prostaglandins;

2) instrumental — curettage or vacuum-excoriation;

3) manual removal with subsequent vacuum-excoriation;

4) hysterotomy and hysterectomy (supravaginal amputation or extirpation of the uterus).

Before the introduction into practice of the vacuum-excoriation, with the size of the uterus larger than for 12–14 week pregnancy, hysterotomy was used more often. Today the use of hysterotomy is limited exclusively to cases connected with intensive bleedings. The given method of evacuation of the vesicular tissue can be used and with the size of the uterus corresponding to 20 week term, blood loss thus is moderate. Before the operation, 2–3 bottles of compatible integral blood are prepared.

Evacuation of the hydatidiform mole is most expedient by *vacuum-aspiration*. When the hydatidiform mole tissue is practically removed, oxytocin intravenously is entered with the purpose of better contraction of the implantation zone and reducing the risk of perforating the uterus. After aspiration curettage, sharp curettage is conducted, thus the taken tissue is sent for histological study.

Evacuation of the hydatidiform masses is a radical method of treatment for many women with the given pathology. As a rule, complete involution of the uterus occurs in 2–3 weeks, the titre of CG is reduced to negative indices, bloody discharge from the vagina stop, the menstrual cycle restors. Such patients should remain under constant clinical-hormonal follow-up.

At large sizes of the uterus and the presence of bleeding (if there is no data on the condition of the myometrium) *hysterotomy* may be conducted (an operation like a caesarean section in the lower segment).

In 10–12% of cases with hydatidiform moles, the attempts to remove the hydatidiform mass from the uterus by curettage are unsuccessful, subsequent chemotherapy is inefficient. *Hysterectomy* is recommended to such patients (after carrying out topical diagnosis of the intrauterine defects with the help of angiohysterography). If during hysterectomy ovarian cysts are found, the ovaries are not removed, or with a decrease in the titre of CG to negative values, they return to normal sizes due to the regression of the cyst. Even in case of hysterectomy, patients should be under the constant supervision of a doctor with dynamic exam of the CG level (with an interval of 1–2 weeks before receiving two negative results), as well as after the use of other methods of evacuation of the hydatidiform tissue.

With desire of the woman to terminate the reproductive function, especially for women older than 40, hysterectomy is preferred to prevent the development of choriocarcinoma.

After evacuation of the hydatidiform mole, a series of exams of the CG level are conducted. If the level of CG is normal, spontaneous remission, developing in 80% of patients with complete hydatidiform mole, takes place. The period for the occurring of negative titres of CG after evacuation of the hydatidiform mole on average is 73 days.

With the presence of spontaneous remission, the CG titre is checked 1 time every 2 months within a year. It is extremely necessary that women use contraception becasue the following normal pregnancy cannot be differentiated with trophoblastic disease by the CG titre.

Regular vaginal examinations are necessary 1 time every 2 weeks till the occurrence of negative CG titres. Within the first year, exams should be carried out once every 3 months. Patients with spontaneous remission (negative CG titres, data of objective and radiological examination for the first year) and women wishing to become pregnant should stop the use of contraception.

Indications for *chemotherapy* for patients with hydatidiform moles are the following conditions:

1) slow involution of the uterus;

2) plateau of CG for 2–3 weeks or an increased level of CG for 60 days after evacuation of the hydatidiform mole;

3) constant bloody discharge;

4) the presence of ovarian cysts;

5) the presence of metastases.

Polychemotherapy is conducted till complete regression of the CG titres, reduction in the size of the uterus and ovaries, liquidation of metastases.

Small ovarian cysts regress independently against a background of chemotherapy, and with the treatment of patients with large cysts active tactics is recommended (transabdominal or transvaginal puncture of the cyst). Punctures of the cyst if necessary are conducted (2 to 12 times) controlled by the data from the ultrasonsography.

Indications to surgical treatment of patients with hydatidiform mole include:

1) twisting of the ovarian cyst's pedicle;

2) rupture of the cystic walls;

3) when conservative treatment is impossible, with the presence of significant destruction or perforation of the uterus by the tumour.

Destructive (invasive) hydatidiform mole is characterized by the penetration of hydatidiform moles into the myometrium and other organs (vagina, parametrium, lungs).

The *clinical picture* is characterized by continuation of bloody discharge from the uterus after the removal of the hydatidiform mole, an increase in its size, constant pain in the lower abdomen and sacrum, persisting theca-lutein ovarian cysts, the occurrence of metastases in other organs. A high level of CG α-subunits is maintained in the blood.

Diagnosis is based on data from the histological study of the tumour and the presence of metastatic defects.

Treatment is only surgical and consists of *extirpation* of the uterus; in the postoperative period *polychemotherapy* is conducted. By indications metastatic nodes of hydatidiform mole in other organs are removed.

The following recommendations are given to reveal any attributes of malignant transformation in patients:

1. Avoid pregnancy for no less than a year after the removal of hydatidiform mole. In order to prevent pregnancy and suppress the luteinizing hormone release by the hypophysis some authors recommend the use of oestrogen-gestagen oral contraceptives under the control of the CG level.
2. Measure the CG level every 2 weeks.
3. Do not use chemotherapy during the period of regression of the CG level. An increase or persistent serum level of CG is an indication for chemotherapy.
4. With a normal level of serum CG, i.e. with the reaching a low level (0–5 IU), it should be examined no less than once a month for 6 months or every 2 months for 1 year.
5. After 1 year observation can be stopped and pregnancy is allowed. However, in early term of the following pregnancy ultrasonographic examination is performed.

The level of CG should be reduced progressively to the minimal value (0–5 IU), otherwise persistency of the disease takes place.

To compare the data before and after the evacuation of the hydatidiform mole, it is necessary to perform roentgenography of the organs of the thorax.

After the evacuation of the hydatidiform mole about 20% of patients are subject to further treatment in connection with the suspicion of persistent trophoblastic disease and the development of choriocarcinoma. If the serum level of CG does not decrease or increases and thus there are no defects beyond the uterus, *hysterectomy* is performed (especially if the woman does not wish further pregnancies). In case of the necessity to preserve the reproductive function or defects of the lungs or vagina, chemotherapy with or without curettage is conducted. *Chemotherapy* consists of the application of methotrexate or actinomycin D as monotherapy, or their combinations with other chemotherapeutic agents (methotrexate-dactinomycin-chlorambucil), which, as a rule, are effective.

Prognosis. Approximately in 20% of cases of complete hydatidiform mole and in 5% of cases of partial, choriocarcinoma develops. Sometimes a trophoblastic tumour can form in some years after the removal of the hydatidiform mole.

The following pregnancy can be complicated with the development of anaemia, intrauterine infections and sepsis.

Choriocarcinoma (chorionepithelioma) — an extremely malignant tumour developing from epithelial cells of the trophoblast, more often from hydatidiform moles. Proliferation of cytotrophoblasts (Langhans' cells) and syntrophoblast occurs in a choriocarcinoma. The absence of fibres, stroma and blood vessels are characteristic for this tumour. The tumour is located in the corpus uteri more often, rarely — in the Fallopian tubes, ovaries and abdominal cavity (ectopic choriocarcinoma). The site of the choriocarcinoma coincides with the place of nidation of the fetal egg. The tumour can be of various sizes, have blue and crimson colour. With exophytic growth the choriocarcinoma grows in the uterine cavity; with endophytic — in the thickness of the myometrium.

The trophoblastic cells are characterized by the ability to destruct the blood vessels and penetrate into their lumen, which results in the fast mass of haematogenous metastases in the vagina, lungs, and brain.

Clinical picture. The patients complain of the presence of bloody discharge, appearing after the removal of hydatidiform mole, as well as after an abortion or birth; nausea, vomiting, pain in the lower abdomen, sometimes — the discharge of colostrum from the mammary glands are observed. The occurrence of a cough with bloody mucous and obvious emaciation, as a rule, are symptoms of pulmonary metastases. During gynaecologic examination, cyanosis and hypostasis of the mucous membrane of the vagina and cervix uteri are noticed. With the presence of intramuscular primary foci of defect, the uterus can be a little enlarged. Metastases in the vagina (mainly in its lower third) look like projecting single or multiple violet elastic masses (from 0.5 to 5–8 cm) which can bleed.

With the mass of parametrial infiltration the uterus loses its mobility. In case of the development of submucous nodes the uterine tumour can have a spherical form, dough-like consistency. With infringement of the integrity of the endometrium, bleedings of various intensity can occur; sometimes the discharge have the colour of "raspberry jelly".

The addition of an infection changes the patient's condition (increase in the body temperature, intensification of the abdominal pain) and the character of the discharge, which become purulent-bloody.

Recurring bleeding, accompanying the infection, results in intoxication, anaemia, deterioration of the patient's general condition.

Diagnosis is based on the data from the clinical, laboratory and morphological study.

The basis of modern diagnosis of choriocarcinoma — determining the contents of CG β-subunit and trophoblastic β-globulin. Though CG is not a specific marker of a tumour (it appears in biological substrata normally in both unpregnant and pregnant women), its concentration, exceeding 500 IU, testifies to the presence of choriocarcinoma.

Due to the haematogenous character of metastasing, it is necessary to carry out complex examination of the organs and systems in which metastases (lungs, liver, brain, kidneys) are more often formed.

Roentgenography of the thorax allows to receive data on the presence of metastases in the lungs (the basic site). Metastases of the tumour look like soft shadows with a spherical form with a diameter from 0.5 to 2 cm; they can be single or multiple, like pneumonia or a "snow storm" due to the embolism of the pulmonary vessels with bubbles.

During *ultrasound study* the tumour nodes in the uterus, their site, thickness of the myometrium, condition of the endometrium, ovaries (polycystosis, ovarian cysts, metastases), and the presence of metastases in the liver and kidneys can be revealed. With the help of a *hysterosalpingography* deformity of the uterus, unevenness of its contours, impregnation of the uterine walls by contrast substances, obstruction of the Fallopian tubes can be determined. During *angiography* asymmetry, wavity, delation and deformity of the intramural vessels, delay of the radiopaque substances in tumours, dilation of veins are observed.

Treatment, prognosis. Now the treatment of patients with choriocarcinoma is more effective than earlier when the only hope for treatment was hysterectomy or resection of the metastatic lesions.

The use of methotrexate and other antineoplastic preparations, especially actinomycin D, has improved the results of treatment to 90%. Practically all such patients now have a favourable prognosis concerning treatment. If patients do not react to the given therapy, the course of the choriocarcinoma quickly progresses. Death due to massive bleeding can occur in a few months.

Treatment more often begins with *chemotherapy* depending on the patient's condition (degree of anaemia, intoxication, parameters of CG release, features of metastatic process). A distinctive feature of a choriocarcinoma is its exclusive sensitivity to chemotherapy.

System chemotherapy is usually performed intravenously, on occasion — endarterial, with the presence of metastases in the brain, chemopreparations are entered into the spinal cord.

At the given stage of treatment polychemotherapy is mainly used, which includes alkaloids (vinblastin, vincristin, rosevin), antibiotics (rubomycin, dactinomycin, adriamycin), alkylated preparations (cyclophosphan tyo-TEP), antimetabolites (methotrexate, 6-mercaptopurine, 5-fluorurcil), preparations of platinum (platidiam, cisplatin, etc.).

Treatment is performed as a cycle of intravenous infusion therapy by one of the two following schemes:

1) 24 hours before the infusion of chemopreparations intravenously enter 1 mg of vincristin or 10 mg of vinblastin or rosevin is introducted. The infusion of methotrexate at a dose of 60–70 mg/m^2; 5-fluorurcil — 1–1.2 g/m^2, cisplatin — 50–60 mg/m^2 is performed the next day;

2) methotrexate — 60–70 mg/m^2, cyclophosphan — 0.8 g/m^2, cisplatin — 60 mg/m^2.

Each preparation is dissolved in 400 ml of an isotonic solution of sodium chloride. With the use of nephrotoxic preparations (methotrexate or platinum) it is necessary to conduct prehydration of the organism (hemodilution) with an isotonic solution of sodium chloride or 5% solution of glucose in the dose of 800–1,000 ml and 200 ml of a 5% solution of sodium hydrocarbonate, and at the end of the infusion conduct dehydration by the introduction of mannite, mannitol, diuretic preparations. Taking into account the high level of toxicity of the given preparations and the significant oppression of the endocrine glands function by them, during infusion 30–60 mg of prednisolon are entered.

The cycles of infusion are necessary to repeat in 6–7 days under the control of the parameters of the haemogram, hemodynamics, urine analysis, functional ability of the kidneys, the patient's general condition.

The test for the sensitivity of the tumour to cytostatics is contents of choriogonin: already after the first infusion of chemopreparation, as a rule, the CG titre begins to decrease, which after 3–4 infusions can reach normal values, as a result there is a reduction in the size of the uterus and ovarian cysts (if there are any) to the normal, metastases decrease or disappear.

With the presence of negative reactions to CG it is necessary to perform 1–2 polychemotherapy cycles more. During the whole course of chemotherapy and in the intercyclic periods patients take prednisolon in the dose of 15–20 mg/day. After each infusion of chemopreparations, detoxication therapy is conducted with the use of infused solutions, essentiale (10 ml in 100 ml of solution). The total amount of infusions is 1.5–2 l.

After the end of the chemotherapy course the daily dose of prednisolon (5 mg a week) is gradually reduced till its full termination. In the intercourse period regular studies of the CG level are conducted.

Complications of medicamentous therapy can be advanced leukopenia and thrombocytopenia with a

decrease in the amount of leukocytes up to 1 • 10^9 G/l and lower. In such cases, a transfusion of fresh donor blood, leukocytic-thrombocytic mass, plasma is recommended. The doses of prednisolon are increased up to 90–120–150 mg (intramuscularly or intravenously). After an increase in the amount of leukocytes the dose of corticosteroids is gradually reduced to 30 mg, with further use of corticosteroids internally till there complete termination of the therapy.

Indications for surgical treatment of patients with choriocarcinoma are the following:

Absolute:

1) intraabdominal or external bleeding, resistant to conservative therapy;

2) the threat of uterine rupture because of the tumour;

3) acute abdomen (due to the twisting of the ovarian cyst's pedicle or a rupture of the capsule).

Relative:

1) the size of the uterus is larger than 10–11 week pregnancy, the presence of intramural tumour nodes;

2) the age of the woman is more than 40, the presence of children, desire to terminate the reproductive function;

3) resistance of the tumour to chemotherapy.

The volume of the surgical intervention depends on the stage of the disease, size of the tumour, its site in the uterus. With high-grade topical diagnosis, establishing the limited defect of the uterus (in the myometrium, uterine corners), the organ-sparing operation (enucleation of the tumour) with subsequent courses of polychemotherapy can be carried out. In some cases, if there is limited injury to the uterus, it is possible perform hysterectomy with the removal of the Fallopian tubes (the ovaries are preserved).

In connection with the fact that ovaries are involved seldom (1% of cases), some clinical physicians consider that surgical treatment can be limited to hysterectomy with the removal of the Fallopian tubes.

Depending on the results of topical diagnosis, the extent of surgical intervention is different: from hysterectomy without removing the ovaries with a limited process to panhysterectomy with significant spread of the neoplastic process of the uterus or the presence of metastases. In case of metastatic lesions of the intestines, bladder, liver, lungs, combined operations are performed.

While solving the problem of the extent of operation concerning choriocarcinoma, a prominent aspect as for preserving or removing the ovaries is clarified. If the patient has a single small lesion in the uterus (tumour node), it is possible to perform hysterectomy while preserving the ovaries. When metastases are found or there is suspicion of their presence, it is necessary to perform extirpation of the uterus with the appendages, for the kept sex glands will cause persisting metastases with subsequent progressing of the process. So, among patients who have had hysterectomy while keeping the ovaries, the death rate is twice more than for patients who had extirpation of the uterus with its appendages done.

After adequate surgical intervention, even with a decrease in the CG titre, to prevent metastases or for the lysis of undiagnosed metastases, a course of polychemotherapy, consisting of several cycles, is conducted. With the complete disappearance of CG in the urine and blood it is necessary to conduct 2 more cycles of treatment (with a total after the operation — 4–5 cycles). The longer the pathological process, the longer the treatment. During the whole period of therapy, control of the hematological, hormonal, radiological and ultrasonographic data is conducted.

Radiation therapy is used in case of the tumour's resistance to chemotherapy, slowed reduction of the distant metastases. Radiation therapy (at a dose of 25–30 Gr) is necessary to carry out against a background of polychemotherapy to prevent relapses of the tumour.

Contraindications to conducting polychemotherapy in patients with trophoblastic disease are decompensation of the functions of the cardiovascular systems, advanced disorders of the function of the kidney and liver, anemia.

Surgical treatment of patients with choriocarcinoma is contraindicated only in case of emergency.

The *prevention* of choriocarcinoma is early diagnosis and adequate treatment of the hydatidiform mole. All women with extensive bloody discharge after an abortion or birth should have screening-diagnosis for trophoblastic diseases done by determining the CG level in the blood serum, as well as histological study of scraping from the uterus.

RECOMMENDED READING

7; 12; 13; 16; 21; 24; 49; 50; 79; 86; 90; 93; 94; 96; 104; 108.

Chapter 14

STATES OF EMERGENCY IN GYNAECOLOGY

ECTOPIC PREGNANCY

With a normal intrauterine pregnancy the blastocyst is implanted in the endometrium of the uterine cavity.

Extrauterine, or ectopic, pregnancy *(graviditas extrauterina s. ectopica)* is an implantation of the fetal egg outside of the uterine cavity (Fig. 58).

For last two decades an increase in reproductive losses connected to disorder of implantation (nidation) of the fertilized ovum is observed. Increases in the amount of abnormal embryos during tubal pregnancies is not marked.

The incidence of ectopic pregnancy is about 1–2.5% of all births, and in 7–15% of cases it is repeated. The risk of the mother's death due to ectopic pregnancy is 10 times higher than for spontaneous birth, and is 50 times as much than for induced abortions. Besides, the prognosis of a successful pregnancy considerably worsens for women having even one ectopic pregnancy, especially the first one, at the age of 30 or more.

More than 95% of cases of ectopic pregnancy are tubal pregnancies. Pregnancy in the ampullar part of the Fallopian tubes is observed most often (55% of cases); in the isthmical part it develops in 25% of cases, in the fimbrial — in 17%, in the angular part — 2%; very seldom a bilateral ectopic pregnancy takes place. Ovarian pregnancy occurs in 0.5% of cases, abdominal — in 1 in 15,000, cervical — in 0.3–0.4% of cases. A combination of uterine and ectopic pregnancy (combined, multifetal, heterotopic pregnancy) 1 : (17,000–30,000) cases. An extremely rare variant of ectopic pregnancy — intraligamentous pregnancy (in the broad uterine ligament).

Variants of ectopic pregnancy also include pregnancy in the rudimentary horn of the uterus.

Etiology, pathogenesis. The reasons for the development of ectopic pregnancy can be the following:

1. *Mechanical factors* (interfere with the passage of the fertilized ovum to the uterus or restrain it):

— salpingitis;

— peritubal adhesions (after an abortion, postnatal infection, perisalpingitis, endometriosis, appendicitis);

— developmental anomalies of the Fallopian tubes (hypoplasia, diverticulum);

— previous ectopic pregnancy (7–15 %);

— operations on the Fallopian tubes (canalization, sterilization);

— numerous previous induced abortions;

— tumours of the uterus and appendages;

— intrauterine spiral.

2. *Functional factors* (restrain the moving of the fertilized ovum to the uterus):

— disorder of oestrogens and progesterone production;

— change in the amount and activity of the adrenergic receptors in the mucous membrane of the Fallopian tubes;

— the pregnant woman taking pure progestin oral contraceptives;

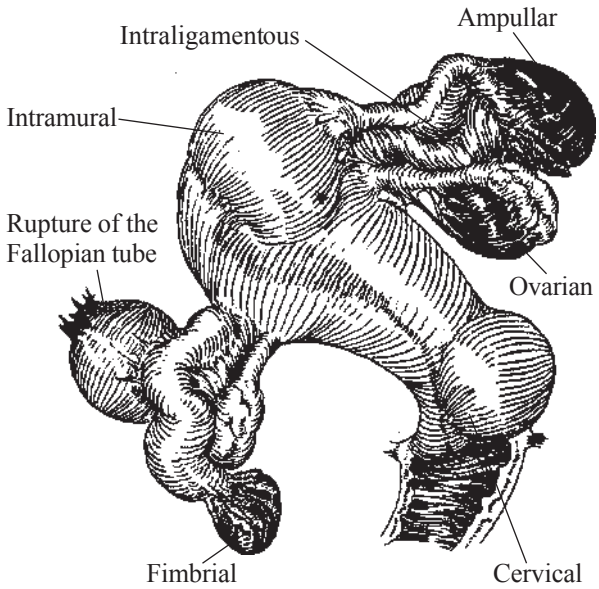


Fig. 58. Location of ectopic pregnancy

— an increase in the sensitivity of the receptors of the mucous membrane of the Fallopian tubes to the fertilized ovum;

— ectopia of the endometrial elements in the Fallopian tubes.

The implantation of the zygote during tubal pregnancy occurs in the epithelium of the mucous membrane of the Fallopian tube; invasion of the proliferated trophoblast in the muscular membrane of the tube and its penetration of the mother's vessels occurs. The changes characteristic for early uterine pregnancy (decidual reaction) take place in the mucous membrane of the uterus during this time; the uterus increases, its cervix softens. External bleeding during ectopic pregnancy is connected to the degeneration and discharge of the uterine decidual tissue. However the absence of the decidual tissue does not exclude ectopic pregnancy.

Clinical picture. Clinically progressing and interrupted tubal pregnancy, abdominal, intraligamentous and intramural (interstitial) pregnancy are distinguished.

With a **progressing tubal pregnancy** the ovum is implanted into the mucous membrane of the Fallopian tubes (endosalpinx), and then invades the muscular layer, loosens and destroys it. The tube increases in size on account of the ovum and gets a spindle-shaped form. Signs of pregnancy appear (delay of menstruation, changes in appetite, nausea, hypersalivation, swelling of the breast, cyanosis of the vagina and cervix, small increase and softening of the uterus). The size of the uterus lags behind the prospective pregnancy term. Sometimes insignificant bloody discharge from the uterus are observed. During bimanual gynaecologic examination it is possible to find a tumour mass located to the side and behind the uterus.

Abdominal pregnancy is possible due to a delay of a significant part of the placenta in the Fallopian tube; the fetus pushed from the tube can develop some time in the abdominal cavity, attaching to an organ. Cases of a full term abdominal pregnancy are known; delivery in this case is abdominal. Attempts to remove the placenta during an abdominal pregnancy, as a rule, are accompanied by profuse bleeding.

Intraligamentous pregnancy (in the broad uterine ligament) occurs due to the implantation of the zygote into the mesentery of the Fallopian tube.

Intramural (interstitial) pregnancy is characterized by the penetration of the fertilized ovum into the uterine wall (more often in the area of the uterine corner). Disorder of the interstitial pregnancy occurs later, at the term of 9–16 weeks. Bleeding in this case can be fatal.

Interruption of tubal pregnancy usually occurs by tubal abortion (with the site in the amullar part) or tubal rupture (with the site in the isthmus).

Classical symptoms of ruptured ectopic pregnancy are the following:

— abdominal or pelvic pain (100% of cases);

— delay in menstruation from several days to 2–3 weeks or insignificant bloody vaginal discharge, "spotting" (60–80% of cases);

— vasculomotor disorders (with small bleeding

— normal or a little increased arterial pressure; with extensive bleeding — tachycardia, decrease in ABP, dizziness, loss of consciousness (60% of cases) as a result of oligemia); sometimes oliguria is observed;

— dyspeptic signs (nausea, vomiting — 80% of cases);

— pain during palpation of the abdomen, posterior ("Douglas' cry") and lateral vaults of the vagina and cervical excursion (75% of cases);

— enlargement of the uterus, its shift to the side; unilateral adnexal enlargement (20% of cases), pain during palpation;

— with the presence of blood in the abdominal cavity symptoms of irritation of the peritoneum and *n. phrenicus* can be observed (pain in the area of the neck, shoulders during breathing), "muscular protection".

The absence of the next menstruation is not obligatory for ectopic pregnancy. So, women can wrongly believe bloody vaginal discharge, frequently accompanying ectopic pregnancy, for the last normal menstruation.

With *tubal abortion* the fetal egg partially or completely exfoliates from the wall of the Fallopian tube and by contractions is expulsed into the abdominal cavity through the ampullar end (abdominal aperture) of the Fallopian tubes. Clinically it appears as pain in the ileal area with irradiation into the rectum, hip, sacrum, clavicle, scapula (irritation of *n. phrenicus* — "phrenicus-symptom"). The pain attack can be accompanied by dizziness, loss of consciousness. Due to thrombogenesis in the blood vessels, bleeding can stop and the pain decreases; later the symptoms of expulsion of the fetal egg can repeat.

With a *complete tubal abortion* the fetal egg is expulsed into the abdominal cavity. More often the bleeding proceeds until the egg remains in the Fallopian tubes, thus blood flows down into the rectouterine cul-de-sac with the formation of a postuterine haematoma. As a result of an occlusion of the ampullar part of the Fallopian tube and healing of rupture, *hematosalpinx* is formed.

After an *incomplete tubal abortion* the rests of the placenta or membrane can remain in the wall of the Fallopian tubes and (after the deposit of fibrin in them) can be transformed into a placentar polyp (the same as for an incomplete uterine abortion).

Rupture of the Fallopian tubes occurs within the first several weeks of pregnancy with the site of the fetal egg in the area of the isthmus, interstitial part or a bit later with another site. In this case profuse internal bleeding occurs, accompanied by oligemia and quite often shock, collapse, acute anaemia.

Clinical picture of a rupture of the Fallopian tube is very well expressed. The most typical sign is a sudden acute pain in the ileal areas with irradiation to the rectum, clavicle. The pain can be accompanied by short-term loss of consciousness, dizziness, nausea, vomiting, hiccups. The patient becomes adynamic, not very contactful. The pain intensifies with an attempt to rise or turn. The skin is pale, acrocyanosis, cold sweat are observed. Pulse is accelerated, of weak filling and pressure, ABP falls. The abdomen inflated, painful during palpation, barely participates in the act of breathing, during percussion, a blunt percussed sound is marked. The positive Schetkin—Blumberg's sign can be observed.

After acute bleeding, the body temperature can be normal or a little lowered. However, it can raise up to 38°C in connection with the development of hemoperitoneum. The temperature above 38°C demands differentiation of tubal rupture with acute salpingitis.

Laboratory changes. After bleeding, the volume of blood is restored due to hemodilution. However, within the first hours after acute bleeding a decrease in the level of haemoglobin and hematocrit numbers can be observed. The amount of leukocytes in half of the patients is normal; leukocytosis up to 30 • 10^9 in 1 l can occur.

Diagnosis. The most informative modern methods of diagnosis of ectopic pregnancy are following:

1. Study of the level of CG in the urine or blood serum (pregnancy test) or its β-subunits (β-CG). With ectopic pregnancy in conformity to its term, the level of CG, as a rule, is lower than for uterine. The most exact method is determining the serum level of CG β-subunits (critical level — 2,000–6,000 mUI/ml).

2. Ultrasound study (transabdominal and transvaginal).

3. Laparoscopy.

The complex of such attributes as the absence of the fetal eggs in the uterus, positive pregnancy test, the presence of liquid in the rectouterine pouch and adnexal enlargement on one side, more often testifies to ectopic pregnancy.

Ultrasonography. Identification of the fetal egg in the Fallopian tubes is complex. However, detection of the fetal egg in the uterine cavity in most cases excludes the diagnosis of ectopic pregnancy. Besides, with the absence of an increase in the level of CG β-subunits in 48 h (with uterine pregnancy the CG level is doubled) and the presence of an "empty uterus" during ultrasonographic study, the diagnosis of ectopic pregnancy can be probable.

Transvaginal ultrasonography together with determining the serum level of β-subunits of CG is the most sensitive methods of early pregnancy diagnosis.

The advantages of transvaginal ultrasonography is the absence of necessity to fill the urinary bladder, which is of great importance for the given condition of the patient. This method allows diagnosing a pregnancy starting with 1.5 weeks after fertilisation (a mass with a diameter of 4–5 mm). The fetal heartbeat is observed on 3rd–4th week after fertilisation.

Additional methods of diagnosis of ectopic pregnancy are also culdocentesis, diagnostic curettage of the uterus, laparoscopy (Fig. 59), laparotomy.

Culdocentesis is performed for diagnosis of intraabdominal bleeding. The cervix is grasped by bullet forceps and is pulled in the direction of the pubic symphysis; with a long wide needle a puncture is made in the Douglas' cul-de-sac through the posterior vaginal fornix; the liquid is aspirated. If the blood received during aspiration does not coagulate, the diagnosis of intraabdominal bleeding is probable.

Results from the culdocentesis can be unsatisfactory for women with previous salpingitis or pelviperitonitis and obliteration of the rectouterine pouch.

Curettage of the uterine cavity helps perform differential diagnosis of an incomplete abortion with tubal pregnancy. With the presence of fetal or placentar elements in the uterus the diagnosis of ectopic pregnancy is improbable. If the specified structures are absent, the diagnosis of ectopic pregnancy is possible. Identification of the Arias—Stella's phenomenon (the presence of cells with hyperchromatic hyperplastic fragmented nucleus and vacuolation cytoplasm in the decidual membrane) is a significant witness to ectopic pregnancy. The presence of decidual tissue in the uterus is possible in case of complete spontaneous abortion.

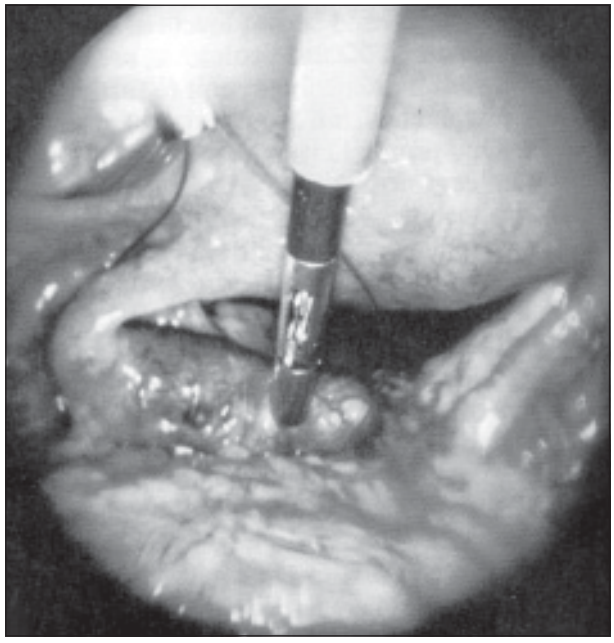


Fig. 59. Laparoscopic picture of an unruptured tubal pregnancy

Laparoscopy is an important diagnostic procedure, especially with an unruptured ectopic pregnancy, and allows to perform an organ-sparing operation. Laparoscopy can be not informative as a result of inflammatory processes of the pelvic organs, bleeding or progressing tubal pregnancy with its short term even with full visualization of the Fallopian tube.

Laparotomy is performed mainly with ruptured ectopic pregnancy. A delay in performing the operation can lead to catastrophic consequences. The first stages of treatment are bring the patient out of shock, stopping the bleeding and supporting the function of blood circulation.

Differential diagnosis (Table 18) is conducted between ectopic pregnancy and the following diseases:

— acute or chronic salpingitis;

— threat of abortion or an incomplete abortion and uterine pregnancy;

— rupture of the corpus luteum and follicular cyst with intraabdominal bleeding (apoplexy);

— twisting of ovarian cysts;

— appendicitis, gastroenteritis, intestinal obstruction, gastric ulcer, cholecystitis, renal colic;

— discomfort in connection with an intrauterine device.

Treatment for ectopic pregnancy is usually complex: operation, antishock and infusion therapy, regenerative treatment, rehabilitation of the reproductive function.

Surgical treatment in most cases consists of salpingectomy. The purpose of such treatment is to save the woman's life. Simultaneously with operative intervention, hemotransfusion of compatible blood is done depending on the severity of the woman's condition, volume of blood loss. In cases of uncomplicated intensive bleeding organ-sparing operations can be carried out.

Last few years due to the opportunity of early diagnosis (determining the β-CG level, transvaginal ultrasonography) laparoscopic treatment of women with unruptured ectopic pregnancy, as well as with tubal abortion accompanied by insignificant blood loss assumed ever greater importance.

Radical operations. *Salpingectomy* — the removal of the Fallopian tube. While performing the operation no more than a third of the interstitial part is left to prevent a relapse of ectopic pregnancy or rupture of the uterus during a uterine pregnancy.

Sterilization is performed if the patient has no desire for further pregnancy.

Table 18. **Differential diagnosis of ectopic pregnancy**

Symptoms	Ectopic pregnancy	Abortion	Salpingitis	Rupture of the cyst of the corpus luteum
Pain	Unilateral spasmodic pain before the rupturing of the Fallopian tube	Abdominal spasmodic	As a rule, in both lower quadrants (irritation of peritoneum) Sometimes dysuria	Unilateral, extended with bleeding
Nausea, vomiting	Sometimes before the rupturing of the Fallopian tube, frequently after it	Almost never	Rarely	Rarely; pregnancy signs are absent
Menstruation	Missing a menstruation, scanty bloody discharge	Long-term amenorrhea, then bloody discharge, bleeding	Hypermenorrhoea and (or) metrorrhagia	Delay in menstruation, further bleeding with pain
Body temperature and pulse	37.2–37.8°C; normal pulse before the rupturing of the Fallopian tubes and accelerated after it	37.2°C with spontaneous; up to 40°C with infected	37.2–40.0°C; pulse is accelerated proportional to the body temperature	No higher than 37.2°C; pulse is normal, with bleeding accelerated
Pelvic examination	Unilateral tenderness, especially during cervical excursion; unilateral tomour masses in the Douglas' cul-de-sac	Cervix is a little opened, uterus is a little enlarged, irregularly softening; tenderness only in case of infection	Bilateral tenderness during excursion of the cervix; tumour masses with hydro- or pyosalpinx	Tenderness over the affected ovary; tumour masses are absent; uterus is hard, not enlarged
Laboratory data	Leukocytes — $15 \cdot 10^9$ in 1 l; elevated ESR; erythrocytes are decreased with significant blood loss	Leukocytes — $15 \cdot 10^9$ in 1 l with spontaneous and up to $30 \cdot 10^9$ in 1 l with infected abortions; amount of erythrocytes is normal	Negative β-CG; leukocytes — $(15–30) \cdot 10^9$ in 1 l, elevated ESR; number of erythrocytes is normal	Negative β-CG; leukocytes — $10 \cdot 10^9$ in 1 l; ESR is normal; number of erythrocytes is normal

Conservative operations on the Fallopian tubes have the best prognosis if they are conducted in unruptured tubal pregnancy before the rupture of the Fallopian tubes in women before the age of 30, with high parity, absence of infertility in the history, salpingitis, and operations on the Fallopian tubes.

Salpingotomy is a vertical cut along the free edge of the Fallopian tube above the fetal egg. The fetal egg is removed by means of forceps or cautiously pumping out; the open Fallopian tube is washed with the Ringer-lactate solution *(nonisotonic solution of sodium chloride)* to identify the bleeding and control the bleeding. Whenever possible the cut is not continued to the end of the ampulalr part of the Fallopian tube. The place of the cut is stitched or not stitched (Fig. 60, *a*).

Segmentary resection and anastomosis are recommended for unruptured tubal pregnancy with the site of the fetal egg in the isthmus (Fig. 60, *b*).

Fimbrial evacuation — removal or pumping out the fetal egg through the ampullar part of the Fallopian tube. It is conducted under the condition of distal site of the fetal egg. This operation has its own opponents in connection with an increase in ectopic pregnancy relapses incidence and risk of developing trophoblastic disease.

Other conservative operations on the Fallopian tubes are carried out after scrupulous stopping the bleeding and irrigation of the abdominal cavity with Ringer-lactate solution.

In connection with a certain risk of developing trophoblastic disease, exam of the CG level 2–3 weeks after the operation to compare with its previous level is recommended. With a persistent or increased CG level a repeated analysis should be done or treatment with methotrexate should be prescribed.

In case of progressing ectopic pregnancy ***medicamentous treatment is prescribed*** with methotrexate. However, independently this method is seldom used.

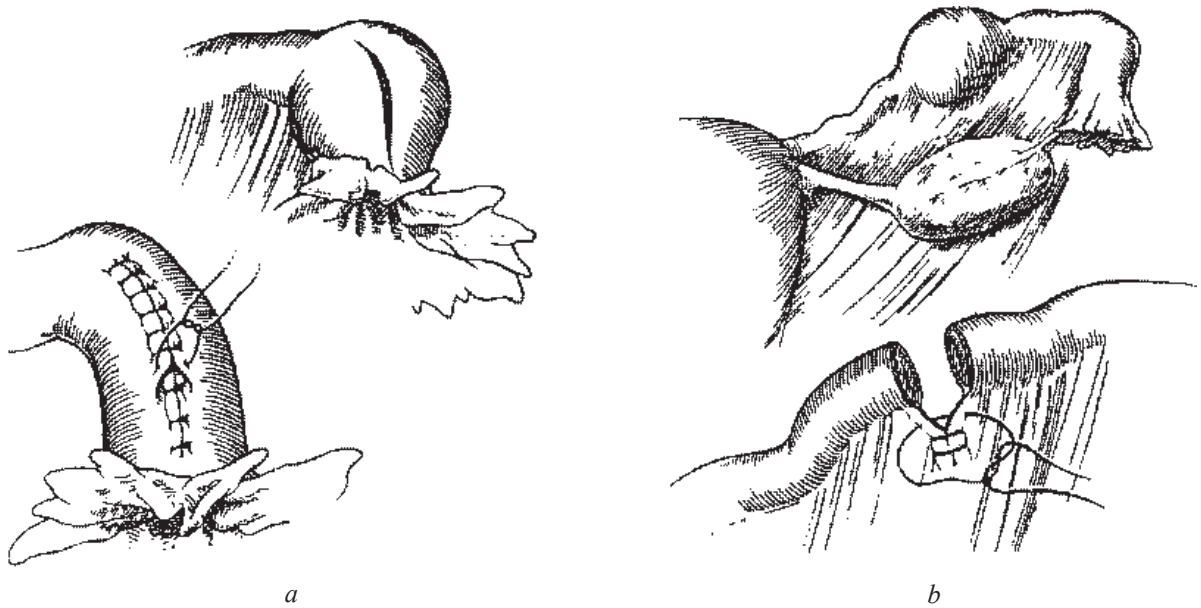
To prevent Rh-isoimmunization of Rh-negative unsensibilized patients, wishing to keep the reproductive function, anti-Rhesus immunoglobulin is recommended.

Prognosis. After performing a resection of ectopic pregnancy 14% of women have ovulation no later than the 19th day; 64% — in 24 days. 30 days after the operation ovulation is restored in 3/4 of the patients. Therefore, contraceptive preparations (more desirable the combined oral contraceptives) are necessary to begin right after the operation.

Abdominal pregnancy. The fetal egg after leaving the Fallopian tube can be implanted on adjacent serous membranes of organs. The fetus (even without the amnion) can develop some time in the abdominal cavity. However, its place in the abdominal cavity is very unreliable; the probability of its destruction is very high. In every second case of abdominal pregnancy the fetus has congenital developmental anomalies.

Diagnosis of abdominal pregnancy is frequently retrospective. A large fetus, as a rule, occupies a diagonal or horizontal position, during palpation an increase in the tone, is not determined as for uterine pregnancy. The cervix is frequently located eccentric.

Data from the ultrasound study are frequently unsatisfactory; they essentially help in the diagnosis if the head of the fetus is located near the mother's bladder, but has no connection with the uterine tissue. In doubtful cases, to establish the diagnosis it is



a *b*

Fig. 60. Conservative operation in case of unruptured tubal pregnancy:
a — salpingotomy; *b* — segmentary resection and anastomosis of the Fallopian tubes

possible to use nuclear magnetic resonance or computer tomography.

Treatment. During the operation, concerning abdominal pregnancy, there can be massive bleeding and significant technical difficulties. Before the operation no less than 2 l of blood should be prepared and the infusion of solutions in two veins is begun. The operation is frequently accompanied by clearing the intestines of any fusions with the placenta and membrane, therefore intraoperative and postoperative introduction of antibiotics, as a rule, cephalosporin line, are recommended.

If the placenta can not be removed completely, it is left in the abdominal cavity and therapy with methotrexate sodium is prescribed, which promotes a faster destruction of the placenta. Due to its use there can be an accumulation of necrotic tissue which increases the risk of infection.

Partial removal of the placenta should be avoided, because bleeding from the placental bed frequently is very strong (profuse) and uncontrollable.

Potential *postoperative complications* connected to the remains of the placenta include secondary bleedings, hypofibrinogenemia, obstruction or perforation of the intestines, peritonitis, development of choriocarcinoma.

The prognosis for abdominal pregnancy improves, and the risk to the woman's life decreases under the condition of duly diagnosis in the I trimester of pregnancy.

Ovarian pregnancy. Diagnostic criteria for ovarian pregnancy are the following attributes:

— the Fallopian tube on the affected side is intact;

— the fetal egg is placed in the ovary;

— the ovary is connected to the uterus by the ovarian ligament;

— well defined ovarian tissue is found in the wall of the fetal sac.

Symptoms of ovarian pregnancy are similar to those for tubal pregnancy or rupture of the cyst of the corpus luteum. During the operation differential diagnosis of ovarian pregnancy with the cyst of the corpus luteum or bleeding from it is done. With small terms of the ovarian pregnancy you can be limited to resection of the ovary or cystectomy; in other cases oophorectomy is performed.

Cervical pregnancy is observed very seldom and characterized by the implantation of the ovum into the cervix uteri below the level of the internal os. The trophoblast tears the mucous membrane (endocervix), and the pregnancy progresses in the fibrous tissue of the cervix.

The first symptom of cervical pregnancy can be painless bleeding occurring a short time after the implantation of the fertilized ovum. With the progressing pregnancy dilation of the cervical walls results in the opening of the internal os. Above the dilated cervix a little enlarged uterine fundus being palpated.

Cervical pregnancy seldom lasts more than 20 weeks. Also rather seldom can calcification of the fetal egg occur.

Treatment of patients with cervical pregnancy is surgical; it is performed immediately after establishing the diagnosis of threat to the woman's life from profuse bleeding. Attempts to remove the placenta from the cervix by vaginal access can lead to uncontrollable bleeding and the patient's death.

The operation of choice is extirpation of the uterus, which is performed in three stages:

1) laparotomy, ligation of the vessels;

2) resuscitation measures;

3) extirpation of the uterus.

Sometimes methotrexate therapy is successful in treatment of patients with cervical pregnancy.

OVARIAN APOPLEXY

Ovarian apoplexy is a sudden ovarian haemorrhage, accompanied by infringement of the integrity of the ovarian tissue and abdominal bleeding. Ovarian apoplexy is 0.5–2.5% of cases of all intraabdominal bleedings. Most frequently the disease develops in the active reproductive period of the woman (16–35 years) and is connected to the rupture of the cyst of the corpus luteum (II phase of the cycle) or with the rupture of the follicle (ovulation phase).

Etiology, pathogenesis. The factors promoting the occurrence of such bleeding, can be trauma to the abdomen, physical loads, sexual intercourse, etc. In many patients, ovarian bleeding can occur without provoking factors. Thus, in the ovary a haematoma is formed, the ovary enlarges.

Clinical picture and *diagnosis*. The clinical picture of the disease is caused by the character of the internal bleeding and the accompanying diseases. If the bleeding is connected to the rupture of the follicle, symptoms of the disease, as a rule, appear between the 12th and 16th days of the menstrual cycle. At this time ovulation occurs, which serves as the direct reason for the bleeding. Due to the rupture of the corpus luteum symptoms appear the last week of the menstrual cycle or during menstruation.

Pain and signs of internal bleeding are characteristic for ovarian apoplexy. In connection with the prevalence of this or that symptom, *anaemic and pain forms* of the disease are conditionally distinguished; with identical expressiveness of these symptoms a mixed form of ovarian apoplexy is also distinguished.

The disease frequently begins suddenly: there is an acute pain in the lower abdomen, in the iliac area, with irradiation into the rectum, hip.

The anaemic form of the disease should be differentiated with ruptured tubal pregnancy (screening pregnancy test on the basis of CG determining is performed), the painful one — with appendicitis.

The absence of delay of menstruation and attributes of pregnancy are characteristic for ovarian bleedings. In case of strong bleedings the final diagnosis is established with the help of laparotomy.

If abdominal bleeding is massive, symptoms of haemorhagic shock, anaemia develop. Pale colour of the skin and mucous membranes is observed, elevated pulse, decreased ABP. During abdominal palpation the patient feels pain, sometimes tension of the anterior abdominal wall in the area of the defect and symptoms of peritoneal irritation.

Gynaecologic examination confirms the absence of signs of pregnancy; the pain is marked during palpation of the uterine appendages in the area of the lesion.

With not so strong bleedings from the right ovary the differentiation with an attack of acute appendicitis is required. The pain during appendicitis is located first in the areas of the naval and epigastria, and in case of acute ovarian bleedings it irradiates to the leg or rectum. For differential diagnosis of appendicitis with ovarian bleeding the *Promptov's sign* matters: with appendicitis examination through the rectum causes an acute pain in the area of the Douglas' culde-sac, moving the uterus is painful; with apoplexy tenderness of the fundus of the rectouterine pouch is insignificant while raising the uterus causes an acute pain. A significant rise of ESR and number of leukocytes in the blood in dynamics are characteristic for appendicitis.

Laparoscopy plays an important role in the differential diagnosis of ovarian apoplexy, tubal pregnancy, diseases of the organs of the pelvis and abdominal cavity.

Treatment of patients with ovarian apoplexy depends on her health condition. With mild bleeding and satisfactory condition of the patient the application of conservative therapy with constant hospital supervision (rest, cold on the lower abdomen, infusive therapy, haemostatic means) is possible. In case of strong bleeding it is recommended to perform surgical treatment: laparoscopy, laparotomy, resection, coagulation or stitching the ovary.

TWISTING OF THE OVARIAN TUMOUR'S PEDICLE

The term "anatomic pedicle of the ovarian tumour" means anatomic masses of the ovary: ovarian mesentery, ovarian ligament, infundibulopelvic ligament. Blood vessels (ovarian artery, veins of the same name, its anastomosis with the uterine artery), lymph vessels and nerves pass in the pedicle of the ovarian tumour.

The surgical pedicle formed due to the twisting of a tumour, can include other organs: hyperinflated Fallopian tube, omentum, intestinal loops. More often only the Fallopian tube is in the surgical pedicle of the ovarian tumour (Fig. 61).

Etiology, pathogenesis. The reasons for the twisting of the ovarian tumour's pedicle are always obvious. More often it occurs in women who have given birth many times with a hyperinflated anterior abdominal wall. Twisting of the pedicle of the tumour can occur due to physical loads, sharp turns of the trunk.

Clinical picture. As a result of the twisting of the pedicle of the tumour its nutrient supply first of all is damaged, which explains the development of characteristic clinical symptoms. The twisting of the tumour pedicle can occur quickly or gradually; be complete (360° or more) and partial (less than 360°). With gradual twisting, first of all the outflow of blood in more thin-walled venous vessels is disturbed, and the blood flow does not stop along the arteries with more elastic walls. In a tumour there is venous stasis, it enlarges, there are haemorrhages, rupture of the tumour capsule with abdominal bleeding is possible. The tumour first gets a dark-cherry colour, then brown. With more significant twisting of the pedicle the tumour loses its nutrition and necrotic changes occur in it. Necrosis of the tumour promotes the development of secondary infection, which with the absence of duly diagnosis and treatment can lead to severe septic complications (peritonitis).

More often the twisting of dermoid cysts, having a long pedicle, occurs, less often — paraovarian cysts, fibromas and ovarian cysts.

Diagnosis. With acute twisting of the tumour's pedicle, which was revealed earlier, establishing the

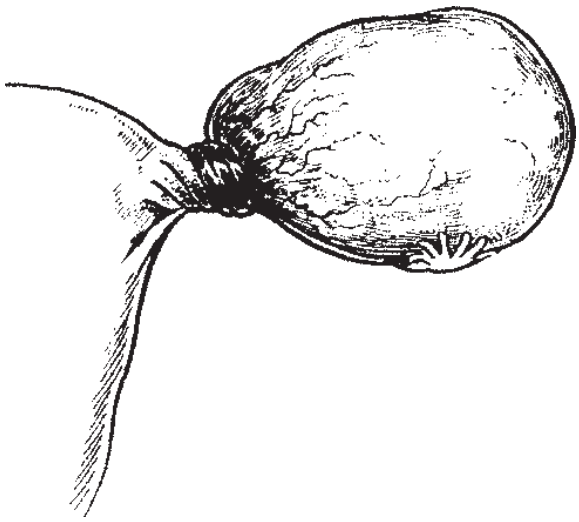


Fig. 61. Twisting of the ovarian tumour's pedicle

diagnosis, as a rule, does not present difficulty. The disease begins with acute pain of spasmodic character with irradiation to the pedicle, sacrum. Nausea, vomiting, constipation, meteorism can be observed. The pulse is accelerated; the body temperature is normal or subfebrile. The abdomen is inflated, during palpation rigidity of the muscles of the anterior abdominal wall and symptoms of irritation of the peritoneum (picture of acute abdomen, shock can develop) are determined.

During gynaecologic examination in the adnexal area, a tumour-like mass of oval form, elastic consistence, limited mobility, acute pain during palpation, are found. The uterus and appendages on the other side are usually not changed. Frequently because of tension and pain occurring during palpation of the anterior abdominal wall, it is hard to reveal a tumour mass in the small pelvis.

If twisting of the tumour's pedicle occurs gradually, symptoms are expressed less acutely.

Differential diagnosis is conducted with ruptured ectopic pregnancy and acute appendicitis. Carefully collected anamnesis, attributes of pregnancy, picture of internal bleeding, bloody discharge from the sexual path, positive reaction to CG, puncture of the posterior vaginal vault (detection of blood) help establish the diagnosis.

Treatment is surgical. After laparotomy on the twisted tumour's pedicle clips are put on and a cut is made between them. The pedicle is not untwisted to prevent the development of thrombembolism. Peritonization of the stump is conducted with the help of the leaves of the broad uterine ligament. The removed tumour is opened and histological study is carried out.

UTERINE MYOMA

Emergency surgery for a uterine myoma can be necessary for such complications:

— birth of submucous node of myoma;

— disorder of the blood supply and dystrophic changes in the myomatous node;

— twisting of a pedicle of a subserous node of a uterine myoma.

The birth of a submucous node of myoma is frequently accompanied by profuse uterine bleeding, spasmodic pain in the lower abdomen, disorder of blood circulation in the node.

The birth of a submucous node of myoma is accompanied by the smoothing and opening of the cervical canal, thus the submucous node can be born in the cervical canal or in the vagina. In such cases urgent surgical intervention is done. In aseptic conditions, after processing the operational area with antiseptic solutions, with Muso's forceps they grasp the top of the node and maximal by pull to the bottom, then with scissors cut its basis and with rotary movements twist the node off, then without difficulties it separates from the uterine wall.

If the pedicle of the node is located high, they preliminary cut the anterior cervical labia to create access to the pedicle and cut the node. Sometimes a born submucous node of myoma necrotizes due to acute **disorder of blood circulation** and gets grey and black. Necrosis of the node can be accompanied by rise in the body temperature, leukocytosis, and elevated ESR.

Indication for operative intervention is pain in the area of the myomatous node due to nutrition disorder. As a rule, first conservative treatment is used (infusive, antibacterial therapy, spasmolytics). If the pain syndrome is not liquidated, rise in the body temperature and leukocytosis is observed, then laparotomy, amputation or extirpation of the uterus is performed.

The picture of an acute abdomen can appear with the **twisting of the pedicle of the epigastric myomatous node.**

During gynaecologic examination of the patient with **subserous node** of a uterine myoma, a painful dense mass connected to the uterus is revealed. Palpation can be complicated because of tenderness and tension of the anterior abdominal wall. With the twisting of the pedicle of such a node, conservative myomectomy or removal of the uterus are possible.

TRAUMATIC DAMAGE TO THE GENITALIA

Damage to the external genitalia and vagina can take place while giving birth, during sexual intercourse, and rape. Cases of deliberate traumatism, industrial traumas are seldom observed. Thermal and chemical burns are also rare. Damages of the iatrogenic character are possible due to radiation therapy for malignant neoplasms, careless examination with specula of older women with atrophic changes of the vaginal mucous membrane.

Clinical picture. The basic symptoms of damage to the external genitalia and vagina are pain and bleeding. As a result of trauma to the bladder, rectum, incontinence of urine, gases and feces can occur.

Closed damages to the vulva are characterized by expressed vascularization of the organ and are accompanied by hypostasis, development of haematomas; open traumas cause bleeding. The mass of haematoma is accompanied by the feeling of pressure in the area of the genitalia, pain, tenesmus, anaemia (large progressing haematomas). With traumas to the vagina, the integrity of the urethra, bladder, rectum and adjoining fat can be damaged, result-

ing in the further formation of intestinal-vaginal and urinogenital fistulas.

Diagnosis is based on the history data, inspection, vaginal and rectovaginal examinations. With the suspicion of damages penetrating into the abdominal cavity, wounds to the bladder, cytoscopy, laparoscopy, diagnostic laparotomy are performed.

Treatment with the absence of severe damages and bleedings is limited to local application of antiseptic solutions; in case of severe trauma surgical operations are indicated. The first step of treatment is to stop the bleeding and normalize the patient's hemodynamics, shock therapy. Wide-spectrum antibiotics are prescribed. If the wound is infected, antitetanic and antigangrenous serums are entered. Primary processing of the wound is conducted according to general surgical principles. With clean fresh wounds in the perineal area, catgut sutures are put on the mucous membrane of the vagina, on the skin — catgut or silk sutures. If the wound is located near the urethra, it is sutured while a metal catheter is put in the urethra, which is later replaced by elastic one and is left in the bladder, taking into account the possible reflex of urinary retention. In case of bleeding from the wound in the area of the vaginal threshold they impose sutures while leading the ligature to the periosteum, so not to injure the venous plexus while suturing. With insignificant parenchymatous bleeding, hard tamponade of the bleeding area and imposing a hard bandage are used.

With haematoma formation, which doesn't enlarge, a hard bandage is applied, haematostatic means are prescribed (calcium chloride, vicasol, dicynon, B vitamins, nicotinic, ascorbic acid). An increasing as well as infected haematomas are opened and the bleeding vessels are tied.

If perineal rupture is accompanied by trauma to the rectum and pollution of the wound with faecal matter, the wound and rectum are washed out with a 5% solution of potassium permanganate or other antiseptic solutions and tamponed. The patient is prescribed liquid food, antibacterial, desintoxication therapy, analgesics. Vishnevsky ointment tampons, on the 6th–7th day laxative means are prescribed, on the 10th–11th day walking is allowed, and in 2–3 months operative treatment depending on the character of the trauma is conducted.

Damage to the cervix and corpus uteri. Such traumas include delivery traumatism of the mother (ruptures during birth and obstetric operations) more often, but can occur during an artificial abortion, diagnostic curettage of the uterine mucous membrane, hysteroscopy, introduction of intrauterine devices, during other intrauterine manipulations.

Perforation of the uterus can be caused by a uterine intubation, Hegar's dilator, curette, or the tip of a vacuum-excochleator's cap. Perforation is promoted by the wrong positions of the uterus (hyperanteflexia, retroflexia), as well as destructive changes in the uterine wall (in women who have given birth many times, due to tumours of the uterus, inflammatory changes of the uterine tissue, etc.).

The extent of trauma because of uterine perforation can vary. Trauma to the endo- and myometrium may not be accompanied by damage to the uterine peritoneum (perimetrium). In severe cases organs of the abdominal cavity can be damaged: intestines, bladder, omentum. Uterine perforation can be located in the area of the fundus, anterior, posterior walls, isthmus, rib of the uterus in the zone of the vascular fascicle.

Clinical picture, diagnosis. Clinical signs of uterine perforation depend on the site, extent of damage and disorder of the integrity of adjacent organs. Perforation with a uterine intubation without peritoneal injury and with the absence of bleeding can proceed asymptomatic. Perforation of the uterus in the zone of the vascular fascicle (uterine artery and vein) is accompanied by a clinical picture of strong internal or external bleeding. Perforation with damage to the peritoneum appears as acute pain reaction.

Important symptoms of uterine perforation are penetration of the instrument (intubation, dilator, curette) into a depth, considerably exceeding the length of the uterine cavity; extraction of the omentum, intestinal loops from the perforated aperture, acute pain. Haematoma between the leaves of the broad uterine ligament can be formed with damage to the uterine vessels without trauma to the visceral peritoneum. Haematoma can be diagnosed during palpation of the abdomen, bimanual gynaecologic examination as a painful mass with an elastic consistency with indistinct contours. To specify the diagnosis of perforation penetrating into the abdominal cavity, laparoscopy is used.

Tactics of the surgeon for perforation of the uterus or suspicion of this complication consists of immediate stopping all further manipulations and depends on the site of the trauma and the instrument which imposed it.

In case of uterine perforation of the uterus by intubation or a small dilator, the patient is put to bed, cold is put on the lower abdomen and the condition of hemodynamics (ABP, pulse), symptoms of uterine bleeding from the reproductive tract, the body temperature, common blood analysis, diuresis are observed. With the absence of symptoms of peritoneal irritation and intraabdominal bleeding conservative treatment is continued while prescribing antibacterial, infusive therapy (blood substitutes), oxytocin. If the pulse is accelerated, the body temperature rises, a puncture of the posterior vaginal vault is recommended. If blood is detected in the Douglas' culde-sac laparotomy is performed. An increase in the symptoms of peritoneal irritation and internal bleeding require epigastrial section, even with negative results from the puncture.

With perforation of the uterus, imposed by a large dilator in the zone of the rib of the uterus (Fig. 62, *a*), curette (Fig. 62, *b*) during a criminal or septic abortion or while pulling internal organs out of the perforated aperture (intestines, omentum), a laparoscopy or laparotomy is immediately performed. The question about the extent of the operation (suturing the apertures, removing the uterus) are solved depending on the sizes and sites of the damage, age and condition of the patient, presence of an infection. If there is an opportunity to suture the damage, its edges are cut, curettage of the uterine cavity through the perforated aperture is conducted and it is sutured. Supravaginal amputation of the uterus is conducted with multiple perforations to the corpus uteri, major defects of its walls, trauma of the ascending branches of the uterine arteries. Extirpation of the uterus with the Fallopian tubes is conducted with accompanying endomyometritis, sepsis, damage to the cervix spreading to the corpus uteri, as well as ruptures of the vascular bunches with the development of retroperitoneal haematomas.

Damage to the cervix more often is the result of excessive force during intubation and the dilation of the cervical canal without taking into account the position of the uterus. With the perforation of the cervix there can be wounds penetrating into the abdominal cavity, into the broad uterine ligament with the formation of haematomas.

In case of perforation of the cervical wall with a dilator or during intubation the doctor who with difficulties entered the instrument, feels a sudden plunge, and then free movement into significant depth. With perforation especially with damage to the peritoneum and the hematoma formation in the broad ligament, the patient feels a strong pain, besides of internal, external bleeding from the reproductive tract may take place. The diagnosis of a penetrating wound to the cervix is proven by cautious intubation. If the diagnosis of perforation is established, all further manipulations are stopped, and treatment of the patient is conducted, the same as for perforation of the corpus uteri.

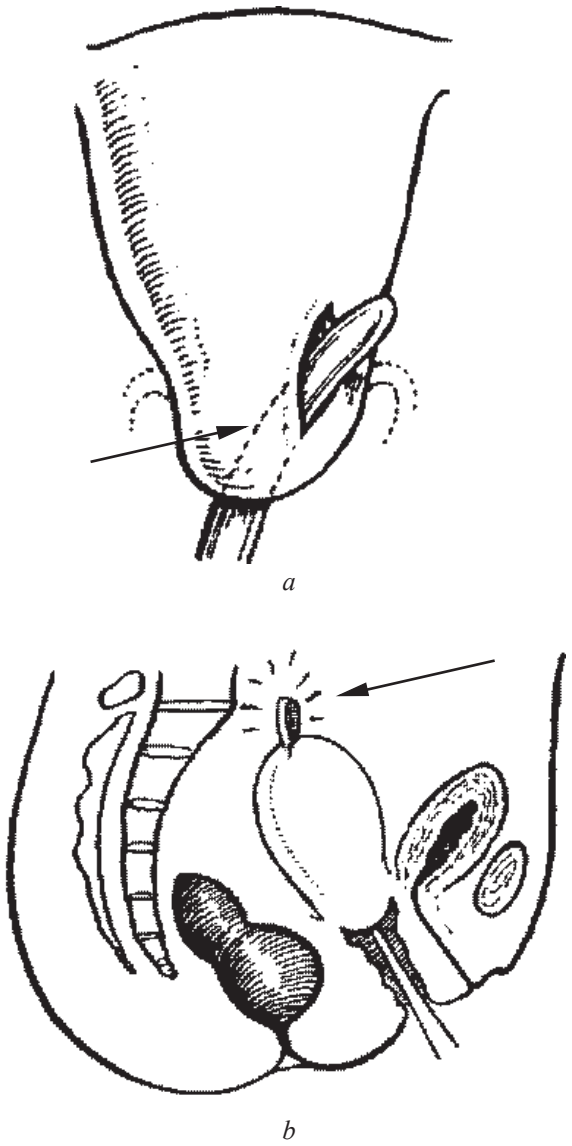


Fig. 62. Perforation of the uterus:
a — by Hegar's dilator; *b* — by curette

Rectovaginal fistula, as a rule, occurs due to traumatic damage to tissue during pathological, especially operative, deliveries (narrow pelvis, large baby, obstetric forceps, delivery operations), trauma during gynaecologic operations, especially with purulent inflammatory processes of the pelvic organs, as well as paraproctitis, after radiation concerning malignant neoplasms of the female genitalia (cervical cancer, etc.).

Clinical picture. Patients complain of the gas, pus, feces discharge from the vagina. During gynaecological examination hyperemia, maceration of the mucous membrane of the vagina and skin of the external genitalia are revealed. Examining the vagina with the help of vaginal specula, on its posterior wall the external aperture of a fistula with a diameter from 1 mm to several centimetres is found. The sizes of the internal aperture of a fistula on the anterior wall of the rectum is determine during cautious intubation through the external aperture of fistula, while simultaneously carrying out manual examination of the rectum.

The fistula can be cylindrical (the whole length along has approximately an identical diameter), funnelled (diameter of one of the apertures is more than the other one), compound form.

Diagnosis is based on the history data, typical complaints of the patient and gynaecologic examination. With a small diameter of the external aperture of a fistula, a colour solution (methylene blue, etc.) is entered into the rectum and its discharge into the vagina is observed.

The treatment of patients with rectovaginal fistulas is surgical.

Urinogenital fistula is rather frequent and severe complication in urogynaecology which is accom-

panied by deterioration of the patient's life, deep psychological trauma, although it does not directly threaten her life.

Etiology, pathogenesis. A urinogenital fistula occurs due to wounds to the urinogenital organs, trophic disorders during pathological deliveries, as a result of obstetric and gynaecologic operations. Rare reasons for the occurrence of a fistula are chemical burns, household traumas, gunshot wounds.

An obstetric fistula is formed due to long-term compression of the urinogenital organs, blood and lymph circulation disorders with subsequent necrosis of tissue (narrow pelvis, big fetus, the use of obstetric forceps, delivery operations, rarely — caesarean section with subsequent hysterectomy). A trophic fistula is formed 8–12 days after labour or operations. In the gynaecologic practice the formation of fistulas is observed more often after extirpation of the uterus, criminal abortion, as well as as a complication of radiation therapy concerning malignant tumours of the genitalia, in case of disintegration of tumours.

The most often pathology is a vesicovaginal fistula. Ureterovaginal, vesicocervical, vesicouterine and compound fistulas are rarely formed.

Clinical picture, diagnosis. Characteristic symptoms for all forms of fistulas are dripping of urine, discharge of urine from vagina. The size of a fistula can fluctuate from several millimetres to several centimetres. The amount of leaking urine depends on the size of the fistula. For an ureterovaginal fistula constant urine leakage together with normal urination is typical.

For vesicocervical and vesicouterine fistulas enuresis is not always observed in connection with the features of the site and a small aperture. Characteristic symptoms are the colouring of the urine with blood during menstruation, pain in the bladder, vagina in connection with the development of accompanying inflammatory processes. The formation of an ureterovaginal fistula is preceded by fever and dysuria.

The site of a fistula and the sizes of its aperture are determined during gynaecologic examination, examination with specula. For more exact diagnosis a colour solution (for example, methylene blue) is entered into the bladder, which with the presence of a fistula pours into the vagina. An ureter fistula, as a rule, is located in the vaginal vault and represents complexity for catheterization.

To specify the site of a fistula in the bladder, cystoscopy is performed. With the purpose of diagnosis of an ureterovaginal fistula, radiological research is used.

Treatment. Conservative treatment of patients with urinogenital fistulas consists of the used coagulative solutions — 5% solution of silver nitrate, 5% alcoholic solution of iodine, diathermic current — during the first 2–3 weeks after the formation of a fistula. These methods are directed on the formation of a scab in the area of the fistula; after its tearing away the fistula can cicatrize. Such treatment is conducted with the presence of a urethral catheter entered on the 8th–10th day. Ureterovaginal fistulas give in to therapy by catheterization of the ureter in which the catheter is for 6th–8th days. Such fistulas can close independently in 1 to 3 months; however the termination of urine discharge always is connected to the destruction of the renal parenchima. Conservative methods of treatment are inefficient for patients with postradiation and complicated fistulas.

The purpose of plastic operations on the urinogenital organs is to restore urination while preserving the necessary anatomic and physiological relations between urinogenital organs. The operation, as a rule, is performed 4–6 months after the formation of fistulas (in 5–6 weeks with the presence of ureterovaginal fistulas and in 1 year — with postradiation fistulas). Preoperative preparation, which is continued until the disappearance of symptoms of inflammatory processes (vaginal syringing, flushing the bladder lavage with antiseptic solutions, antibacterial therapy while taking into account the sensitivity of the pathogenic microorganisms excreted from the vaginal discharge and urine, desintoxication, general revitalizing, sedative therapy) has great value for the consequences of the operation.

The plastic of fistulas is performed by using various accesses: transvaginal, transvesicular or transabdominal.

The *prognosis* for the majority of patients after plastic operations is mainly favourable, except for postradiation fistulas.

Prevention of urinogenital and rectovaginal fistulas consists of rational conducting of delivery, the application of anatomic operative technics.

PURULENT TUBAL-OVARIAN TUMOURS

Purulent tubal-ovarian tumours of the uterine appendages (pyosalpinx, pyo-ovarium) frequently are indications to urgent surgery.

Clinical picture. With the presence of purulent tubal-ovarian adnexal masses the inflammatory process involves the peritoneum, omentum, intestinal loops with the formation of a single inflammatory conglomerate. The picture of acute abdomen develops: the body temperature rises, fever, nausea, vomiting, leukocytosis with a left shift of the leukocytic formula, elevated ESR.

During gynaecologic examination, tumour painful masses with a dense capsule and indistinct borders, due to the fusion with adjacent organs, are found. With an increase in the symptoms of acute

abdomen there is a threat of the purulent tumours rupturing with the pus entering the abdominal cavity and the purulent general peritonitis development. The pus can also rupture into the bladder, rectum and vagina with the formation of fistulas.

Symptoms of the threat of the adnexal purulent tumour rupturing into the rectum are tenesmus, mucous discharge and quite often diarrhoea; with the rupture into the bladder — frequent and painful urinations.

Diagnosis. The diagnosis is based on the history data (adnexal inflammation with frequent exacerbations), objective examination. Additional informative methods of diagnosis is ultrasound study, laparoscopy. With the picture of peritonitis, the final diagnosis is established during laparotomy.

Treatment of patients with tubal-ovarian purulent masses should be individual, complex. With the picture of acute abdomen against a background of intensive infusive and antibacterial therapy, surgical intervention with the removal of the affected appendages is performed. In the climacteric period, the operative intervention, as a rule, is extended to supravaginal amputation or extirpation of the uterus with the appendages. A long course of the inflammatory disease with the development of promoted abdominal adhesions may present significant technical difficulties for performing operation.

With accompanying peritonitis the drainage of the abdominal cavity through the lateral canals and leaving microirrigators in them for the introduction of antibiotics and peritoneal dialysis are recommended.

RECOMMENDED READING

7; 16; 21; 24; 71; 79; 90; 92; 93; 94; 104; 108.

Chapter 15

SURGERY IN GYNAECOLOGY

MINOR SURGERY

Minor gynaecological surgery includes cervical biopsy, uterine intubation, polypectomy, curettage of the mucous membrane of the uterus, puncture of the abdominal cavity through the posterior vaginal vault, vacuum-aspiration of the fetal egg, artificial abortion at the term before 12 weeks of gestation and other diagnostic and medical procedures (hysterosalpingography, introduction of intrauterine devices, etc.).

Cervical biopsy. The cervix is limited by the specula, fixed by the bullet forceps behind the affected area. On the border between the healthy and affected tissue with conchotome or scalpel the cervical tissue is cut and the wound is sutured with catgut stitches (as a wedge). After using a conchotome, tamponade of the vagina with a tampon moistened in 5% solution of aminocaproic acid is done. The taken material is subject to histological study.

Intubation of the uterus. This operation is conducted while observing all the rules of aseptics and antiseptics. Before intubating the uterus, bacterioscopic exam of the discharge from the urethra, cervical canal and posterior vaginal vault, and bimanual examination to specify the position of the uterus are necessary. The intubation tube has a length of 25 cm, width of 1–5 mm (N 1–5), a handle and a rounded end. The normal length of the uterine cavity is about 7 cm. The width of the tube is selected depending on the passability of the cervical canal.

Preparation for the operation is standard for all operative interventions and includes emptying the bladder, lubricating the external genitalia and internal surface of the hips with chlorhexydin or iodonate. The patient is put in the gynaecological chair. The vagina is opened with Simpson's specula; the vagina and cervix are lubricated with alcohol or iodonate. Then the vaginal specula are moved deeper into the vaginal vault so as not to compress the cervix and isthmus and not create additional obstacles when entering the intubation tube. The cervix is fixated with bullet forceps, which are put on the anterior lip. Straightening the cervical canal in the lower segment of the uterus is achieved by pulling the cervix upward with the bullet forceps and backward (for anteflexia of the uterus) or forward (for retroflexia). Entering the intubation tube is performed while taking into consideration the shift of the uterus to this or that side.

The tube is held with three fingers of the right hand: big, index and middle. Till the internal os the probe, as a rule, passes easily. Some obstacles in this segment of the cervical canal can occur because of the presence a polyp, adhesions. In the uterine cavity the tube moves forward easily to the uterine fundus where it faces an obstacle. To prevent perforating the uterus, while entering the tube, it is impossible to use force, it is necessary to cautiously manipulate it to bypass obstacles.

Polypectomy and fractional curettage of the uterine cavity. For anaesthesia during the operation inhalation (dinitrogen oxide), intravenous (kalipsol, ketalar, diprivan) narcosis, infiltration anaesthesia of 0.25% solution of novocaine are used.

Before the operation, the doctor carefully washes his hands, puts on sterile gloves, examines the vagina and cervix with specula, and performs bimanual gynaecological examination. After vaginal examination, the surgeon processes his hands with an antiseptic solution, puts on sterile gloves, processes the woman's external genitalia with an antiseptic solution, and the vagina and cervix — first with a dry wadded tampon, then a tampon moistened in alcohol. Further the cervix is fixated with bullet forceps.

A polyp on a thin pedicle is removed by twisting, on a wide base — by cutting.

The next procedure is intubation of the uterus: the uterine tube is entered in the cervical canal until the tip of the tube touches the uterine fundus. The length of the uterus is determined by the scale on the tube.

After intubation of the uterus, the cervical canal is dilated with Hegar's N 7–8 dilators. The curette is

entered into the cervical canal and curettage of the cervical canal is performed by back and forth movements of the curette.

The curette N 2 is entered into the uterine cavity and curettage of the uterine wall is performed by back and forth movements of the curette (Fig. 63), consistently going over the whole uterine wall and area of the tubal corners clockwise. The contents of the uterus are removed by removing the curette from the uterine cavity after every 3–4 movements. After finishing curettage the bullet forceps are removed, the cervix is processed with a tampon moistened in alcohol or 2–5% solution of iodine, then the specula are taken out and cold is applied on the lower abdomen for 2 h. The received material (polyp, tissue from the cervical canal and uterine cavity) are placed in a vial with formalin (everything separately) and sent for histological study with indicating each material's orientation separately.

Puncture of the abdominal cavity through the posterior vaginal vault. In aseptic conditions with the help of specula the vaginal part of the cervix is exposed and processed with an antiseptic solution. By way of taking the posterior lip the cervix is fixed with bullet forceps and pulled forward and upward (Fig. 64). The posterior vaginal vault is processed with alcohol, 0.25% solution of novocaine is entered at the site of the planned puncture; further in the thickness of the posterior vaginal vault a thick puncture needle with a length of no less than 12 cm at a depth of no more than 1.5–2 cm is introduced. The contents of the abdominal cavity is removed with a syringe, the punctate is pour into a sterile test tube and macroscopically analysed. If there are ruptured ectopic pregnancy, ovarian apoplexy, other intraabdominal bleeding, the punctate contains blood with microclots. With purulent peritonitis, pyosalpinx, pyo-ovarium the punctate, as a rule, contains pus and is subject to bacteriological examination. In case of revealing transudate (ascitic liquid) during the puncture, it is sent for cytological study.

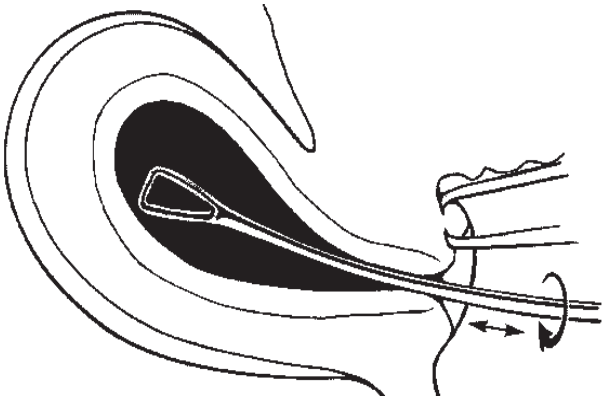


Fig. 63. Entering and movements of the curette during curettage of the uterine cavity

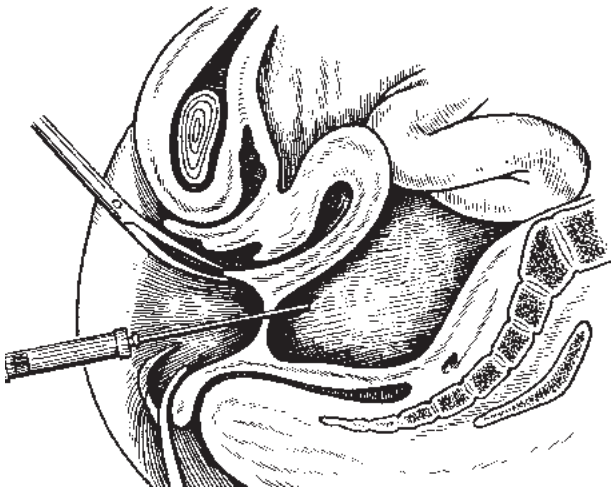


Fig. 64. Diagnostic puncture of the abdominal cavity through the posterior vaginal fornix

Artificial abortion before 12 weeks. The patient is put in the gynaecological chair. The patient's external genitalia and the surgeon's hands are processed the same as for fractional curettage of the uterus. The operation is performed under intravenous, inhalation or infiltration novocaine narcosis. After bimanual examination the hands are processed again, gloves are changed. They expose the cervix in the specula and grasp it with bullet forceps by the anterior lip. After fixating the cervix the anterior mirror is taken out, and the posterior one is given to the assistant to hold. The vagina and cervix are repeatedly processed with antiseptic solutions. Further the cervix is pulled downward and intubation of the uterus is carried out, specifying thus its position and length. The cervical canal is dilated with metal Hegar's dilators (N 4–12), putting the end of the dilator behind the internal os.

The fetal egg is removed with a curette or fenestrated forcepts. In the beginning, a large curette is used (N 6). After removing the basic mass of the fetal egg and contraction of the uterus (reduction of its cavity) the curette N 4 is used. Curettage is finished with a small curette (N 2) till achieving the uterine contraction, the bleeding stops, hearing the characteristic sound.

After removing the fetal egg the bullet forceps are taken off, the cervix is processed with an antiseptic solution.

CERVICAL PROCEDURES

There are following cervical procedures: removal of polyps, diathermocoagulation, diathermoexcision, cryolysis, amputation, cervicoplasty.

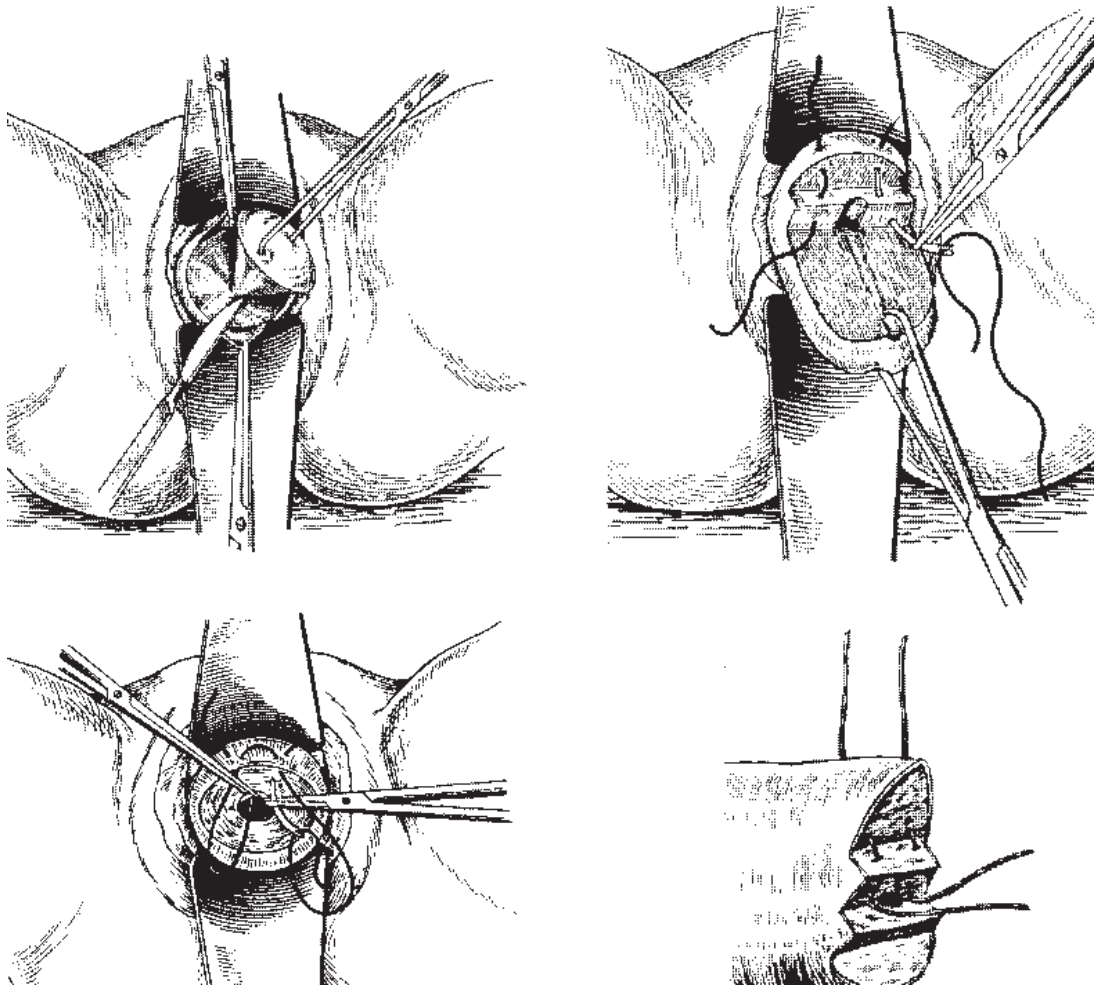
Cervical conization by Shturmdorf. Indications for the operation are hypertrophy and cervical anatomic deformation of the cervix.

Technics of the operation. The vagina is open with the specula; the vaginal part of the cervix is grasped with the bullet forceps and pulling downward to the entrance into the vagina. A circular cut of the mucous membrane of the vaginal part of the cervix is done at a distance of 1 cm above the borders of the pathological tissue. With a scalpel the tissue is cut (cervical mucosa, muscular tissue and mucous membrane of the canal) in the shape of a cone, with the edge directed into the cervical canal (Fig. 65, *a*). The cut cone is removed. The vaginal part of the cervix from the canal side that was left is grasped with clamps. On the border of the cut the edges of the vaginal mucous membrane are separated in front and behind at a depth of 2 cm and it is sutured with the cut cervix by means of special V-shaped stitches.

The stitch is put on the anterior edge of the off-separated vaginal mucous membrane (having receded 0.5 cm from the edge). After suturing the edges of the mucous membrane the ligature is performed from the cervical canal through its whole thickness to the anterior wall of the vagina at a distance of 2 cm above the previous stick. The end of the stitch is clamped, and the opposite end of the catgut string is passed through the eye of the needle and the course of the suture is repeated next to the previous one. Both of the removed ligatures are clamped. On the posterior cervical wall they impose a similar suture, and then connect the upper and lower ligatures, thus forming a cervical canal, which patency is checked by means of intubation.

Wedge-shaped amputation of the cervix by Shredder. The operation is performed in cases of cervical ectropion.

Technics of the operation. On the right and left side of the cervical canal they make cuts on the vaginal part of the cervix (Fig. 65, *b*). The depth of the cut depends on the extent of the amputation. They make a wedge-like cut of the anterior lip of the cervix, the edges are sutured with individual stitches, leading them through the whole thickness of the tissue. Then the same manipulation is performed on the posterior cervical lip with its subsequent suturing with separate catgut sutures. At the end of the operation lateral sutures are put on the cervix; checking the canal's patency with a tube.



a *b*

Fig. 65. Amputation of the cervix:
a — conization by Sturmdorf; *b* — wedge-shaped amputation by Shredder

SURGERY DURING GENITAL PROLAPSE

With the genital prolapse anterior colporrhaphy, posterior (colpoperineorrhaphy) and middle (Le Fort—Neugebauer operation) are performed.

Anterior colporrhaphy. Indications for an anterior colporrhaphy are prolapse of the anterior vaginal wall, prolapse of the anterior vaginal wall and posterior wall of the bladder (cystocele).

Technics. The vagina is opened with the specula; the cervix is grasped with the bullet forceps and pulled toward the entrance into the vagina. On the anterior vaginal wall with a scalpel limit an oval formed area of the mucous membrane (Fig. 66, *a*). The upper edge of this area should be at a distance of 1.5–2 cm below the external aperture of the urethra, and the lower — by 1.5–2 cm from the uterine aperture. The upper edge is grasped with clamps, and partly in a sharp partly in a blunt way separate and cut this area of the mucous membrane. Haemostasis is carefully performed. They impose separate submersed catgut sutures, then with continuous catgut stitches suture the edges of the vaginal mucous membrane with the earlier submersed sutures.

Posterior colporrhaphy (colpoperineorrhaphy). Indications for colpoperineorrhaphy are prolapse of the posterior vaginal wall due to previous perineal ruptures, rectocele, decrease in the tone of the tissue of the pelvic fundus.

Technics. The specula are entered into the vagina; the cervix is grasped by the bullet forceps and pulled upward. A triangle on the posterior vaginal wall is limited with three clamps, two of them being imposed on the right and left side on the border of the vaginal mucous membrane and the skin of the

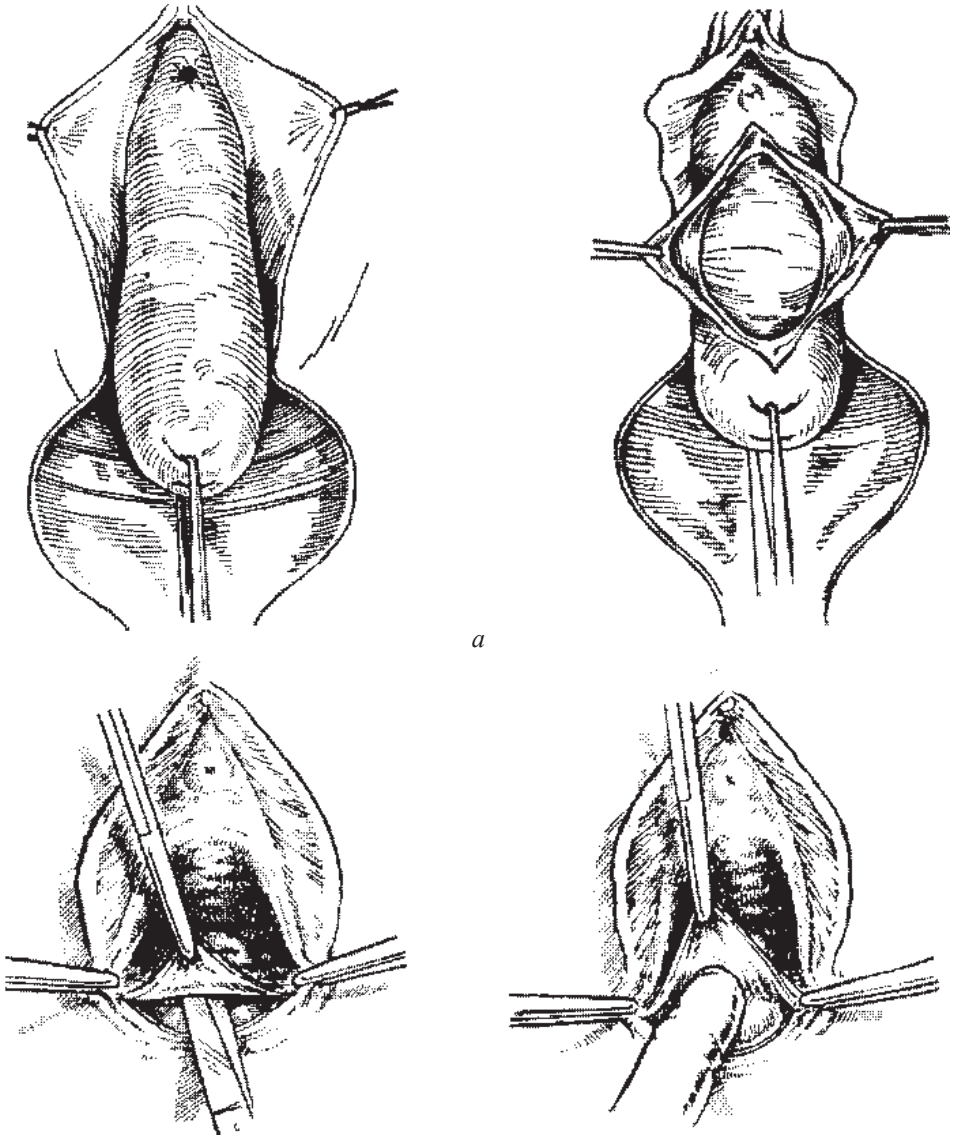


Fig. 66. Colporrhaphy:
a — anterior (pulling the cervix to the vaginal aperture and cutting the anterior vaginal wall);
b — posterior (removing an area of the posterior vaginal wall)

perineum, and the third one — on the posterior vaginal wall on the middle line. The mucous membrane of the posterior vaginal wall is off-separated by the sharp (scalpel) and blunt (swab) ways within the limits of this triangle (Fig. 65, *b*). It is necessary to remember, that the internal surface of the triangle borders (adjoins) the anterior wall of the rectum. After removing this area of the mucous membrane, they expose the levators and connect them with the help of catgut ligatures. With several individual sutures they connect the tissue above the levator; then suture the mucous membrane of the posterior vaginal wall with continuous catgut sutures.

Middle colporrhaphy (Le Fort—Neugebauer operation). The indication for this operation is complete prolapse of the uterus in elderly women, having no sexual intercourses, with the absence of uterine and cervical cancer.

Technics. The anterior and posterior cervical lips are grasped with bullet forceps; the uterus and vagina are removed from the sexual rima. Separate and cut rectangular areas of the mucous membrane from the anterior and posterior vaginal walls, identical in size and form. Further with nodular catgut stitches suture first the anterior edges of the surface of the wound, then — the lateral and posterior ones. The cervix is diped into the vagina. On the right and left side the lateral canals are left for the cervical and uterine discharge outflow.

A shortcoming of operation is the cervix inaccessibility for examination; besides as a result of this surgical intervention the woman cannot have sexual intercourses.

OPERATIONS ON THE UTERINE APPENDAGES

Operations on the uterine appendages are performed concerning ectopic (tubal, ovarian) pregnancy, hydro- and pyosalpinx, pyo-ovarium, with the purpose of sterilization. Plastic operations are performed on the Fallopian tubes for tubal and peritoneal infertility, cysts and ovarian tumours.

Removal of the Fallopian tubes (tubectomy). With a ruptured ectopic pregnancy more often the operation to remove the Fallopian tubes is performed.

Technics. The abdominal cavity is opened below the median with a vertical or horizontal cut. The uterus is grasped with the hand, moved into the operational wound, then is stitched in the area of the fundus by a strong ligature without piercing the endometrium. After that, the pathological changes are revealed in the Fallopian tubes and two clamps are quickly imposed: the one — on the tube in the area of the uterine corner, the second — on the mesentery of the tubes (mesosalpinx) from the side of the ampullar part. A tube is cut above the clamps; the mesentery under the clamps is stitched with catgut and sutured (Fig. 67, *a*). Peritonization is performed with the help of the round ligament of the uterus, which is stitched with several catgut sutures to the posterior surface of the uterus.

Salpingostomy is referred to plastic operations on the Fallopian tubes and consists of X-like incisions in the ampullar part of the tube with subsequent suturing with catgut the cut areas to tubal peritoneum. The fimbria are artificially tried to be formed. The ampullar end of the tube sometimes is fixed near the ovary.

Salpingolysis is an operation to clear the Fallopian tubes from adhesions, which are cut in the sharp way or coagulated, while supervising haemostasis. The prevailing majority of such operations are conducted with the help of laparoscopy.

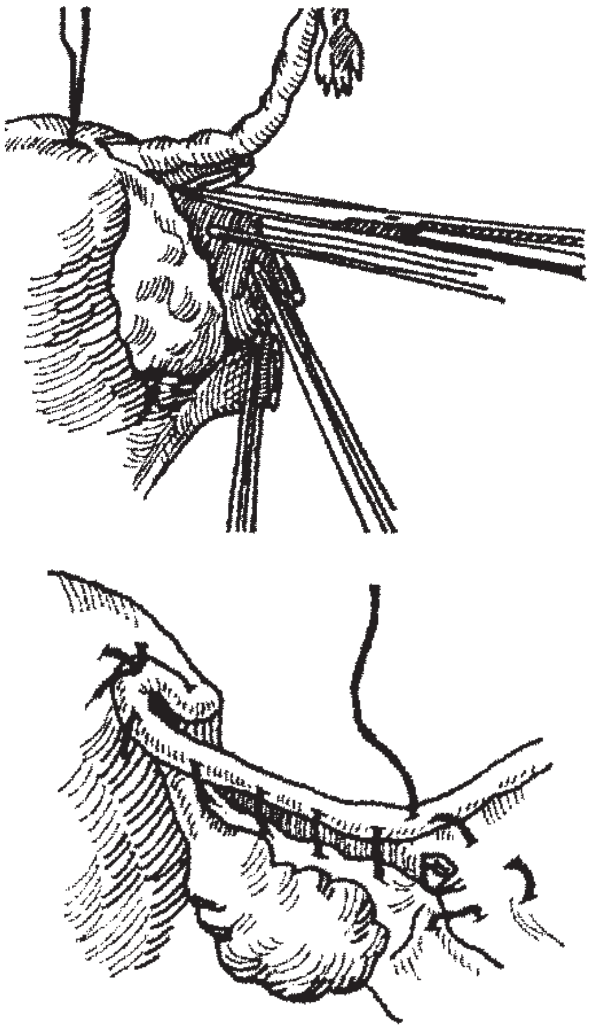
Resection of the ovary. A resection, or removal of a part of the ovary (or ovaries), is performed mainly in young women in cases of cystic masses (large persistent follicular cyst, cysts of the corpus luteum), ovarian apoplexy, as well as in clomephene-resistant patients with polycystic ovarian syndrome (both ovaries are subject to resection).

Technics. The abdominal cavity is opened with a transverse suprapubic incision. The ovary is moved to the wound and wrapped in the surgical drape. To reduce the trauma, clamps are not imposed on the tissue, and the ovary is taken in a catgut ligature, imposed on both sides. The pathologically changed part of the ovary is excised wedge-like with the scalpel, the edge of the wedge being directed to the gate of the organ; the ovary is closed with several separate catgut sutures at a distance of 0.5–0.8 cm from each other, using thin round needles and thin catgut.

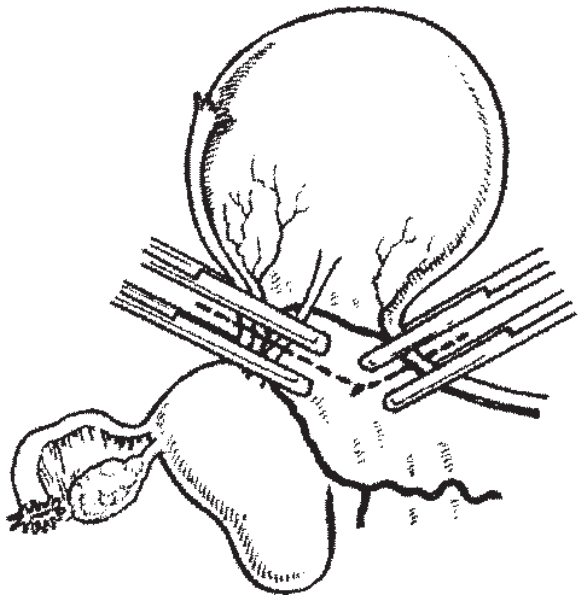
Ovariectomy. The operation, basically, is recommended for pathological changes (cyst, tumour) of the whole ovary.

Technics. Laparotomy is performed with a transverse suprapubic or vertical incision. The small mobile tumour of the ovary can be easily moved into the operational wound. If the tumour is large, it is expedient to perform the vertical incision (in case of need it can be continued upwards, bypassing the naval to the left). With the presence of adhesions with the uterus and intestines, friable adhesions are separated in the blunt way; dense fusions are cut with scissors closer to the tumoural surface, trying not to damage the intestinal wall. If the tumour is very large and is filled with liquid, it is necessary to release the liquid by a puncture with the help of trocar.

Punctures should not be made in dense tuberous masses outwardly similar to malignant. After removing the cystic mass the place of the puncture is closed, as a rule, with a purse-string suture. Then the cyst or tumour is moved into the operational wound, wraped in a surgical drape and clamps are



a



b

Fig. 67. Operation on the uterine appendages: *a* — tubectomy; *b* — adnexectomy

imposed on its pedicle, which consists of the ovarian ligament, infundibulopelvic ligament, ovarian mesentery (mesoovarium), sometimes — Fallopian tubes. In case of the tumour's pedicle twisting clamps are imposed below the twisted place, but do not untwist the pedicle. If the tumour's pedicle is thick, it is possible to separately compress and ligate separate anatomic masses which compose its structure.

They cut the tissue between the clamps with the scissors, remove the tumour, the stump is sutured and legated. Peritonization is performed with a purse-string suture, starting from the corner of the uterus, with consecutive suturing of the anterior and posterior leaves of the broad uterine ligament. The stump is immersed in the created purse-string and the suture is tighten. The abdominal cavity is layer-by-layer tightly sutured. With the presence of inflammatory changes in the tumour or in the abdominal cavity drainage tube is left.

Adnexectomy. If the contents of the ovarian tumour's pedicle includes a Fallopian tube, as well as with the presence of tuboovarian inflammatory masses of the appendages, their removal (adnexectomy) is performed.

After opening the abdominal cavity it is necessary to be oriented in the anatomic-topographical relationships of the pelvic organs, usually changed due to inflammation and adhesions. Having limited the operational area with surgical drapes, they separate the adhesions in the sharp and blunt ways (first the omentum is separated, then it is pulled upwards and cautiously separate the intestinal loops, bladder from tuboovarian inflammatory masses). Clamps are imposed on the infundibulopelvic ligament, further in the direction towards the corner of the uterus the upper part of the broad ligament is grasped together with the ovarian ligament and uterine end of the Fallopian tube (Fig. 67, *b*). The grasped tissue is cut and ligated with catgut. Peritonization is performed with the help of the round and broad uterine ligaments.

OPERATIONS ON THE UTERUS

The following operations are performed on the uterus: conservative (preserving the organ or most of it which allows keeping the woman's menstrual and reproductive functions); plastic (for congenital maldevelopments and disorders of the reproductive function); radical (removal of the whole uterus or most of it). Due to radical operations on the uterus the woman loses menstrual and reproductive functions.

Operations on the uterus are performed concerning a uterine myoma, adenomyosis, atypical hyper-

plasia of the endometrium, endometrial cancer, as well as developmental anomalies.

Conservative operations on the uterus include conservative myomectomy, defundation of the uterus, removal of subserous node on a pedicle, removal of the submucous node born through the vagina.

Conservative myomectomy. After opening the anterior abdominal wall the uterus is moved into the operational wound and a catgut ligature is stitched. Then a circumferential incision is made above the *subserous* myomatous node, which is grasped with the bullet forceps, lifted and separated in the blunt way. The clamps are imposed on the tense muscular fibres and the node is removed. Haemostasis in the wound is conducted by imposing catgut muscular-muscular sutures. Peritonization is performed with the help of the serous cover of the node.

With submucous (intramural) site of the myomatous node the peritoneum and thinned muscular tissue (capsule) above the tumour are excised. The node is grasped with biserrate and with the help of Cooper's (curved) scissors in the blunt and sharp way they remove it. Haemostasis is conducted by imposing multi-storeyed catgut sutures (last line of sutures — muscular-peritoneal).

Defundation (removal of the fundus) of the uterus is performed with the purpose of preserving the menstrual function in young women with the site of the myomatous nodes in the area of uterine fundus.

Technics. After laparotomy the uterus is grasped with Muso's forceps and moved to the wound. Kocher's forcepts are imposed on the Fallopian tubes and ovarian ligament on both sides; the appendages are excised from the uterus; the clamps are replaced with catgut ligatures. The round uterine ligaments frequently are possible to preserve. After separating the appendages, ligation and excision of the ascending branch of the uterine artery a little lower than the planned place of defundation of the uterus take place.

The removal of the uterine fundus is performed with the help of the incision parallel to the uterine fundus. The wound on the uterus is sutured with a two-storeyed suture with subsequent peritonization. The first line of sutures is mucous-muscular, with the

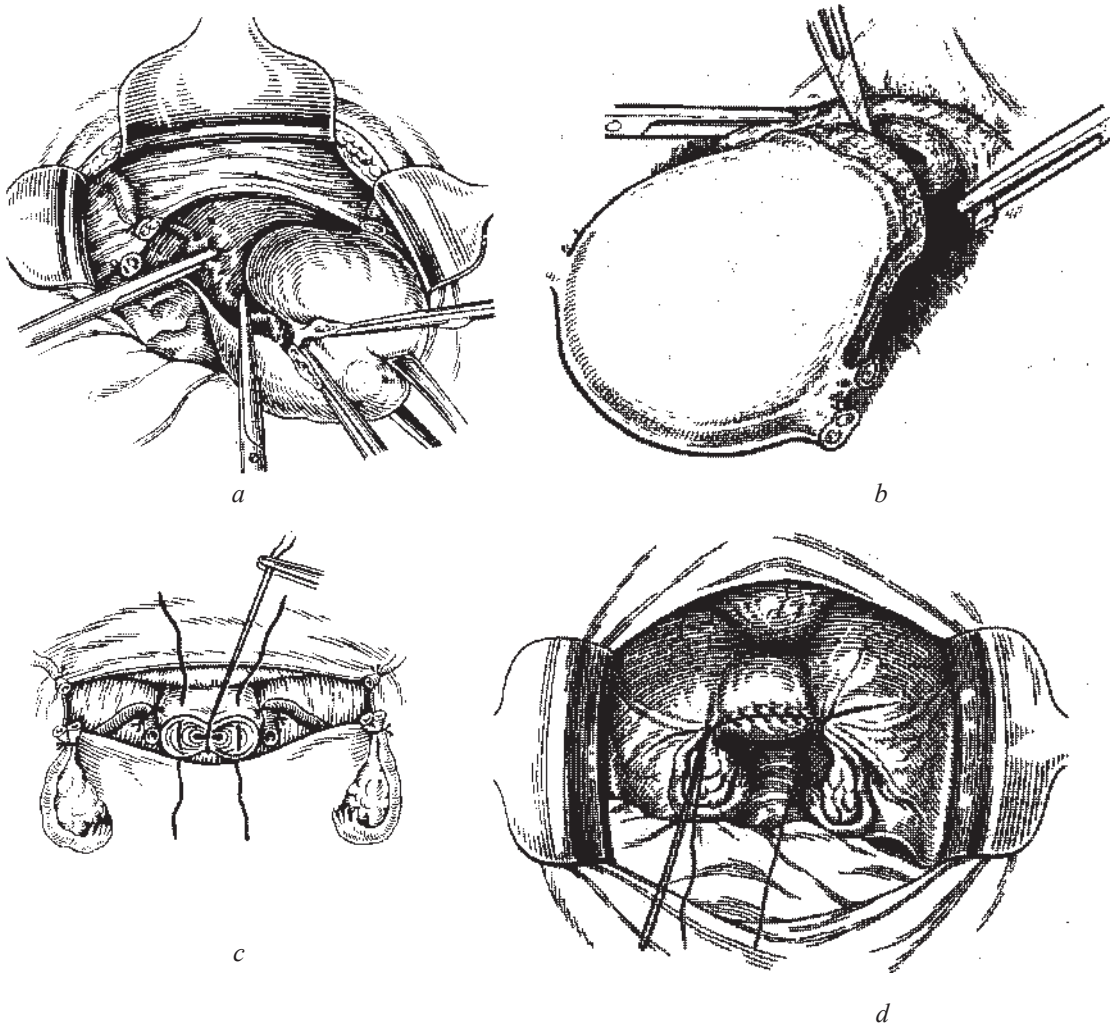


Fig. 68. Supravaginal amputation of the uterus without the appendages:
a — imposing the clamps on the uterine artery; *b* — cutting the uterus; *c* — suturing the stump of the cervix; *d* — peritonization with the immersion of the ligamentous stumps

site of the nodes to the side of the uterine cavity; the second line is muscular-serous, with the ligature tying on the surface of the uterus. Peritonization is performed with the closing of the wound, with the excised appendages and round uterine ligaments.

Supravaginal amputation of the uterus without the appendages is performed concerning a uterine myoma more often.

Technics (Fig. 68, *a–d*). After laparotomy, the uterus in the area of the fundus is grasped with bullet forceps or suture with catgut, and then is moved into the operational wound. With the presence of uterine adhesions with the intestines or omentum, they are separated.

The both sides of the uterine ribs are imposed two parallel straight long clamps at a distance of 1.5 cm from each other, confining the Fallopian tube, the ovarian ligament and round uterine ligament. The uterine appendages and the round ligament are excised and ligated. The clamps are removed, but the ligatures are left.

The round ligaments' stumps on both sides are lifted by the ligatures, simultaneously with the forcepts lift the vesicouterine fold of the peritoneum in the area of its mobile part (above the friable layer of the fat) and with the scissors cut it from one round ligament to the other one. The cut edge of the peritoneum together with the bladder with a gauze swab is cautiously moved from downward. After that the posterior parts of the broad ligaments near the uterine rib are excised a little to release the vascular vascicles.

To cut the vascular vascicles it is necessary to impose two parallel clamps perpendicularly to the uterine rib at the level of the internal os. Between the clamps the vessels are dissected down to the muscular tissue of the cervix. While imposing the clamps and cutting the vascular vascicles, the uterus is pulled to the opposite direction. Under a clamp, the vessels are sutured with catgut while confining the tissue of the cervix and ligated near the end of the clamp while going around it; then the clamps are cautiously removed. Further with the scalpel the corpus uteri from the cervix is excised at a distance of 1–2 cm above the level of the ligation. It is expedient to make a cone incision of the uterus for that the scalpel should be inclined downwards, toward the cervical canal. After dissecting the corpus uteri, the cervical canal is lubricated with 5% alcohol solution of iodine, and the cervical stump is sutured with separate 8-shaped catgut sutures, without involving cervical mucosa.

Peritonization of the cervical stump is performed with the help of the vesicouterine fold of the peritoneum. For peritonization of the adnexal stumps and the round uterine ligaments the posterior leaf of the broad ligament (at the cervical stump), peritoneum of the Fallopian tubes, peritoneum of the round ligament (below the site of the ligation) and the anterior leaf of the broad uterine ligament are sutured successively in each side with continuous catgut sutures. The stump is immersed inside, the sutures are tightened. Before peritonization the stump is examined to be convinced of the consistency of the imposed ligatures and the absence of bleeding.

Supravaginal amputation of the uterus with the appendages is performed in case of ovarian tumours, combinations of defect of the uterus and appendages with an unchanged cervix.

Technics. After moving the uterus into the operational wound on the infundibulopelvic ligaments, closer to the ovaries, two parallel clamps imposed on both sides. The tissues between them are dissected, and the stump is sutured under the clamps and ligated twice; then the clamps are removed. Under the control of the eye, the posterior leaf of the broad uterine ligament is excised and shifted downwards with a swab. Further the operation is performed the same as for supravaginal amputation of the uterus without the appendages. For peritonization of the stump of the round and infundibulopelvic ligaments, with a continuous suture consistently stitch the posterior leaf of the peritoneum of the broad ligament, the peritoneum of the infundibulopelvic and round ligaments and the anterior leaf of the broad ligament. After that the stump is immersed in the purse-string suture and it is tightened.

Extirpation of the uterus with the appendages (Fig. 69, *a–f*) is performed for endometrial cancer, uterine myoma, ovarian tumours, inflammatory diseases of the pelvic organs.

Technics. Before the operation the vaginal syringing is done, with the vagina and the cervix subsequent processing with alcohol and 5% alcohol solution of iodine. The vagina tamponed with sterile bandages, the end of which is moved beyond the sexual rima and clamped. Urine is delivered with a catheter or a constant catheter is put in for the period of the operation. The operation begins the same as for the supravaginal amputation of the uterus with the appendages. It differs from the moment of separating the bladder. The bladder is separated from the cervix on the whole extent down to the anterior vaginal vault. For this purpose after cutting the vesicouterine fold, it is lifted with the forcepts; dissected the connective tissue fibres between the bladder and the cervix are with the scissors. With a blunt small swab the bladder is move downwards, then with the help of the specula it is moved to the pubic symphysis. The uterus is pulled forward, and the sacrouterine ligament separately clamped near the uterine end. Above the clamps the tissues are dissected with scissors on both sides, the stumps are sutured and ligated; the clamps are removed. Between the sacrouterine ligaments the peritoneum of the rectouterine pouch is dissected and with a hard swab the rectum is separated. Then both the leaves of the broad uterine ligament under the appendages, performing the incision parallel to the ovarian

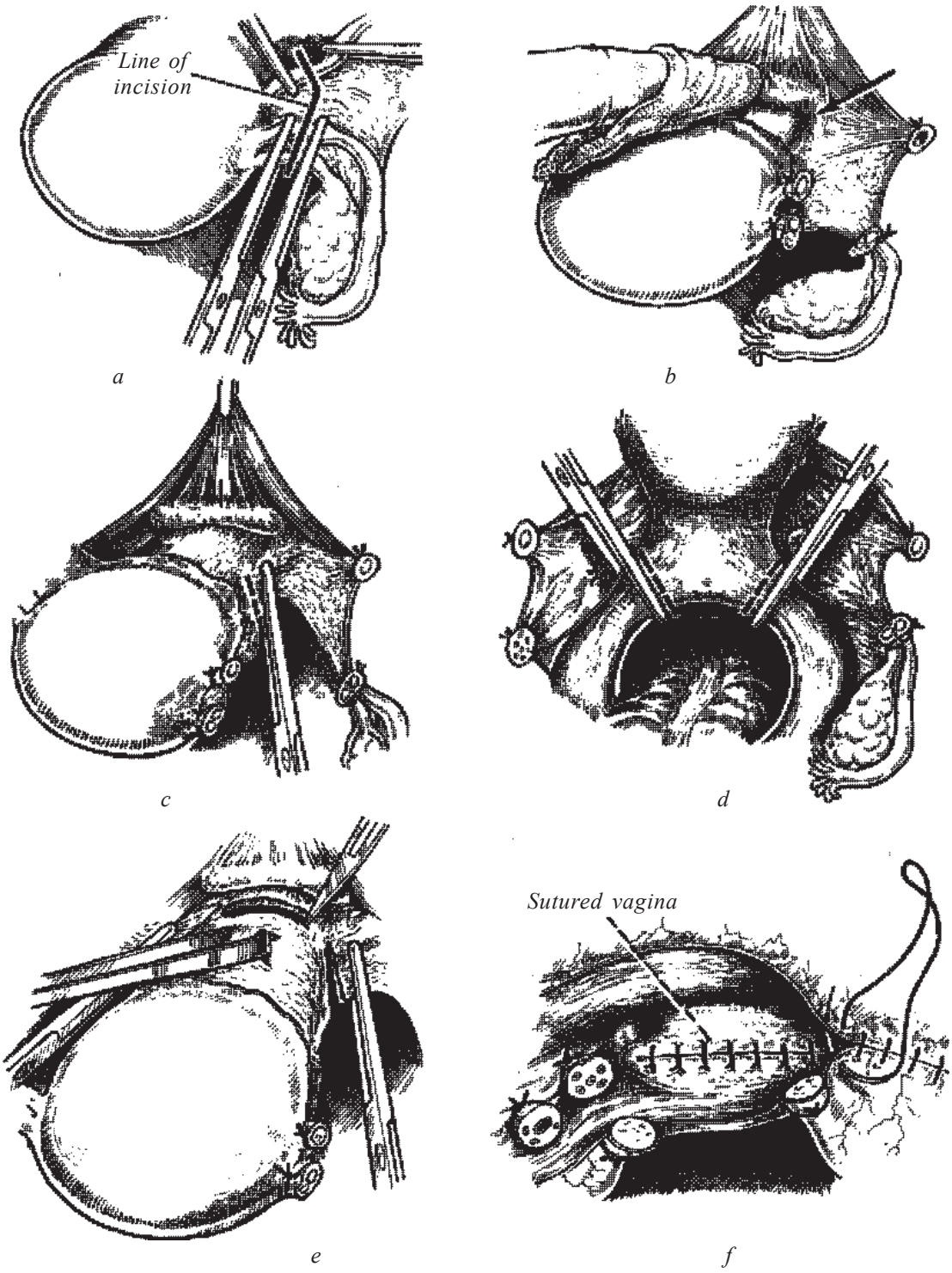


Fig. 69. Extirpation of the uterus:
a — imposing the clamps on the ovarian ligament, fallopian tubes and round ligament; *b* — clearing the vesicouterine ligament; *c* — imposing the clamps on the parametrium and uterine artery; *d* — cutting the sacrouterine ligament; *e* — cutting the vaginal apex; *f* — suturing the vagina

ligament. While cutting the posterior leaf of the broad ligament, it is necessary to watch closely the ureteral track in order to prevent trauma to them. After that two parallel clamps are imposed on both sides on the vascular fascicles between which the vessels are dissected. While ligating the vessels their stumps should be left mobile instead of fixating to the cervix.

A doctor or nurse not participating in the operation remove the tampon from the vagina. After that two long clamps are imposed on the anterior vaginal wall at a level lower than the cervix and excise the vaginal wall at a length of 2 cm between them (Fig. 69, *e*, *f*). A long surgical drape wetted with 5% alcohol solution of iodine is entered into the aperture.

The aperture is gradually dilated; the vaginal part of the cervix is grasped with the bullet forceps and delivered to the wound. The vagina is dissected around the cervix; its edges are grasped with clamps. The uterus with the appendages is removed; the vagina is sutured with separate catgut ligatures. Peritonization is performed with continuous catgut sutures, thus consistently suturing the leaf of the broad ligament, vesicouterine fold and the peritoneum of the rectouterine pouch. The surgical drape is taken from the vagina after the operation.

DIAGNOSTIC AND SURGICAL ENDOSCOPY

Surgical endoscopic methods most frequently used in gynaecology include diagnostic and surgical hysteroscopy and laparoscopy.

Hysteroscopy (from Greek *hystera* — uterus and *scopio* — to look) is an operative method of research of the uterine cavity with the help of an optical device entered into the uterus through the cervical canal. The operation was performed for the first time in 1869 by D. Pantaleoni, who used a tube with external illumination for this purpose. Hysteroscopy can be a usual panoramic and panoramic with magnification. With the help of a hysterofiberscope, hysterofiberscopy is performed, and with hysteroresectoscope — hysteroresectoscopy is conducted. Suturing the uterine cavity can be done with the help of gas (CO_2) — gas hysteroscopy or with a liquid (reopolyglukin, 32% solution of dextrans, solution of dextrose, sterile water, isotonic solution of sodium chloride, glycine, mannitol) — liquid hysteroscopy.

Indications: suspicion of adenomyosis, submucous myomatous node, intrauterine synechia, remains of a fetal egg, the presence of foreign objects, cervical cancer, endometrial cancer, perforation of the uterus, pathology of the endometrium, as well as to specify the character of uterine maldevelopments, the site of an intrauterine device. Disorders of the menstrual cycle in the reproductive age, bleeding in the postmenopause, infertility; necessity of performing control research of the uterine cavity after an operation on the uterus, hydatidiform mole, as well as for miscarriages and after hormonal treatment may be indications too.

Contraindications: inflammatory process of the genitalia, pregnancy, strong uterine bleeding, recent perforation of the uterus, stenosis, and extensive cervical cancer.

Preparation for hysteroscopy and examination of the patient are performed the same as before diagnostic curettage of the endometrium (general clinical analysis of the blood and urine, RW, HIV, Australian antigene, smears for flora, coagulogram, electrocardiogram and hepatic tests for women older than 40).

On the operation day patient should not eat or drink. With suspicion of an organic pathology of the uterus (uterine myoma, endometriosis) in women of the reproductive age the examination is conducted at the early follicular phase (on the 7th–9th day of the menstrual cycle) in connection with the best visibility (endometrium is thin and minimally vascularized). For a functional estimation of the endometrium, hysteroscopy is performed at the II phase of the menstrual cycle.

For hysteroresectoscopy in connection with the presence of intrauterine septums, synechias, submucous myomas of the uterus, as well as for the removal of the endometrium (ablation), 1–3 months before operation preparation of the endometrium should be done with antigonadotrophin (danazol, danogen) or agonists of Gn-RH ("Decapeptil-depot", nafarelin, zoladex). It is desirable that the width of the endometrium decrease to 0.5 mm.

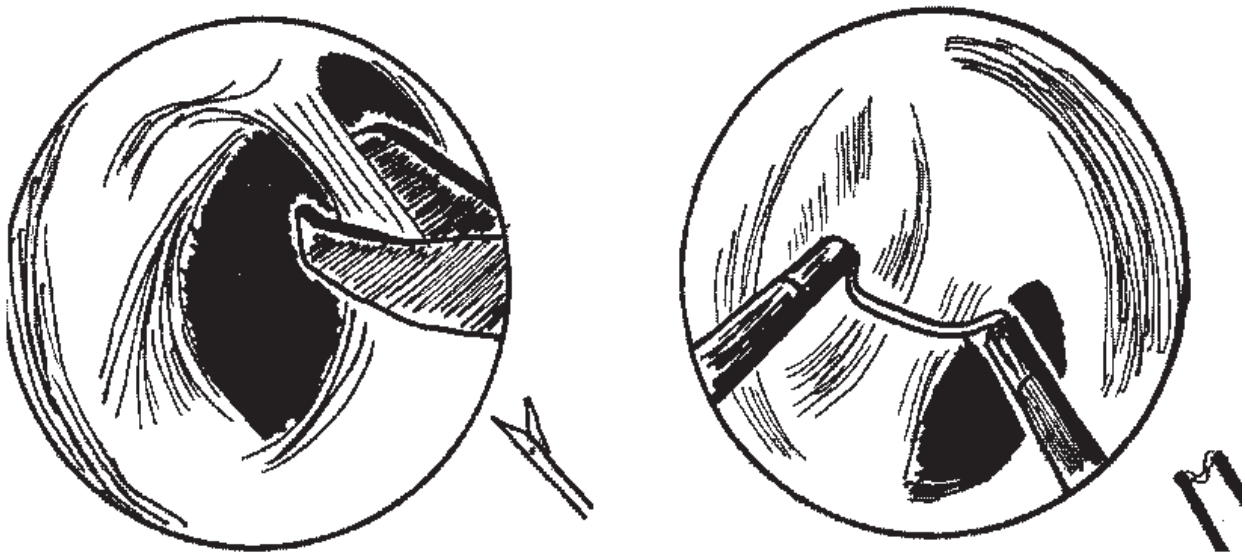
Hysteroscopy is possible with the dilation and without the dilation of the cervical canal (diagnostic hysteroscopy). If indicated the canal is dilated and the operational hysteroscope is entered.

The method of choice for anaesthesia during hysteroscopy is temporary intravenous narcosis.

Technics. The patient is put in the gynaecological chair; the external genitalia and internal surface of the hips are processed. The cervix is opened in the specula, processed with a disinfectant solution. The anterior cervical lip is fixed with the help of bullet forceps and is lowered downwards. The diagnostic hysterofiberscope is connected to a light source and system for providing liquid. The distal working end of the device is cautiously, without force, like for intubation, entered through the cervical canal (without its dilation) into the uterine cavity and examine it.

If dilation of the cervical canal is necessary after intubation and to measure the length of the uterus with the tube, the cervical canal is dilated with Hegar's dilators (from N 3 to N 9–10.5) to maintain the outflow of liquid from the uterine cavity. The hysteroscope is entered into the uterine cavity; the uterine cavity and walls are examined. The size and form of the uterine cavity, the type of its walls, condition of the endometrium (colour, thickness, folds, vascular figure), apertures of the Fallopian tubes are taken notice. Consistently, clockwise the uterine fundus, tubal corners, lateral walls, isthmus, cervical canal are examined.

Hysteroscopic operations include: hysteroscopic septectomy (Fig. 70, *a*, *b*), hysteroscopic myomectomy, hysteroscopic ablation (resection) of the endometrium. The basic surgical procedures used during hysteroscopic operations — incision, removal, coagulation and vaporization of tissue (lysis of intrauterine fusions, incision of intrauterine septa, polypec-



a *b*

Fig. 70. Histeroscopic septectomy:
a — with cissors; *b* — with resectoscope

tomy, target endometrial biopsy, partial or complete removal of the endometrium, myomectomy, removal of the remains of intrauterine devices, foreign bodies, tubal catheterization, introduction of intratubal contraceptives, tuboscopy).

Laparoscopy — examination of the organs of the abdominal cavity with the help of an optical instrument — laparoscope.

Pelvioscopy — examination of the pelvic organs. Laparoscopy as well as hysteroscopy can be diagnostic, surgical and control. Indications for laparoscopy expand every year in connection with the advantages of this method: low invasiveness, decrease in the time of a patient's stay in the hospital, acceleration in the restoration of vital functions after an operation (hospital within 1–2 days).

Indications for diagnostic laparoscopy in gynaecology are diagnosis and differential diagnosis of pathological processes of the internal female genitalia. Most frequently laparoscopy is used to find the reason for acute (ectopic pregnancy, rupture or twisting of an ovarian cyst, appendicitis, salpingitis, uterine myoma) and chronic pelvic pains (endometriosis, infection), diagnosis of genital anomalies. Laparoscopy is used for sterilization, salpingostomy, treatment of women with tubal and peritoneal infertility (separation of adhesions, salpingolysis), ectopic pregnancy, endometriosis, polycystic ovaries, as well as for myomectomy, resections of the ovaries, removal of cysts and ovarian cysts. Last years laparoscopic oophor- and hysterectomy, endoscopic modification of the Wertheim's operation, laparoscopic paraaortic, pararectal and pelvic lymphadenectomy, etc. have received further development.

Contraindications (non-absolute) to laparoscopy are cardiovascular diseases at the stage of decompensation, acute hepatic-renal insufficiency, diabetes at the stage of decompensation, comas, acute infectious diseases, extensive abdominal adhesions, diaphragmal hernia, promoted obesity.

Preoperative preparation is performed the same as and for abdominal operations (see "Preoperative preparation of gynaecological patients p. 202"). Narcosis, as a rule, is endotracheal.

Technics. By the method of penetrating into the abdominal cavity, open and closed laparoscopies are distinguished.

Open laparoscopy includes: 1) performing mini-laparotomy; 2) introduction of special trocar through a mini-laparotomy aperture into the abdominal cavity; 3) fixing the sleeve of a trocar to the abdominal wall for its pressurization; 4) creation of pneumoperitoneum through the sleeve of a trocar. This technique is considered safer, than closed laparoscopy. However, more labour-intensive, especially in obese patients. Open laparoscopy is performed in cases of promoted abdominal adhesions after previous laparotomies.

When performing *closed laparoscopy,* the patient should be in a position hips spread out (the hips should be in the plane parallel to the anterior abdominal wall). From the beginning of the operation till the moment of introducing the basic trocar, the patient's position is horizontal, and then moved to the Trendelenburg's position (15–30°).

Veress' needle is the instrument to create pneumoperitoneum, which is entered into the abdominal cavity through the naval or a little lower than the umbilical ring. With the presence in the anamnesis of previous laparotomy, the Veress' needle is entered at a distance of 2–3 cm above and more to the left of the naval to prevent wounding the round liga-

ment of the liver. The trocar is entered through the incision in the skin, with moderate pressure, at a 90° angle to the peritoneum and at this moment with one movement turn upwards at 45°, with a turn of the wrist at 90°. The intraabdominal pressure should not exceed 15 mmHg.

After introducing the basic trocar, its stilet is taken out and the laparoscope (diagnostic or operational) is entered into the abdominal cavity. The patient is moved into the Trendelenburg's position; examine the abdominal cavity, including its upper segment.

Secondary trocars (trocars-manipulators) are entered usually in the right and left lower quadrant of the abdomen on the border with the pubic hair. As a rule, two secondary punctures are used. Some surgeons use a third secondary puncture on the middle line in the centre between the naval and pubis.

During laparoscopy they dissect the tissue, remove the pathological masses, perform haemostasis and restore the normal anatomic relations between organs. Besides of mechanical, laser, ultrasonic instruments, an apparatus for high-frequency coagulation in bipolar and monopolar modes, etc. are used.

The laparoscopic operation is completed with the abdominal cavity irrigation with a significant amount of sodium chloride isotonic solution, under haemostasis control. The patient is moved into the horizontal position. The pneumoperitoneum is removed from the abdominal cavity by opening the valve of the sleeve of the basic trocar and putting it in a horizontal position. Separate sutures or brackets are imposed on the skin.

After uncomplicated laparoscopic operations the patient can get out of bed in 4–5 h. The first day after the operation the zero diet is recommended. Prevention with antibiotics is done during the operation, by introducing 1–2 g of cephalosporin. If necessary, intravenous injections of antibiotics are prolonged for the first day (twice a day). With the pain syndrome, non-narcotic analgesics are prescribed. For meteorism stimulation of peristalsis with neostigmine methylsulfate, cerucal, cleansing clyster are used.

Complications occurring after laparoscopy are divided into intra- and postoperative. Intraoperative can be specific, i.e. connected with the pneumoperitoneum (hypodermic and subfascial emphysema, gas embolism), introduction of the Veress' needle and trocars (wound to large vessels, internal organs), and nonspecific, connected with the operation or anaesthesia.

Postoperative complications include intraabdominal bleeding, the occurrence of retroperitoneal haematomas, etc.

PREOPERATIVE PREPARATION OF GYNAECOLOGICAL PATIENTS

The success of surgical intervention depends a lot on the preoperative measures, such as: examination of the patients, clinical, laboratory, functional exams, correction of functional disorders of the organism, improvement in the clinical course of accompanying diseases, determining the degree of the operational risk, choice of methods of premedication and anaesthesia. With chronic extragenital diseases (hypertension, ischemic heart disease, rheumatism, liver diseases) the question about the terms of the operation after treatment, is solved together with the corresponding specialist. The allergology history with obligatory specification of medical products and products to which the patient had a reaction are established.

Before an elective operation the following examinations are necessary:

— clinical blood and urine analysis;

— bacterioscopic and bacteriological examination of the discharge from the reproductive tract;

— cytology of cervical and os smears;

— the blood group and Rh-factor determining;

— biochemical exam of the blood (general protein, bilirubin, urea, residual nitrogen, glucose, electrolytes);

— RW, HIV, Australian antigen blood analysis;

— coagulogramma;

— AP, ECG and roentgenography of the thorax;

— by indications additional examinations: ultrasonography, hysteroscopy, colposcopy, hysterosalpingography, endometrial biopsy (histological study of the endometrium), hormonal examination, lymphography, computer tomography, etc.

While preparing patients suffering from vaginitis of III–IV degree of cleanness for **vaginal operations**, anti-inflammatory therapy is prescribed. In case of uterine prolapse the vagina is processed with hydrogen peroxide, peroxide compound; and then the uterus is repositioned and tampons moistened with synthomycin emulsion are entered. With the presence of trophic ulcers, pseudo-erosion, leukoplakia and other pathological changes of the cervix and vaginal walls, a dilated colposcopy with biopsy and subsequent histological study are performed. Depending on the received data the problem of the extent of the operation is solved.

Preparation of patients for **emergency surgery** (intraabdominal bleeding, twisting of the cyst's pedicle, etc.) is reduced to a minimum. Urgently, the blood group and Rh-factor are determined, clinical analysis of the blood and urine are performed, the glucose content in the blood, general protein in the blood are determined, coagulogramma. The stomach is irrigated or its contents is removed with intubation, a cleansing clyster is applied. For a ruptured ectopic pregnan-

cy, accompanied by profuse bleeding, a cleansing clyster is contraindicated (bleeding may intensify). The patient in the condition of haemorhagic shock is transported from the admission office into the operational room, where simultaneously hemotransfusion (after determining the blood group and Rh-factor) and laparotomy are performed.

For patients with tuboovarian inflammatory masses during preparation for an operation, infusion therapy is recommended. Preoperative preparation of patients older than 50 is directed mainly on the improvement of cardiovascular function.

Patients with a uterine myoma frequently have iron deficiency anaemia. In connection with this during preoperative preparation internal preparations of iron for 1–2 months till restoration of the haemoglobin level is prescribed. If there are indications to urgent surgery and anaemia is found (even without disorders of hemodynamics) hemotransfusion is necessary.

With the presence of inflammatory diseases of the veins (phlebites, thrombophlebites) in the pre- and postoperative periods anticoagulants of direct action (heparin, fraxiparin, calciparin) are recommended. 2–3 days prior to the operation anticoagulant therapy is stopped. For varix dilation of the lower extremities, it is necessary to compress them with elastic stockings or elastic bandages.

When determining the time for the operation it is necessary to take into account the phase of the menstrual cycle. Operative interventions are not performed 2–3 days prior to the beginning and during menstruation, in connection with the physiological increase of pelvic bleedings. Elective operations are expedient to conduct during the first phase of the menstrual cycle.

Elective operations are not appointed, and already appointed are postponed, in case of acute inflammatory processes of the upper respiratory tract, internal organs, infectious defects of the skin, increase in the body temperature, change in the parameters of the blood or urine.

To improve the compensatory prospect of the respiratory system before an operation, patients should regularly (4–5 times a day) carry out special physical exercises.

During preparation for surgery, the patient should receive high-calorie foods with small fat contents. 14–16 h before the operation, eating is stopped (one day prior to the operation light dinner-liquid soup, bullion, in the evening — sweet tea). In the evening before and the morning of the operation day cleansing clysters are performed to prevent postoperative meteorism and intestinal paresis, sanitary processing (hygienic baths) are performed.

Before an operation medicamentous preparation of the patient is conducted with the purpose of eliminating psychological strain and normalizing sleep (sibazon — 0.01 g, nozepam — 0.01 g, elenium — 0.005 g; antihistamines (dimedrol 0.01 — 0.02 g, suprastin — 0.025 g, tavegil — 0.01 g). 30–40 min before the operation premedication is performed: intramuscularly — anticholinergic means (atrophine — 0.5 mg, methacin 0.5–0.8 mg), narcotic analgesics (promedol — 20 mg, fentanyl — 0.1 mg), antihistamines (dimedrol — 20 mg).

Directly before the operation urine is removed with a catheter or a constant catheter for the whole time of the operation is entered, because due to the filled bladder it may be wounded when the abdominal cavity is opened and trauma with the pubic specula during the operation. The day of the operation the vagina is processed with alcohol, dioxydin and a sterile tampon is entered.

During gynaecological operations most often combined endotracheal narcosis with myorelaxants and artificial ventilation of the lungs are used.

POSTOPERATIVE OBSERVATION OF GYNAECOLOGICAL PATIENTS

Management of the postoperative period is directed on the prevention and duly revealing of possible complications.

The patient is moved into the postoperative room only after restoration of adequate breathing, consciousness, muscular tone, reflex activity, normalization of hemodynamics. If artificial respiration is necessary as well as in case of severe condition the patient is transported to the unit of resuscitation and intensive care.

The postoperative room should be equipped with oxygen, narcotic equipment and a set of medical instruments for providing emergency cover (respiratory apparatus, laryngoscope, antidote, myorelaxants, disposable systems, cardiostimulators, respiratory anleptics, infusion solutions, etc.). Supervision of the patient during the postoperative period is carried out by the operating surgeon and anaesthesiologist.

During postoperative observation of patients it is necessary to take into account their age, somatic diseases, volume of operative intervention, complications during the operation. The most critical ones are the first 48–72 h after an operation.

The patient is moved to a preliminary warmed functional bed. During the first 6 h after an operation, arterial pressure, pulse and respiratory rate is measured hourly, the condition of the bandage, vaginal discharge are checked, symptoms of internal and external bleeding, bladder empting are watched for. With the absence of independent urination during the first 8–10 h, the urine delay is liquidated if possible with medicamentous and reflex means

(warm vessel, pour water) or its catheterization is performed.

After **abdominal operations** immediately on the area of the postoperative wound for 3–4 h the weight (sack with sand) is put on for haemostasis and to preserve the anterior abdominal wall during vomiting or coughing. For additional haemostasis, reduction of postoperative hypostasis of the wound, analgesia it is expedient to apply dosed local hypothermia (cold on the area of the postoperative wound for 30 min with an interval of 1.5–2 h for the first two days).

Conducting the early postoperative period includes adequate anaesthesia, support of normal respiration, infusive therapy, antibacterial therapy if indicated, prevention of bleeding and thrombembolism, elimination of postoperative complications.

The pain syndrome after an operation negatively influences the postoperative period course. As anaesthesia analgesics are recommended, if necessary every 4–6 h after an operation (promedol, tramal, tramadol, baralgin, etc.). Adequate anaesthesia allows the patient to breathe deeply, execute necessary ventilation of the lungs. On the 2nd–3rd day analgesics whenever possible are limited to 1 time a day (at night).

The patient should have an active position in bed by the end of the first day. Turns on the side, bending of the leg, deep breaths, respiratory gymnastics are recommended in 6–8 h after an operation to prevent pneumonia. With the purpose of preventing thrombembolia complications it is recommended to get out of bed early with the presence of a doctor or nurse (if there are no contraindications).

To prevent pulmonary complications (postoperative pneumonia) oxygen therapy (if necessary), position for drainage, stimulation of cough, mucolytics, round jars and mustard plasters for the thorax (morning-evening) are recommended. It is necessary to watch the patient's hygiene (sanitation and toilet of the oral cavity, external genitalia, hygienic rubdowns, prevention of decubitus).

During the whole postoperative period it is necessary to observe closely the general condition of the patient (the body temperature, ABP, pulse, respiratory rate), condition of the postoperative wound, discharge from the drainages and catheters, duly emptying of the bladder and intestines. Carefully palpation of the abdomen to determine the presence or absence of attributes of peritoneal irritation, conditions of the intestines. Laboratory control of the condition of the basic vital functions of an organism is performed.

Within the first hours after an operation the patient's lips are moistened with a damp napkin, on the second day liquid consumption is not limited (1.5–2 l). Boiled water or tea without sugar with lemon, extract of dogrose without sugar, alkaline mineral waters without gas are recommended to drink.

Infusive-transfusive therapy is performed within the first days after an operation (2–2.5 l.) and further if indicated for the correction of hemodynamic disorders, restoration of general blood circulation, normalization of rheological properties of the blood and microcirculation, electrolytic balance and acid-alkaline condition (blood, plasma, albumin, colloids and crystalloid solutions — Ringer's, Ringer—Lock's solution, isotonic solution of sodium chloride, 5% solution of glucose, lactasol, 4% solution of potassium chloride — 30–40 ml/kg. The character and volume of infusive therapy should depend on the basic disease, features of the operative intervention and age of the patient. Thus, daily diuresis should be 1,200–1,400 ml. The amount of entered liquid is twice reduced if the patient before the operation had signs of heart insufficiency. Antibiotic therapy is prescribed with the presence of inflammatory processes in the small pelvis, after trauma operations, for repeated operations, high risk of infection.

20–40% solution of glucose, osmotic diuretics (mannitol), saluretic (lasix) are entered to support kidney function; function of the liver — essentiale, cocarboxylase; stimulation of the cardiovascular system — strophanthin, korglykon, euphyllin, papaverin.

In a complex of actions to prevent thrombembolism complications at the early postoperative period alongside with sufficient hydration, active postoperative behaviour (active and passive gymnastics, getting out of bed) especially for women in the risk group, direct anticoagulants (heparin in a dose of 5,000 U under the skin of the anterior abdominal wall three times a day, or low-molecular heparin (fraxiparin), or unfractionated heparin (calciparin) — at one injection a day, aspirin — 125 mg/day) are recommended.

The condition of the intestines is normalized, as a rule, on the 2nd–3rd day after the operation (normalization of peristalsis, independent removal of gases; on the 3rd day it is recommended to use cleansing or hypertonic (100 ml) clysters).

The patients can begin to eat after the intestines functioning, as a rule, on the 2nd day after the operation (low-fat chicken broth, fish broth, tomato juice, tea). On the 3rd day it is possible to add buttermilk, boiled grated chicken meat, eggs, soup, baked apples, crackers. Further the menu is gradually expanded till the usual.

2–3 days after an operation the bandage on the abdomen is replaced, and the sutures are processed with alcohol, iodine, alcohol solution of diamond green. On the 7th–8th day the stitches are removed and gynaecological examination is performed. In patients with obesity the stitches are removed gradually (every other one), and finally — on the 9th–10th day.

After ***vaginal operations*** the patients should observe such rules: strict bed confinement, application of analgesics and antibiotics (if indicated), respirato-

ry gymnastics, regulation of intestinal and bladder functions.

After the operation cold is applied to the area of the perineum for 1–1.5 h, with hypostasis of the sutures cold is applied for the first day after the operation, for 30 min with an interval of 1.5–2 h. The first day after the operation it is expedient to leave the patient's pedicle together. Starting the second day they can be bent in the knee joints. However, not to separate them: turn in the bed with pedicle together.

The tampon from the vagina is taken out 6–8 h after the operation.

After ***operations on the muscles of the pelvic fundus*** defecation is detained for 5 days. The delay is provided by careful cleansing of the intestines before the operation and a liquid diet for the first 5 days after it (unsweeten tea, fish broth, juices). Starting the 6th day the diet is gradually expand (grated baked fruits, vegetables, kissel, one-day buttermilk); the food should contain low contents of fat. Before removing the sutures, 30 g glycerine is prescribed internally. During the operation with plastic of the bladder it is expedient to apply a thin elastic constant catheter, which is entered on the 3rd–4th day. The bladder is flushed out through the catheter once a day with solution of furacilin. It reduces the incidence of postoperative cystitis, postoperative atony of the bladder.

Care of the postoperative wound in the perineum is carried out in the open way 2 times a day. The vagina is irrigated with 0.1% solution of potassium permanganate, solution of furacilin. On the 5th day a clyster is used, on the 6th — the sutures are removed.

The patients can go home on the 12th–14th day after the operation. Further, for at least three months, they are not allowed to lift heavy things (more than 3 kg). Women operated on should be released from heavy physical work for 6 months.

Complications in the postoperative period can be life threatening to the patients, immediate diagnosis and adequate duly treatment therefore is required. Early (within the first hours after the operation) and late (on the 2nd–8th day) postoperative complications are distinguished.

With *urination delay* it is necessary to find its reason (reflex, psychogenic). The absence of urine during catheterization of the bladder testifies to anuria, the reason of which should be revealed and removed immediately (unnoticed trauma to the bladder or ureter during the operation, disorder of renal function due to sepsis, shock, unrestored blood loss).

A frequent complication in the postoperative period is *nausea* and *vomitting.* Within the first hours after the operation nausea can be connected to the anaesthetics. In such cases the patient's head is turned to the side, tray with a towel is given. In connection with possible aspiration of the vomiting masses, a nurse should constantly be near the patient. Nausea and vomiting can be the result of acidosis, the beginning of peritonitis, intestinal atony, relapse of digestive tract chronic diseases.

Eneteroparesis may occur in many gynaecological patients after abdominal operations. Hypotonia of the intestines is connected with bradyperistalsis. The patient with paresis of the intestines is inserted a gas emission tube, siphon or oil clysters, cholinesterase inhibitors (neostigmine methylsulfate 0.05% — 1 ml, cerucal — 1–2 ml intramuscularly), intravenously glucose-potassium mix, hypertonic solution of sodium chloride (10–20 ml of a 10% of solution) are prescribed. In case of *hypotonia of the abdomen* it is irrigated with the help of a nasogastric tube.

Intestinal obstruction is a late (opposite to enteroparesis) and vitally dangerous complication. Patients complain of nausea, vomiting, swelling of the abdomen. Peristalsis is loud, excessively active. During a survey roentgenogram of the abdominal cavity air-liquid levels (Kloiber's symptom) and dilated intestinal loops proximal from the place of obstruction are observed. Treatment consists of decompression of the intestines and infusive therapy with electrolytes solutions.

The serious, however, extremely rare today complication, is *intestinal eventeration* due to the separating of the sutures in all layers of the postoperative wound with the development of peritonitis. The first symptom is sudden strong infiltration of the postoperative bandage with serous or purulent contents. Treatment consists of relaparotomy, audits and toilet of the abdominal organs, imposing secondary sutures on all layers of the abdominal wall.

Postoperative disorders of hemodynamics are caused more often *by internal bleeding* due to the poor ligation of large vessels more often. The patients have pallor skin and visible mucous membranes, decrease in ABP, weak rapid pulse. With bleeding from the hypodermic layer the wound bandage on the abdominal wall is soaked with blood. Significant long-term bloody vaginal discharge also testify to internal bleeding and require, as a rule, relaparotomy and the bleeding vessels legation. After the bleeding stops, intensive infusive therapy is conducted surgically (polyglucin, gelatinol, erythrocytic mass, frozen plasma, Ringer's solution, isotonic solution of sodium chloride). The volume of the entered solutions should exceed the blood loss by 25–30%. If the volume of blood loss exceeds 30% of the general circulating blood, blood should be 50% of the entered volume of solutions; with blood loss more than 3 l — 75%. About 500 ml of infused blood promotes an increase in the hematocrit number by 3–5%. The speed of introduction of solutions has great value in bringing patients out of haemorhagic shock: with systolic ABP less than 60 mmHg — 100 ml/min, with stabilized ABP higher than 100 mmHg — 10–20 ml/min. Infusions are performed in 2–3 veins. Patients with coagulation disorders are recommend-

ed frozen plasma, cryoprecipitate and thrombocytes.

To stabilize the ABP large doses of glycocorticoid (hydrocortisone — 1,000–1,200 μg, prednisolon — 200 mg), dopamine (2–5 μg/kg per 1 min) are used. To stimulate diuresis, with the introduction of a great volume of solutions, lasix is prescribed — 1 mg/kg (critical diuresis — 30–50 ml/h testifies to the restoration of organ blood flow).

To improve the rheological properties of the blood, microcirculation on the background of restoration of general circulating blood they apply rheopolyglucin, rheogluman, droperidol, aminazine, dipiridamol, trental. Taking into account the parameters of ABC, metabolic acidosis is corrected.

Haematoma can develop rather quickly and progress to large sizes which results in the hypovolemic shock development, especially as a result of its occurrence in the retroperitoneal space. However, in most cases haematoma develops gradually, its pressure upon open vessels frequently is sufficient to be tamponed by the released blood.

Clinical symptoms of haematoma depend on its size and site. Most frequently subaponeurotic (subfascial) postoperative haematoma develops. The patient, as a rule, complains of pain in the area of the postoperative wound, subfebrile temperature. Haematoma of the wound is easily accessible during palpation as opposed to pre-wall haematomas of the pelvis (in this case ultrasound, computer tomography are used). A large progressing haematoma can lead to anaemia of the patient.

Treatment of the patient with haematoma consists of surgically stopping the bleeding (relaparotomy, legation) and subsequent substitute infusive therapy (blood, plasma, etc.). In case of a small uninfected haematoma it is possible to use conservative therapy.

Pulmonary complications include atelectasis, pneumonia, aspiration pneumonia, embolism of the pulmonary arteries.

Atelectasis of the lungs occurs due to superficial respiration because of postoperative pain. It is an early complication (during the first 24 h) which is characterized by subfebrile temperature, weakening or disappearance of respiratory noises above the lungs, at times — inspiratory rales. To *prevent* atelectasis, the patients are recommended to cough slightly, breathe deeply, take a drainage position, get out of bed early, do respiratory gymnastics.

Aspiration syndrome (Mendelson's syndrome) was described for the first time in 1946 by the obstetrian Curtis Mendelson and it was connected with the gastric contents aspiration. Clinical symptoms are dyspnea, tachypnea, bronchospasm, rales, tachycardia, cyanosis and acute hypoxia.

Treatment consists of artificial respiratory ventilation, introduction of large doses of glycocorticoids and antibiotics. To prevent this complication antacids and inhibitors of H_2-receptors of the abdomen before the use of anaesthesia are prescribed.

In case of *pneumonia* the patients condition is sever: fever, tachypnea, steady cough. Considering the prevailing role of polymicrobic associations, treatment with cephalosporins of the II–III lines or broad-spectrum penicillins are prescribed.

The risk of *pulmonary embolism* increases in patients after previous operations on pelvic organs due to long immobilization, with obesity, in the elderly. The classical triad of symptoms of pulmonary embolism includes chest pain, dyspnea and tachycardia; cough, pleural outpouring, leukocytosis, elevated ESR can also be observed.

Treatment consists of heparin therapy (intravenously 1,000 U/h) for 7 days, then the patient is prescribed indirect coagulants to maintain the prothrombin level (50% of the normal amount) for 2–3 months.

Infected wounds is a frequent complication, especially in patients with obesity (5–10% after abdominal hysterectomy). With the presence of infiltrate in the area of the suture the therapy directed on the restriction and liquidation of the inflammatory process is conducted. On the 3rd–5th day after the operation symptoms of the postoperative wound infection (as a rule, in the area of the hypodermic basis, less often — under the aponeurosis) can be seen. Patients complain of pulsating pain in the area of the postoperative wound, increase in the body temperature. If infection occurs in this area, they remove the sutures, bath the wound with 3% solution of hydrogen peroxide, put on a bandage moistened in a hypertonic solution and with Vishnevsky ointment; prescribe parenteral antibacterial therapy with broad-spectrum antibiotics (cephalosporins, metronidazole) taking into account the polymicrobic etiology of the given infection. Such wounds heal with secondary tension. Therapy with three antibiotics (ampicillin + clindamycin + gentamycin) is prescribed in case of the pelvic abscesses development.

RECOMMENDED READING

2; 6; 7; 16; 21; 24; 32; 46; 51; 57; 79; 81; 90; 92; 93; 94; 96; 98; 103; 108.

Chapter 16

BREAST DISEASES

Breast diseases are a challenge both for the patient, and for the doctor. Gynaecologists pay more attention to them, because the incidence of benign and malignant breast diseases increases.

The breast of an adult woman is a large modified sebaceous gland, which is placed on the superficial fascia of the thorax; its weight averages 200–300 g. The structural elements of the breast are fatty tissue, fibrous septums (septi), and glandular structures. It consists of 12–20 lobes, lactiferous ducts and secretory cells, contained in the alveoles. Each of these lobes has lactiferous ducts which open into the nipple. The breast has rich blood and lymph systems which causes fast metastasing as a result of malignancy. Additional nipples *(polythelia)* are observed more often than additional mammary glands *(polymastia)*.

The breast tissue is very sensitive to hormonal changes. During puberty breast development is connected to action of hormones. The breast is also very sensitive to the level of hormones during the menstrual cycle.

Pathological changes can develop in each tissue of the breast: *fibro-cystic mastopathy and fibroadenoma* — from the connective tissue, lipoma — from the fatty tissue, as well as due to trauma. The duct system of the breast sometimes expand (ductular ectasia, galactocele), can contain papillary tumours or subject to malignant changes. Infectious disease of the breast — mastitis — develops in feeding mothers.

Breast cancer makes up 25% of all malignancies in women and develops mainly after the age of 40–45.

BENIGN DISEASES

Mastodynia — pain in the breast, connected to the cyclic hypostasis of the breast due to venous stasis and hypostasis of the glands stroma before menstruation; during this time the breasts increase by almost 15%.

Treatment is the same, as for premenstrual syndrome (nonsteroid antiinflammatory means, diuretics, pregnin, norcolut, dufastone, urogestan, projestogel, parlodel).

Fibrocystic mastopathy (FCM), by definition of the WHO, — fibrocystic disease characterized by a complex of proliferative and regressive changes in the breast with a disorder in the ratio between epithelial and connective tissue components. Proliferative processes include hyperplasia, proliferation of the lobes, ducts, connective tissue; regressive — atrophy, fibrosis, mass of cysts.

FCM is the most widespread disease of the breasts (peak incidence — 45 years old). The risk of breast cancer development with mastopathy with hyperplastic processes increases 2.6 times, in case of atypical changes — 6 times.

The term "fibrocystic mastopathy" covers more than 35 various pathological processes. These conditions can occur in connection with an increased sensitivity to the action of hormones and consequently most are frequently observed in the reproductive period or in women who have received oestrogen replacement therapy in postmenopause. The reason for them also can be inadequate secretion of oestrogen, progesterone or an increase in the prolactin level. There is no proof of the influence of hormonal contraceptives on the development of benign breast diseases.

Histological fibrocystic changes go through three stages. The first stage — *proliferation of the stroma,* especially in the upper quadrant of the gland, resulting in induration and causing pain in patients. The second stage is *adenosis,* causing the mass of cysts with various sizes: from microscopic to 1 cm in diameter. During the adenosis stage significant proliferation of the ducts and alveolar cells develops. The last, third stage of fibrocystic changes is characterized by the mass of *large cysts. However,* with less sensation of pain (except for cases of fast cyst growth). Proliferative changes occur in all the breast structures. In case of the occurrence of atypical cells

in the ducts or apocrine tissue, the risk of developing breast cancer increases 5 times.

The following forms of FCM are distinguished:

1) diffuse:

a) with the prevalence of the glandular component (adenosis);

b) with the prevalence of the fibrous component;

c) with the prevalence of the cystic component;

d) mixed;

2) nodular.

Etiology and pathogenesis of FCM are not established. A certain role is played by hormonal disorders: hyperoestrogenism, deficiency of progesterone, hyperprolactinemia.

Clinical picture. Fibrocystic mastopathy, as a rule, is accompanied by cyclic, bilateral pain *(mastalgia)* and breast swelling. The pain connected to the fibrocystic changes, in most cases is diffuse, frequently with irradiation into the shoulder. The located pain can occur due to fast growing cysts. During examination of the breasts, their nodularity is found. Large cysts can be felt as filled with liquid. These changes are most expressed before menstruation. However, may not have a cyclic character. Up to 15% of women, as a rule, do not complain of pain. However, during palpation of the breasts zones of nodularity are found in them.

Diagnosis is based on history data, clinical picture, palpation of the breasts, ultrasound study. The diagnosis is confirmed with data from special investigationes (mammography, thermography, punctual biopsy). A biopsy consists of aspiration of cystic masses; this procedure simultaneously is also therapeutic. The tissue received by aspiration is subject to cytological investigation. The cystic masses may fully disappear after aspiration; in such cases patients should have a repeated examination in 3–6 months. With the presence of solid masses, histological study is required by aspiration or open biopsy. Mammography is recommended to women over the age of 35 having a high risk of developing breast cancer. Such breast diseases as *sclerosing adenosis, apocrine metaplasia, ectasia of the ducts, fibroadenoma, fibrosis, mild hyperplasia, mastitis and squamous metaplasia* do not increase the risk of developing breast cancer.

Treatment of patients with fibrocystic mastopathy is medicamentous. With this purpose they use oral contraceptives (method of choice), gestagens, danazol, antioestrogen (tamoxifen, nolvadex), antiprolactin preparations (parlodel, bromcriptin), microdoses of iodine, vitamins. In every second patient who is treated with danazol 12 months after the termination of therapy symptoms repeat. Parlodel, as a rule, has bad tolerance (nausea, vomiting). Such patients are recommended to limit the use methylxanthin (coffee, tea, chocolate).

Fibroadenoma has the second rate among benign breast diseases. It develops mostly in young women (21–25 years). It is revealed as a firm, painless, freely mobile mass in the breast usually with a diameter of 2–3 cm. In most cases fibroadenoma is single; multiple tumours can be formed in 15–20% of all cases. Fibroadenoma does not undergo changes during the menstrual cycle and, as a rule, grows slowly.

The diagnosis is established during objective examination and is confirmed by aspiration biopsy with subsequent histological study. Patients can find a tumour independently during breast self-examination.

Treatment of patients with fibroadenoma consists of surgical removal of the tumour, though in some cases treatment with danazol or tamoxifen is effective.

Lipoma, fatty necrosis. In the fatty tissue of the breasts benign tumours which at times are difficult to distinguish from carcinomas can develop. *Lipoma,* as a rule*,* is not sensitive during palpation. However, the diffuse character can resemble malignant neoplasm. Secondary changes, characteristic for cancer (change of skin, nipple), in most cases are absent. *Fatty necrosis* develops extremely seldom due to trauma; its reason is not completely known. The patient complains of firm painful masses in the breast; in some cases retraction of the skin is present. To specify the diagnosis, mammography and biopsy of the breast are done.

Intraductal papilloma is the frequent reason for discharge from the nipple of one breast, including bloody. This tumour is solitary; multiple papillomas (papillomatosis) are possible. With the presence of thick discharge in a combination to a tumour mass in the breasts the differentiation with carcinoma is necessary.

Mammary duct ectasia occurs in the perimenopausal period (in women over the age of 55) more often and is characterized by an increase, reddening and hardening of the breasts, the presence of grey, greenish, even black, discharge from the nipple, having a consistency of toothpaste. Ectasia of the mammary ducts is connected to their chronic inflammation and can be accompanied by local lymph nodes enlargement. The presence of local firm masses and enlarged lymph nodes demand their differentiation with carcinoma. Mammary duct ectasia can independently regress.

BREAST CANCER

Within the last 10 years the case rate of breast cancer in Ukraine has almost doubled, and in 1996 was 51.2 in 100 thousand of the female population.

The basic epidemiological factors influencing the development of breast cancer are submitted below.

Etiology. The reason for cancer is unknown. However, it is considered oestrogen-dependant. A

Epidemiological factors influencing the development of breast cancer

Increase the risk	*Uncertain or absence of the effect*	*Decrease the risk*
Radiation	Lactation	Surgical menopause
Menarche before the age of 12	Oestrogentherapy	First delivery before the age of 25
Menopause after the age of 55	Use of oral contraceptives	
First delivery after the age of 30	Use of caffeine	
Use of alcohol	Smoking	
Burdened familial hystory	Increased amount of fats in the diet	

significant role in the development of this disease is played by heredity and factors of the environment.

Clinical picture, diagnosis. Early symptoms of breast cancer can be absent or characterized by the mass of small insensitive mobile masses in the breasts. The growth of a tumour is accompanied by disorder of its mobility, fixation, pink or orange discharge from the nipple.

Screening of breast cancer is conducted during objective examination of each patient no less than once a year, as well as during self-examination. Mammography (Fig. 71) is performed in patients over the age of 35; till the age of 50 the given investigation should be performed every 1–2 years; after 50 — annually. Additional methods of investigation are thermography, nuclear magnetic resonance, determining oncoantigen MCA. The final diagnosis of breast cancer is established during histological study. Breast tissue is obtained by open or aspiration biopsy.

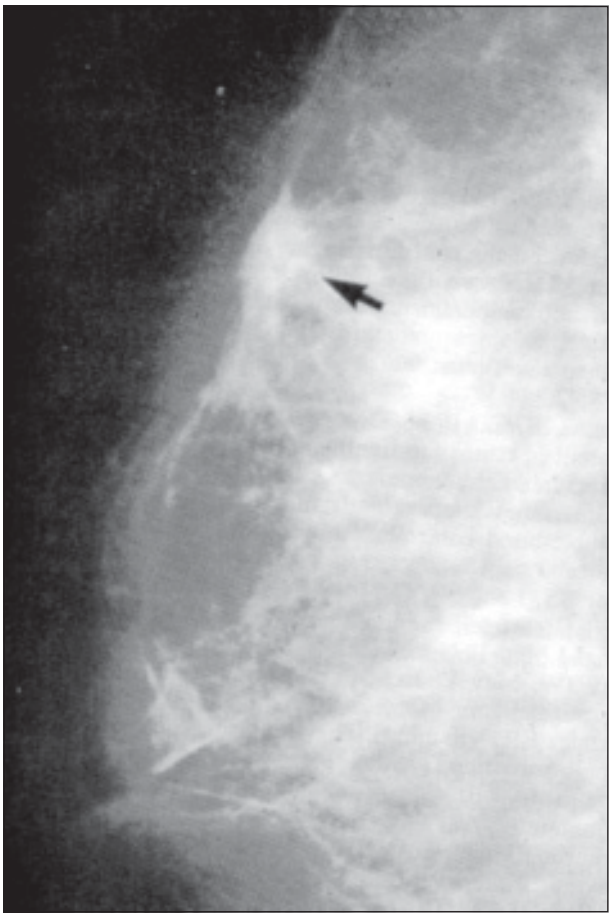


Fig. 71. Mammogram: breast cancer

Breast cancer spreads as a result of direct infiltration, through the lymphatic system of the glands, as well as haematogenously. Clinical attributes of direct infiltration: tumour fixing to the fascia, muscles or thorax, change in the skin above the tumour (hypostasis, ulcers), enlarged regional lymph nodes.

Palpation of the axillary and supraclavicular lymph nodes helps to determine lymphatic distribution of a tumour. If these groups of lymph nodes are affected, the prognosis of the disease worsens. 40–50% of patients with the affection of the axillary lymph nodes have metastases in the parasternal lymph nodes, and only 4% of patients have single metastases in the parasternal nodes. The most often sites of metastases in distant organs are the bones (especially cartilages), basin, lungs, liver and brain.

Other prognostic factors include the histological type and aggression of the tumour, the presence of hormonal receptors in it, vascular invasion. Breast cancer develops from the epithelium of large or medium ducts ("ductal") or from the epithelium of the terminal ducts of the lobes ("globular"). The most often type of cancer is infiltrating ductal carcinoma (70–80% of cases), having a poor prognosis. Other histological types of ductal carcinomas— medullar (5–8%), mucinous (2–4%) and papillary cancer (1–2%). Invasive lobular carcinoma is formed in 6–8% of patients, other kinds of cancer — less than in 1% of patients. The majority of breast cancer types of the moderate histological degree can have aggressive features. Vascular invasion of tumours always worsens the prognosis of the disease.

Treatment of patients with breast cancer is in the competence of oncologists.

Standard *surgical treatment* of patients with breast cancer is *radical mastectomy* (by Holisted): the removal of the mammary gland, chest muscles and axillary lymph nodes. In addition radiation, hormonal therapy, cytotoxic chemotherapy are applied. Less extensive procedures at the early stages of t he disease are *lumpectomy* (wide local excision of the primary tumour), partial mastectomy (removal of the segment or quadrant of the mammary gland with the primary tumour), and simple mastectomy (removal

of the mammary gland affected with the primary tumour). Dissection of the axillary lymph nodes is performed together with less extensive procedures with the purpose of not only treatment, but also revealing the necessity of chemo- or radiation therapy. The combination of simple mastectomy with the removal of the axillary lymph nodes received the name *"modified radical mastectomy"*.

Hormonal treatment is conducted to eliminate hormonal stimulation of the tumour. As an alternative to bilateral oophorectomy some women are prescribed antioestrogen tamoxifen.

The tumours containing receptors to oestrogen (ER+) and to progesterone (PR+), are more differentiated in comparison to tumours which do not have those receptors (ER- or PR-). Highly differentiated tumours have more favourable prognosis. The presence of oestrogen and progesterone receptors in a tumour determines its sensitivity to hormonal therapy. About 40% of tumours contain progesterone receptors. 25% of primary tumours are characterized by the absence of the receptors. Such patients, as a rule, have no corresponding response to hormonal therapy. Other tumours contain oestrogen receptors and have no progesterone receptors: the more receptors present in the tumour the better the prognosis in these cases.

Cytotoxic chemotherapy is used as adjuvant in patients with breast carcinoma. Combinations are applied: adriamycin-vincristin; 5-fluoruracil-adriamycin-cyclophosphamid; adriamycin-cyclophosphamid.

The prognosis concerning treatment of breast cancer depends on the disease extent with the establishment of the diagnosis and character of growth of the tumour (in some patients its aggressive growth can occur). So, the 5-year survival rate of patients with I stage breast cancer is 85%, II stage — 66%, III — 41%, IV — 10% of cases. With the presence of very early stage cancer (invasive tumour with a diameter of less than 0.5 cm — 0 stage or carcinoma *in situ*) the survival rate of patients is 100% within 15 years.

RECOMMENDED READING

7; 16; 21; 24; 90; 92; 93; 94; 96; 98; 103; 108.

Chapter 17
CONTRACEPTION

Modern methods of contraception reduce the risk of the complications connected to undesirable pregnancy and include:

1) hormonal methods (oral steroid contraceptives, injections or implants of steroid contraceptives);

2) intrauterine contraception (intrauterine spirals: non-medicamentous — inert and medicamentous — with copper, progesterone);

3) barrier methods (physical and chemical);

4) traditional methods (rhythm-method, or the Ogino—Knaus method, lactational amenorrhoea, coitus interruption);

5) surgical (tubal sterilization, vasectomy).

The frequency of inefficiency of the typical use of contraceptive methods (Perla's index) is submitted below.

Contraceptives	*Perl's index, %*
Injecable contraceptives	0.25
Combined oral contraceptives	2
Pure progestin contraceptives	2.5
Intrauterine spirals	5
Condoms	10
Diaphragm (with spermicides)	19
Sponge (with spermicides)	10–20
Creams, gels with spermicides	18
Interruption of sexual intercourse	23
Physiological method (periodic rhythmic abstinence)	24
Syringing	40
Absence of contraception	90

Hormonal contraceptives. The combined oral contraceptives represent a complex of oestrogen and progesterone; they are taken daily for 3 weeks with a week break during which withdrawel bleeding occurs. The oestrogen in modern preparations is acetenyl estradiol or mestranol, and progestin component — norethindrone, norgestrel, desogestrel and other progestins.

Mechanism of action. The combined oral contraceptives protect from fertilisation in several ways. Prevention of ovulaion is achieved by suppression of hypothalamic releasing-factors, which, in turn, results in inadequate secretion of folli- and lutrophin. Other effects are disorder in the endometrial maturing which does not promote the process of implantation even with the development of a blastocyst, and the production of thick cervical mucous impeding the penetration of spermatozoon. Disorder of the normal peristalsis of the Fallopian tubes and the uterus may also play a role.

In order to avoid ovulation, as well as to recognize pregnancy in the early terms, as a rule, the use of oral contraceptives is recommended to begin in one of the first 7 days of the menstrual cycle. It is possible to begin right after giving birth or abortion. If the contraceptives were not started within the first 7 days of the menstrual cycle or 3 weeks after giving birth to reduce the risk ovulation it is necessary to use one more of the methods of contraception.

To achieve the maximal contraceptive effect it is important to take the preparation daily, approximately at the same time. In case of missing one dose, the next day the dose is doubled. If more than one doses are missed, it is recommended to use simultaneously one more additional method of contraception (for example, barrier). Taking contraceptives is renewed after the beginning of withdrawel bleeding. With the absence of withdrawel bleeding it is necessary to rule out pregnancy.

Taking oral contraceptives it is necessary to use the minimal doses of hormonal preparations (30–50 μg of acetenyl estradiol or mestranol).

Three-phase contraceptives were offered to reduce the dose of the progestin component. Reduction of the dose of progestin was achieved by its use in small doses from the very beginning of the contraceptive cycle. The dose of oestrogen can remain constant or increases during the cycle little, but should not exceed 30–40 μg of acetenyl estradiol.

Positive and side effects. Combined oestrogen-gestagen contraceptives taken daily for 3 weeks, are

the most effective method of contraception. Positive effects include the reduction of menstrual blood loss, displays of premenstrual syndrome, algodysmenorrhoea, functional ovarian cysts, salpingitis, rheumatoid arthritis, the incidence of ovarian and endometrial cancer, benign breast diseases and, probably, breast cancer.

The possibility of side-effects of these preparations increases in case of diseases where the use of hormonal contraceptives is contraindicated. It is connected to some adverse metabolic and cardiovascular effects. The majority of side-effects depending mainly on the oestrogen component have been described in connection with the use of contraceptives containing over 50 μg oestrogen (now such preparations are not made); these effects from the action of the drugs having low doses of oestrogen (20–30–35 μg) are much less often observed.

Contraindications to the use of oestrogen-gestagen contraceptives:

1. Thrombembolism in the anamnesis.
2. Cerebrovascular diseases.
3. Diseases of the coronary arteries.
4. Disorder of the liver function.
5. Adenoma of the liver.
6. Breast cancer.
7. Arterial hypertension.
8. Diabetes.
9. Diseases of the gallbladder.
10. Cholestasia during pregnancy.
11. Sickle cell coagulopathy.
12. Possible surgical operations within next 4 weeks.
13. Immobilization of the lower extremities.
14. Excessive smoking, especially in women over the age of 35.
15. Family hyperlipidemia.
16. Antiphospholipid antibodies.

The risk of death due to the use oral contraceptives is very low for healthy non smoking women less than 35 years old and much smaller than that one connected with pregnancy.

Influence on reproduction and breast feeding. Ovulation, as a rule, is quickly restored after discontinuing the hormonal contraceptives (90% of women previously having ovulatory cycles) and happens within 3 months. In unusual cases women with amenorrhoea after discontinuing hormonal contraception do not require long treatment to restore the ability to fertilisation.

The use of hormonal contraceptives by feeding mothers results in a reduction of the production of milk, thus only a small amount of oestrogen excretes with the milk.

Progestin-only contraceptives (mini-pili) contain less than 0.5 mg of progestin in one dose. They have not gained popularity in connection with a higher, in comparison with preparations of combined oestrogen-gestagen, incidence of pregnancy and irregular intramenstrual bleedings. The influence of the progestin component on the prevention of fertilisation consists mainly in thickening of the cervical mucous complicating the penetration of spermatozoon, in disorders in the maturing of the endometrium and as a result deterioration in the conditions for implantation of the blastocyst.

Injectable hormonal contraceptives. The use of injectable medoxyprogesterone acetate ("Depot-provera") is accompanied by the contraceptive effect similar to those for the use of combined oral contraceptives. The duration of action (injection 2–4 times a year), absence of influence on lactation promote the popularity of this method. The mechanism of action of injection contraceptives is multicomponent and includes the suppression of ovulation, increases the thickness of the cervical mucous and changes the endometrium impeding implantation.

Side-effects of the action of "Depot-provera" are long amenorrhoea or uterine bleedings during or after the use of the preparation, prolonged anovulation after the drug cessation, as well as an increase in the risk of developing thrombosis and thrombembolia.

Hormonal implants containing progestin (norplant) are an effective method of contraception. Norplant is six silastic capsules, each of which contains 36 mg of L-norgestrel. The capsules are implanted under the skin of the internal surface of the shoulder. The mechanism of action consists of inhibiting ovulation and an increase in the thickness of cervical mucosa. The duration of its contraceptive action is 5 years.

Postcoital contraception. It is possible to be protected from pregnancy by means of using large doses of acetenyl estradiol or conjugated oestrogens within several days after sexual intercourse without safety means, as well as with the use of the preparation "Postinor".

Intrauterine contraception. There are two types of intrauterine spirals: 1) chemically inert made from a non-absorbent material, more often polythene, with impregnation of sulfate barium for radiopaque; 2) with constant discharge of chemically active substances (progesterone, copper).

The mechanism of action of chemically inert spirals is not completely known. However, it is quite possible that a defect of implantation of the fertilized ovum takes place due to the development of local inflammatory processes resulting in damage to the blastocysts by lysosome and phagocytosis of the spermatozoon. The contraceptive effect of the use of chemically inert spirals usually increases due to the increase in their sizes and external contact with the endometrium.

Side-effects include perforation of the uterus, rupture of existing undesirable pregnancy, spontaneous expulsion, painful strong menstrual bleedings, pelvic infectious diseases. The possibility of perforating the uterus is insignificant (mainly during the introduction of the spiral) and depends on the skills

of the operator. Pelvic infectious diseases can be severe (septic abortion, uni- or bilateral tuboovarian abscesses and sepsis).

In connection with the risk the occurrence of salpingitis, pelvic peritonitis, pelvic abscess and subsequent sterility intrauterine spirals are not recommended to young (under 25) women who have not yet given birth or women with low parity, as well as to patients in the risk group for developing infections of the pelvic organs, having numerous sexual partners.

Uterine pregnancy and spirals. With the development of uterine pregnancy in a patient with an intrauterine spiral the risk rises to both her health and the baby's. If the "tail" of the spiral is visualized, the latter is removed to reduce the risk of spontaneous abortion, sepsis and premature birth. The incidence of spontaneous abortion is 50% when the spirals are left and 25% if it is removed. With the absence of visualization of the spiral's "tail", attempts to remove it with the help of instruments can lead to abortion.

The risk for the mother consists of possible expulsion of the spiral into the abdominal cavity. The spiral is removed during the delivery.

Ectopic pregnancy and spiral. The spiral to a greater extent protects from uterine than ectopic pregnancy. Hence, the women who have previously had salpingitis, ectopic pregnancy, operation on the Fallopian tubes shouldn't use intrauterine spirals.

Barrier methods of contraception. *Condoms* can effectively protect from conception if they are used correctly. Advantages of this method are also effective prevention of sexually transmitted diseases, including gonorrhoea, syphilis, genital herpes, clamidiosis, trichomoniasis and HIV-infection. The use of a condom prevents the development of premalignant changes in the cervix to a certain extent.

Barrier contraceptives can be used as an alternative of other methods or temporary protection, for example, for the 1st week after starting oral contraceptives, or during lactation amenorrhoea. They can be *creams, gels, suppositories, sponges, aerosols*, etc. The mechanism of their action consists in the creation of a physical barrier for penetration of spermatozoon due to the action of chemical spermicides. Active spermicidal agents include nonoxunol-9. For the maximal efficiency, spermicides are entered high in the vagina (to the cervix uteri) directly before sexual intercourse. The duration of their action, as a rule, does not exceed one hour. Before subsequent sexual intercourse it is necessary to enter the spermicides into the vagina again. Syringing can be carried out no earlier than 6 h after sexual intercourse.

Diaphragm with spermicides. The vaginal diaphragm, consisting of a rubber dome and the supporting metal ring, also is used for contraception in combination with spermicidal gels and creams. The spermicidal agent is put on the anterior surface of the diaphragm and it is placed in the vagina so that the cervix, vaults and anterior vaginal wall have been effectively isolated from the penis and other parts of the vagina. The diaphragm with spermicidal agents should be put 1 h before a sexual intercourse; extraction — 6 h after a sexual intercourse.

Physiological method of contraception *(rhythm-method, periodic (rhythmic) abstention)* is based on the fact that ovulation most frequently occurs 14 days after the beginning of menstruation. But numerous variations of the occurrence of ovulation (early, late), as well as unequal life expectancy of spermatozoon (on average — 3 days) makes this method insufficiently effective.

Lactational amenorrhoea. Ovulation before the 10th week after giving birth is improbable for breast feeding mothers. However, breast feeding is not an effective method of contraception for mothers whose children receive additional food and have a night break in breast feeding. Ovulation of lactational women can anticipate menstruation. After the first menstruation contraception is necessary.

Surgical contraception. *Tubal sterilization* can be performed right after giving birth or during caesarean section, as well as during any other time; it is an irreversible method of contraception. It can be performed by laparotomy, transvaginally or during laparoscopy.

Vasectomy consists of tying off the ductus deferens to block spermatozoons from leaving the testicles and it is performed as out-patient under local anaesthesia.

RECOMMENDED READINGS

7; 21; 24; 58; 90; 92; 93; 94; 102; 108.

Chapter 1

COMMON SYMPTOMATOLOGY OF GYNAECOLOGICAL DISEASES. METHODS OF GYNAECOLOGICAL EXAMINATION

1. A patient of 30 years old with initial infertility within 7 years. The menses last since 14 years, for 5–7 days with 35–45-day interval, moderate, painless. The woman of a superfluous feed. External genitalia are advanced correctly, the growing of hair of a female type, the body of the uterus is reduced in the size, the ovaries from both sides are 3×4×4 cm, dense, mobile, painless. According to results of the tests of functional diagnosis, the basal temperature is monophase, the cariopicnotic index makes 60–70 %. The spermogramma of her husband is without pathological changes. What is the policy of the patient treatment?

A. Laparotomy, a bilateral resection of the ovaries.
B. Cyclic hormonal therapy during 6–12 months.
C. Bilateral resection of the ovaries with the subsequent hormonal therapy.
D. Antibacterial therapy by riphampicins and immunomodulators.
E. Extracorporal fertilization.

2. A patient of 34 years old with initial infertility within 7 years. On a curve of the basal temperature — a single-phase and biphasic cycles with the second phase short up to 4–5 days. At X-ray hysterosalpingography the Fallopian tubes are carried out by contrast substance up to ampular parts, their exit in an abdominal cavity is not marked. Spermal study of the husband reveals asteno- and oligozoospermy of the II degree. After treatment of the husband by the andrologist it is kept the astenozoospermy of the II degree. What is the most rational way of treatment of infertility?

A. Microsurgical plastics by the uterine tubes.
B. Assignment of stimulators of the ovulation in a combination with medical hydrotubation.
C. Artificial insemination by the donor sperm.
D. Extracorporal fertilization with transfer of the embryo.
E. Yield to no treatment.

3. A patient of 27 years old with complaints of infertility has addressed to the maternity welfare centre. Sexual life lasts in marriage for 4 years, contraception was not applied. There were no pregnancies. At the inspection of the woman it is established: development of female genitalia without anomalies. The Fallopain tubes are passable. The basal (rectal) temperature during three menstrual cycles is singlephase. Name the most probable reason for infertility in this case.

A. Chronic adnexitis.
B. Anovulatory menstrual cycle.
C. Genital maldevelopments.
D. Immunological infertility.
E. Genital endometriosis.

4. A woman complains of slight dark bloody discharge and mild pains in the lower abdomen for several days. Last menses were 7 weeks ago. The test for pregnancy is positive. Bimanual exam: the body of the uterus is about 5–6 weeks of pregnancy, has softish consistence, painless. On the left side there is a retortlike adnexal mass, with dimensions of 7×5 cm, mobile, painless. What is necessary to carry out to determine the site ot the fetus?

A. Hysteroscopy.
B. Chromohydrotubation.
C. Ultrasound.
D. Colposcopy.
E. Cystoscopy.

5. A 24-year old woman, never pregnant before, terminated to accept oral contraceptives. After last reception of a drug she had one menses, and then within 6 months amenorrhoea was observed. Choose the most appropriate investigation:

A. Determination of the level of gonadotrophins.
B. Pelvic ultrasound.
C. Progesteron test.
D. Computer tomography of the head.
E. Determination of the contents of testosteron in blood serum.

6. A 12-year old girl complains of abdominal sudden cramp-like pain which appeared during a physical activity, as well as nausea, vomiting. The body temperature is 38ºC. At abdominal palpation — the Schetkin's sign is positive in the right ileac area. What study is most informative for statement of the diagnosis?

A. Clinical analysis of the urine.
B. Clinical analysis of the blood.
C. Pelvic ultrasound.
D. Rectal investigation.
E. X-ray study of the abdominal cavity.

7. A 24-year old patient has addressed with the complaint of amenorrhoea in 13 months after the first labor. Pregnancy has concluded by the Cesarian section concerning to premature detachment of normally posed placenta and an intrauterine fetal asphyxia, haemorhage was 2,000 ml owing to impaired blood coagulability. Choose the most suitable investigation:

A. Determination of the level of gonadotrophins.
B. Pelvic ultrasound.
C. Progesterone test.
D. Computer tomography of the head.
E. Determination of testosterone in the blood serum.

8. A 28 year old woman has visited the gynecological department with complaints of pain in the lower abdomen at the left and slight bloody discharge within last 2 days. 2 labors in the anamnesis. Last menses were 6 weeks ago. Infringements of the menstrual cycle till that time were not observed. She was preserved from pregnancy with the help of an endometrial contraceptive. The ABP at admission was 110/70 mmHg, haemoglobin 124 g/l. What method of examination is most informative?

A. X-ray film of the sella turcica.
B. Definition of CG level in the urine.
C. Tests of function diagnosis.
D. Transvaginal echography.
E. A diagnostic currettage of uterine mucosa.

9. A 28 year old woman was delivered to the gynaecological department with complaints of acute pain in the right ileac area which appeared after lifting weight. Last menses were 10 days ago, in time. At survey in specula: the vagina and cervix without changes. At the vaginal examination the uterus and appendages are not accessible for palpation because of painfulness and muscle tension of the anterior abdominal wall. The posterior fornix overhangs, painful. What it is necessary to make for specification of the diagnosis?

A. Hysteroscopy.
B. Colposcopy.
C. Culdoscopy.
D. Define CG.
E. A puncture of the abdominal cavity through the back vault of the vagina.

10. It is established that a healthy woman at colpocytological investigation on 15th day of the menstrual cycle has the maturing index is 0/12/88, the karyopyknotic index is 80%. What does this index testify to?

A. An approach of the phase of early proliferation.
B. Profound endocrine disorders.
C. Ovulation approach.
D. An approach of the late ovulation phase.
E. An approach of the secretion phase.

Chapter 2
INFLAMMATORY DISEASES OF FEMALE GENITALIA

1. A patient of 40 years old shows complaints of yellow vaginal discharge; in the anamnesis — 1 labor and 2 artificial abortions. At specula exam: mucosa is hyperaemic, on the posterior labium of the cervix there are hazy fields with legible contours. Bimanual exam: the body of the uterus and appendages are without pathological changes. The discharge are white, foamy, in smears — vaginal *Trichomonas vaginalis* and mixed flora. Colposcopy: two hazy fields on the anterior labium, iodine-negative. Your policy of treatment?

A. Treatment of mycotic colpitis.
B. Cervical diathermocoagulation.
C. A target biopsy after treatment of colpitis.
D. Cervical amputation.
E. Cervical cryolysis.

2. A 23-years old woman has addressed with complaints of serous-purulent vaginal discharge, pain in the lower abdomen, the temperature rise at the end of menses.

The most probable cause of the disorder?

A. Gardnerellosis.
B. Clamidiosis.

C. Gonococcus.
D. Shankroid.
E. Inguinal granuloma.

3. In a 18-year old woman never given birth gonorrhoea was revealed 6 months ago. She received ampicillin per os. Last month she also received ampicillin concerning inflammatory process of the pelvic organs. At palpation the expressed abdominal tenderness is marked. Gonadotrophin contents is normal. The prescribed treatment:
A. Doxycycline per os.
B. Penicillin i/m.
C. Cephotoxin and a doxycycline in a hospital.
D. Isoniazid.
E. Spektinomycin.

4. At the gynaecological department a woman with complaints of acute pain in the lower abdomen, the temperature rise up to 38°C, the purulent vaginal discharge is delivered. Sexual life is episodic. At bimanual exam the tender uterine appendages, and purulent discharge are defined. The following diagnostic measures are necessary:
A. Uterine currettage.
B. Colposcopy.
C. Uterine intubation.
D. Bacteriologic study of vaginal discharge.
E. Cytologic study of vaginal discharge.

5. A patient of 35 years old, single, has addressed to the gynaecologist with complaints of purulent discharge, often and painful urination, and itching in the urethral region which have appeared on the 5th day after a casual sexual contact. Objective data: mucosa of the urethra is edematic, discharge from the urethra are purulent. What is the preliminary diagnosis?
A. Gardnerellosis.
B. A chronic gonorrhoeal urethritis.
C. Clamidiosis.
D. Acute gonorrhoeal urethritis.
E. Ureaplasmosis.

6. A patient of 18 years old comlains of the pains in the lower abdomen, the temperature rise up to 37.5ºC, purulent discharge from the reproductive tract, painful urination. The disease had an acute onset on the 7th day of the menstrual cycle, when the mentioned above signs had appeared. The urethra is infiltrated, the cervix is edematic, with extensive anabrosis, from the cervical canal — abundant mucopurulent discharge. The uterus is not enlarged, tender, appendages are thickened, tender. In smears for vaginal flora — extra- and intracellular gonococci. Your diagnosis?
A. Fresh acute gonorrhoea of the lower reproductive tract.
B. Fresh acute ascending gonorrhoea.
C. Subacute ascending gonorrhoea.
D. Chronic gonorrhoea of the inferior department of genitourinary tract.
E. Torpid gonorrhoea.

7. A patient of 18 years old complains of the pain in the lower abdomen, the temperature rise up to 37.5ºC, purulent vaginal discharge, pain at urination. The disease had an acute onset on the 7th day of the menstrual cycle, when the mentioned above signs had appeared. The urethra is infiltrated, the cervix is edematic, with extensive anabrosis, from the cervical canal — abundant mucopurulent discharge. The uterus is not enlarged, tender, appendages are thickened, tender. In smears for vaginal flora — extra- and intracellular gonococci. The management of the doctor of the maternity welfare centre:
A. To carry out the course of antibacterial therapy.
B. To send the patient to the clinic for skin and venereal diseases for the profound inspection and treatment.
C. To hospitalize the patient to the gynaecological department for inspection and treatment.
D. To recommend a planned hospitalization to the gynaecological department after obtaining the results of laboratory inspection (blood, urine analysis, Wassermann reaction, the blood analysis for HIV antibodies), consultations of the specialist in skin and venereal diseases, urologist.
E. Hospitalization to the clinic for skin and venereal diseases.

8. A 18-year old woman having infertility in the anamnesis has addressed to the gynaecologist to make chlamidia analysis. The sexual partner of the patient has recently completed the treatment of clamidiosis. Prescribe the "gold standard" in diagnosis of urogenital clamidiosis:
A. Immuno-enzyme analysis.
B. Polymerase chain reaction.
C. Cytologic.
D. Serologic.
E. Cultural.

9. A woman of 28 years old complains of watery vaginal discharge with an unpleasent fish odour. The microscopy of vaginal discharge revealed key cells. The amine test is positive. Your diagnosis?
A. Bacterial vaginosis.
B. Trichomoniasis.
C. Gonorrhoea.
D. Candidiasis.
E. Clamidiosis.

10. A patient complains of an intolerable itch and burning sensation in the vagina intensifying at night. At exam acute hyperemia of the vulva, vaginal mucosa and vaginal part of the cervix are revealed. Discharge are liquid, abundant, foamy with tints of green. At exam of the uterus and appendages no pathology was revealed.

What disease should be suspected?

A. Urogenital herpes.
B. Gonococcal infection.
C. Bacterial vaginosis.
D. Urogenital candidiasis.
E. Urogenital trichomoniasis.

11. A woman of 27 years old has addressed to the maternity welfare centre with complaints of growths in the vulvar area. At exam separated growths with the size from 2 up to 5 mm were revealed. Internal genitalia are without pathology. The diagnosis: condyloma acuminata. What is the most probable cause of this pathology?

A. Papillomavirus infection.
B. Herpes infection.
C. Clamidiosis.
D. Mycoplasmosis.
E. Syphilis.

12. A woman of 32 years old has addressed to the venerologist with the purpose of preventive inspection as her sexual partner with whom she had contact 1.5 months ago had informed her that he was that time on hospitalization in the clinic for skin and venereal diseases concerning the secondary relapsing syphilis. Objective exam revealed no signs of the disease, serological tests are negative. Management of the doctor:

A. Preventive treatment.
B. Out-patient treatment.
C. Symptomatic treatment.
D. Preventive treatmen.
E. Repeated inspection in a month.

13. A woman of 23 years old has addressed to the maternity welfare centre with complaints of pain, itching, burning sensation in the vulvar region, the general weakness, malaise, the temperature rise up to 37.2ºC, headache. At exam against a background of hyperemia and mucous edema multiple vesicles up to 2–3 mm in diameter with transparent contents are detected in the vulvar region. What is the provisional diagnosis?

A. Genital herpes infection.
B. Primary syphilis.
C. Papillomavirus infection.
D. Vulvar cancer.
E. Cytomegaloviral infection.

14. A patient of 20 years old has arrived to the gynaecological department with the diagnosis: an acute bilaterial adnexitis. She got ill 3 days ago when after a casual sexual intercourse in a day began to feel pain in the lower abdomen and at urination, abundent purulent vaginal discharge, the temperature rise up to 37.8ºC. At additional exam the 4th degree of vaginal purity, leucocytes through the whole field of vision, bacteria, diplococci extra- and intracellularly are revealed. What etiology is acute adnexitis?

A. Trichomonal.
B. Collibacillary.
C. Clamidial.
D. Gonorrhoeal.
E. Staphylococcal.

Chapter 3
DISORDERS OF THE MENSTRUAL FUNCTION

1. A 24-year old woman with a regular menstrual cycle before has addressed to the doctor with complaints of the irregular menstrual cycle. The prolactin level in the blood is elevated. The most informative method of examination:

A. Definition of the gonadotrophin level.
B. Definition of the prolactin level.
C. Progesterone test.
D. Definition of the thyroid-stimulating hormone level.
E. Definition of the testosterone level in the blood.

2. A patient of 38 years old visited the maternity welfare centre with complaints of moderate bloody vaginal discharge which have appeared after a delay of the next menses by 1.5 months. At gynaecologic examination: the neck of the uterus is epithelized, the pupil's sign (++), the uterus is not enlarged, dense, mobile, painless, appendages from both sides are not enlarged, painless, fornices are deep. The most probable diagnosis?

A. Dysfunctional bleeding.
B. Internal endometriosis.
C. Ectopic pregnancy.
D. Submucous hysteromyoma.
E. Endometrial cancer.

3. A patient of 38 years old visited the maternity welfare centre with complaints of moderate bloody vaginal discharge which have appeared after a delay of the next menses by 1.5 months. At gynaecologic examination: the neck of the uterus is epithelized, the pupil's sign (++), the uterus is not enlarged, dense, mobile, painless, appendages from both sides are not enlarged, painless, fornices are deep. Management of the doctor:

A. To make cytologic examination of the uterine aspirate, to refer the patient to the oncologist.
B. To register the patient in a dispensary, to prescribe haemostatic and uterotonic drugs.
C. To make pelvic ultrasound; in case of absence of pathological changes to make a hormonal haemostasis.
D. To refer the patient to the gynaecological department.
E. To make a hormonal hemostasis under observation of the doctor of the maternity welfare centre; in case of absence of effect a planned hospitalization.

4. A girl of 12 years visited the gynaecological department with complaints of vaginal bleeding within 2 weeks after a delay of menses within 3 months, weakness, headache, giddiness. Menses since 10 years. At the age of 10 years got ill with scarlatina. Objective exam: integuments cyanotic, tachycardia, the blood pressure — 100/60. In analysis of blood Hgb = 100 g/l, thrombocytes number is 200 thousand. Gynaecologic examination: virgo. Rectal examination: the uterus and appendages without pathology. The preliminary diagnosis?
A. Juvenile bleeding.
B. Broken pregnancy.
C. The Werlhof's disease.
D. Sclerocystic ovarian syndrom.
E. Haemorrhagic diathesis.

5. A girl of 15 years complains of bloody vaginal discharge during 2 weeks which has appeared after a 3 month menses delay. Menarche occured at 13 years. The menstrual cycle is irregular. Blood analysis: Hgb — 90 g/l, erythrocytes — $2.0 \cdot 10^{12}$/l, leucocytes — $5.6 \cdot 10^{9}$/l. At rectal examination: the uterus of the normal size, appendages are not palpated. What diagnosis is most probable?
A. Juvenile bleeding.
B. Endometrial polyp.
C. Impaired coagulation.
D. Endometrial cancer.
E. Incomplete abortion.

6. A 14-year old girl was delivered to the gynaecological department with complaints of abundant bloody discharge during 3 days. From the anamnesis: menses since 12 years, irregular, with periodic delays about 10–15 days. Sexual life is absent. Extragenital pathology is not revealed. At ultrasound the uterus of the normal size, ovaries without pathological changes. Optimal medical policy:
A. Hormonal hemostasis with combined oestrogen-gestagen drugs.
B. Uterine curettage.
C. Roborant, haemostatic therapy, agents reducing the uterus.
D. A hormonal hemostasis with oestrogens.
E. Hemotransfusion.

7. A 14 year old girl was delivered to the gynaecological department with complaints of abundant bloody discharge during 3 days. From the anamnesis: menses since 12 years, irregular, with periodic delays about 10–15 days. Sexual life is absent. Extragenital pathology is not revealed. At ultrasound the uterus of the normal size, ovaries without pathological changes. The diagnosis?
A. A fibromyoma of the uterus.
B. Dysfunctional bleeding of the reproductive period.
C. Internal endometriosis.
D. Dysfunctional bleeding of the juvenile period.
E. Polycystic ovaries.

8. A girl of 11 years with uterine bleeding which has arisen after menses delay is delivered to the hospital. Mild degree anemia. Sexual formula A×2 P3 Ma2 Me+. Virgo. Rectal exam revealed no pathology. Treatment of the patient should be started with:
A. A diagnostic uterine curettage.
B. Infusive therapy with the use of agents reducing the uterus and other drugs.
C. Hormonal hemostasis.
D. Antianaemic therapy.
E. Intramuscular introduction of medicines reducing the uterus.

9. A woman of 26 years had urgent physiological labor 10 months ago. She visited the maternity welfare centre with complaints of absence of menses. Breast feeding is on. At the bimanual examination the uterus is of the normal size, dense consistence, mobile, painless. Appendages are not determined.
What is the most probable diagnosis?
A. Physiological amenorrhoea.
B. Schihan's syndrome.
C. Pseudoamenorrhoea.
D. Ashermann's syndrome.
E. Pregnancy.

10. A woman of 35 years complains of absence of menses after the psychic stress. Menses are absent during one year. The diagnosis?
A. Epimenorrhoea.
B. Hypomenstrual syndrome.
C. Hyperpolymenorrhoea.
D. Psychogenic amenorrhoea.
E. Algodismenorrhoea.

Chapter 4
VIRIL SYNDROMES

1. A woman of 28 years old complains of absence of menses, growing of hair on the face, extremities. She is married. Menses since 14 years, scanty, in two years were stopped. Objective exam: body height — 160 cm, the body weight — 65 kg. Female constitution. The skin of normal colour and humidity. The growing of hair on the face as backenbards, on the upper lip, chin, forearms, hips, calfs by the man's type. External genitalia of a normal constitution. The uterus size is normal, ovaries at palpation are a little bit enlarged. The diagnosis:

A. Corticoandrosteroma.
B. Itsenko—Cushing's syndrome.
C. Adrenogenital syndrome.
D. Androsteroma.
E. Stein—Leventhal's syndrome.

2. A 23-year old infertile woman complains of a 2–6 month delay of menses. For last year her body weight has considerably increased. At inspection the growing of hair on the pubis by man's type, an exuberant pilosis of hips; the uterus of the normal size, ovaries are enlarged, dense at bimanual inspection, painless. The basal temperature is monophasal, the pupil's and fern signs are sharply positive. The probable diagnosis:

A. Adrenogenital syndrome.
B. Sclerocystic ovaries.
C. Inflammation of the uterine appendages.
D. Gonadal dysgenesis.
E. Itsenko—Cushing's syndrome.

3. A married woman of 26 years old complains of growing of hair on the face, extremities. Menses since 14 years, 5–7 days long, interval — 29–30 days, ovulatory. Objective exam: the growing of hair on the face as backenbards, on the upper lip, chin, forearms, hips, calfs by man's type. External genitalia are of normal constitution. The androgens level in the blood serum is normal. The probable diagnosis:

A. Adrenogenital syndrome.
B. Sclerocystic ovaries.
C. Idiopathic hyrsutism.
D. Gonadal dysgenesis.
E. Itsenko—Cushing's syndrome.

4. A woman of 21 years old complains of amenorrea. She is married. In the anamnesis — one spontaneous abortion. Menses since 14 years, 5–6 days long, interval — 31 days, anovulatory. Objective exam: hypertrichosis, acne vulgaris, the hair growing on the hips, upper extremities. External genitalia are of normal constitution. The level of the androgens is increased. After dexamethasone test — decreasing of dehydroepiandrosterone in the serum and 17-corticosteroids in the urine. The probable diagnosis:

A. Postpubertal adrenogenital syndrome.
B. Sclerocystic ovaries.
C. Idiopathic hyrsutism.
D. Gonadal dysgenesis.
E. Itsenko—Cushing's syndrome.

5. A woman of 24 years old complains of amenorrea. She is married. In anamnesis — one spontaneous abortion. Menses since 14 years, 5–6 days long, interval — 31 days, irregular, anovulatory. Objective exam: hypertrichosis, acne vulgaris, the growing of hair on the hips, upper extremities. What are the most probable reasons of clinical signs of hyperandrogenemia?

A. Hyperproduction of androgens, relapsing of testosterone-linking globulin, increasing of enzyme activity of androgen receptors.
B. Hypersecretion of oestrogens by tissues, excessive transformation of preandrogens from fatty tissue.
C. Poor aromatization of preandrogens owing to hypothyroidism. The elevated contents of FSH.
D. Oversecretion of androgens by the cortex of adrenals, increased content of prolactin.
E. Hyperproduction of testosterone-linking globulin, decreasing of enzyme activity of androgen receptors.

6. A woman of 20 years old complains of irregular menstruations. Menses since 13 years, 7 days long, interval — 29 days, irregular, anovulatory. Objective exam: hypertrichosis, the hair growing on the hips, upper extremities. The uterus is without changes, both ovaries are enlarged, painless, mobile. In the blood test there is significant decrease in cortisole level. After corticotrophin test — increase in 17-α-hydroxyprogesterone.

The probable diagnosis:

A. Postpubertal adrenogenital syndrome.
B. Sclerocystic ovaries.
C. Idiopathic hyrsutism.
D. Congenital adrenogenital syndrome.
E. Itsenko—Cushing's syndrome

7. A woman of 25 years old complains of irregular menses, weakness. Menses since 14 years, 5–6 days long, interval — 31 days, anovulatory, nullipara. Objective exam: obesity, hypertrichosis, stria gravidarum on the anterior abdominal wall, mammary glands, hair growing on the hips, upper extremities. Pulse 82 b/min, the body temperature — 36.6°C, AP 130/90. External genitalias of normal constitution. At internal examination the uterus is without changes, both ovaries are enlarged, painless, mobile. After the dexamethasone test (1 mg, 23.00) — no

change of cortisole level in the next morning urine (8.00). The probable diagnosis?

A. Postpubertal adrenogenital syndrome.
B. Sclerocystic ovaries.
C. Idiopathic hyrsutism.
D. Congenital adrenogenital syndrome.
E. Itsenko—Cushing's syndrome.

8. A woman of 26 years old complains of irregular menses. Menses since 13 y. o., 5–6 days long, interval — 29 days, anovulatory, nullipara. Objective exam: obesity, hypertrichosis, the hair growing on the hips, upper extremities. External genitalia of normal constitution. The uterus — without changes, both ovaries are enlarged, painless, mobile. The level of androgens in the serum and 17-corticosteroids in the urine are increased. The test of night suppression of cortisole level is negative. What is the most adequate additional examination?

A. Pelvic ultrasound.
B. X-ray examination of the skull.
C. CT-scanning of suprarenal gland.
D. Ultrasound examination of suprarenal gland.
E. Gonadotrophins level in the serum.

9. A woman of 26 years old complains of irregular menses. Menses since 13 years old, 5–6 days long, interval — 29 days, anovulatory, nullipara. Objective exam: obesity, hypertrichosis, growing of hair on the hips, upper extremities. External genitalia of normal constitution. The uterus without changes, both ovaries are enlarged, painless, mobile. Ultrasound examination: enlarged ovaries, 7 follicular cysts, increased density of their stroma. Ratio LH/FSH = 2.4 in the serum. What is the most probable diagnosis?

A. Postpubertal adrenogenital syndrome.
B. Polycystic ovarian syndrome.
C. Idiopathic hyrsutism.
D. Congenital adrenogenital syndrome.
E. Itsenko—Cushing's syndrome.

10. A woman of 26 years old complains of irregular menses, sudden intensive hair growth on the face, upper extremities, hips. Menses since 12 y. o., 3–5 days long, interval — 28 days, irregular last 6 months; 1 labor, 1 artificial abortion. Objective exam: hypertrichosis, excessive growing of hair; mail voice type. External genitalia of normal constitution. At internal examination the uterus — without peculiarities, in the region of the left ovary — a tumour-like mass, 7 cm in diameter, of hard density, mobile, painless. What is the most probable plan of treatment?

A. Anti-inflammatory treatment.
B. Surgical treatment.
C. Hormonal treatment.
D. Ionizing radiation treatment.
E. Chemotherapy.

Chapter 5
NEUROENDOCRINE SYNDROMES

1. A 3 week aged girl suffers from multiple "projectile" vomiting, not connected with nutrition, periodically infrequent defecation, a decrease of the body weight. At exam: the child is dehydrated, weak. Hypertrophy of the clitoris attracts attention. What disease is meant?

A. Acute intestinal infection.
B. Pylorostenosis.
C. High intestinal obstruction.
D. True hermaphroditism.
E. Congenital adrenogenital syndrome, salt-loosing form.

2. A patient of 26 years old has addressed to the gynaecologist with complaints of tightening and tenderness of breasts, oedema of the face and shins, abdominal distention, irritability, sweating. She consideres herself to be ill within 3 years. The signs occur at the second phase of the menstrual cycle and stop after the next menses. In the course of time severity of clinical signs does not aggrivate. At gynaecologic exam the pathological changes are not revealed. What form of the premenstrual syndrome is the most probable?

A. Cephalgic.
B. Psychologic.
C. Crisis.
D. Edematic.
E. Atypical.

3. A woman of 30 years old with complaints of infrequent, scanty menses, absence of pregnancy for 6 years. Menses since 17 years, irregular, with delays from 30 to 60 days. At exam — the adult male pattern of hair distribution, excessive body weight. At bimanual exam: the reduced uterus, painless. Ovaries from both sides are enlarged, of dense consistence. Ultrasound reveals small ovarian cysts, the size of 6.0 × 4.5 mm and 5.5 × 4.5 mm, with a dense capsule. The basal temperature is monophasal. What is the most probable diagnosis?

A. Polycystic ovarian syndrome.
B. Follicular cysts.
C. Bilaterial adnexitis.
D. Cysts of the corpus luteum.
E. Ovarian cancer.

4. A 16-year old girl has a primary amenorrhoea, absence of hair-growing in the armpits and on the pubis, normal development of breasts, a genotype 46XY, absence of the uterus and the vagina. The diagnosis:

A. Rokitansky—Küster syndrome.
B. Testicular feminization syndrome.
C. Itsenko—Cushing's syndrome.
D. Shihan's syndrome.
E. Itsenko—Cushing's disease.

5. A 24-year old woman after labor has addressed to the doctor with complaints of absence of menses within 6 months. The first pregnancy was finished with the caesarian section under indications: premature detachment of a normally posed placenta, intrauterine asphyxia of the fetus. The haemorhage was 2,000 ml.

The most informative exam:
A. Definition of the gonadotrophins level.
B. Definition of the prolactin level in the blood.
C. Progesterone test.
D. Definition of the thyroid hormone level.
E. Definition of the testosterone level in the blood.

6. A woman of 30 years old complains of the absence of menses during 2 years after labor. Labor have become complicated by a massive bleeding. After labor the patient has noted falling of hair, weight loss. At bimanual exam the uterus is reduced, vulvar lips are hypoplastic. Specify the etiological factor of complication:
A. An age involution of hypothalamic structures.
B. Hereditary factor.
C. Simultaneous deenergizing of function of ovaries.
D. A long stimulation of ovulation.
E. Necrotic changes in the adenohypophysis owing to haemorhagic shock in labor.

7. A patient complains of the irregular menstrual cycle, substantial growth of the body weight, hirsutism, infertility. At bimanual exam the uterus is a little bit less than normal, dense from both sides, mobile painless ovaries with the size of 4 × 5 × 4 cm are defined. What pathology is meant?
A. Bilateral ovarian cysts.
B. Bilateral chronic adnexitis.
C. Tuberculosis of uterine appendages.
D. Polycystic ovarian syndrom.
E. Ovarian endometriosis.

8. A woman of 20 years old has addressed with complaints of periodic delays of menses after the beginning of sexual life from 2 about 4 months. The excessive pilosis of the anterior abdominal wall, breasts, legs has appeared. Last year she's gained 14 kg. Exam revealed: the cervix is conic, the fauces are closed, the epithelium is intact. The body of the uterus is in the anteflexio position, a little reduced, mobile, painless. From both sides from the uterus the ovaries with the size of 4 × 6 cm, painless, dense are palpated. Fornices of the vagina are deep. Discharge are mucous. The probable diagnosis?
A. Itsenko—Cushing's syndrome.
B. Ovarian adenoblastoma.
C. Simmonds—Shihan's syndrome.
D. Stein—Leventhal's syndrome.
E. Adrenogenital syndrome.

9. A woman of 27 years old has addressed with complaints of irregular menses, infertility during 4 years. Obesity, hypertrichosis are marked. At bimanual exam: a small uterus, enlarged and dense ovaries. The basal temperature is monophase. The diagnosis?
A. Genital tuberculosis.
B. Polycystic ovarian syndrome.
C. Shihan's syndrome.
D. Simmonds' syndrome.
E. Adrenogenital syndrome.

10. After 3 days after clomephene citrate withdrawel a patient has an abdominal pain, nausea, vomiting, meteorism, malaise, dyspnea. Objective exam: muscle tension of the anterior abdominal wall, enlarged painful ovaries. ABP falls, tachycardia is defined. Specify pathogenesis of the complication:
A. Ovarian hyperstimulation.
B. Ovarian inflammation.
C. Intra-abdominal bleeding.
D. The DIC syndrome.
E. Pulmonary embolism.

Chapter 6
INFERTILITY

1. A woman of 26 years old has addressed with complaints of infertility within 3 years. In the anamnesis: menses since 14 years, painless, moderate. The cycle 4–5/28, regular. At the age of 16 years had appendectomy. Postcoital test and analysis of the husband's sperm within the norm. According to the basal temperature data the cycles are ovulatory, the lutein phase makes 12–14 days. Define the most expedient method of diagnosis:
A. Laparoscopy and chromosalpingography.
B. Hysteroscopy.
C. Colposcopy.
D. Endometrial biopsy.
E. Hysterosalpingography.

2. 150. A woman of 28 years old has addressed to the gynaecologist with complaints of infertility. From the anamnesis: in marriage for 6 years, the first pregnancy occured at the first year of marriage and completed with the artificial abortion which has become complicated by inflammation of the uterus. The menstrual cycle disorders were not noticed. There were pregnancies no more. What exam should be carried out?

A. Spermogramma.
B. Metrosalpingography.
C. Tests of function diagnosis.
D. Hormonal analysis of the blood on the 7th–8th day of the cycle.
E. Bacteriologicalal investigation of discharge from the reproductive tract.

3. A 25-year old woman visited the maternity welfare centre with complaints of infertility. She is married for 1 year, does not use contraceptives. From anamnesis it is known, that it was repeatedly treated in the gynaecological department concerning exacerbations of chronic adnexitis. What is the diagnosis?
A. Secondary infertility.
B. Chronic adnexitis.
C. Initial infertility.
D. Ovarian apoplexy.
E. Pelviperitonitis.

4. A 18 year old woman complains of absence of pregnancy during 1 year of the regular sexual life. From pregnancy she did not preserved. Pregnancies were absent. At bimanual exam no pathology is revealed. What method of evaluation should be used?
A. Spermogramma.
B. Hysterosalpingography.
C. Laparoscopy.
D. Tests of function diagnosis.
E. Bacterial inoculation.

5. A patient of 29 years old with complains of infertility. Sexual life in the marriage for 4 years, did not preserve from pregnancies. Pregnancies were absent. At exam of the woman it is revealed: development of genitalia without deviations from the norm. The Fallopain tubes are passable. The basal temperature during three menstrual cycles is single-phase. The most probable cause of infertility?
A. Anovulatory menstrual cycle.
B. Chronic adnexitis.
C. Anomalies of development of genitalia.
D. Immunological infertility.
E. Genital endometriosis.

6. A woman complains of the irregular menstrual cycle within 2 years. Duration of the menstrual cycle is 30–50 days. During one year there were no pregnancies. What exam should be appointed first of all for specification of the causes of infertility?
A. Laparoscopy.
B. Spermogramma of the sexual partner.
C. Measuring basal temperature.
D. Postcoital test.
E. Hysteroscopy.

7. A patient of 29 years old with 3 still pregnancies in the anamnesis, during last 3 years hasn't become pregnant. What is it necessary to do for revealing the cause of the given pathology?
A. Bacteriological investigation of the vaginal contents.
B. Inspection on syphilis.
C. Inspection on tuberculosis.
D. Clinical blood analysis.
E. Inspection on TORCH-infection, medicogenetic consultation.

8. A patient of 28 years old with complaints of infertility within 2 years has arrived to the gynaecological department. From the anamnesis: 3 induced abortions, the menstrual cycle without features. The husband is examined — spermogramma is normal. What method should be carried out the first?
A. Metrosalpingography.
B. Laparoscopy.
C. A stimulation of ovulation.
D. Courses of hydrotubation.
E. Insemination with the donor's sperm.

9. A woman visited the doctor with complaints of infertility. The basic signs: obesity, hirsutism, hypomenstrual syndrome. At pelvic ultrasound endometrial hyperplasia is revealed. The sign of which condition is the given conclusion?
A. Persistence of the corpus luteum.
B. Inflammatory process of the endometrium.
C. Chronic anovulation.
D. Hypothyroidism.
E. Endometrium in the norm.

10. A women of 28 years old with complaints of the secondary infertility at a diagnostic laparoscopy is fixed internal endometriosis. In the anamnesis — chronic salpingo-oophoritis. The most probable pathogenetic factor of infertility at the given woman is:
A. A local secretion of prostaglandins.
B. Infringement of hydrocortisone synthesis in the adrenal glands.
C. A thickening of the ovarian tunica albuginea.
D. A congenital underdevelopment of genetalia.
E. Rising of cervical mucosa viscosity.

Chapter 7
ENDOMETRIOSIS

1. A patient of 38 years within 3 years complains of painful menses, bloody brown discharge before and after menses. In the anamnesis 5 induced abortions. At examination the uterus mild consistence, tender, a little bit enlarged, circumscribed mobile. At ultrasound the myometrium is granular, honey comb. The diagnosis?

A. Adenomyosis.
B. Hysteromyoma.
C. Endometriosis.
D. Dysfunctional uterine bleeding.
E. Endometrial polyps.

2. A patient of 35 years visited the gynaecological department with complaints of periodic pains in the lower abdomen which strengthen during menses, dark brown discharge from the reproductive tract. At the bimanual examination: the uterus a little bit enlarged, appendages are not determined. At exam of the cervix in specula cyanotic "eyes" are found. What diagnosis is the most probable?
A. Cervical fibroid.
B. Cervical anabrosis.
C. Cervical polyp.
D. Cervical cancer.
E. Cervical endometriosis.

3. A woman of 34 years complains of bloody discharge from the reproductive tract some days before the menses. In the anamnesis — diathermocoagulation 2 years ago. At exam of the cervix in specula cyanotic "eyes" are revealed. For confirmation of the diagnosis it is necessary to appoint:
A. Laparoscopy.
B. Smear for cytologic examination.
C. Colposcopy.
D. Cervical biopsy.
E. Pelvic ultrasound.

4. A patient complains of pain in the lower abdomen which intensifies during menses and coitus and irradiates to the vagina. From the anamnesis: 2 years ago endometriosis was suspected. At the bimanual examination — to the back from the uterus the dense, nodular, tender masses are determined. The preliminary diagnosis?
A. Retrocervical endometriosis.
B. Adenomyosis.
C. Cervical endometriosis.
D. Chronic inflammation of the uterine appendages.
E. Parametritis.

5. Colposcopy revealed endometriosis of the vaginal part of the cervix. What, in your opinion, is the most justified policy of treatment?
A. Hysterectomy with appendages.
B. Cervical diathermocoagulation.
C. Laser vaporization of the endometriosis loci.
D. Supravaginal ablation of the uterus.
E. Anti-inflammatory treatment.

6. A patient of 25 years old has addressed to the doctor with complaints of long painful menses, with long premenstrual discharge, infertility during 5 years. At exam of the cervix in specula —the "eyes" type inclusions. The preliminary diagnosis?
A. Endometriosis.
B. Menstrual cycle disorder.
C. Cervical erosion.
D. Cervical cancer.
E. Cervical polyp.

7. During the last 10 years a woman of 42 years has menses by type of hyperpolymenorrhoea and progressing algodysmonorrhoea. Vaginal examination revealed unchanged cervix, moderate chocolate discharge, the enlarged uterus, tuberous, little bit painful, appendages are not palpated, fornices are deep, painless. What is most probable diagnosis?
A. A submucous fibromyoma of the uterus.
B. Endometrial cancer.
C. Uterine endometriosis.
D. Endometritis.
E. Endometriosis of the appendages.

8. A patient of 32 years complains of a nagging pain in the lower abdomen, it is especially before and during menses, brown discharge before menses. At the bimanual examination the uterus is little bit enlarged, more in the isthmical area, painful at palpation, a spherical form. Appendages from both sides without features. The preliminary diagnosis — endometriosis. The most informative method for diagnosis of the given disease:
A. Laparoscopy.
B. Hysterosalpingography.
C. Colposcopy.
D. Culdoscopy.
E. Bimanual examination.

9. A patient of 32 years complains of a nagging pain in the lower abdomen, in particular before and during menses, "spotting" brown discharge before menses. At the bimanual examination the uterus a little bit enlarged, more in the isthmical area, painful at shifting, of a spherical form. Appendages from both sides without features. The most probable diagnosis?
A. Uterine fibromyoma.
B. Internal endometriosis.
C. Dysfunctional uterine bleeding.
D. Endometrial cancer.
E. Incomplete abortion.

10. A 28-year old patient complains of abundant, painful and long-term menses. Before and after menses during 4–6 days it is observed bloody discharge. At the bimanual examination: the uterus is enlarged corresponds to 5–6 weeks of pregnancy, circumscribed, mobile, tender. Appendages are not palpated. At exam in dynamics for 15th day of the menstrual cycle the uterus is of the normal size, painless. On the establishment of complaints and objective examination it is diagnosed internal endometriosis. Appoint treatment.

A. Sinestrol.
B. Dufaston.
C. Parlodel.
D. Ovidon.
E. Folliculin.

Chapter 8
DEVELOPMENTAL DISORDERS OF THE REPRODUCTIVE SYSTEM

1. A 18-year old woman has addressed to the doctor with complaints of absence of menses, monthly abdominal pains. Sexual life is not present. At exam: breasts and external genitalia are developed correctly, the hair growth by the female type. The orifice in the vagina is closed by mucosa of cyanotic colour which is a little stuck out. At rectal investigation the uterus and appendages without pathology, in range of the vagina elastic mass is palpated. The most probable diagnosis?
A. Overgrowing of the hymen.
B. Vaginal aplasia.
C. The Gartner's cyst.
D. Vulvar haematoma.
E. Vaginal atresia.

2. A patient of 15 years old complains of absence of menses, periodic abdominal pain. At exam of the external genitalia: the hair by female type, the large pudendal lips are developed normally, cover the small pudendal lips, the orifice to the vagina is closed by the septum of cyanotic-crimson colour which sticks out. The diagnosis:
A. Vulvar endometriosis.
B. Atresia of the hymen.
C. Genital infantilism.
D. Amenorrhoea of unknown ethiology.
E. Ovarian dysfunction.

3. A 18 year old girl has visited the doctor of the maternity welfare centre with complaints of impossibility of the sexual life, absence of menses. The patient with a normal constitution, the secondary sexual characters correspond to the age. At exam: external genitalia are in the norm, the vagina is absent. At rectoabdominal exam: the uterus is not found out, at its place transversal band is palpated. The uterine appendages are not changed. The karyotype — 46XX. What is the diagnosis?
A. Aplasia of the ovaries.
B. Aplasia of the vagina and uterus.
C. Testicular feminization.
D. Gonadal dysgenesis.
E. Atresia of the hymen.

4. A 7-year old girl addressed to the gynaecologist with complaints of bloody discharge from genitalia, sudden intensive hair growth in the pubic region and growth of mammary glands. Ultrasound examination revealed the tumour in the region of right ovary, 9 cm in diameter, unicameral. What is the diagnosis?
A. Premature incomplete sexual development, ovarian origin.
B. Premature sexual development, central origin.
C. Premature sexual development, suprarenal origin.
D. Testicular feminization.
E. Gonadal dysgenesis.

5. A 16-year old girl addressed to the gynaecologist with complaints of absence of menses. In anamnesis — acute meningitis at 5 years old. At objective examination: height — 170.0 cm, relatively short trunk, hypoplasya of the mammary glands. Level of gonadotrophins in the serum and urine is decreased, osseal age corresponds to the calendar. Diagnose is retardation of sexual development of the central origin. What is the most adequate treatment:
A. Oestrogens during one month.
B. Progestagens during three months.
C. Oestrogen-gestagen complex during three months.
D. Vitamin therapy.
E. Physiotherapy.

6. A 15-year old girl addressed to the gynaecologist with complaints of absence of menses. At objective examination: infantile body type, hypoplasya of the mammary glands. Level of gonadotrophins in serum and urine is decreased, osseal age is less than calendar. At ultrasound — hypoplasya of genitalia. Gonadotrophins level is strongly increased in the serum, oestrogen level — decreased. What is the most probable diagnosis:
A. Itsenko—Kushing's syndrome.
B. Retardation of sexual development of the central origin.
C. Retardation of sexual development of the ovarian origin.
D. Sexual infantilism.
E. Adrenogenital syndrome.

7. 15-year old girl addressed to the gynaecologist with complaints of algodysmenorrhoea. Menses since 14 year old, 1–2 days long in 28 days interval. At objective examination: normal body type, hypoplasya of the mammary glands. Level of gonadotrophins in serum and urine is decreased, osseal age is less than the calendar one. At ultrasound — uterus infantilis 3.5 cm, cervix/body ratio 3 : 1. What is the most probable diagnosis?

A. Itsenko—Kushing's syndrome.
B. Retardation of sexual development of central origin.
C. Retardation of sexual development of ovarian origin.
D. Sexual infantilism.
E. Adrenogenital syndrome.

8. A 16-year old girl addressed to the gynaecologist with complaints of algodysmenorrhoea. Menses since 14 years old, 1–2 days long in 28 days interval. At objective examination: normal body type, hypoplasya of the mammary glands. Level of estrones and progesterone is decreased in serum. Content of sexual chromatin and cariotype is normal. At ultrasound — uterus infantilis 3.5 cm, cervix/body ratio 3 : 1. What is the most probable diagnosis:
A. Polycystic ovarian syndrome.
B. Gonadal disgenesis, clear form.
C. Retardation of sexual development of ovarian origin.
D. Sexual infantilism.
E. Adrenogenital syndrome.

9. A 16-year old girl addressed to the gynaecologist with complaints of algodysmenorrhoea. Menses since 14 year old, 1–2 days long in 28 days interval. At objective examination: normal body type, hypoplasya of the mammary glands. Level of oestrones and progesterone is decreased in serum. Content of sexual chromatin and cariotype is normal. At ultrasound — uterus hypoplastic, 5 cm length, normal cervix/body ratio. Complex treatment should include the listed below, except:
A. Cyclic replacement oestrogen-gestagen complex therapy.
B. Physiotherapy.
C. Physical exercises.
D. Balneal therapy.
E. Coneform resection of ovaries.

10. A 16-year old girl addressed to the gynaecologist with complaints of algodysmenorrhoea. Menses since 14 years old, 1–2 days long in 28 days interval. At objective examination: normal body type, hypoplasya of the mammary glands, justo minor pelvis. Level of estrones and progesterone is decreased in serum. Content of sexual chromatin and cariotype is normal. At ultrasound — uterus fetalis, 2 cm length. What is the prognosis for reproductive function?
A. Unfavorable.
B. Favorable.
C. Favorable in case of cyclic replacement oestrogen-gestagen complex therapy.
D. Favorable in case of physiotherapy.
E. Favorable in case of reflex therapy.

Chapter 9
ANOMALIES OF POSITION OF THE FEMALE GENITALIA

1. A patient of 14 years old complains of heaviness and pain in the lower abdomen, intensifyed. For the first time such sensations have appeared 3 months ago. Body height 155 cm., weight 40 kg. The sexual formula — A×2 P2 Ma2 Me0. At exam of the external genitalia the diverticulum of the hymen with dark contents of the vagina is revealed. What anomaly of generative organs is meant?
A. Artesia of the vagina.
B. The septum of the vagina.
C. Overgrowing of the hymen.
D. Hypoplasia of the labia pudendi.
E. Synechias of the vulva.

2. A 14-year old girl with algodismenorrhoea according to ultrasound data was established the diagnosis: an additional functioning uterine horn with infringement of outflow. The method of treatment:
A. Erasion of the additional horn of the uterus with the ovary.
B. Treatment with gestagens.
C. Treatment with oestrogens.
D. Hysterectomy.
E. Laparotomy. Erasion of the additional horn of the uterus.

3. A girl of 13 years old complains of abdominal pain with an interval of 24–30 days that is accompanied by vomiting, subfebrile temperature. At intubation of the vagina the probe passes only 1 cm. Ultrasound reveals a tumour-like mass outside from the rectum. The diagnosis:
A. Atresia of the vagina, hematocolpos.
B. Paraovarian oothecoma.
C. A tumour of the ovary.
D. Ingenious endometriosis.
E. Initial algodismenorrhoea.

4. A woman of 24 years old complains of abdominal pain betweem menstruations, algodismenorrhoea, constipations. In anamnesis — chronic inflammatory disease of genitalia, spontaneous abortion. At bimanual examination — retrodeviation of the uterus. Normal enforced replacement of the uterus is impossible. What is the most adequate procedure to conduct differential diagnosing:
A. Laparoscopy.
B. Ultrasound examination.
C. Hysteroscopy.
D. Hysterosalpingography.
E. Culdoscopy.

5. A patient of 55 years old has addressed to the gynaecologist with complaints of constant nagging

pain in the lower abdomen, difficulty of urination. In the anamnesis one labor with a large fetus which has become complicated by perineal rupture of II degree. The somatic anamnesis is not burdened. Postmenopause lasts for 4 years. The gynaecologic status: there are disjointed pedicles of the muscles lifting the anus; at staining effort outside the vulvar ring the uterus is defined, enlongated and hypertrophic cervix. The anterior and posterior walls of the vagina are lowered. The diagnosis:

A. Inversion of the uterus.
B. An incomplete prolapse of the uterus, failure of the muscles of the pelvic floor, enlongated cervix.
C. A complete prolapse of the uterus, failure of muscles of the pelvic floor, enlongated cervix, cysto- and rectocele.
D. Ptosis of the vagina's walls, failure of muscles of the pelvic floor.
E. Elogation of the cervix, cysto- and rectocele.

6. A patient of 55 years old has addressed to the gynaecologist with complaints of constant nagging pain in the lower abdomen, difficulty of urination. In the anamnesis one labor with the large fetus which has become complicated by perineal rupture of II degree. The somatic anamnesis is not burdened. Postmenopause lasts for 4 years. The gynaecologic status: there are disjointed pedicles of the muscles lifting the anus; at staining effort outside the vulvar ring the uterus is defined, enlongated and hypertrophic cervix. The anterior and posterior walls of the vagina are lowered. What policy of treatment of the patient?

A. Constant bandage wearing, medical gymnastics directed on strengthening of muscles of the pelvic floor.
B. Use of a pessary (the uterine ring).
C. Laparotomy, hysterectomy with appendages.
D. Vaginal hysterectomy, anterior and back colporrhaphy, levators plasctics.
E. Amputation of the cervix, colpoperineorrhaphy.

7. A women of 60 years in the anamnesis of 2 labor with newborns' weight 4,500 and 4,800, hard physical job. Complaints of often urination, nagging pains in the lower abdomen and in the loin. At physical load a tumour-like mass appear from the pudendal fissure which is easily replaced. It is impossible to bring fingers together above the perineum near the vagina. The diagnosis:

A. A complete prolapse of the uterus.
B. An incomplete prolapse of the uterus, cystocele.
C. A cyst of the Gartner's duct.
D. Bearing myomatous node.
E. A cyst of the Bartholin's gland.

8. In a woman of 45 years who works as a house painter, ptosis of the vaginal walls of the II degree is revealed at vocational exam. The cause of disease:

A. Erosion of the cervix.
B. A birth trauma.
C. Inflammatory disease of the vagina.
D. Hard physical job.
E. Intestinal disorder.

9. A woman of 62 years old complains of difficulty at urination and defecation, a diverticulum from the pudendal fissure which hinders walking. Menses are abundant. The gynaecologic status: a tumour on which inferior pole the os is seen, pouches out from the pudendal fissure. The tumour's walls remind a mat-glittering dry skin, some ulcers are visible. In the tumour a part of the uterus which completely leaves the pudendal fissure is palpated. The diagnosis:

A. Cervical prolaps with decubituses.
B. Ptosis of the anterior wall of the vagina.
C. An incomplete prolapse of the uterus with cervical ulcers.
D. A complete prolapse of the uterus with decubital ulcers.
E. Prolaps of the posterior wall of the vagina.

10. A woman of 24 years old complains of algodismenorrhoea, constant pelvic pain, dispareunia. Menses since 14 year old, 2–3 days, 28 day interval, regular, painful; infertility during two year marriage. In the anamnesis — chronic inflammatory disease of genitalia. At bimanual examination — acute angle between the uterine body and cervix, reduction of sizes of the uterus, flat vaginal fornices. What is the primary step of treatment?

A. Anti-inflammatory therapy.
B. Surgical treatment.
C. Hormonal therapy.
D. Analgesics.
E. Physiotherapy.

Chapter 10
BACKGROUND AND PRECANCER DISEASES OF THE FEMALE GENITALIA

1. In a woman of 45 years old the cytological investigation of the vaginal smears revealed pelvic displasy of the mild degree, at colposcopy — a zone of transformation, clinical colpitis is not present. Appoint the treatment:

A. Chemical coagulation of the cervix of the uterus.
B. Cervical conization.
C. Cervical criodestruction.

D. Radical hysterectomy.
E. Amputation of the cervix.

2. In a 38-year old woman at cytological investigation of the vaginal smears non-typical cells are not revealed. Non-typical cells are revealed in the smears from the cervical channel. Policy of the doctor:
A. To repeat the smear for non-typical cells in 3 months.
B. To repeat colposcopy in 3 months.
C. Cervical conization.
D. Vaginal hysterectomy.
E. The further observation is not necessary.

3. A 25 year old patient has addressed with complaints of the intensification of the vaginal discharge during 2 months. 2 years ago in the anamnesis there were labor which have become complicated by the cervical rupture. At exam in specula: the cervix is of a cylindrical form. On the anterior lip an erosioned surface is defined, which isn't bleeding when touched. Bimanually — painless displacement of the cervix. A tip of a finger passes through the external os. The uterus is of the usual sizes, mobile, painless. The probable diagnosis:
A. Cervical erosion.
B. Cervical cancer.
C. Decubital ulcer.
D. Leykoplakia.
E. Cervical polyp.

4. A 22-year old patient visited the maternity welfare centre with complaints of contact bloody vaginal discharge which has noticed after the sexual intercourses within last two weeks. Survey of the cervix and the vagina in specula: the cervix is of a conic form, the external os is dotty, bloody discharge. On the anterior lip of the cervix it is defined the erosioned surface of the sizes of 0.5–1 cm; at contact bleeds. Cytology — type II. The II degree of vaginal cleanliness. The method of treatment:
A. Criodestruction.
B. Diathermcoagulation.
C. Laser therapy.
D. Extirpation of the uterus with appendages.
E. Chemotherapy

5. In a 30-year old pregnant woman on the cervix a crimson spot up to 1 cm which is not painted by the Lugol's solution is revealed, at a touch does not bleed. What additional investigation is indicated?
A. Biopsy.
B. No examinations.
C. Inspection is possible only after labor.
D. Diagnostic excision of the cervix.
E. Colposcopy.

6. In a woman of 46 years at annual cytologic investigation of vaginal smears dysplasia of mild degree was revealed. The data of colposcopy: precise transition of the squamous epithelium into the cylindrical one. What should the doctor appoint?
A. Cervical diathermoconization.
B. Fractional diagnostic curettage of the uterine mucosa.
C. Cervical biopsy.
D. Cervical cryodestruction.
E. Anti-inflammatory therapy.

7. In a 32-year old woman the cervical exam revealed hyperemy of the cervical channel and vaginal part of the uterus. With the help of what method is it possible to establish a pathology of the cervix?
A. Separate diagnostic scraping of the uterine mucosa.
B. Culdoscopy.
C. Colpocytology.
D. Colposcopy with biopsy and the subsequent histological study.
E. Ultrasound study.

8. A patient of 40 years old complains of contact bloody vaginal discharge. Gynaecological exam: the cervix is erosioned, hypertrophic, deformed owing to postnatal ruptures, the external os gaps. The uterus and appendages without pathologicalal changes, parametries are free. Expanded colposcopy revealed the extensive zone of transformation with a plenty open and closed glands, a site of ectopy on the anterior lip, leukoplakia — on 12 o'clock. What treatment is necessary to recommend to the patient?
A. Local application of tampons with the ointments containing antibiotics and preparations, increasing regenerative ability of the epithelium.
B. Processing of the cervix with a beam of the helium-neon laser.
C. Electrosurgery or cryogenic treatment.
D. Surgical treatment.
E. Supervision.

9. A woman of 32 year sold complaints of leukorrhoea, irritation, itching of vulva, pain in the lower abdomen, dispareunia, disuria. At exam of the cervix of the uterus in specula it is revealed the looseness, fragility, icreased vascularisation, infection of glands of vaginal part of the uterus. In bacteriological investigation *Staphylococcus epidermicus and Chlamidia trachomatis* are revealed. What treatment is necessary to recommend to the patient?
A. Anty-inflammatory treatment.
B. Processing of the cervix with a beam of the helium-neon laser.
C. Electrosurgery or cryogenic treatment.
D. Surgical treatment.
E. Supervision.

10. A woman of 51 year old with dysfunctional uterine bleeding was conducted the separate curettage of uterine mucous. The data of histological examination — atypical hyperplasia of the endometrium. What method of treatment is it necessary to choose?

A. Total hysterectomy with bilateral adnexectomy.
B. Progesteron therapy.
C. Hysterectomy without appendages.
D. Gonadoliberin agonists therapy.
E. Cryodestruction of the endometrium.

Chapter 11
BENIGN TUMOURS AND TUMOUR-LIKE CONDITIONS OF THE FEMALE GENITALIA

1. A patient of 46 years old complains of often urination. The urinary system is without pathology. Bimanual exam: the uterus is enlarged up to 14 weeks of pregnancy, multiple myomatous nodes, on the anterior wall of the uterus — a node up to 8 cm in diameter is defined. The appendages are not defined. The discharge are mucous, moderate. The data of the histological study of the mucosa of the cervical channel — a grandular polyp; the uterus — endometrial polyps. Colposcopy reveals the cervical ectropion. Choose the treatment mode:

A. Supravaginal amputation of the uterus without appendages.
B. Extirpation of the uterus with appendages.
C. Expanded extirpation of the uterus.
D. Supravaginal amputation of the uterus with appendages.
E. Extirpation of the uterus without appendages.

2. A woman of 38 years old complains of long and plentiful menses within a half-year, nagging pains in the lower abdomen, weakness. Gynaecologic exam reveals the enlarged uterus up to 11–12 weeks of pregnancy, dense, mobile, painless. In the analysis of blood — anaemia; Hb = 90 g/l. What pathology can be suspected?

A. A uterine myoma.
B. Endometrial cancer.
C. Pregnancy.
D. Cystoma of the uterus.
E. Dysfunctional uterine bleeding.

3. A 46-year old woman has addressed to the doctor with the diagnosis: uterine myoma. The menstrual cycle lasts for 30–50 days, with 7-day plentiful bleeding, intermenstrual bloody discharge. What method of inspection is not informative for definition of policy of the doctor?

A. Intravenous pyeloureterography.
B. Pelvic ultrasound.
C. General blood analysis.
D. Endometrial biopsy.
E. Hysterosalpingography.

4. A 47-year old woman visited the maternity welfare centre with complaints of plentiful menstruation. Last menstruation was 10 days ago. At gynaecologic investigation: the cervix of the uterus is of a cylindrical form, it is deformed by old postnatal ruptures, on the anterior lip — leukoplakia. The uterus is enlarged up to 14–15 weeks of pregnancy, with a rough surface, dense, mobile, painless. Appendages are not palpated. The fornices are deep. The discharge are mucous. What method of treatment is expedient for appointing?

A. Extirpation of the uterus.
B. Hormonal therapy.
C. Supravaginal amputation of the uterus.
D. Haemostatic therapy.
E. Conservative myomectomy.

5. A 40-year old woman complains of intensive pains during the menstruation which is accompanied with increased haemorhage. What disease is it typical for?

A. Subserous myoma.
B. Submucous myoma.
C. Retention tumour of the ovary.
D. Trophoblastic disease.
E. Ovarian cancer.

6. A 30-year old woman, suffering from infertility within 10 years, complains of plentiful, long menses, accompanying with intensive pains. At bimanual exam: the uterus is enlarged up to 8 weeks of pregnancy, appendages are not defined. The exam of the uterine cavity reveals its deformation. What is the most probable diagnosis?

A. Submucous uterine myoma.
B. Chronic endometritis.
C. Metrorrhage.
D. Algodismenorrhoea.
E. The uterine pregnancy.

7. A patient of 40 years old within one year pays heed to plentiful menses, accompanying with the intensive pains in the lower abdomen. During next menses it is made the vaginal exam: a mass with a diameter up to 5 cm of a dense consistence is defined in the channel of the cervix. The uterus is increased accordingly to 5–6 weeks of pregnancy of normal consistence, mobile, painful. The appendages are not defined. The discharge are bloody, plentiful. What diagnosis can be assumed?

A. Born submucous fibromatous node.
B. Abortion in the course.
C. Cervical cancer.

D. Cervical myoma.
E. Algodismenorrhoea.

8. A 47 year old patient suffers from hysteromyoma for 8 years, it was not treated. For last year the tumour has grown up to the size of 15-week pregnancy. Management of the doctor:
A. To make a diagnostic uterine curettage. Surgical treatment after the histological conclusion.
B. To make a diagnostic uterine curettage. Dispensary observation.
C. Urgent surgical treatment.
D. To appoint hormonal therapy.
E. Ultrasound dispensary observation.

9. In a women with infertility in the anamnesis the intramural fibromyoma with the size up to 6 cm which deforms the uterine cavity is revealed. What drug is more preferable at the conservative treatment?
A. Zoladex.
B. Depot-Provera 150 mg.
C. 17-pregnenoldione capronate.
D. Omnodren.
E. Diane 35.

10. A patient of 27 years with initial infertility visited the gynaecological department for surgical treatment concerning submucous hysteromyoma. Optimum extent of the operation?
A. Hysterectomy.
B. Defundation.
C. Supravaginal ablation of the uterus without appendages.
D. A conservative myomectomy.
E. Supravaginal ablation of the uterus, ovarian biopsy.

Chapter 12
MALIGNANT TUMOURS OF THE FEMALE GENITALIA

1. A patient of 70 years, who has been disturbed for many years by itching of the vulva, is determined an ulcer with the dense edges and a necrotic bottom on the labium majora. The Chrobak's test is positive. What disease is it typical for?
A. Vulvar cancer.
B. Craurosis of the vulva with secondary infection.
C. Syphilis.
D. Leukoplakia.
E. Tuberculosis cutis.

2. A patient of 45 years old has arrived with complaints of bloody discharge after the sexual intercourse. Within last 2 years watery vaginal discharge. At exam in specula the cervix is hypertrophic, there are growths bleeding at a touch. At the bimanual examination the uterus is a little enlarged, mobile, painless. Appendages are not determined. Fornices of the vagina, parametria are free. Discharge after survey are dark, bloody. The most informative examination:
A. Histological examination of the cervical bioptate.
B. Colposcopy.
C. Cytologic examination of smear.
D. Shiller's test.
E. Pelvic lympho- and vasography.

3. A patient of 31 years complains of steady spotting bloody discharge from the reproductive tract during last 3 months, contact bleedings. At the bimanual examination: the cervix is elongated, restricted in motility, dense at palpation. At exam in specula the crateriform ulcer at the center is determined. The Chrobak's test is positive. The most probable diagnosis:
A. Cervical cancer.
B. Erosion of the cervix.
C. Cervical polyp.
D. Cervical pregnancy.
E. Cervical leukoplakia.

4. A patient of 50 years complaints of leukorrhoea. Discharge strengthen after lifting weight. Gynaecologic examination reveals cervical ulcer covered by dirtly and grey membrane. Vaginal discharge with unpleasent odour. The probable diagnosis:
A. Cervical cancer.
B. Metaplasia of the cylindrical epithelium.
C. Senile colpitis.
D. Cervical erosion.
E. A hard ulcer.

5. A patient of 45 years. During carrying out of routine exam she does not show complaints. At colposcopy and carrying out the Shiller's probe a iodine-negative zone is revealed on the anterior labia of the cervix. The provisional diagnosis:
A. Cervical cancer.
B. Cervical polyp.
C. Senile colpitis.
D. Cervical erosion.
E. Leukoplakia.

6. A patient of 45 years complains of contact bleedings within last 5 months. At exam in specula: the cervix is hypertrophic, looks like a cauliflower, bleeds at a sond touch. At the bimanual examination: the cervix is of dense consistence. The uterus is not enlarged, mobile circumscribed. Appendages are not palpated, parametria are free. Fornices are deep. The most probable diagnosis?
A. Cervical cancer.
B. Hysterocarcinoma.

C. Born fibromatous node.
D. Cervical pregnancy.
E. Cervical polyps.

7. A patient of 59 years complains of whining, gnawing pain in the left-hand ileac area, in the leg, particularly at night. Urine and feces contain blood. At internal obstetric examination: the vagina is short; on the cervix a crater with necrotic masses is determined. Discharge have meat-slops color. In the small pelvis a tumour conglomerate of dense consistence which reaches the pelvic bones, fixed, and painful is determined. What most probable diagnosis?
A. Cancer of the urinary bladder.
B. Cervical cancer of the II stage.
C. Cancer of the rectum.
D. Cervical cancer of the III stage.
E. Cervical cancer of the IV stage.

8. The vagina is involved in the patient suffering from cervical cancer. A biopsy of this site has revealed the invasive squamous carcinoma. The vaginal examination of the parametral area presents the induration on the right, which does not reach the pelvic walls. Term the cancer stage:
A. I-a.
B. I-b.
C. II-a.
D. II-b.
E. IV-a.

9. In a patient with the invasive squamous cancer of the cervix, which is spread to the inferior third of the vagina, during examination the right-hand hydronephrosis is revealed. Determine the cancer stage:
A. I-a.
B. II-b.
C. II-a.
D. III-a.
E. IV-a.

10. A patient of 54 years is made cervical biopsy. Histological examination of the bioptate presents a pattern of squamous non-keratinizing cancer. Depth of invasion is 5 mm. Determine the extent and policy of treatment of the patient.
A. Cervical electroconization with the subsequent distant radial therapy.
B. The Werteheim's operation with the subsequent hormonal therapy.
C. Hysterectomy without appendages with the subsequent polychemotherapy.
D. The Werteheim's operation with the subsequent radial therapy.
E. A symptomatic treatment.

Chapter 13
TROPHOBLASTIC DISEASE

1. A woman of 45 years old complains of 2-month menstruation delay, nausea and vomiting, pain in the lower abdomen, bloody discharge from genitalia. The exam: external genitalia are cyanotic and edematic. The uterus is enlarged up to 12 weeks of pregnancy, round shape, homogeneous, mobile, painless, slightly contracts at palpation. Both ovaries are enlarged up to 8 cm. The level of β-CG is 8 times increased as compared to normal pregnancy. At ultrasound — a sign of "snow storm", cysts of both ovaries — 6 cm. What is the most probable diagnosis?
A. Ectopic pregnancy.
B. Missed abortion.
C. Incomplete abortion.
D. Placental polyp.
E. Hydatidiform mole.

2. A patient with 5-month menstruation delay visited the maternity polyclinic to be accounted at dispensary observation as a pregnant for the first time. At objective examination ABP — 145/90 mm, edema of lower extremities, protein in the urine — 0.126 g/l. The uterus is enlarged up to 36 weeks of pregnancy. At ultrasound examination — a sign of "snow storm", gigantic cysts of both ovaries. What should the treatment start from?
A. Removing of masses of hydatiform mole.
B. Treatment of gestosis.
C. Surgical treatment of ovarian cysts.
D. Hypotensive therapy.
E. Chemotherapy.

3. An incomplete hydatidiform mole was diagnosed in a patient of 37 years old with 4 month long menstruation delay. What method of removing of hydatidiform mole masses is preferable?
A. Vacuum aspiration.
B. Acute curettage.
C. Hysterectomy.
D. Digital removing.
E. Medicamentous.

4. A patient complains of bloody discharge, constant pain in the lower abdomen and sacrum region two months after removing of masses of hydatidiform mole. At exam: sizes of the uterus are increased up to 8 weeks of pregnancy, cysts in both ovaries of elastic consistence; high level of β-CG. What is the probable diagnosis?
A. Invasive hydatidiform mole.
B. Endometritis after removing of hydatidiform mole.
C. Chorionic polyp.
D. Ectopic pregnancy.
E. Acute adnexitis.

5. A patient is one month after removing of masses of hydatidiform mole. Complaints of bloody jelly-like discharge from genitalia, nausea, vomiting, discharge of colostrums from the mammary glands, constant pain in the lower abdomen, cough with bloody discharge . At exam: external genital organs are cyanotic and edematic, in the lower region of the vagina three elastic cyanotic protruding masses, 3–5 cm, sizes of the uterus are increased up to 8 weeks of pregnancy, the uterus is soft, limited in mobility. Content of CG in the serum — 800 IU. What is the most adequate method of treatment:

A. Surgical therapy.
B. Systemic chemotherapy.
C. Surgical therapy + chemotherapy.
D. Hormonal therapy.
E. Anty-inflammatory therapy.

Chapter 14
STATES OF EMERGENCY IN GYNAECOLOGY

1. A woman complains of suddenly arosen pains in the lower abdomen, irradiating to the anus, nausea, giddiness, bloody dark discharge from the reproductive tract within one week, a delay of menses for 4 weeks. Signs of peritoneal irritation are positive. In specula: cyanosis of the cervical and vaginal mucosa. At the bimanual examination the sign of a "floating uterus", diverticulum and painfulness of the posterior and dextral lateral fornices of the vagina are revealed. The most probable diagnosis:

A. Acute appendicitis.
B. Ovarian apoplexy.
C. Acute right-hand adnexitis.
D. Torsion of the ovarian tumour's pedicle.
E. Broken ectopic pregnancy.

2. A 24-year old woman complains of staining bloody vaginal discharge and pains in the dextral ileac area. In the anamnesis the irregular menstrual cycle. Last menses are 7 weeks ago. At the bimanual examination the uterus is not enlarged, painless. The titer of CG is 1,000. The management of the doctor:

A. Diagnostic laparoscopy.
B. Pelvic ultrasound.
C. Culdoscopy.
D. Repeated definition of CG in 24 h.
E. Repeated definition of CG in one week.

3. A woman of 17 years old complains of pains in the lower abdomen during 12 h, gradually increasing, weakness, giddiness. Menses since 14 years for 3–4/26–28. A delay of menses for 2 weeks. Sexual life within one year. From pregnancy did not preserved. The abdomen is intense. At the bimanual examination the uterus is slightly enlarged, shifting is painful. Appendages are not precisely contured, the posterior vault outpouches. Discharge from the reproductive tract are dark and bloody, scanty. The preliminary diagnosis?

A. Appendicitis.
B. Ovarian apoplexy .
C. Broken ectopic pregnancy.
D. Torsion of the oothecomas.
E. Sponteneous abortion.

4. A woman of 17 years is disturbed with an acute pain in the lower abdomen. 2 weeks menses delay. Sexual life within one year. She preserved from pregnancy by the interrupted sexual act. Objective exam: integuments are cyanotic. The body temperature 36.6°C, the blood pressure is 95/60 mmHg, Pulse is 90 b/min. At the bimanual examination slightly enlarged uterus, cervical excursions are painful, appendages are not precisely contured, the posterior vault outpouches. Discharge from the reproductive tract are dark-bloody, scanty. The most informative method:

A. Pelvic ultrasound.
B. Clinical blood analysis.
C. An abdominal puncture through the posterior vaginal fornix.
D. Colposcopy.
E. Laparoscopy.

5. A woman is disturbed with acute abdominal pains, the temperature is up to 38.0°C. She knows about presence of hysteromyoma within 3 years. Signs of peritoneal irritation are positive in the lower abdomen. Leukocytes 10.2 T/l, ESR 28 mm/h. At the bimanual examination the uterus is enlarged up to 8–9 weeks of pregnancy, on a anterior surface — sharply tender myomatous node with the size of 4 × 4 cm, uterine appendages are without changes. Ultrasound confirms the presence of the subserous myomatous node. What diagnosis is the most probable?

A. Internal endometriosis.
B. A tubo-ovarian tumour.
C. Necrosis of the myomatous node.
D. Acute adnexitis.
E. Perimetritis.

6. A woman with complaints of pains in the lower abdomen irradiating to the anus, giddiness which has arisen after coitus. In the anamnesis inflammation of the uterine appendages during 7 years. The 15th day of the menstrual cycle. Integuments are cyanotic, the abdomen is mild, tender at palpation, positive signs of peritoneal irritation. The pulse is 110 b/min. At the bimanual examination the enlarged globe-shaped, painful left ovary is determined. The posterior and dextral lateral fornices of the vagina are painful too. There are no bloody discharge. The probable cause of the acute abdomen:

A. A tumour of the ovary with infringement of feeding.

B. Ovarian apoplexy.
C. Interrupted ectopic pregnancy by tubal abortion type.
D. Interrupted ectopic pregnancy by tubal rupture type.
E. Exacerbation of chronic adnexitis.

7. A patient of 20 years old with complaints of acute pains in the lower abdomen after physical load has arrived to the gynaecological department. Last menses were 2 weeks ago. At the vaginal examination the uterus is not enlarged, painless, on the left the appendages are sharply painful at palpation that impedes examination. The Promtov's sign is positive. The posterior vault overhangs, painful. The pulse is 96 b/min, the blood pressure is 100/60 mmHg. What pathology is meant?
A. Acute left-hand salpingo-oophoritis.
B. Apoplexy of the left-hand ovary.
C. Pyosalpinx on the left.
D. The broken left-hand tubal pregnancy.
E. A tumour of the left ovary.

8. A woman of 26 years old is delivered to the reception with complaints of a sudden pain in the lower abdomen, weakness, loss of consciousness. Last menses were 2 months ago. Hb 106 g/l, the pulse is 120 b/min, the blood pressure is 80/50 mmHg. Painfulness and signs of peritoneal irritation below on the right. What diagnosis is the most probable?
A. Ovarian apoplexy.
B. Torsion of a tumour's pedicle.
C. Acute appendicitis.
D. Acute adnexitis.
E. Broken tubal pregnancy.

9. A woman with complaints of acute pain in the lower abdomen has arrived to the gynaecologic hospital. One year ago at the routine inspection a tumour of the left ovary was diagnosed. She refused the operation. The positive signs of peritoneal irritation attract attention. Bimanually — the uterus of the normal size, painless, on the right a mass with the size up to 8 cm, acutely painful, dense, with precise contours is determined. The probable diagnosis?
A. Torsion of the ovarian cyst's pedicle.
B. Ectopic pregnancy.
C. Acute right-hand adnexitis.
D. Ovarian cyst rupture.
E. Pelviperitonitis.

10. A patient of 29 years complains of acute pain in the lower abdomen, vomiting. The blood pressure is 120/80 mmHg. The pulse is 108 b/min. The abdomen is moderately bloated, acutely painful in the inferior parts. The Schetkin—Blumberg's sign is positive. At the bimanual examination: the uterus is not enlarged, mobile, painless. On the right from the uterus a mass with the size of 7 × 7 cm, elastic consistence, acutely painful is palpated. The left appendages are not palpated. The most probable diagnosis?
A. Torsion of the ovarian cyst's pedicle.
B. Acute adnexitis.
C. Broken ectopic pregnancy.
D. Ovarian apoplexy.
E. Intestinal obstruction.

Chapter 15
SURGERY IN GYNAECOLOGY

1. During the operation of induced abortion at the gestation term of 10 weeks in a woman of 25 years old the uterus was perforated in the area of the anterior wall. What should be subsequent management of the doctor?
A. Perform laparotomy, removal of the fetal egg remnants and suture plication.
B. Complete the fetal egg remnants removal through the cervical canal.
C. Perform laparotomy and supravaginal ablation of the uterus.
D. Perform laparotomy and hysterectomy.
E. Observe the patient and perform a surgical intervention only at appearance of peritonitis signs.

2. A 24-year old patient was made a criminal abortion at home in the gestation term of 18 weeks. Objective exam: the body temperature is 39.4°C, fever, the general condition is severe, the pulse is 120 b/min, the blood pressure is 80/60 mmHg. The uterine fundus is 4 cm higher than the bosom, the uterus is painful at palpation. Diuresis within 6 h — 100 ml. The diagnosis is established: a septic shock. What should be subsequent management?
A. Operative treatment — removal of the uterus with appendages against a background of the infusive therapy.
B. Instrumental revision of the uterine cavity.
C. Antibacterial therapy.
D. Carrying out artificial diuresis.
E. Treatment in the nephrological department.

3. A patient of 47 years old was operated concerning uterine myoma. 2 days ago supravaginal ablation of the uterus was performed. Objective exam: the general condition is moderate, the body temperature is 37.4, the pulse is 92 b/min, the blood pressure is 95/75 mmHg, heart sounds are muffled, rough breath sounds. A postoperative wound is satisfactory. Physiological functions are in the norm. At the given stage of treatment your tactics:
A. Exercise therapy is contraindicated.
B. To appoint morning remedial gymnastics.
C. To appoint remedial gymnastics.

D. To appoint remedial gymnastics and massage.
E. To appoint massage

4. A pregnant woman of 25 years has been admitted to the hospital with complaints of pains in the lower abdomen and bloody discharge from the reproductive tract. Bimanually: the uterus is mild, enlarged up to about 9 weeks of pregnancy, the cervical canal easily passes a finger. In the external os the parts of embryonic tissues are palpated. From the vagina — a moderate bleeding. What treatment should be conducted?
A. Instrumental removal of embryonic tissues.
B. Observing the patient.
C. Appointment of hormones.
D. Hemostatic and antianemic therapy.
E. Appointment of pregnancy maintenance therapy.

5. A patient of 39 years old with complaints of acute pains in the lower abdomen, vomiting, often urination. At exam: the abdomen is moderately bloated, the Schetkin—Blumberg's sign is positive. The pulse is 88 b/min, the body temperature is 37°C. At the bimanual examination: the uterus is dense, not enlarged, mobile, painless, on the right and in front of the uterus a mass with the size of 6×6 cm, elastic consistence, acutely painful when shifted is palpated; left appendages are not determined; fornices are free; discharge are mucous. What diagnosis is the most probable?
A. Intestinal obstruction.
B. Renal colic.
C. Ovarian apoplexy.
D. Torsion of the ovarian tumour's pedicle.
E. An acute inflammation of uterine appendages with tubo-ovarian mass on the right.

6. A patient of 39 years old with complains of acute pains in the lower abdomen, vomiting, often urination. At exam: the abdomen is moderately bloated, the Schetkin—Blumberg's sign is positive. The pulse is 88 b/min, the body temperature is 37°C. At the bimanual examination: the uterus is dense, not enlarged, mobile, painless, on the right and in front of the uterus mass in the size 6×6 cm, elastic consistence, acutely painful is palpated when shifted; left appendages are not determined; fornices are free; discharge are mucous. An additional method of exam:
A. Roentgeno-television hysterosalpingography.
B. Excretory urography.
C. Transvaginal echography.
D. Abdominal puncture through the posterior vaginal fornix.
E. All listed above.

7. A patient of 39 years with complaints of acute pains in the lower abdomen, vomiting, often urination. At exam: the abdomen is moderately bloated, Schetkin—Blumberg's positive sign. The pulse is 88 b/min, the body temperature is 37°C. At the bimanual examination: the uterus is dense, not enlarged, mobile, painless, on the right and in the front from the uterus a mass with the size of 6×6 cm, elastic consistence, acutely painful is palpated when shifted; left appendages are not determined; fornices are free; discharge are mucous. Policy of conducting the patient:
A. Cold on the abdomen, antibacterial, infusive, spasmolytic therapy.
B. Emergency laparotomy, exision of the left uterine appendages.
C. Emergency laparotomy, resection of the left ovary.
D. Laparotomy in the scheduled order in case of failure of conservative therapy.
E. A puncture of the pathological mass under the check for transvaginal echography with the subsequent cytologic examination of the aspirate.

8. A patient of 28 years has addressed with complaints of violent abdominal pains in the inferior parts of the abdomen, the temperature rise is up to 39ºC, nausea. She got ill after menses. Sexual life is out of wedlock. The abdomen is painful at palpation. The Schetkin—Blumberg's sign is positive. At examination: contours of the uterus and appendages are not precisely determined because of tension of the anterior abdominal wall. The posterior fornix is acutely painful. Discharge are purulent. What diagnosis is the most probable?
A. Adenomyosis.
B. Parametritis.
C. Pelvioperitonitis.
D. Appendicitis.
E. Torsion of the ovarian cyst's pedicle.

9. A patient of 29 years has addressed with complaints of bursting pain in the lower abdomen. The menses are absent within 2.5 months after an induced abortion. At the bimanual examination: the external os is closed, the uterus enlarged, painful. The appendages are not determined. Fornices are deep, painless. Discharge are absent. At ultrasound: the enlarged uterine cavity, overfilled with homogeneous fluid. What diagnosis is most probable?
A. Stein—Leventhal's syndrome.
B. Hematometer.
C. Shihan's syndrome.
D. Ectopic pregnancy.
E. Chiary—Frommel's syndrome.

10. A patient of 32 years is delivered to the gynaecological department with complaints of acute pain in the lower abdomen. Menses — 2 weeks ago, in time. Bimanual examination: the vagina and cervix without changes, survey of the uterus and appendag-

es is impossible because of painfulness and tension of the anterior abdominal wall. The posterior fornix overhangs, painful. What is it necessary to make for improvement of the diagnosis:

A. Culdoscopy.
B. To repeat bimanual examination under narcosis.
C. Ultrasound.
D. A puncture of the abdominal cavity through the posterior vaginal fornix.
E. Hysteroscopy.

Chapter 16
BREAST DISEASES

1. A patient of 23 years old addressed to gynaecologist with complaints of breast pain 3 days prior to menstruation. Menses since 12 years, 3–5 days in 28 days intervals, regular, last menses finished one week ago. At objective examination: normal body structure, mammary glands are well developed, painless at palpation, without violations of their tissue, no discharge from pupils. Peripheral lymphatic nodes are not enlarged. What kind of therapy is the most preferable:

A. Nonsteroid anti-nflammatory, diuretics, bromcriptine.
B. Oestrogen-gestagen complex.
C. Oestrogens.
D. Gestagens.
E. Androgens

2. A patient of 35 years old addressed to the gynaecologist with complaints of pain in the mammary glands 3–5 days prior to menstruation with irradiation to shoulder region. Menses since 12 years, 3–5 days in 28 days intervals, regular, last menses finished three weeks ago. At objective examination: normal body structure, mammary glands are well developed, at palpation numerous node-like masses are determined, no discharge from pupils. Peripheral lymphatic nodes are not enlarged. What kind of examination is the most informative:

A. Ultrasound examination of the mammary glands.
B. Mammography.
C. CA 19-9.
D. MCA.
E. Prolactin analysis.

3. A patient of 35 year old addressed to gynaecologist with complaints of pain in the mammary glands 3–5 days prior to menstruation with irradiation to the shoulder region. Menses since 12 years, 3–5 days in 28-day intervals, regular. At objective examination: normal body structure, the mammary glands are well developed, at palpation numerous node-like masses are determined, no discharge from pupils. Peripheral lymph nodes are not enlarged. Results of mammography: fibrous-cystic mastopathy. Everything listed below can be proposed for treatment, except:

A. Diet (limitation of coffee, tea, chocolate), vitamins.
B. Oral contraceptives.
C. Antioestrogens.
D. Antiprolactins.
E. Oestrogens.

4. A patient of 24 year old addressed to gynaecologist with complaints of presence of a tumour like mass in the left mammary gland, that she had found at self-examination. Menses since 12 years, 3–5 days in 28 days intervals, regular. At objective examination: normal body structure, the mammary glands are well developed, at palpation a round shape mass is determined in the upper external region of left mammary gland, the right one — without alteration. No discharge from pupils. Peripheral lymph nodes are not enlarged. What method of treatment of listed below can be chosen:

A. Aspiration of a tumour mass.
B. Resection of the tumour.
C. Diet (limitation of coffee, tea, chocolate), vitamins.
D. Oral contraceptives.
E. Antiprolactins.

5. A patient of 50 years old addressed to the gynaecologist with complaints of discharge from the mammary glands. At objective examination: normal body structure, the pupil of right mammary gland is retracted. Rose color discharge is marked from the pupil. Axillary and supraclavian lymph nodes are enlarged. What method of treatment from listed below can be chosen:

A. Surgical treatment.
B. Ionizing radiation.
C. Cytotoxic therapy.
D. Hormonal therapy.
E. Physiotherapy.

Chapter 17
CONTRACEPTION

1. On consultation a woman of 17 years old. Married for 6 months. The menses since 13 years, 3–4/28. The sexual formula — A×3 P3 Ma2 Me+. Height 168 cm, weight 64 kg. At gynaecologic investigation the deviations from the norm are not revealed. With the purpose of contraception the woman wishes to use an intrauterine device. What investigation is it necessary to do?

A. Bacterioscopy of the uterine smears.
B. Smear for cytology.
C. Pelvic ultrasound.

D. Bacterial inoculation.
E. Colposcopy.

2. A patient of 29 years old addressed for consultation concerning method of reversible contraception. Menses since 12 years, 3–5/28, regular. The sexual formula — A×3 P3 Ma2 Me+. Height 168 cm, weight 64 kg. At gynaecological investigation no violations were revealed. Has a harmful habit — smoking. At laboratory examination: liver test: ASAT — 1.45 U, ALAT — 1.50, cholesterol level — 6.8 mmol/l. What method of contraception is contraindicated?

A. Oestrogen-gestagen complex.
B. Intrauterine device.
C. Barrier methods.
D. Physiological method.
E. Surgical contraception.

3. A patient of 25 years old addressed to the gynaecologist with complaints of two month delay of menses and pain in the lower abdomen. A year ago the intrauterine device was applied. At gynaecologic examination: the enlargement of uterus was revealed which corresponds to 8 weeks of pregnancy, external parts of intrauterine device are visualized in the uterine cervix channel. At ultrasound examination: pregnancy, 8 weeks, loop inside uterine cavity, near the internal os of the uterine cervix. What is it necessary to conduct?

A. Treatment of threaten abortion.
B. Removing of the device.
C. Induced abortion.
D. Antibacterial treatment.
E. Surgical treatment

4. A patient addressed to the gynaecologist for consultation about preventing an undesirable pregnancy after sexual intercourse (the day before) without birth control methods. What is necessary to recommend?

A. Postinor.
B. Oestrogen-gestagen complex.
C. Depo-provera.
D. Norplant.
E. Local spermicidal means.

5. A 24-year old woman, never pregnant before terminated to take oral contraceptives. After last reception of the drug she had one menses, and then within 6 months amenorrhoea was observed. Choose the most suitable investigation:

A. Determination of the level of gonadotrophins.
B. Pelvic ultrasound.
C. Progesterone test.
D. Computer tomography of the head.
E. Determination of the testosterone in the blood serum.

ANSWERS

Chapter 1: 1 A; 2 D; 3 B; 4 A; 5 B; 6 C; 7 A; 8 D; 9 E; 10 C
Chapter 2: 1 C; 2 C; 3 C; 4 D; 5 D; 6 B; 7 C; 8 E; 9 A; 10 E; 11 A; 12 D; 13 A; 14 D
Chapter 3: 1 D; 2 A; 3 D; 4 A; 5 A; 6 C; 7 D; 8 B; 9 A; 10 D
Chapter 4: 1 E; 2 B; 3 C; 4 A; 5 A; 6 D; 7 E; 8 C; 9 B; 10 B
Chapter 5: 1 E; 2 D; 3 A; 4 B; 5 A; 6 E; 7 D; 8 D; 9 B; 10 A
Chapter 6: 1 A; 2 B; 3 C; 4 A; 5 A; 6 C; 7 E; 8 A; 9 C; 10 A
Chapter 7: 1 A; 2 E; 3 E; 4 A; 5 C; 6 A; 7 C; 8 B; 9 B; 10 B
Chapter 8: 1 A; 2 B; 3 B; 4 A; 5 C; 6 C; 7 D; 8 D; 9 E; 10 A
Chapter 9: 1 C; 2 E; 3 A; 4 A; 5 C; 6 D; 7 B; 8 D; 9 D; 10 A
Chapter 10: 1 C; 2 C; 3 A; 4 A; 5 A; 6 B; 7 D; 8 D; 9 A; 10 A
Chapter 11: 1 B; 2 A; 3 E; 4 A; 5 B; 6 A; 7 A; 8 A; 9 A; 10 D
Chapter 12: 1 A; 2 A; 3 A; 4 A; 5 A; 6 A; 7 E; 8 D; 9 D; 10 D
Chapter 13: 1 E; 2 A; 3 A; 4 A; 5 B
Chapter 14: 1 E; 2 D; 3 C; 4 E; 5 C; 6 B; 7 B; 8 E; 9 A; 10 A
Chapter 15: 1 A; 2 A; 3 A; 4 A; 5 D; 6 C; 7 B; 8 C; 9 B; 10 D
Chapter 16: 1 A; 2 B; 3 E; 4 B; 5 E
Chapter 17: 1 A; 2 A; 3 B; 4 A; 5 B

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