OBSTETRICS AND GYNECOLOGY

Textbook in 4 volumes

I.S. Sidorova, N.A. Nikitina

Volume I

PHYSIOLOGICAL OBSTETRICS

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Сеченовский Университет

Федеральное государственное автономное образовательное учреждение высшего образования Первый Московский государственный медицинский университет имени И.М. Сеченова Министерства здравоохранения Российской Федерации (Сеченовский Университет)

УЧЕБНИК

АКУШЕРСТВО И ГИНЕКОЛОГИЯ

Учебник в 4 томах

И.С. Сидорова, Н.А. Никитина

Том I

ФИЗИОЛОГИЧЕСКОЕ АКУШЕРСТВО

SECHENOV UNIVERSITY

Федеральное государственное автономное образовательное учреждение высшего образования Первый Московский государственный медицинский университет имени И.М. Сеченова Министерства здравоохранения Российской Федерации (Сеченовский Университет)

TEXTBOOK

OBSTETRICS AND GYNECOLOGY

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Volume I

PHYSIOLOGICAL OBSTETRICS

Министерство науки и высшего образования РФ

Рекомендовано Координационным советом по области образования «Здравоохранение и медицинские науки» в качестве учебника для использования в образовательных учреждениях, реализующих основные профессиональные образовательные программы высшего образования по направлению подготовки специалитета по специальности 31.05.01 «Лечебное дело»

Регистрационный номер рецензии 1087 от 02 июля 2020 года

Moscow
«GEOTAR-Media»
PUBLISHING GROUP
2021

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Chapter 11

INVESTIGATIONS DURING PREGNANCY

11.1. MEDICAL HISTORY AND PHYSICAL EXAMINATION

Medical history and physical examination in obstetrics differ from those in therapeutic or surgical practice. Care and delicacy should be employed during physical examination. Always introduce yourself to the patient, be polite.

Order of history taking. When taking a history, the doctor asks a set of standard questions. The list of these questions and the order of registering answers in a medical record are presented below.

Demographic data:

- full name;
- age;
- occupation, current employment status;
- reason for referral to the hospital/women's health clinic/maternity hospital.

Social factors:

- marital status;
- living conditions;
- smoking (cigarettes per day);
- alcohol consumption;
- substance abuse (which drugs and how often, route of administration).

Additional data:

- blood type and rhesus-factor;
- past history of rubella;
- hepatitis B, C, HIV status.

Allergies:

- ask if the patient has an allergy, how it manifests, which medications she takes;
- ask about hypersensitivity to antibiotics and anesthetics.

Family history:

- diseases in relatives (thrombosis, endocrinopathy, cancers, etc.).

Somatic history (extragenital disorders):

- past diseases of internal organs;
- previous surgeries, type of anesthesia.

Gynecological history:

- age at menarche;
- features of menstrual cycle (regularity, duration of periods, etc.);
- which methods of contraception were used; when their use was stopped;
- past STDs (inflammatory diseases of the female genital organs, chlamydiosis, gonorrhea, etc.);
- date and results of the last pap smear and cytology;
- past gynecological diseases and surgeries.

Information on the course and outcomes of previous pregnancies and labors:

- number of pregnancies which resulted in the delivery of a live baby. Term of labor, method of delivery, sex and weight of the baby. Complications of previous pregnancies;
- number of stillbirths, children, who died in the neonatal period;
- number of artificial and spontaneous abortions, ectopic pregnancies.

Current pregnancy:

- gestational age;
- date of last period;
- date of delivery, estimated according to the date of the last period. Discrepancies between this term and the term according to the ultrasound data;
- singleton or multiple gestation;
- type of placentation;
- was it a planned pregnancy?
- Does the woman feel fetal movements after the 20th week of gestation?
- Did she note abnormal vaginal discharge?

Complications of current pregnancy:

- complaints (in detail);
- term of pregnancy at which the complication developed;
- signs and symptoms of the complication;
- medical measures, employed for management of this complication;
- the most probable prognosis in this condition;

- results of ultrasound investigations (number of investigations, results obtained).

Medications:

- does the woman currently take iron or folic acid supplements, vitamins?
- Does she take other medications (antihypertensive, antiepileptic, thyroid hormones, etc.)?

When taking family history, specific attention should be paid to such diseases as diabetes mellitus, venous thromboembolic complications, myocardial infarction, stroke (especially under the age of 40), hypertension, tuberculosis, mental disorders, multiple pregnancy, family history of congenital abnormalities, etc.

It is necessary to collect information about past diseases, particularly, rubella, toxoplasmosis, genital herpes, disorders of kidneys, lungs, liver, cardiovascular or endocrine disease, surgeries, blood transfusion, allergies, etc.

Major underlying disorders complicating the course of pregnancy:

- diabetes mellitus (hypo- and hyperglycemia, developmental abnormalities, macrosomy, stillbirth);
- hypertension;
- kidney diseases (urinary tract infection);
- history of deep vein thrombosis or pulmonary embolism;
- connective tissue disorders;
- antiphospholipid syndrome;
- epilepsy;
- thyroid diseases.

Special attention is paid to history of thrombosis and hemorrhage for the purpose of prevention of thromboembolic events and bleeding during pregnancy, labor and in the postpartum period.

Obstetric and gynecological history should include data on the menstrual and reproductive function, including data on the number of pregnancies, time intervals between pregnancies, duration, course and outcomes of previous pregnancies, complications in labor, in postpartum period and after abortions, birth weight of the newborns, development and state of health of other children in the family, use of contraceptives.

Ask about the state of health of the husband, his blood type and Rh-factor, as well as exposure to occupational hazards and bad habits in partners.

The gestational age and estimated date of delivery can be deetrmined before the 20th week of pregnancy:

1) according to the first day of the last period (estimated due date should be adjusted depending on the duration of menstrual cycle: with a cycle of

32 days or longer — reduce the term; with a cycle of 24–26 days or less — increase the term);

2) according to the date of conception, if the patient can precisely indicate it (when estimating the gestational age one should add 2 weeks to the date of conception);
3) according to the ovulation (add two weeks);
4) according to the ultrasound data (in irregular menstrual cycle, unknown date of the last period, 5-day or more discrepancy of the gestational age with that estimated based on the date of the last period). Ultrasound at 10–14 weeks gestation allows the most precise determination of the gestational age. If 10–14-week ultrasound data are unavailable, data of the investigation at the term of 16–22 weeks are used.
5) in case of IVF — according to the follicle puncture date (add 2 weeks) or date of embryo transfer (add 2 weeks and the age of the embryo).

When taking history, it is important to clarify whether this pregnancy has occurred naturally or as a result of the use of assisted reproductive technologies, which increases the risk of some obstetric complications. The following aspects should be considered:

- what is the cause of infertility (tubal obstruction, polycystic ovarian syndrome, presence of male factor);
- were donor oocytes and sperm used (these data are confidential);
- how many attempts of IVF were made before the development of this pregnancy.

Physical examination. Height measurement at the first examination. Body weight is measured and registered at each examination.

BMI is calculated at the first appointment. Assessment for abnormal change in body weight at each appointment is recommended. Patients with BMI <20 kg/m^2 should be instructed on proper nutrition, and the increased risk of IUGR syndrome. In case of obesity (BMI ⩾30 kg/m^2) additional recommendations for pregnancy management are necessary:

- counseling on weight gain, nutrition and regular exercises;
- informing about the correlation between obesity and gestational hypertension, gestational diabetes, macrosomy, greater risk of the need for cesarean section and complications during labor and in the postpartum period;
- fasting glucose — at first appointment to diagnose diabetes mellitus.

Additional investigaitons:

- at BMI ⩾35 kg/m^2 in combination with hypertension or diabetes, echocardiography is necessary;
- at BMI ⩾40 kg/m^2 — additional ultrasound of the fetus on the 26th and 32nd weeks gestation of gestation;
- BMI ⩾50 kg/m^2 — consultation of anesthesiologist in the III trimester;
- BP is measured at each visit;
- inspection of breasts at the first appointment;
- vaginal examination at the first visit (including tests for chlamydiosis and gonorrhea, pap smear, assessment of the cervix, uterine size according to the term of pregnancy, vagina and external genital organs).

Rules of BP measurement

The most accurate results can be obtained with the use of mercurial sphygmomanometer (all used instruments should be calibrated on its basis).

Sitting in a comfortable position, the arm rests on the table at the heart level. The lower edge of the standard cuff (width 12–13 cm, length 35 cm) must be 2 cm over the elbow. Cuff size must correspond to the size of the arm.

The moment of hearing the first sounds corresponds to the I phase of Korotkoff sounds and indicates systolic BP; it is recommended to assess diastolic BP in the V phase of Korotkoff sounds (termination).

BP is measured at rest (after 5-minute rest) twice, with not less than 2-minute interval; in case of difference of 5 mm Hg or more, one additional measurement is conducted with averaging results of two last measurements.

BP is measured on both arms. In case of different results, the higher indicators are considered.

In patients with diabetes mellitus BP should be measured in sitting and lying positions.

Values should be registered with the precision of 2 mm Hg.

Fetus. Heart rate starting from the 12th week of gestation (using fetal Doppler apparatus).

Fundal height should be assessed at each visit from 20 to 36 weeks gestation. The table presents correspondence of fundal height to gestational age. When fundal height deviates from the norm for gestational age by 4 cm or more, ultrasound is necessary to assess fetal development and the amount of amniotic fluid.

Fetal lie and presentation are determined after the 34th week of gestation with the help of Leopold's maneuver and/or ultrasound.

11.2. SPECIAL OBSTETRIC EXAMINATIONS

Examination methods for pregnant women at a term, close to delivery are as follows:

- general examination of the woman's abdomen, assessment of body type, performed in the supine and standing position;
- external pelvic measurement using pelvimeter;
- measurement of fundal height and abdominal circumference using measuring tape;
- palpation of the abdomen (uterus) with Leopold's maneuvers;
- auscultation of fetal heartbeat;
- ultrasound, Doppler ultrasound, cardiotocography.

These methods allow establishing the presence and term of pregnancy, the state of uterus, fetus, birth canal and *answer the questions*:

- is the woman pregnant, and what is the gestational age?
- What is the approximate obstetric status (pelvic measurements)?
- Is the fetus located in the uterus properly (longitudinal or transverse lie)?
- Is this a singleton or multiple pregnancy?
- Is the fetus alive or dead? Do fetal dimensions correspond to the estimated pregnancy term (fetometry using ultrasound)?
- Is this the first or repeated pregnancy?
- Is the woman in labor or not? If she is in labor, in which period is she?

During a general examination of a pregnant woman the obstetrician pays attention to the height, body type, shape of the abdomen, state of the anterior abdominal wall, mammary glands, and the contours (shape) of lumbosacral rhombus (rhombus of Michaelis) (fig. 11.1). In well-built women, the rhombus of Michaelis is close to the shape of square.

The horizontal diagonal line of the rhombus of Michaelis is 10 cm and the vertical one is 11 cm.

External pelvic measurement. Three transverse diameters are measured (fig. 11.2):

- distance between the most distant iliac points, i.e. between anterior superior iliac spines — *interspinous distance* (26 cm) (fig. 11.3, a);
- distance (see fig. 11.3, b) between the most distant points of the iliac crests — *intercristal distance* (29 cm);
- distance (see fig. 11.3, c) between the most distant points of two trochanters — *intertrochanteric distance* (32 cm).

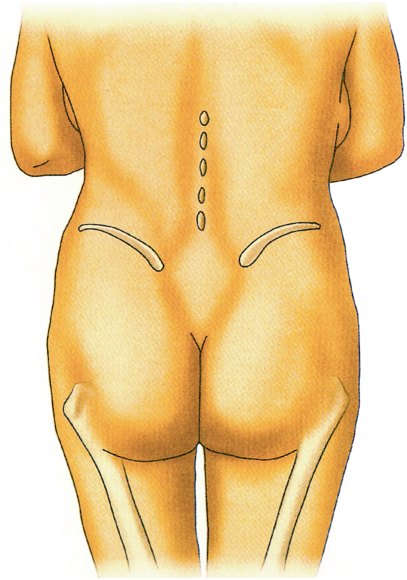

Fig. 11.1. Lumbosacral rhombus (rhombus of Michaelis)

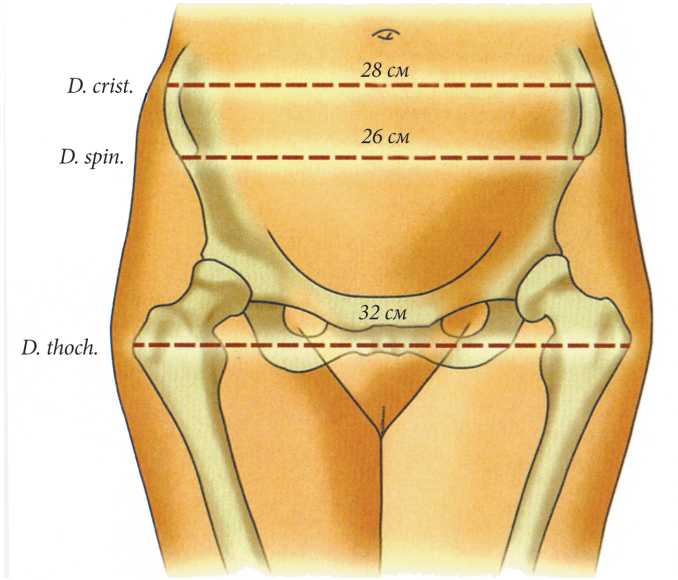

Fig. 11.2. Transverse pelvic diameters

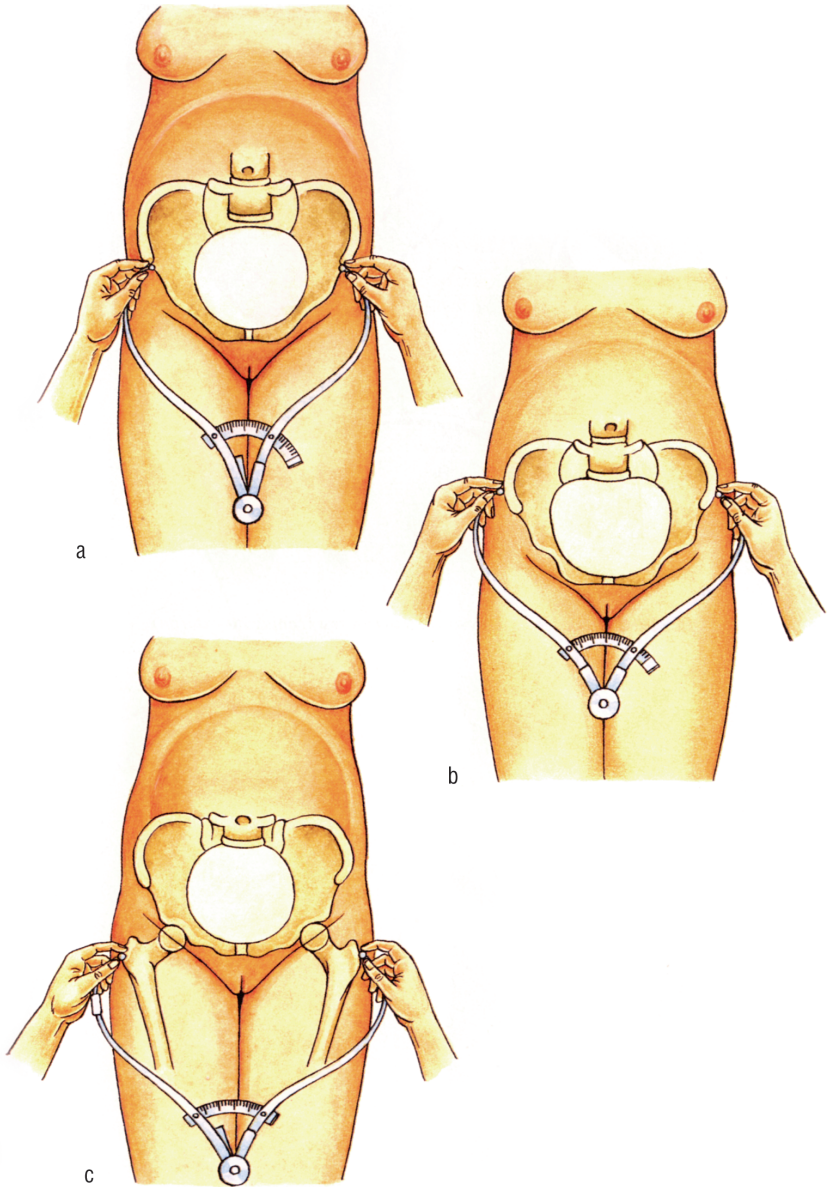

Fig. 11.3. Measurement of transverse pelvic diameters: a — interspinous distance; b — intercristal distance; c — intertrochanteric distance

The external conjugate diameter (*conjugata externa*) is measured. The pelvimeter button is placed not on the spinous process of L5 but in the supersacral fossa located below between the spinous processes of L5 and S1. This fossa corresponds to the upper angle of lumbosacral rhombus (fig. 11.4).

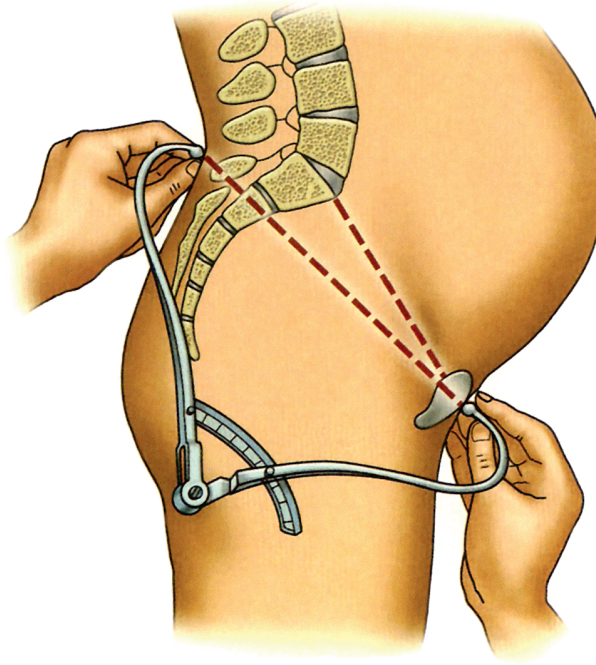

Fig. 11.4. Measurement of external conjugate diameter (conjugata externa)

In case of coxalgic (obliquely oval contracted) pelvis, oblique diameters are measured.

Fundal height (FH) and *abdominal circumference* (AC) are measured using measuring tape (fig. 11.5). At the end of pregnancy FH is 36–37 cm, AC is not more than 100 cm. The size (circumference) of the wrist joint (Soloviev index) is measured. Normally it is 14–15 cm (fig. 11.6).

Further fundal position, orientation of the fetal spine (on the left — I position, on the right — II position) and the small fetal parts are determined using ***external palpation of uterus***. The presenting part (cephalic, breech) and humeral prominence of the fetus are determined using III and IV Leopold's maneuvers. In more detail, external palpation of uterus according to Leopold Levitsky is presented in chapter 13.4.

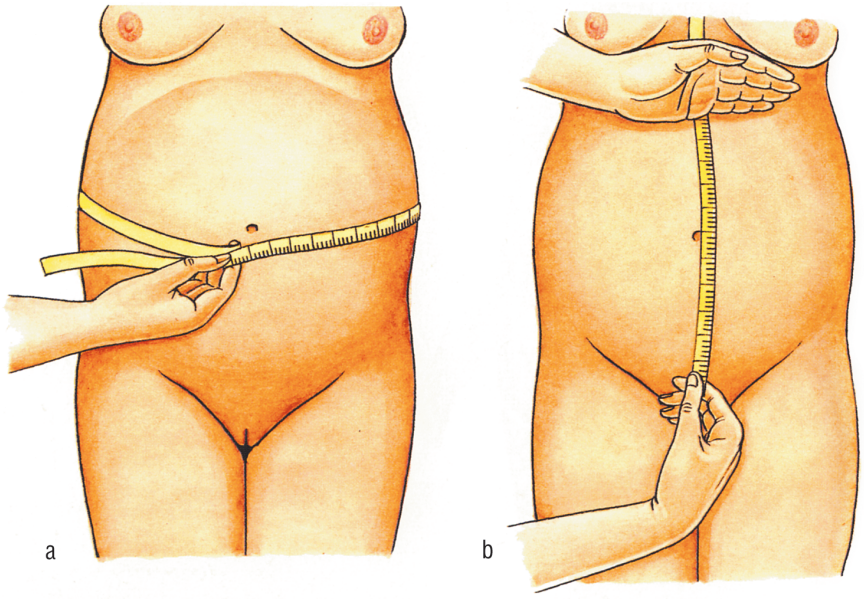

Fig. 11.5. Measurement of abdominal circumference (a) and fundal height (b)

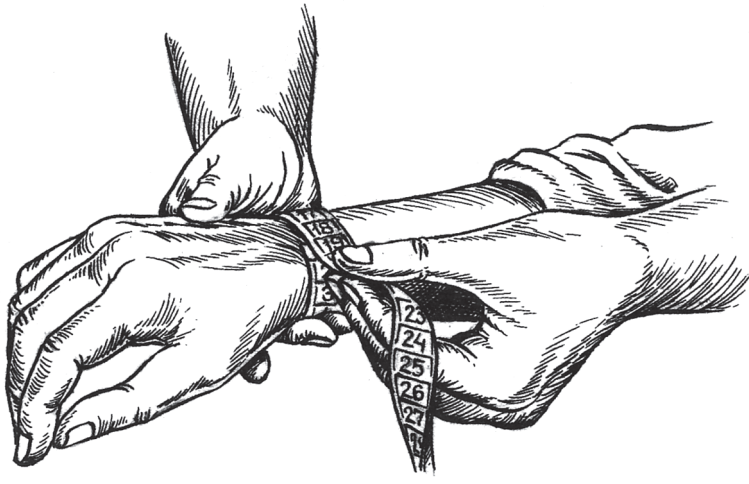

Fig. 11.6. Measurement of size (circumference) of wrist joint (Soloviev index)

Auscultation of fetal heartbeats is performed using fetoscope (after the 20th week of pregnancy). The fetal heartbeat is heard most clearly in the area of fetal chest, back and shoulder (fig. 11.7). The fetal heartbeat is characterized by double frequent beats with a very short pause, which resemble the ticking of a wristwatch. Fetal heart rate is 140–160 beats per minute. In the second half of pregnancy, cardiotocography, Doppler ultrasound, and other methods of fetal assessment are used.

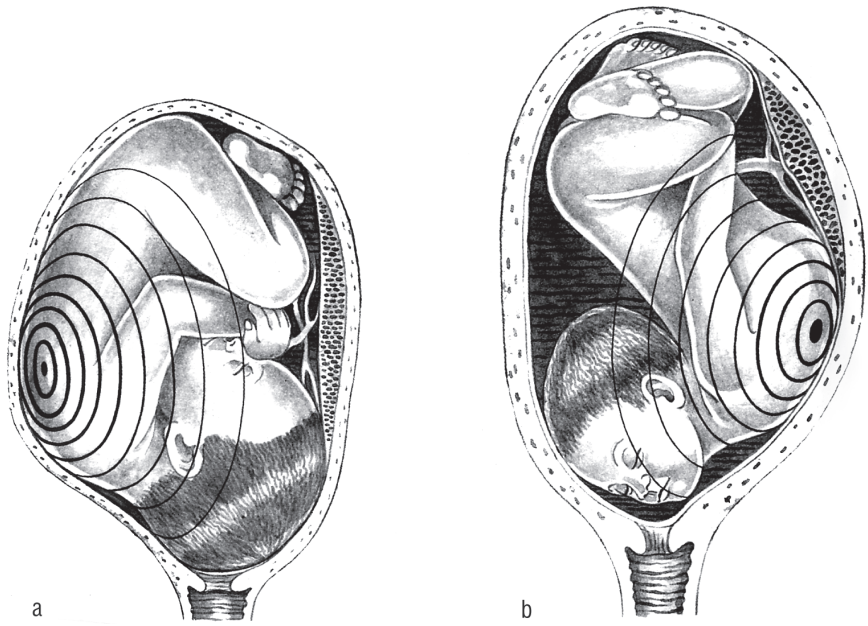

Fig. 11.7. Fetal heart tones conduction: a — with the head flexed; b — at maximum extension of the head

After taking medical history, external examination, general clinical and external pelvic measurements, ***one performa a vaginal examination*** to assess the state of the perineum, vagina, cervix uteri, uterine size, signs of pregnancy, and takes smears for the analysis of vaginal flora and possible presence of bacterial infection.

The pregnant woman is examined on a gynecological chair in compliance with aseptics principles (fig. 11.8).

Examination of external genital organs. During examination of external genital organs the following is noted: type of hair growth (female or male type),

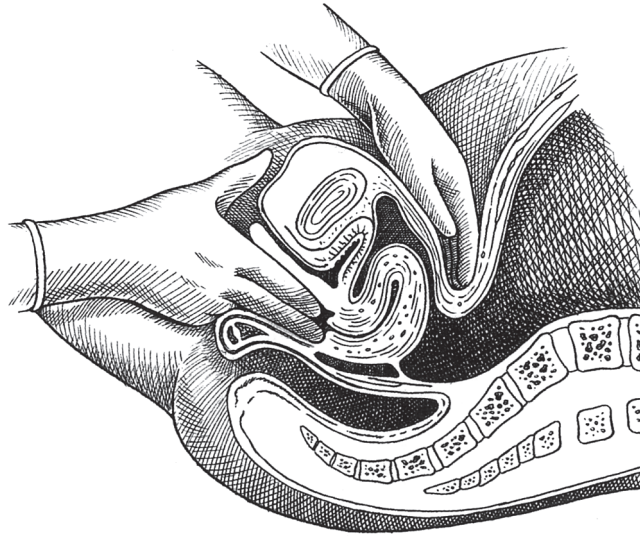

Fig. 11.8. Bimanual abdominovaginal examination in early gestational age

development of the labia minora and labia majora, state of the perineum (high, low); presence of abnormalities: inflammation, tumors, condylomas, fistulas, scars after tears in the perineal area. During examination of the anal orifice area, attention is payed to the presence of hemorrhoids.

Spreading the labia minora with fingers, one examines the vulva and vaginal orifice, state of the external urethral opening, paraurethral passages and openings of ducts of Bartholin's glands.

Examination and assessment of cervix uteri state using speculum. During examination, a bivalved speculum or vaginal retractor is used. The following is assessed: color of the mucosa of the cervix uteri and vagina, nature of the secretion, size and shape of the cervix uteri and the external os, any abnormalities in the cervix (cicatricial deformity, ectropion, ectopy, leukoplakia, cervical canal polyp, condylomas) and vaginal walls.

Moreover, at an early gestational age such signs as cyanosis of cervix uteri and vaginal walls are determined. At the same time, one takes a smear (discharge from cervical canal, from vaginal fornices, from urethra and paraurethral passages) for cytological examination and identification of pathogens of the urinary and genital tract.

Internal obstetric examination. Internal (vaginal) examination as well as external examination are major examination techniques in obstetrics. In la-

bor, this examination allows determining fetal presentation, state of the cervix, presence or absence of fetal membranes, monitoring the dynamics of cervical dilatation and the biomechanism of engagement of presenting part and passing through the birth canal.

As a rule, an obstetric vaginal examination is carried out with two fingers — index finger and the median (long) finger of the hand which the obstetrician is able to use better. The index and median fingers should be extended, the third finger and little finger flexed and pressed to the palm of the hand, the thumb is extended and maximally abducted to the side.

During a vaginal examination, the diagonal conjugate diameter (*conjugata diagonalis*) is determined: the distance between the promontory and the lower edge of pubis (normal distance is 12.5 cm). For this purpose the physician tries to reach promontory with the introduced fingers, and puts the index or median finger of the external hand under the lower edge of the symphysis and notes the site of contact of the introduced hand with the lower edge of pubis (fig. 11.9).

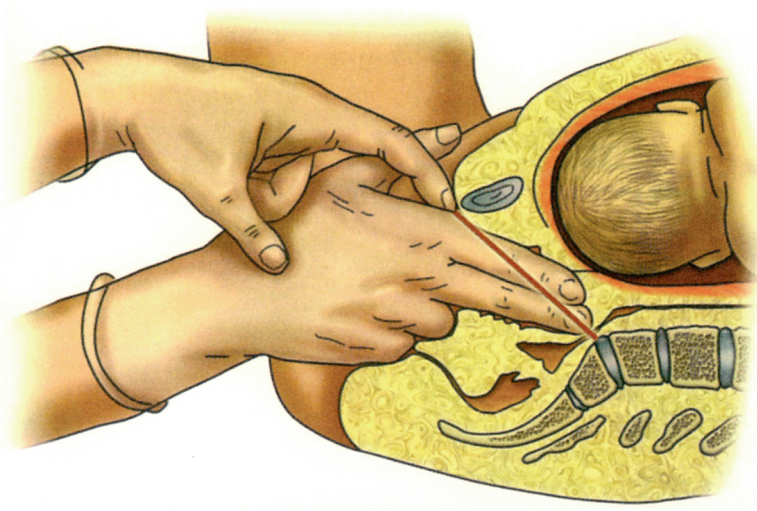

Fig. 11.9. Internal obstetric examination. Determination of diagonal conjugate diameter

The measured distance is determined. Based on the measured diagonal conjugate diameter, the true (obstetric) conjugate is calculated. For this purpose, 1.5–2 cm is subtracted from the length of diagonal conjugate.

11.3. PREGNANCY DETECTION. DETERMINATION OF GESTATIONAL AGE AND DUE DATE

In case of a missed period in women of childbearing age and absence of infertility, the possibility of pregnancy should be taken into account.

Knowledge of clinical methods for diagnosing pregnancy is important for the establishment of *preliminary diagnosis,* which requires confirmation by instrumental and laboratory methods (primarily by ultrasound).

Clinical signs of pregnancy. Nowadays, determination of specific clinical signs of pregnancy is *auxiliary.* According to their diagnostic value, specific signs of pregnancy can be divided into three groups:

1) doubtful (presumptive) signs are associated with the subjective sensations of the pregnant woman and somatic changes in her body;
2) probable ones include signs determined by objective examination of reproductive organs, and positive immunological tests for pregnancy;
3) positive (apparent) are objective signs associated with the presence of the fetus.

Presumptive signs of pregnancy. These include:

- changes in appetite, nausea, vomiting in the morning;
- changing in olfactory sensations;
- skin pigmentation on the face, along the white line, nipples and areolae;
- breast tenderness;
- abdomen enlargement.

Probable signs of pregnancy. Probable signs include the following:

- delay in menstrual period;
- appearance of colostrum if the breast is squeezed;
- bluish discoloration (cyanosis) of vaginal and cervical mucosa;
- increase of uterine size;
- softening of the uterus (change in its density);
- asymmetry of structure, increased excitability at palpation.

Delay of menses is an important sign, especially in women with a regular menstrual cycle. The value of this sign is still greater if it is combined with breast tenderness and appearance of colostrum in them, with the presence of cyanosis of the vaginal mucosa and especially vaginal part of uterine cervix.

At 8 weeks gestation, uterine body is enlarged 2 times compared with the initial size, at 10 weeks — 3 times, at 12 weeks — 4 times.

The following signs determined at a vaginal examination also indicate the presence of pregnancy.

Hegar's sign. *Change in uterus density (consistency).* The consistency of the pregnant uterus is soft, and softening is especially significant in the isthmus. On bimanual examination, the fiingers of both hands come close in the area of uterine isthmus with almost no resistance.

Snegiryev's sign. Greater uterine excitability and tone is specific for pregnancy. On bimanual examination a softened pregnant uterus become denser in response to mechanical irritation. When the irritation discontinues, the uterus softens again.

Piskacek's sign. At an early gestational age an asymmetry of uterus, manifesting as the right or left lateral bulge, is often noted from 7–8 weeks gestation. The protrusion corresponds to the site of implantation. As the ovum (gestational sac) grows, the protrusion gradually disappears (by the 10th week of pregnancy)

Gubarev and Gaus noted mild cervical mobility at an early gestational age. Easy cervical displaceability is related to significant softening of the isthmus.

Genter's sign. At an early gestational age, the uterus is in pronounced anteversion appearing as a result of significant softening of the isthmus as well as a crest-like thickening (protrusion) on the anterior surface of the uterus in the midline. This thickening is not always present.

Positive signs of pregnancy. These include:

- visualization of gestational sac or fetus in the uterine cavity using ultrasound is the most reliable method to determine pregnancy;
- palpation of fetal parts. In the second half of pregnancy the head, back and small parts (extremities of fetus) are determined during palpation of the uterus;
- auscultation of fetal heart tones. Fetal heartbeat can be heard during auscultation (using fetoscope) after 18–20 weeks gestation;
- feeling of fetal movements during palpation of the uterus on obstetric examination.

The diagnosis of pregnancy is accurate even in the presence of one true sign.

Determination of gestational age and due date. Determination of gestational age is based on history data and results of objective examination.

- *According to the date of last menstrual period.* The gestational age can be calculated based on the time since the 1st day of the last menstruation (if the menstrual cycle is regular). To estimate the delivery date, one has to subtract 3 months from the date of the last menstruation and add 7 days (Naegele rule).

- *According to ovulation*. When the date of conception is known, it is necessary to subtract 3 months and 7 days to estimate the delivery date (Naegele rule modification) or add 266 days (38 weeks).
- *According to the first visit to women's health clinics*. Data from history and examination of a pregnant woman are taken into account.
- *According to the date of the first quickening*. When determining the gestational age and date of delivery, one takes into account the time of the first quickening, which is felt by a primigravida after 20 weeks gestation, by multigravida — about 2 weeks earlier. This sensation is subjective and its value is limited. To determine the delivery date in primigravida, 20 weeks are added to the date of the first quickening (20 weeks gestation), in multigravida — 22 weeks are added to the date of the first quickening (18 weeks gestation).

Special pregnancy tables — gravidometers (they are accurate enough) are used for faster calculation of gestational age and delivery date according to the date of last menstruation and according to quickening.

In addition, the gestational age can be determined based on the data of a physical examination.

An insignificant enlargment of uterus is noted at 4 weeks of pregnancy. At this gestational age, no reliable determination of pregnancy using non-instrumental methods is possible.

At 8 weeks the size of uterus increases 2 times and approximately corresponds to the size of a female fist.

At 12 weeks the asymmetry of uterus disappears, its fundus reaches the edge of the pubic arch.

From 16 weeks gestation, uterine fundus is palpated through the anterior abdominal wall and the gestational age is judged based on the fundal height (FH) (Table 11.1 and fig. 11.10). It is important to remember that fetal size, excess amniotic fluid (AF), twins, fetal mal position and other features of pregnancy can affect FH. Therefore, when determining the gestational age, FH is compared with other signs (last period, quickening, etc.).

Table 11.1. Fundal height at different gestational age

Gestational age, weeks	Location of uterine fundus	
	Anatomic landmarks	Height, cm
16	Midpoint between pubis and umbilicus	6
20	Two fingers below the umbilicus	11–12
24	On the level of the umbilicus	22–24

End of the table 11.1

Gestational age, weeks	Location of uterine fundus	
	Anatomic landmarks	Height, cm
28	Two fingers above the umbilicus	28
32	Midpoint between the umbilicus and xyphoid process	32
36	At the level of xyphoid process and costal arches	36
40	Midpoint between the umbilicus and xyphoid process	32

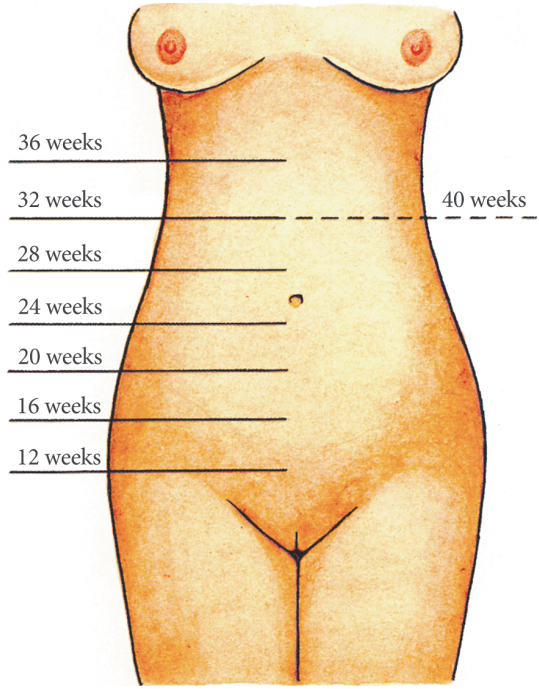

Fig. 11.10. Fundal height at different gestational age

Additional tests confirming the diagnosis of pregnancy. Currently, a combination of two methods is considered the gold standard for diagnosing pregnancy of any location:

- determination of β-HCG;
- ultrasound using abdominal or transvaginal probe.

These two diagnostic techniques ascertain the presence or absence of pregnancy and almost exclude the possibility of a false positive or false negative result.

Human chorionic gonadotropin is produced by syncytiotrophoblast of the growing villous chorion. As early as day 7–9 after conception (3 weeks of the obstetric term), β-subunit of this hormone is found in the blood which coincides with implantation of fertilized ovum into the endometrium. The level of β-HCG is constantly increasing, reaching a maximum at 8 weeks, then its level decreases 2–3 times and remains unchanged until the end of pregnancy. This hormone is no longer detected in the blood 2 weeks after delivery. In addition to early diagnosis of normally developing uterine pregnancy, quantitative determination of β-HCG allows distinguishing normal uterine pregnancy from pathological (ectopic, non-developing) pregnancy.

β-HCG levels are measured in the blood using an immunological method, or in the urine. In the first case, more reliable results are obtained.

The detection of HCG in the woman's blood is not an absolute confirmation of pregnancy without ultrasound and clinical signs.

Using transvaginal ultrasound, the presence of pregnancy can be reliably established at 4–5 weeks. At this term, the diagnosis of pregnancy is determined based on the presence of gestational sac in the uterine cavity.

Starting from 6–7 weeks the embryo and yolk sac are visualized in the amniotic cavity, the heartbeat of the embryo (HB +) is recorded facilitating the diagnosis (fig. 11.11, 11.12).

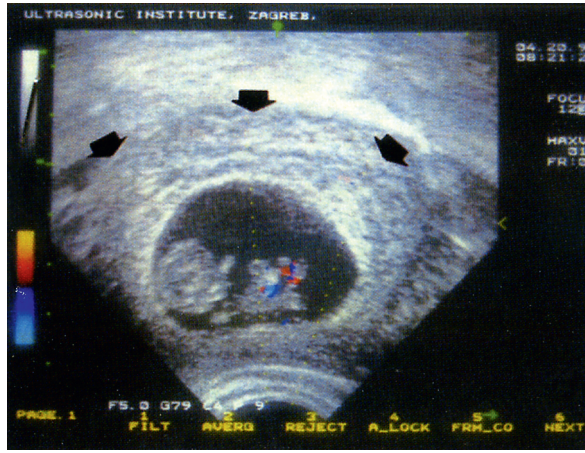

Fig. 11.11. Fetal ultrasound. Gestational age 10 weeks (transvaginal sonography)

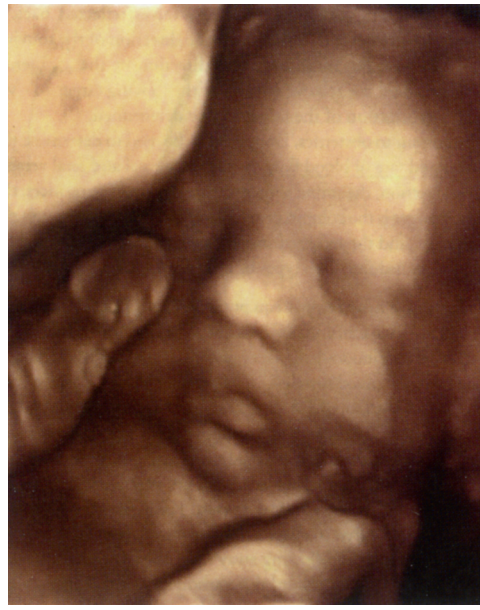

Fig. 11.12. Three-dimensional ultrasonography. Face of fetus. Gestational age 33 weeks

11.4. LABORATORY TESTS

Complete blood count. In a workup of a pregnant woman, complete blood count includes the following: red blood cell count, white blood cell count, platelets, reticulocytes count, WBC differential, hemoglobin concentration, ESR, color index, and hematocrit (Ht) (table 11.2).

Table 11.2. Normal hematological parameters in non-pregnant and pregnant women

Parameter	Non pregnant women	Pregnant women		
		I trimester	II trimester	III trimester
Hemoglobin (Hb), g/l	139 (115–152)	131 (112–165)	120 (108–144)	112 (110–140)
Hematocrit (Ht), % (capillary blood)	35–36	33–34	30–34	30–34
Arterial blood	35	33	36	34
Venous blood	40 (33–44)	36	33	32

End of the table 11.2

Parameter	Non pregnant women	Pregnant women		
		I trimester	II trimester	III trimester
Red blood cells, $\times 10^{12}$/L	4.2–5.4 (3.5–5)	4.2–5.4	3.5–4.8	3.7–5.0
Blood color index	0.85–1.05	0.85–1.05	0.85–1.05	0.85–1.05
Platelets, $\times 10^{9}$/L	180–320	180–320	180–320	350–380
Neutrophils, %	7.4 (4–8.8)	10.2	10.5	10.4
Band neutrophils	55 (45–70)	66	69	69.6
Segmented neutrophils	1–5	1–5	1–5	1–5
Basophils, %	40–70	40–70	40–70	40–70
Eosinophils, %	0.5 (0–1)	0.2	0.2	0.1
Lymphocytes, %	2.0 (1–5)	1.7	1.5	1.5
Monocytes, %	38.0 (20–45)	27.9	25.2	25.3
ESR, mm/h	4.0 (0.93–8)	3.9	4.0	4.5

Complete urinalysis. Normal urinalysis of pregnant women includes the following parameters (table 11.3).

Table 11.3. Normal parameters of complete urinalysis in pregnant women

Parameter	Characteristics or value
Quantity	150–250 mL
Color	From straw yellow to amber yellow
Transparency	Full
Specific gravity	1.015–1.030
pH	5.0–7.0
Protein	Absent or less than 0.075 g/L
Glucose	Absent
Bilirubin	Absent
Urobilinogen	Traces
Ketone bodies	Absent

End of the table 11.3

Parameter	Characteristics or value
Red blood cells	Solitary in the preparation
White blood cells	Up to 5 in the preparation and in the field of view
Epithelium	Single squamous and transient epithelial cells in the field of view
Casts	Absent
Salts	Solitary amorphous urates and oxalates in the field of view

Basic metabolic panel. The following parameters (table 11.4) are determined:

- protein and protein fractions;
- indices of nitrogen metabolism. Urea, the end product of metabolism;
- creatinine;
- glucose;
- indices of pigment metabolism;
- total cholesterol;
- electrolyte balance: potassium, sodium, calcium, phosphorus, magnesium, chloride;
- indices of iron metabolism.

Table 11.4. Biochemical blood parameters in non-pregnant and pregnant women by the trimester of gestation

Parameter	Non-pregnant women	Pregnant women		
		I trimester	II trimester	III trimester
Total protein, g/L	71.0	66.0	64.0	62.0
Albumin, g/L	34.0	32.0	28.0	25.6
Globulins, g/L: α_1-globulins	0.36	0.40	0.44	0.51
α_2-globulins	0.68	0.70	0.77	0.87
β-globulins	1.01	0.96	1.2	1.4
γ-globulins	0.97	0.73	0.69	0.68
Albumin/globulin	1.32	1.26	1.06	0.84
Urea, mmol/L	4.5	4.5	4.3	4.0

End of the table 11.4

Parameter	Non-pregnant women	Pregnant women		
		I trimester	II trimester	III trimester
Creatinine, μmol/L	73.0	65.0	51.0	47.0
Glucose, mmol/L	4.5–5.0	4.2	3.9	3.8
Bilirubin, μmol/L	3.4–17.1	–	–	–
Direct bilirubin, μmol/L	0–3.4	–	–	3.0
Indirect bilirubin, μmol/L	3.4–13.7	–	–	–
Alanine transaminase, IU/L	7–40	–	–	–
Aspartate transaminase,, IU/L	10–30	–	–	–
Alkaline phosphatase, IU	25	26	50	75
Sodium, mmol/L	142.0	139.0	137.0	134.0
Potassium, mmol/L	4.8	4.9	4.8	4.0
Chloride, mmol/L	107.0	102.0	98.0	99.0
Calcium, mmol/L	4.9	4.5	4.1	4.1
Magnesium, mmol/L	2.2	2.0	1.7	1.4
Phosphorus, mmol/l	2.0	1.57	1.53	1.47
Iron, mmol/L	13–32	21	14.6	10.6

Hormonal profile during pregnancy. Hormonal tests are administered if required, for early detection of anomalies during pregnancy.

The concentration of hormones in the blood of a pregnant woman. The concentration of *hydroxyprogesterone* is determined to diagnose congenital adrenal hyperplasia.

Determination of *prolactin* allows monitoring the state of fetus, its energy supply.

In case of intrauterine death of the fetus, prolactin concentration drops much earlier than the fetal heartbeat stops. Seriual assessment of this hormone level allows monitoring the placental function throughout pregnancy and diagnosing placental insufficiency. It has been found that a critical decrease of prolactin by 30% below the average level for a given gestational age, gives ground to suspect the development of IUGR. A decrease in concentration of 80% or more indicates fetal demise.

According to its biological activity, *estradiol* holds the leading position among estrogens. It provides for growth and development of uterus during pregnancy.

During normally developing pregnancy, blood *estriol* level rises with the increase in gestational age and fetal growth. Determination of estriol level is a method of monitoring fetal state during pregnancy.

Progesterone concentration is determined when the placental function is evaluated in complicated pregnancy. Blood progesterone level decreases in case of threatened miscarriage (fig. 11.13).

During pregnancy (especially in the third trimester), blood *triiodothyronine concentration* (T_3) elevates 1.5 times. After the delivery, the hormone level normalizes within a week.

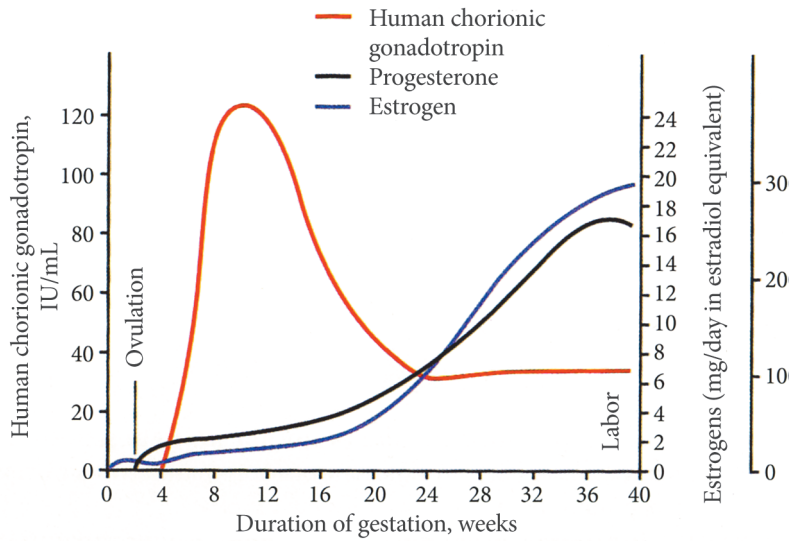

Fig. 11.13. Levels of estrogen (mg/day) in estradiol equivalent, chorionic gonadotropin (IU/mL) and progesterone during pregnancy

Testosterone concentration in the blood and amniotic fluid allows detecting maternal hyperandrogenism.

The assessment of blood clotting function is especially important in identifying disorders that can cause obstetric bleeding due to hypocoagulation or thrombosis and thromboembolism. Currently, assessment of hemostasis is made as a screening test if the pregnant woman has risk factors.

Laboratory assessment of hemostasis. Under normal conditions, functioning of the hemostatic system depends on the state of the vascular wall, platelets, blood coagulation factors, and fibrinolysis. During pregnancy, significant changes in the system of coagulation and fibrinolysis occur. The activity of coagulation factors, especially fibrinogen, increases. Fibrin is deposited on the walls of blood vessels of the uteroplacental system, and fibrinolysis is suppressed. These changes along with an increase of circulating blood volume prevent bleeding during detachment of placenta, contribute to formation of intravascular blood clots, and play an important role in prevention of pregnancy complications such as thromboembolism and bleeding.

During normal pregnancy, significant changes occur in the hemostatic system: plasma concentrations of VII, VIII, X coagulation factors, and especially fibrinogen increase (table 11.5).

Table 11.5. The most important parameters of hemostatic system during pregnancy

Parameter	Trimester of pregnancy		
	first	end of the second	end of the third
Fibrinogen, g/L	2.98±0.08	3.11±0.31	4.95±0.62
APTT, s	39.2±4.1	36.5±2.1	34.1±2.5
ART, s	64.4±6.9	61.4± 5.9	51.1±4.8
Prothrombin index, %	89.3±4.5	95.4±5.3	108.8±3.3
FDP, μg/ml	<2.0	<2.0	5.7 ±0.9
Antithrombin III, g/L	0.222±0.032	0.175±0.013	0.15±0.019
TPI in thromboelastography c.u.	8.5±1.3	10.4±1.9	18.1±3.4
Platelets, $\times 10^9$/L	302±14,5	288±12	350±14

Note. APTT — activated partial thromboplastin time; ART — activated recalcification time; FDP — fibrinogen degradation products; TPI — thrombodynamic potential index.

Fibrinolytic activity of plasma is decreased during pregnancy reaching its minimum in labor and returning to the baseline level one hour after the delivery of placenta (end of labor).

11.5. PRENATAL SCREENING DURING PREGNANCY

Screening is a set of measures and medical investigations, tests and other procedures aiming at preliminary identification of individuals among whom the probability of certain disease is higher than in the rest of examined population.

Sensitivity of a screening test is the ability to correctly identify individuals who have the disease that they were screened for.

Specificity is the ability of the test to correctly identify individuals without this disease.

The probability of the presence of disease in the case of known result of the test is called its **predictive value**.

Each pregnant woman has a certain risk of chromosomal abnormality. The baseline (initial) risk depends on the woman's age. The individual patient's risk is calculated by multiplying the baseline risk by the value of likelihood ratios for screening tests performed during this pregnancy.

Basic methods of prenatal diagnostics include:

- sonography (ultrasound investigation of fetal state and dynamics of fetal growth in the I (10–14 weeks), II (20–24 weeks) and III (30–34 weeks);
- invasive diagnostics (chorionic villus sampling, amniocentesis, placentocentesis and cordocentesis), only if required;
- biochemical screening for fetal genetic abnormality (markers of chromosomal abnormality).

Ultrasound investigation (sonography, scanning) is a highly informative, safe, non-invasive method that allows monitoring of the fetus over time from the earliest developmental stages.

In obstetrics, two main methods are most widely used: *transabdominal* and *transvaginal scanning*. Transabdominal scanning uses probes (linear, convex) with the frequency of 3.5 and 5.0 MHz, transvaginal scanning uses sectoral probes with the frequency of 6.5 MHz and higher. The use of transvaginal probes allows diagnosing pregnancy at earlier terms, assessing the development of gestational sac (embryonic and extraembryonic structures) more accurately, and diagnosing most major embryonic/fetal developmental abnormalities starting from the first trimester.

Ultrasound in the I trimester is performed for the following purposes:

- establishing the uterine localization of gestation based on visualization of the gestational sac in the uterine cavity;
- ruling out ectopic (extrauterine) pregnancy;

- diagnosing multiple pregnancy, determining the type of placentation (dichorionic, monochorionic);
- assessing the growth of gestational sac [mean internal diameter of gestational sac, crown rump length (CRL) of embryo/fetus];
- determining the vital activity of embryo (cardiac function, motor activity);
- examining the anatomy of embryo/fetus, detecting sonographic markers of chromosomal abnormality;
- examining extraembryonic structures (yolk sac, amnion, chorion, umbilical cord);
- detecting complications (threatened abortion, incipient abortion, complete abortion, hydatiform mole);
- diagnosing genital disease (uterine fibroids, structural abnormality of uterus, uterine synechiae, ovarian tumors).

Objectives of ultrasound in the II trimester:

- assessing fetal growth in accordance with the estimated gestational age;
- diagnosing developmental abnormalities;
- checking for markers of chromosomal abnormality;
- detecting ultrasound markers of chromosomal abnormality (thickening of nuchal fold);
- revealing early stages of fetal growth retardation;
- assessing the location, thickness and structure of placenta;
- determining the amount of amniotic fluid.

Objectives of ultrasound in the third trimester:

- diagnosing developmental abnormalities with late manifestation;
- determining fetal growth retardation and its severity;
- assessing the functional state of the fetus (assessment of motor activity and respiratory function, blood flow in the maternal–placental–fetal system using Doppler ultrasound).

In this country, ultrasound screening is performed at 10–14, 20–24 and 30–34 weeks.

The yolk sac, whose size varies from 6 to 8 mm is detected from the 4th–5th week of gestation. Physiological reduction of the yolk sac occurs by the 12th week. The absence of yolk sac and its premature reduction are unfavorable prognostic signs.

Gross intrauterine fetal malformations are diagnosed using transvaginal sonography in the I trimester: anencephaly, myelocele, skeletal abnormalities.

At 11–14 weeks it is critical to detect the sonographic markers of chromosomal pathology: hypoplasia or absence of the nasal bone, non-immune hydrops fetalis.

Fetometry (measurement of fetal size) is performed for the assessment of fetal growth in the II and III trimester. Fetometry includes the measurement of biparietal diameter and head circumference, abdominal diameter and circumference, as well as the length of the femur.

The objects of examination are cerebral structures, the skeleton, facial skull, internal organs of the fetus: heart, lungs, liver, stomach, intestine, kidneys, adrenal glands, and therinary bladder. Thanks to ultrasound, it is possible to diagnose most of the developmental abnormalities fetus. For a detailed assessment of the fetal anatomy, three-dimensional sonography is used additionally.

The range of sonographic markers of chromosomal pathology in the fetus detected in the second trimester includes changes in various organs and systems. These include ventriculometry, cysts of choroid plexuses of lateral ventricles, abnormal shape of the skull and cerebellum, hyperechoic intestines, pyeloectasis, single artery of umbilical cord, symmetrical fetal growth restriction.

Using ultrasound, the placenta can be examined in detail, obtaining information on its location, thickness, and structure.

Location of the placenta at different stages of pregnancy can change due to its "migration". If placenta previa is detected before 20 weeks gestation ultrasound should be repeated every 4 weeks. The final conclusion about the location of placenta is possible only at the end of pregnancy.

Placental thickness is an important indicator of its condition. Placental thickness is characterized by a typical growth curve as the pregnancy progresses. Placental growth stops at 36–37 weeks gestation. Further, in a physiological pregnancy, its thickness decreases or remains at the same level, and equals 3.3–3.6 cm.

There are main signs, according to which the degree of placental maturity is determined (table 11.6).

Table 11.6. Placental grading (by P. Grannum)

Degree of placental maturity	Chorionic plate	Parenchyma	Basal plate
0	Straight, smooth	Uniform echogenicity	Not identified
I	Subtle indentations	Occasional hyperechoic areas	Not identified

End of the table 11.6

Degree of placental maturity	Chorionic plate	Parenchyma	Basal plate
II	Deep indentations	Occasional basal calcification/hyperechoic areas	Linear location of small hyperechoic areas (basal dotted line)
III	Interrupted by indentations (frequently calcified)	Roundish indurations with translucency in the center	Significant calcification

Changes in the placental structure can be in the form of cysts, which are visualized as echo-negative formations of various shape and size.

Ultrasound is also used for the diagnostics of *postoperative uterine scar integrity*. A uterine scar in a good condition shows homogeneous structure of tissues and uneven contours of the lower uterine segment. Uterine scar dehiscence is when detecting a defect in the form of deep fossa, thinning in the area of suspected scar, presence of large amount of hyperechoic areas (connective tissue).

Valuable information on the *state of cervix during pregnancy and about the risk of preterm delivery is obtained using ultrasound*. During transvaginal and transabdominal sonography, it is possible to measure the total length of the cervix, assess the state of the cervical canal, degree of the opening of internal uterine os.

Doppler ultrasound for assessment of blood flow in maternal–placental–fetal system. Recently Doppler ultrasound along with cardiotocography became the leading method of examination in obstetrics as it allows assessing the functional state of blood supply to the uterus, placenta, fetus (fig. 11.14).

The essence of the Doppler effect is that ultrasonic vibrations transmit in the examined object in the form of elastic waves. On the border of biological media with a difference in acoustic impedance, a part of the energy of oscillations of elastic waves passes into the second medium, and another part is reflected from the interface. In this case, the frequency of oscillations reflected from a stationary object is not changed and is equal to the initial frequency of the generated ultrasonic impulses.

In medicine, Doppler effect is mainly used to determine blood flow rate. In this case, blood cells, first of all erythrocytes, serve as a reflective surface. The parietal layers of blood in the vessels flow at a much lower rate than the central

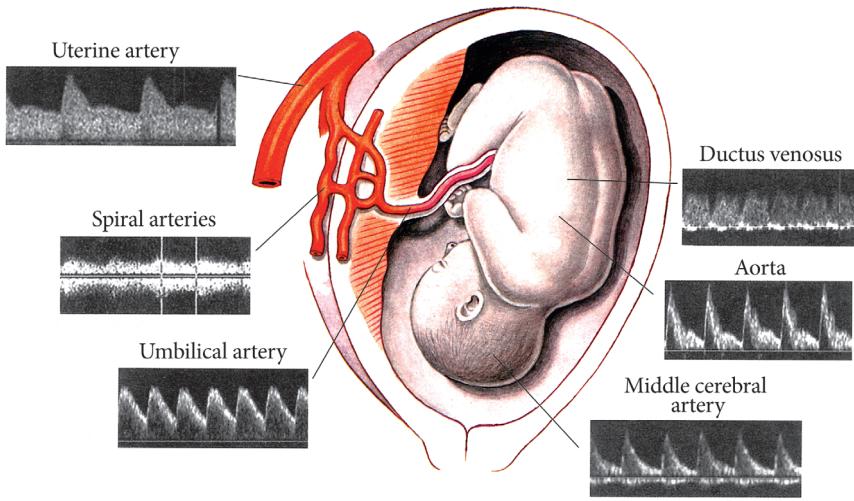

Fig. 11.14. Doppler ultrasound of the blood flow in maternal–placental–fetal system

ones. Thus, the blood flow in the vessel is represented as a certain velocity range, which is reflected in the dopplerogram by the corresponding frequency range that changes throughout the cardiac cycle.

There are quantitative and qualitative methods of assessing of dopplerograms of blood flow in examined vessels. In the quantitative analysis, the volumetric blood flow through a cross section of the vessel per unit of time is determined by multiplying the average linear blood flow velocity by the area of the vascular lumen. Currently, qualitative analysis of spectral curves is widely used for dopplerogram interpretation; its parameters do not depend on the diameter of the vessel and the angle of insonation since qualitative characteristics of the blood flow are based on the ratio of its velocity in different phases of the cardiac cycle:

- systolic-diastolic ratio (A/B) — the ratio of maximum systolic velocity (A) to the final diastolic one (B);
- resistance index (RI): (A–B)/A;
- pulsation index — (A–B)/M, where M is the average blood flow velocity throughout the cardiac cycle.

Assessment of the uteroplacental blood flow in the uterine arteries, their branches (spiral arteries) and umbilical arteries as well as fetal hemodynamics in the aorta and cerebral vessels of the fetus is of greatest practical value during pregnancy.

For an objective assessment of blood circulation in the mother–placenta–fetus system, a classification of disorders of uteroplacental and fetoplacental blood flow is used [A. Strizhakov et al., 1989]. According to the authors, there are three grades of uteroplacental and fetal blood flow impairment.

- I grade:
  - A impairment of uteroplacental blood flow (uterine arteries) with normal fetoplacental blood flow (umbilical artery),
  - B impairment of fetoplacental blood flow with normal uteroplacental blood flow;
- II grade: impairment of uteroplacental and fetoplacental blood flow that does not reach critical values (diastolic blood flow is intact);
- III grade: critical impairment of fetoplacental blood flow ("zero" or retrograde diastolic blood flow with intact or impaired uteroplacental blood flow).

Doppler indices for fetal vessels in the III trimester are provided in table 11.6.

Table 11.6. Doppler indices of blood flow in fetal aorta, umbilical artery and uterine artery in the III trimester of non-complicated pregnancy

Vessel	Systolic-diastolic ratio depending on gestational age, weeks			
	27–29	30–32	33–35	36–41
Aorta	5.69±0.7	5.41±0.53	5.24+0.66	4.94+0.44
Umbilical artery	3.19±0.4	2.88±0.46	2.52±0.31	2.14±0.24
Uterine artery	1.85+0.34	1.78±0.3	1.69+0.3	1.66+0.24

The accuracy of diagnosing fetal disorders using Doppler ultrasound is 70%. There is a clear correlation between changes in Doppler indices and fetal growth restriction. In unilateral decrease of uteroplacental blood flow, fetal growth restriction is noted in 67% of cases, in bilateral decrease of blood flow — in 97%. Upon a simultaneous decrease in uteroplacental and fetoplacental blood flow, fetal growth restriction develops in almost 100%.

A relatively new method based on the Doppler effect is Color Doppler (flow) Mapping (CDM), a combination of two-dimensional pulse-wave and color information on the blood flow velocity in examined organs. Due to the high resolution of devices, it is possible to visualize and identify the smallest vessels of the microvasculature in the mother–placenta–fetus system.

11.6. FETAL MONITORING AND INTERPRETATION OF ITS RESULTS

Cardiotocography is an assessment of fetal cardiac activity during pregnancy and delivery. Parameters of cardiac activity reflect the functional state of the fetus in the ante- and intranatal period. Monitoring of fetal cardiac activity is carried out using a cardiotocograph (fetal heartbeat monitor). The method is based on the Doppler principle, the use of which allows registering abnormal intervals between separate cycles of fetal cardiac activity which are converted into heart rate changes in the form of a graphic image (cardiotocogram). Cardiotocogram (CTG) is two curves combined in time: one of them displays fetal heart rate, and the other one, uterine contractile activity. In addition to uterine contractions the uterine activity curve also detects the motor activity of the fetus.

Cardiac monitoring is a timely diagnostic tool for disorders in fetal functional state allowing a choice of appropriate tactics of therapeutic measures, as well as the optimal time and method of delivery.

Indications for CTG during pregnancy include risk factors for fetal hypoxia in such conditions as preeclampsia, essential hypertension, diabetes mellitus, post-term pregnancy, multiple pregnancy, fetal growth restriction, oligohydramnios, perinatal losses, decreased motor activity of the fetus, hemodynamic disorders in the mother-placenta-fetus system according to Doppler assessment.

During labor, continuous fetal cardiomonitoring is indicated for all parturient women.

During pregnancy, indirect CTG is used.

During cardiotocography, an ultrasound probe is placed on the maternal anterior abdominal wall in the site where fetal cardiac sounds are best heard. CTG is performed with the pregnant woman (parturient woman) on her side or semi-sitting. To obtain accurate information on the fetal condition, cardiac monitoring should be performed for at least 20–30 minutes. This length of observation is explained by the presence of sleep and wake periods in the fetus.

CTG is considered reasonable from the 32nd week of pregnancy. However, the use of devices with **automatic analysis** of cardiotocograms allows evaluating fetal cardiac activity **from the 26th weeks of pregnancy**.

To read a CTG the following is determined:

- baseline heart rate and baseline variability of heart rate;
- amplitude;
- presence of accelerations and decelerations, tachycardia and bradycardia;
- curve of uterine contraction.

Reading of cardiotocogram starts from determination of baseline heart rate. *Baseline heart rate* means an average value between instantaneous values of the fetal heartbeat, which remains unchanged for 10 minutes or more while acceleration and deceleration are taken into account.

When characterizing the baseline heart rate, it is necessary to consider its variability, i.e. frequency and amplitude of instantaneous changes in fetal heart contractions (*oscillations*). The frequency and amplitude of instantaneous oscillations are calculated for each subsequent 10 minutes. The amplitude of oscillations is determined according to the deviation from the baseline heart rate, the frequency is determined according to the number of oscillations per 1 min.

In clinical practice, the following classification of the types of baseline variability is most common:

- silent (smooth) rhythm characterized by low amplitude (0.5 per minute);
- slightly undulating (5–10 per minute);
- undulating (10–15 per minute);
- saltatory (25–30 per minute).

The presence of silent (smooth) and slightly undulating rhythm usually indicates an impairment in fetal functional state. Undulating and saltatory rhythms indicate a satisfactory state of fetus.

In addition to oscillations, in the interpretation of cardiotocograms attention is paid to accelerations a decelerations.

Acceleration is an increase of heart rate by 15–25 beats per minute compared to the initial (baseline) heart rate. Accelerations occur in response to fetal movement, contractions, functional tests. The presence of accelerations is a favorable sign and indicates a satisfactory state of fetus.

Decelerations are episodes of slowing down of the heart rate by 30 beats and more with duration of not more than 30 s. There are three main types of decelerations.

1. *Early decelerations* begin simultaneously with a contraction or with a delay of up to 30 s and have a gradual beginning and end. The duration and amplitude of early decelerations correspond to the duration and in-

tensity of contraction. Early decelerations are a fetal reflex reaction to short-term cerebral ischemia due to the compression of fetal head during contraction. Early decelerations are not considered to be a sign of hypoxia if no other pathologic changes are seen on the CTG.

2. *Late decelerations* are also related to contractions but occur 30 s and more after the start of uterine contraction. Late decelerations achieve their peak after the maximum strain of the uterus, their duration often exceeds the duration of contraction. Late decelerations are a sign of uteroplacental circulation impairment and progressing fetal hypoxia.
3. *Variable decelerations* are varied in time, irrespective of the start of the contraction, and have different (V-, U-, W-like) shape. The appearance of variable decelerations is related to umbilical cord compression during contractions, fetal movement, or oligohydramnios.

The criteria of reassuring antenatal cardiotocogram include:

- baseline rhythm of 120–160 per min;
- amplitude of baseline variability is 10–25 per min;
- absence of decelerations;
- presence of two or more accelerations during 10 minutes of monitoring.

In the presence of *a normal CTG* for 10 minutes, no further monitoring is needed.

The following signs are characteristic for *dubious CTG*:

- baseline rhythm is within 100–120 or 160–180 per min;
- amplitude of baseline variability is less than 10 or more than 25 per min;
- absence of accelerations;
- spontaneous shallow and short decelerations.

If such type of CTG is recorded, one administers a repeated examination after 1–2 hours and additional examination methods to assess the functional state of the fetus.

The following *is indicative of* abnormal CTG:

- baseline rhythm of less than 10 per minute or more than 180 per minute;
- amplitude of baseline variability is less than 5 per min;
- pronounced variable decelerations;
- late decelerations;
- sinusoidal pattern.

Methods of interpretation of CTG results. There is an opinion about inadequate diagnostic value of CTG in the assessment of fetal disorders as evidenced by a considerable number of false-positive results in the group with pathological changes in the cardiotocogram, when compared to outcomes of delivery. According to other data, the accuracy of prediction of satisfactory

condition of newborns coincided with CTG results in more than 90% of cases which indicates a high precision of the method to confirm the normal state of the fetus. However, this is not a sign of CTG method drawback but only indicates a low information value of various approaches to the cardiotocogram analysis.

A most important issue of cardiotocographic monitoring is interpretation of obtained data. Currently existing methods assessing the fetal condition according to CTG data can be nominally divided into two groups.

One group includes *methods of computerized assessment of CTG records* using a special processor integrated in the cardiac monitor or using an additional computer. Moreover, as a rule, these methods need expensive equipment and computer software specially designed for this purpose.

Such method of CTG data reading has a number of advantages: objectivity of fetal state assessment, absence of subjective analysis, reducing the time spent for examination, excluding the effect of fetal sleep phase on the final result, the ability to save and subsequently quickly reproduce the CTG records and calculated parameters. Computed CTG analysis confirms that the following has the best prognostic value: baseline rhythm and its variability, characteristics of accelerations and decelerations.

The second group is represented by the most simple, accessible, and widely used *methods of visual analysis*, often with an assessment of CTG parameters in points. Various scales are currently used to evaluate antenatal CTG. Among them, the most common scales are those proposed by W. Fischer et al. (1976), E.S. Gauthier et al. (1982), as well as their various modifications.

The use of rating scale is based on the fact that the reactivity of the fetal cardiovascular system is assessed utilizing CTG parameters which are characterized by certain normal and pathological signs. Each CTG parameter is rated according to the identified *dominant sign*. The latter includes the one that corresponds to the most significant pathological change of this parameter (the lowest score).

The results of assessment of CTG data correlate with sonographic data used for detection of signs of fetoplacental insufficiency (FPI). Sonographic signs of *compensated* FPI are most often accompanied by early stage of impairment of reactivity of the fetal cardiovascular system. Moderate reactivity impairment is most often observed in pregnant women with sonographic signs of *sub-compensated* FPI. Significant reactivity impairment is observed when pregnant women have sonographic signs of *decompensated* FPI. Both significant and severe impairment of reactivity of fetal cardiovascular system are specific for pregnant women with sonographic signs of *critical* FPI.

11.7. INVASIVE INSTRUMENTAL DIAGNOSTIC METHODS

Saling's test is evaluation of pH of capillary blood taken from the fetal scalp.

Chorionic villus sampling is an invasive procedure that involves obtaining chorionic villi for subsequent investigation in order to diagnose congenital or hereditary diseases of the fetus.

Amniocentesis is a puncture of the amniotic membrane in order to obtain amniotic fluid for subsequent laboratory testing. Amniocentesis can be performed in the I, II and III trimester (most optimally — at 16–20 weeks gestation).

Cordocentesis is puncture of umbilical vessels in order to obtain blood for laboratory tests or for transfusions of blood products and/or medication infusion to the fetus.

To diagnose fetal chromosomal abnormality, it is necessary to obtain material of fetal origin using invasive techniques. Currently the main invasive diagnostic methods are *chorion villus sampling* and *amniocentesis* in which the fetal karyotype is determined.

The incidence of abortion during chorion villus sampling in the first trimester is 1% and does not differ from that after amniocentesis in the second trimester. Chorion villus sampling should not be performed before 10 weeks gestation due to a risk of fetal damage.

Amniocentesis is not recommended before 15 weeks gestation due to the higher incidence of abortion during its early conduction as well as a potential for fetal talipes equinnovarus deformity.

11.8. NONINVASIVE PRENATAL DNA-SCREENING FOR FETAL ANEUPLOIDY

Chromosomal aneuploidy is a genetic abnormality in which one or more extra chromosomes are present or one or more chromosomes are absent: Down's syndrome (trisomy 21), Edwards syndrome (trisomy 18), Patau syndrome (trisomy 13) and others. During standard noninvasive screening of pregnant women (ultrasound and biochemical parameters), only indirect markers of chromosomal abnormalities are evaluated. Currently, a new noninvasive prenatal screening method for direct analysis of fetal extracellular DNA in the maternal blood has been proposed; it has high sensitivity and specificity.

DNA screening is recommended at gestational age of at least 10–11 weeks and no later than 17 weeks (time is required for the test and subsequent confirmatory invasive diagnostics).

Indications for DNA screening:

- screening for fetal aneuploidy in a singleton pregnancy upon patient's request if not contraindicated.

Contraindications for DNA screening:

- oncological diseases in pregnant woman;
- multiple pregnancy (including spontaneous reduction of a twin).

If a high risk of chromosomal abnormalities is detected using noninvasive DNA test, invasive prenatal diagnostics with fetal karyotyping is required to confirm aneuploidy.

11.9. MEDICAL GENETIC COUNSELING AND PRENATAL DIAGNOSIS OF HEREDITARY CONDITIONS

Hereditary diseases (genetic apparatus impairment) and congenital abnormalities (without genetic apparatus impairment) hold the 2nd–3rd place among all causes of perinatal mortality. More than 2,500 nosological entities of hereditary diseases that affect all organs, systems of the body and disrupt its functions are known. Severe hereditary abnormality that causes death or disability of the child occurs in 1–2% of cases.

As a rule, there is no effective therapy for most hereditary diseases; therefore its prevention, which is carried out using genetic counseling and early prenatal diagnosis, plays an important role.

There are the following groups of hereditary diseases: multifactorial, monogenic and chromosomal.

The first, largest group of diseases (detected by medical genetic counseling) is multifactorial, or polygenic, diseases.

Various chemical compounds, ionizing radiation, drugs (antiblastic drugs, some antibiotics, etc.), viral diseases (for example, rubella) should be distinguished among environmental factors that can have an adverse effect on the fetus especially in the first trimester.

It is difficult to assess the genetic hazard of ionizing radiation for humans, therefore all the procedures during which x-ray irradiation of the gonads occurs, should be carried out according to strict indications. Investigations such as urography, hysterosalpingography in the very early stages of pregnancy are undesirable.

The genetic risk of recurrence of multifactorial disease usually does not exceed 5%. Such diseases include isolated congenital abnormalities (for example, anencephaly, various hernias, myelocele, heart defects), some forms of schizophrenia, essential hypertension, atherosclerosis, etc.

The second group includes monogenic diseases. They are due to impairment of one gene.

Diseases with autosomal dominant mode of inheritance are characterized by the same frequency in individuals of different sexes; the presence of condition in one of the parents; transmission of the disease from generation to generation i.e. vertically in 50% of cases.

These diseases include achondroplasia, Marfan syndrome, Ehlers–Danlos disease, neurofibromatosis, etc. As a rule, these diseases are not life-threatening, have a high manifestation (penetrance), the type of inheritance is clear.

The diagnosis and prognosis for the offspring are not difficult to make. Risk assessment is complicated if the disease is not traced in the family pedigree but appears sporadically. In this case, it occurs in the family for the first time due to changes (mutations) in the germ cells of one of the parents; prognosis for the offspring in subsequent pregnancies is usually favorable. The birth of a child with achondroplasia from phenotypically healthy parents does not indicate recurrence of this disease in subsequent children.

Diseases with autosomal recessive mode of inheritance are characterized by the same frequency in individuals of different sexes, absence of disease in the parents (they are usually heterozygous carriers of the pathological gene), transmission of the disease from healthy parents to children, i.e. horizontally in 25% of cases; their frequency increase in case of intermarriage. These diseases are associated with a severe course and high mortality. Examples of such diseases are numerous enzymopathies, phenylketonuria, congenital adrenal hyperplasia (androgenital syndrome), hypothyroidism, cystic fibrosis, some hereditary skin diseases (bullous epidermolysis, ichthyosiform erythroderma), etc.

Sex-linked diseases usually affect males; the mother is a heterozygous carrier of the pathological gene; the disease is transmitted to 50% of sons; all daughters of affected father will be heterozygous carriers.

Examples of this type of disease are hemophilia, Duchenne muscular dystrophy.

The third group of hereditary diseases includes chromosomal diseases. They are characterized by the presence of multiple congenital malformations, impairment of organ and system functions, first of all of the nervous and endocrine system, retardation of mental development. Amenorrhea and infertility can be clinical signs of chromosomal diseases. Diseases caused by a numerical change in chromosomes are classified as random, and do not often affect subsequent conditions. The occurrence of such diseases is facilitated by the same factors that cause multifactorial pathology. The most common diseases of this

group are Down's syndrome (trisomy 21), Patau syndrome (trisomy 13), Edwards syndrome (trisomy 18), Turner syndrome (monosomy X), Klinefelter syndrome (karyotype 47, XXY), etc. The influence of the mother's age on the birth of child with Down's syndrom has been clearly established. For young women (under 35 years old), the population risk is 1:700. For women aged 35–40 years old, it increases to 1:300–1:100, and after 40 years old — up to 1:100–1:40.

Care consists in genetic counseling aiming mainly to identify a genetic risk and prevent the appearance of patients with hereditary disease in the family.

The main objectives of genetic counseling:

1) establishing an accurate diagnosis of hereditary disease;
2) determining the type of inheritance of the disease in this family;
3) assessing the risk of disease recurrence in the family;
4) determining the most effective method of prevention.

Genetic risk is the likelihood of occurrence of a certain hereditary disease in the patient or their offspring. It is determined by calculations based on an analysis of genetic patterns or using empirical data. The possibility of assessing the genetic risk depends mainly on the accuracy of the diagnosis and the completeness of the family pedigree data.

Genetic risk of up to 5% is assessed as low and is not considered a contraindication to childbearing in this family. A risk of 6–20% is considered moderate. In this case, recommendations regarding further pregnancy planning depend on the severity of medical and social consequences of certain hereditary disease and the possibility of prenatal diagnostics. The risk of more than 20% is considered high, and if methods of prenatal diagnosis of the relevant condition are unavailable, further childbearing in this family is not recommended.

The main indications for referral of couples to genetic counseling:

1) birth of a child with hereditary disease or congenital abnormalities;
2) presence of chromosomal rearrangement, hereditary disease or congenital abnormality in one of the partner;
3) intermarriage;
4) maternal age >35 years old;
5) unfavorable effect of environmental factors at an early gestation age;
6) history of spontaneous miscarriage, stillbirth, primary amenorrhea, primary infertility in partners;
7) threatening miscarriage at an early gestational age;
8) administration of drugs at an early gestational age;
9) detection of ultrasound and/or biochemical markers of fetal chromosomal and congenital abnormalities.

Depending on the disease nature, various methods of examination of the patient and their relatives are used during counseling; the main ones include clinical genealogical, cytogenetic, biochemical, immunological, molecular genetic (DNA analysis) methods, and methods of prenatal diagnosis.

The clinical genealogical method, or method of collecting and analyzing the pedigree, provides the necessary information for making a diagnosis or establishing the etiological nature of the disease. The main objective of genealogical method is to determine the hereditary nature of the disease followed by specification of its variety and type of inheritance.

The cytogenetic method allows a direct study of the entire chromosome set of the individual (karyotype). Karyotyping is indicated for women with history of miscarriage, stillbirths or with children who died from unclear causes at a young age, persons with primary amenorrhea or impaired sexual differentiation.

The introduction of prenatal diagnostic methods significantly increased the effectiveness of genetic counseling and allowed a transition from probabilistic to definitive prognosis for the offspring health. Two groups of prenatal diagnostic methods are used: noninvasive and invasive.

Noninvasive methods of prenatal diagnosis (ultrasound in the I and II trimester, tests for alpha-fetoprotein, chorionic gonadotropin, PAPP-A and unconjugated estriol in the maternal blood serum) are screening tests, that is they can be used in examination of all pregnant women.

Invasive methods of prenatal diagnosis include amniocentesis, chorionic (or placental) biopsy, cordocentesis (obtaining fetal blood from the umbilical cord vessels) and fetal skin biopsy. Using these methods fetal cells are obtained for cytogenetic, biochemical, molecular genetics and other types of analysis.

Ultrasound has a special place in prenatal diagnosis. There is a clear relationship between the nature of the defect and the period of its detection using ultrasound. A number of congenital abnormalities can be diagnosed at the end of the I trimester — beginning of the II trimester. Such abnormalities include anencephaly, exencephaly, lymphangiomas of the neck, ophthalmocele, gastroschisis, conjoined twins, amelia, achondrogenesis, craniocerebral and spinal hernias, polycystic kidney disease, imperfect osteogenesis, etc. The accuracy of diagnosis for these abnormalities is approximating to 100% at the end of the second trimester. The accuracy of diagnosis for congenital heart abnormalities in the fetus is 87% in the population, 90% — in the population of high risk.

For timely diagnosis of congenital abnormalities in the fetus, a well-managed organization of ultrasound screening is required: it should cover all preg-

nant women at least 3 times during pregnancy (at 10–12, 20–22 and 30–32 weeks), and if required (history or suspected abnormality), it should be performed more often (after 3–4 weeks) and with careful examination of all organs and systems of the fetus.

At an early gestational age chorion villus sampling is used for prenatal diagnosis. The age of 8–11 weeks gestation is optimal for this procedure. Sampling chorionic tissue is indicated in the following cases:

- abnormal karyotype in one of the parents;
- maternal age >35 years old;
- presence of a child with chromosomal abnormality in the family, sex-linked diseases, metabolic disorders, hemoglobinopathies.

Amniocentesis in the second trimester is a most widespread method of prenatal diagnostics is most widespread. Currently, only transabdominal technique is used. The optimal period for its implementation is 17–20 weeks gestation. During the analysis of amniotic fluid, karyotype of the fetus, the level of various enzymes, hormones can be determined; DNA analysis can be performed and thus fetal chromosomal abnormality, some autosomal recessive and inherited sex-related diseases, CNS malformations can be diagnosed. In some cases, amniocentesis can be performed in the first trimester to diagnose congenital adrenal hyperplasia and chromosomal abnormality.