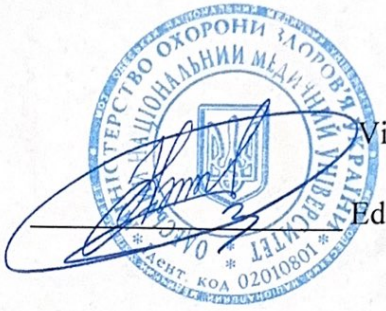
MINISTRY OF HEALTH OF UKRAINE
ODESA NATIONAL MEDICAL UNIVERSITY

International Faculty

Department of obstetrics and gynecology



CONFIRMED by
Vice-rector for scientific and pedagogical work
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September 1, 2023

METHODOLOGICAL RECOMMENDATIONS FOR LECTURE

International Faculty, Course V

Discipline "Obstetrics and Gynecology"

Lecture №2. Topic: Fetal distress. Intrauterine growth restriction.

Approved:

Meeting of the Department of Obstetrics and Gynecology of Odesa National Medical University

Protocol No. 1 dated August 28, 2023.

Head of the Department_____ (Ihor GLADCHUK)

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LECTURE №2:

FETAL DISTRESS. INTRAUTERINE GROWTH RESTRICTION

RELEVANCE: Placenta ("child's place") – is an extremely important organ, which exists only during pregnancy. It connects the functional systems of two organisms – the mother and fetus, providing the fetus with necessary vital substances. Etiology and pathogenesis, clinical features, classification and modern diagnostic methods of placental dysfunction and baby's wellbeing are basic to understand here to provide qualified emergency care, modern principles of prevention and medical rehabilitation of the patients. Unless well studied, this can make impossible to master physiological and pathological obstetric care.

LEARNING OBJECTIVE is to gain basic knowledge about anatomical, physiological and biochemical changes during pregnancy, be familiar with the physiologic adaptations associated with a normal pregnancy, be able to differentiate between certain signs and symptoms that can be common to both disease processes and to physiologic adaptations of pregnancy, obtain knowledge about placenta functions, signs of fetal distress and intrauterine growth restriction, methods of examination of baby's wellbeing, to give appropriate prenatal counseling and supervision in order to provide successful obstetric outcome.

BASIC CONCEPTS: Fertilization and development of a fertilized egg. Placenta, its structure and function. Critical periods of embryo and fetal development. Influence of harmful factors on the embryo and fetus. Physiological changes in a woman's body during pregnancy. Definition, etiology and pathogenesis of placental dysfunction. Classification of placental dysfunction. Evaluation the fetal condition during placental dysfunction depending on the degree of compensatory placental mechanism. Prediction of the course of the pregnancy and the fetal condition depending on the degree of placental dysfunction. definition, etiology and pathogenesis of fetal distress syndrome. Aetiology and pathogenesis of IUGR (retardation, hypotrophy). Hygiene and nutrition of a pregnant woman. Methods of examination of baby's wellbeing. The knowledge of modern methods of diagnostics during the antenatal period during a non-complicated pregnancy helps reveal fetal disorders in the early stages of a pregnancy.

PLAN AND ORGANIZATIONAL STRUCTURE OF THE LECTURE

№	The main stages of the lecture, their content	Type of lecture, equipment of the lecture	Time distribution
1.	*Preparatory stage*		
	▫ Defining of educational goals		3 min

	▫ Providing of positive motivation		2 min
2.	*The main stage*		
	▫ Presentation of lecture material	Clinical	90%
	Plan:		
	– Physiological changes in the mother's body during pregnancy. - Diagnosis of pregnancy. - Methods of examination of pregnant women. - Methods of assessment of fetal wellbeing. - Perinatal protection of the fetus.	Multimedia equipment (computer, projector, screen, TV). Power Point presentation	15 min 15 min 20 min 15 min. 15 min
3.	*The final stage* Lecture summary. Answers to questions. Tasks for self-preparation		5 min

EDUCATIONAL MATERIALS

PLACENTAL DYSFUNCTION. FETAL DISTRESS. INTRAUTERINE GROWTH RESTRICTION

Placenta functions

Placenta ("child's place") – is an extremely important organ, which exists only during pregnancy. It connects the functional systems of two organisms – the mother and fetus, providing the fetus with necessary vital substances. During the course of a normal pregnancy, the placenta is located in the corpus of the uterus on the posterior (more often) or anterior wall. It is completely formed by 15-16 weeks of pregnancy, after 20 weeks is when active exchange through the placenta vessels begins. From 22 to 36 weeks, the placenta increases in weight, and by 36 weeks it reaches it full functional maturity.

The placenta is similar to a round flat disk. By the end of the pregnancy, the placenta weighs 500-600 gr., has a diameter of 15-18 cm and a thickness - 2-3 cm. There are two surfaces distinguished on the placenta: maternal, turned toward the uterine wall, and the fetal – turned toward the amnion cavity.

Normally, the placenta together with its membranes (afterbirth) is born 10-15 minutes after the birth of the fetus. It is attentively examined and sent for morphological research. First, it is very important to be convinced that the placenta was born (detached) entirely (i.e. there are no damages on its surface and no lobes or parts of the placenta have remained inside the uterine cavity). Secondly, the condition of the

placenta can be judged by the course of the pregnancy (whether there was detachment, infectious processes, etc.).

Functions:

Hormons of placenta

Placenta plays the role of an internal secretion gland and synthesizes hormones which provides apropriate growth and development of the fetus.

Placenta produces a variety of hormones of which protein and steroid hormones are significantly important.

Human chorionic gonadotropin (hCG): hCG is a glycoprotein. Its molecular weight is 36000–40000 daltons. It consists of a hormone non-specific **a** (92 amino acids) and a hormone specific **b** (145 amino acids) subunit. hCG is chemically and functionally similar to pituitary luteinizing hormone. The a subunit is biochemically similar to LH, FSH and TSH whereas the b subunit is relatively unique to hCG. Placental GnRH may have a control on hCG formation.

Functions: (1) It acts as a stimulus for the secretion of progesterone by the corpus luteum of pregnancy. The rescue and maintenance of corpus luteum till 6 weeks of pregnancy is the major biological function of hCG.

(2) hCG stimulates Leydig cells of the male fetus to produce testosterone in conjunction with fetal pituitary gonadotropins. It is thus indirectly involved in the development of male external genitalia.

(3) It has got immunosuppressive activity which may inhibit the maternal processes of immunorejection of the fetus as a homograft.

(4) Stimulates both adrenal and placental steroidogenesis.

(5) Stimulates maternal thyroid because of its thyrotropic activity.

(6) Promotes secretion of relaxin from the corpus luteum.

Level of hCG at different periods of pregnancy: hCG is produced by the syncytiotrophoblast of the placenta and secreted into the blood of both mother and fetus. The plasma half life of hCG is about 36 hours. By radioimmunoassay, it can be detected in the maternal serum or urine as early as 8-9 days postfertilization. In the early pregnancy, the doubling time of hCG concentrations in plasma is 1.4–2 days. The blood and urine values reach maximum levels ranging 100 IU and 200 IU/mL between 60–70 days of pregnancy. The concentration falls slowly reaching a low level of 10–20 IU/ mL between 100–130 days. High levels of hCG could be detected in—(a) multiple pregnancy (b) hydatidiform mole or choriocarcinoma and relatively high in—(c) pregnancy with a 21-trisomy fetus (Down's syndrome). Plasma lower levels are found in ectopic pregnancies and in spontaneous abortion. hCG disappears from the circulation within 2 weeks following delivery.

Human placental lactogen (hPL): This is also known as human chorionic somatomammotropin (hCS). The hormone is synthesized by the syncytiotrophoblast

of the placenta. The hormone is chemically and immunologically similar to pituitary growth hormone and prolactin. hPL in maternal serum is first detected during the 3rd week. The level rises progressively from 5 to 25 μg/mL until about 36 weeks. The plasma concentration of hPL is proportional to placental mass.

Functions: hPL antagonises insulin action. High level of maternal insulin helps protein synthesis. hPL causes maternal lipolysis and promotes transfer of glucose and amino acids to the fetus. As a potent angiogenic hormone, it helps to develop fetal vasculature. It promotes growth of breasts for lactation.

Pregnancy associated plasma protein—A (PAPP-A) is secreted by the syncytiotrophoblast. It acts as an immunosuppressant in pregnancy.

Estrogen: In late pregnancy, qualitatively, estriol is the most important amongst the three major estrogens. The site of its production is in the syncytiotrophoblast. The placenta is an incomplete endocrine organ as it has no capability of independent steroidogenesis like that of ovary. For steroidogenesis, it depends much on the precursors derived mainly from the fetal and partly from the maternal sources. Fetal adrenal gland and the placenta contain the complementary enzyme system.

Estriol is first detectable at 9 weeks (0.05 ng/mL) and increases gradually to about 30 ng/mL at term. Fetal death, fetal anomalies (adrenal atrophy, anencephaly, Down's syndrome), hydatidiform moles, placental sulfatase or aromatase deficiency are associated with low estriol.

Progesteron: Before 6 weeks of pregnancy, the corpus luteum secretes 17-ydroxyprogesterone. Following the development of trophoblast, progesterone is synthesized and secreted in increasing amount from the placenta. The daily production rate of progesterone in late normal pregnancy is about 250 mg. Low progesterone levels are observed in ectopic pregnancy and in abortion. High values are observed in hydatidiform mole, Rh-isoimmunization. After delivery, the plasma progesterone decreases rapidly and is not detectable after 24 hours.

Functions of the steroid hormones (estrogen and progesterone):

It is indeed difficult to single out the function of one from the other.

— Together they play an important role in the maintenance of pregnancy. Estrogen causes hypertrophy and hyperplasia of the uterine myometrium, thereby increasing the accommodation capacity and blood flow of the uterus. Progesterone in conjunction with estrogen stimulates growth of the uterus, causes decidual changes of the endometrium required for implantation and it inhibits myometrial contraction.

— Development and hypertrophy of the breasts during pregnancy are achieved by a number of hormones. Hypertrophy and proliferation of the ducts are due to estrogen, while those of lobulo-alveolar system are due to combined action of estrogen and progesterone (details — below).

— Both the steroids are required for the adaptation of the maternal organs to the constantly increasing demands of the growing fetus.

— Progesterone maintains uterine quiescence, by stabilizing lysosomal membranes and inhibiting prostaglandin synthesis. Progesterone and estrogens are antagonistic in the process of labor.

— Estrogens sensitizes the myometrum to oxytocin and prostaglandins. Estrogens ripen the cervix.

— Progesterone along with hCG and decidual cortisol inhibits T-lymphocyte mediated tissue rejection and protects the conceptus.

— Together they cause inhibition of cyclic fluctuating activity of gonadotropin–gonadal axis thereby preserving gonadal function.

Relaxin: It is a peptide hormone structurally related to insulin. The main source of production is the corpus luteum of the ovary but part of it may be also produced by the placenta and decidua. It has been claimed that relaxin relaxes myometrium, the symphysis and sacroiliac joints during pregnancy and also helps in cervical ripening by its biochemical effect.

Gas exchange

Placenta participates in the gas exchange: diffusion of oxygen occurs from the mother's blood to the fetus, and carbonic gas is transported in the opposite direction.

The fetus receives vital substances necessary for its growth and development through the placenta. It is necessary to remember that a lot of substances (alcohol, nicotine, narcotics, many medical preparations, viruses) easily penetrate through the placenta and can harm the fetus. Besides, with the help of the placenta, the fetus gets rid of products of metabolism.

Placenta provides immunological protection for the fetus by detaining the cells of the mother's immune system which, can penetrate to the fetus causing it to be a foreign object and then cause an immune conflict, which could start rejection reactions. At the same time, the placenta passes the maternal antibodies, which protect the fetus from infections.

Placental dysfunction (PD) – a clinical syndrome, caused by morphological and functional changes in the placenta and its infringement of the compensatory-adaptive possibilities. The reasons for placental dysfunction can be infringements of maturing and the formation of the placenta in women with pathologies of the endometrium, ovary-hypophysis and adrenal glands disorders, previous abortions and miscarriages. Pre-eclampsia, risk of miscarriage, overdue pregnancy, iso-serological blood incompatibility of the mother and fetus, genital infantility and other extra-genital pathologies (dysfunction of the adrenal glands, diabetes, thyrotoxicosis, etc.). play a great role in the occurrence of placental dysfunction, Thus, a complex of transport, trophic, endocrine and metabolic disorders of the placenta can occur, which is the basis for pathology of the fetus and newborn. The degree and character of influence of the pathological condition of the pregnant woman on the fetus depends upon many factors:

the term of the pregnancy, the length of influence, condition of compensatory-adaptive mechanisms in the "mother-placenta-fetus" system.

Placental dysfunction – syndrome, caused by morpho-functional changes in the placenta, the result of complex reaction of the placenta and fetus to different pathological conditions in the mother's organism. The basis for the given syndrome is pathological changes in the fetal- and-or uterine-placental complex with infringement of the compensatory-adaptive mechanisms at the molecular, cellular and tissue levels. Thus, a complex of transport, trophic, endocrine and metabolic disorders of the placenta can occur, which is the basis for pathology of the fetus and newborn. The data specifies that the term "feto- or uterine-placental insufficiency", is incomplete because it does not display completely the whole complex of changes in the uterine-placenta-fetus system. In the International Classification of Diseases (ICD-X reviewed in Geneva, 1995) the disease has only one name - "placental insufficiency"; later – placental dysfunction.

Placental ischemia and placental dysfunction are the starting link in the complex chain of pathophysiological mechanisms and progress of gestosis into pre-eclampsia. The condition of the placental complex during a pregnancy is studied completely (hormonal function, uterine-placental blood circulation, activity of the enzymes, ultrasound, tests of the amniotic fluid), especially taking into account the fact that the placenta is a uniform organ, accessible for lifetime pathomorphological research. Changes in the placental complex in pregnant women with different degrees of gestosis allow to track the steps (stages) of formation of placental dysfunction.

No uniform classification of PD exists.

In 1986, M. Ygel offered a classification of placental dysfunction by dividing it into latent placental dysfunction, manifestive and chronic insufficiency. Each division contains minimal, average or severe degree of severity.

In our country, the greatest and most widespread classification of placental dysfunction was offered by M.V. Fedorov and E.P. Kalashnikov (1986), where they distinguish primary (before 16 weeks pregnancy) and secondary (after 16 weeks) PD.

On the basis of the morphological changes in the placenta, I.S. Sidorov and I.O. Makarov (2000), V.I. Kulakov (2004) distinguished compensated, subcompensated, decompensated and critical forms of chronic PD.

Depending on the area of defeat in the placenta, M.V. Fedorov, O.P. Kalashnikov (1986) and H.C. Wallenburg (1990) distinguished relative and absolute placental dysfunction.

V.A. Tsinzerling and co-authors (1998) developed the criteria for morphological diagnostics of the following kinds of functional conditions of the placenta: compensated condition, acute insufficiency, chronic insufficiency with acute decompensation, chronic subcompensated insufficiency, chronic decompensated insufficiency (gradually accruing).

Classification of PD:

I. by the clinical-morphological signs:

a) primary (early) placental insufficiency (before 16 weeks) occurs during the formation of the placenta during implantation, early embryogenesis and placentation under the influence of genetic, endocrine, infectious and other factors. Enzyme insufficiency of the decidual tissue (during dysfunction of the ovaries, anatomical structural disorders, disorders in the location of the placenta attachment, and also defects of vascularization and the problems in the maturing of the chorion) play a valuable role in the development of primary placental dysfunction. Primary insufficiency can assist in the development of congenital disorders of the fetus, stillborn pregnancy. Clinically, it appears as risk of miscarriage in early terms. On occasion, primary placental dysfunction can develop into secondary.

b) secondary (late) placental dysfunction, as a rule, occurs in the late terms of pregnancy, after 16 weeks, under the influence of different maternal factors.

II. by the clinical course:

a) acute – acute disturbances of decidual perfusion and disturbances of the utero-placental blood circulation play a leading role in its development. This kind of placental dysfunction appears as large infarctions of the placenta, preterm detachment of a normally located placenta. As a result, death of the fetus and the termination of the pregnancy can occur quickly.

b) chronic – very frequent pathology (it is observed in approximately every third pregnancy woman in the group of high risk). It can occur in the II trimester and last for a long time.

III. by the condition of the compensatory-adaptive reactions:

a) relative – when the compensatory reactions in the placenta are preserved. Vital support of the fetus is caused by compensatory reactions, which operate on the tissue (increase the number of reabsorbing villa, capillaries of terminal villa, functioning syncytial nodes), cellular and subcellular levels of the syncytiotrophoblast. Infringements of maturing of the placenta and immune disorders have certain value in the development of this type of PD.

b) absolute - most difficult form of chronic PD. It is characterized by the development of damage to the placenta of involution-dystrophic, circulatory and inflammatory character, which is accompanied by the absence of compensatory-adaptive reactions of the chorion at the tissue level.

Diagnostics of disorders of the functions of the placenta.

**1. Determine the degree and character of changes in the placenta. **

a) hormonal researches:

Hormonal methods of diagnostics of PD consist of determining the level of hormones in the amniotic fluid, patient's blood and urine. But, it cannot be limited to the research of one hormone only one time. It is advisable to use dynamic supervision

of a complex of hormones in the placental complex, placental lactogen (PL) and chorionic gonadotropin (CG) – to diagnose the condition of the syncytiotrophoblast of the placenta; estrogen (estradiol-E2 and estriol-E3) – to evaluate the function of the placental complex; progesterone (Pg)-to diagnose the condition of the uterine-placental-fetal system (see table 1).

2. Determine the condition of the fetus and placental system.

a) measure the height of the uterine fundus over the pubis symphysis and the circumference of the abdomen in dynamics.

Special attention should be paid during external measurement in the II and beginning of the III trimester when the received sizes are comparison to the term of the pregnancy, which shows any fetal growth retardation. It is convenient to use a gravidogram, where normal measurements of the height of the uterus fundus are marked. The lack of 20 mm in the size of the uterus or more at 32-33 weeks is basis for considering the presence of hypotrophy of the fetus.

b) determine the sizes of the fetus with an ultrasound.

c) study the respiratory activity of the fetus with an ultrasound.

d) determine the movement activity of the fetus with an ultrasound.

It is performed at 7-8 weeks of pregnancy, but its evaluation has the greatest value in the III trimester when the fetus does 5 and more movements in 30 minutes. Thus, an increase in general movement activity of the fetus is considered compensatory reactions, a decrease - an adverse sign.

e) ultrasound of the urinary functions of the kidneys of the fetus by the amount of excreted urine.

The latter is determined by the difference between the volume of the urinary bladder during the first US and the repeated US in 1 hour. The given test is especially valuable when diagnosing hypotrophy of the fetus, during which the excretion of the urine decreases to 15-18 ml (normal – 24-27 ml). Also consider, that a decrease in the speed of urine excretion of the fetus is observed during gestosis of the pregnant women, in those cases there is no growth retardation by data from the US. The degree of decrease in the production of urine is directly dependant on the severity of gestosis, which is connected not only to fetal growth retardation, but also to the infringement in the regulation of the kidney functions.

f) evaluation of the fetal heart activity.

Along with auscultation, the most accessible and widespread method of evaluating the fetal heart activity is cardiotocography, registration of fetal heart rate (HR). Cardiomonitoring shows initial and expressed signs of suffering of the fetus as a result of fetal distress.

The basic treatment for placental dysfunction:

1) Improving the uterine-placental blood circulation;

2) Normalizing the gas exchange between the mother and fetus;

3) Improving the metabolic functions of the placenta;

4) Acting on the fetus, through the placenta and using the para-placental way of exchange.

Different methods and different means influence multiple functions of the placenta at once. Normalizing the uterine-placental blood flow, certainly, improves the transport of nutrients and gas exchange, which is an important factor in the synthesis of hormones. Correcting the metabolic changes leads to the improvement of gas exchange and normal function of the placenta which in turn, improves the haemodynamics of the placenta.

Normalizing the uterine-placental blood flow is the basic link in normalizing the function of the placenta; it is achieved by using vasodilating means or preparations which relax the uterus, along with actions directed on normalizing the reocoagulate properties of the blood:

a) physical methods of action (electro-relaxation of the uterus, electrophoresis of magnesium, thermal procedures on the renal area, diathermy, inductothermy, etc.) reflex the biometry and lead to the dilation of vessels;

b) abdominal decompression removes extra muscle work of the uterus by overcoming of the tonus of the abdominal muscles. It leads to an increase in blood flow in the uterus and improves placental perfusion. Besides that, it leads to an increase in the synthesis of estriol and an increase in the transport function of the placenta;

c) hyperbaric oxygenation is applied to improve the function of the placenta and fetal condition, especially in pregnant women heart disorders. It preserves the activity of the respiratory enzymes, assists in normalizing the carbohydrate metabolis;

medicament means. Aminophylline or teophylline, vasodilating substances, are used; they can be introduced by i\v by stream or droplet introduction. Complamin, teonicole are used for the same purposes. It should be noted that hypersensibility is possible in pregnant woman and so individual doses of complamin should be selected. Considerable improvement in the uterine-placental blood circulation causes vaso-active preparation trental. It has vasodilating action, decreases the resistance of peripheral vessels, increases the collateral blood circulation. The preparation improves the rheological properties of blood and microcirculation, and it can be used in hospitals and female consultations.

In the female consultation:

Diathermy at the renal area – up to 10 sessions alternating with ultraviolet irradiation (10 sessions).

Diet rich in fiber and vitamins (boiled meat, fish, cheese);

I\v introduction of glucose 40% - 20,0 with corglicon 0,06% - 0,5 ml gradually every day or every other day (10 injections);

Cocarboxilase i\m 50 mg every day, for 10-14 days;

Aminophylline 0,15 gr per os 2 times a day and 0,2 gr suppositories at night, for 14 days (or no-shpa, papaverin);

Trental 1 pill 3 times a day or isadrin 0,005 gr (under tongue) 3 times a day in combination with finoptin (isoptin);

Orotate potassium 0,5 gr 3 times a day;

Ferroplex (conferon) 1 dragee (capsule) 3 time a day;

Methionine 0,5 gr 3 times a day;

Ascorutin 1 pill 3 times a day.

If not effective during 2 weeks – hospitalization

Prevention of placental dysfunction

1) eliminating the influence of harmful factors during the period before conception and especially during the first days and weeks of pregnancy:

a) eliminating smoking, alcohol, taking of medicines (without prescription from the doctor);

b) before pregnancy (and during pregnancy) sanation of sites of infection, treatment of chronic diseases.

2) after the patient becomes pregnant, it is necessary to explain to her the role of high-grade balanced food, high-grade and extra sleep.

3) finding the group of high risks and registering them for regular medical check-ups.

Fetal distress syndrome

According to order of the Ministry of Health of Ukraine №900 from 27.12.2006 about the statement of the clinical report about obstetrical help for "Fetal distress during pregnancy and during birth ", the terms "chronic hypoxia of the fetus ", "acute hypoxia " are not clinical, because for the diagnostics of these disorders, indicators of oxygen contents in the fetus (metabolic acidosis) are not used in routine medical practice. So, all disorders of the functional condition of the fetus at the present are distinguished as "fetal distress". The concept "chronic fetal hypoxia", "acute fetal hypoxia" are not used.
I. In the conditions of a hospital:
Treatment of the basic pathology of pregnancy;

I. In the hospital:

Treatment of the basic pathology of the pregnancy;

Oxygen therapy - inhalation of mixed oxygen for 30-60 minutes 2 times per day;

Preparations which influence metabolism: glutamic acid 1,0 gr. x 3 times a day, methionine 0,25-0,5 gr x 3 times a day.

Galaxorbin as ferroplex 1 tab. x 3 times a day.

Cocarboxilase 50 mg i\m every day.

Vaso-active substances: trental, partusisten, isadrin, aminophylline i\v or per os (i\v with glucose or physiological solution). I\v introduction + 3x per os (in pills).

Course of the vaso-active substances is 4-6 weeks, of them 5-7 days – infusion therapy, and the other days – per os. Complamin (teonicole) 0,15 gr. per os with food 3 times a day can be used as vaso-active substances.

Reopolyglucin 10 % solution 400-500мл every day i\v droplets, 3-4 times, or 2-3 times a week (it can be used as a loading liquid before introducing vaso-active substances).

Native plasma – 150 ml i\v droplets for low protein in the blood (below 6%).

When introducing large doses of glucose it is used with insulin - 1 unit for 4 gr. of dry substance.

II. In the female consultation:

Diathermy at the renal area – up to 10 sessions alternating with ultraviolet irradiation (10 sessions).

Diet rich in fiber and vitamins (boiled meat, fish, cheese);

I\v introduction of glucose 40% - 20,0 with corglicon 0,06% - 0,5 ml gradually every day or every other day (10 injections);

Cocarboxilase i\m 50 mg every day, for 10-14 days;

Aminophylline 0,15 gr per os 2 times a day and 0,2 gr suppositories at night, for 14 days (or no-shpa, papaverin);

Trental 1 pill 3 times a day or isadrin 0,005 gr (under tongue) 3 times a day in combination with finoptin (isoptin);

Orotate potassium 0,5 gr 3 times a day;

Ferroplex (conferon) 1 dragee (capsule) 3 time a day;

Methionine 0,5 gr 3 times a day;

Ascorutin 1 pill 3 times a day.

If not effective during 2 weeks – hospitalization

Respiratory distress syndrome in newborns (respiratory disorder syndrome) – non-infectious pathological processes (primary atelectasis, disease of the hyaline membrane, hydropic- hemorrhagic syndrome) that form in the prenatal and early neonatal periods of development of an infant and breathing; it appears as respiratory disorders. The frequency of development of respiratory distress depends on the degree of immaturity and averages about 60% of children born at the pregnancy term less than 28 weeks, 15-20% -at the term 32-36 weeks and 5% - 37 weeks and more. With rational nursing of such children, the mortality rate is close to 10%.

Fetal distress syndrome means hypoxia.

Hypoxia of the fetus - insufficient supply of oxygen to the tissue and organs or their incomplete digestion of the oxygen. This term was recommended by the World Health Organization, but it is not the only one: the terms fetal distress ("suffering") and asphyxia (without pulse; but has dyspnea, i.e. a lack of oxygen and accumulation of carbonic gas in the organism) also exist. The term hypoxia of the fetus and asphyxia of newborns are not used.

The consequences of oxygen insufficiency for a fetus during different periods of pregnancy are different. In early terms (before 16 weeks), when organs and systems are forming, expressed hypoxia can be accompanied by embryo growth delay and the occurrence of development anomalies. Oxygen starvation in later pregnancy terms can lead to fetal growth retardation, defects of the central nervous system in the fetus and newborns, infringement of the processes of the infant's adaptation after birth; in special cases it can be the reason for stillborn deliveries or death in infants.

Depending on the duration, chronic and acute fetal distress is distinguished. Chronic distress develops when there is an insufficient supply of oxygen to the fetus throughout a long period of time due to diseases of the mother's internal organs (diabetes, chronic diseases of the lungs, kidneys, anemia, etc.), complicated course of the pregnancy (gestosis, risk of miscarriage, over-due pregnancy, immunological incompatibility of the mother and fetus blood by Rhesus factor, pre-natal fetal infection). Chronic distress also can be the result of smoking, use of alcohol, drugs during pregnancy. Acute fetal distress, as a rule, occurs during the delivery (in connection with anomalies of labor activity, entanglement of the umbilical cord, prolapse or compression of loops of the umbilical cord, short umbilical cord). Less often, acute fetal distress is observed during the pregnancy during life-threatening conditions of the mother (premature detachment of the placenta, rupture of the uterus). Sometimes, chronic and acute distress is observed together.

Intrauterine fetal distress - pathological condition connected with oxygen insufficiency during the pregnancy and delivery. It is caused by the reduction or absence of oxygen in the body and the accumulation of metabolism products in the blood. Hypoxia leads to an imbalance in the oxidation-reduction reactions in the fetus's organism resulting in the development of acidosis, when tissue ceases to receive oxygen. Carbonic acid accumulation causes irritation of the respiratory center. The fetus starts to breathe through an open vocal fissure and aspirates amniotic fluid, mucous, blood.

Many kinds of obstetrical pathologies, different extra-genital diseases, dysfunction of the placenta, pathology of the umbilical cord and fetus are just some of the reasons.

Etiology and pathogenesis

The main pathogenesis for distress of the fetus and newborn is placental dysfunction with obstetrical and extra-genital pathologies. Defects in the structure of the placenta and processes of microcirculation in pregnant women with gestosis, the action of medical preparations and other harmful factors lead to chronic oxygen starvation which is accompanied by a decrease of oxygen in blood, hypercapnia, non-compensated acidosis, imbalance in the water-electrolyte exchange, decrease of the contents of corticosteroids. It, in turn, causes dysfunction of the central nervous and cardiovascular systems, homeostasis regulation, and increase in the permeability of

vessels, decrease in the immunological reactance of the fetus's organism. Conditions of fetal hypoxia are connected with the changes in the complex uterine-placental-fetal system. This testifies that the result of the pregnancy for the fetus and in many respects for the mother depends on the condition of the compensatory-reactive mechanisms of the fetoplacental complex and rational correction of disorders.

Acute and chronic fetal distress is distinguished. The symptoms of acute fetal distress usually appear during delivery. Chronic fetal distress (more than 7-10 days) - the consequence of prolonged obstetrical or extragenital pathologies, which lead to fetal development delay.

The reasons for fetal distress and distress in newborns can be divided into 4 groups:

I group - diseases of the mother.

Blood loss during obstetrical bleedings (detachment of the placenta, placental presentation, rupture of the uterus); blood diseases (anemia, leukemia, etc.).
Shock conditions of any origin.
Diseases of the cardiovascular system (congenital and acquired heart disorders with haemodynamic infringement).
Diseases of the respiratory system with gas exchange infringement (bronchial asthma, pneumonia).
Any intoxications.

II group - pathology of the uterine-placental and umbilical cord circulation.

Umbilical cord pathology (umbilical cord knots, entanglement of the umbilical cord around the extremities, prolapse of the umbilical cord, compression of the umbilical cord during delivery in pelvic presentation).
Bleedings (detachment of the placenta, placental presentation, rupture of vessels with membrane attachment of the umbilical cord).
Defects in the placental blood circulation in connection with dystrophic changes of the vessels (during gestosis, over-due pregnancy).
Anomalies of the birth activity (very long or fast contractions, discoordination of the birth activity).

III group - reasons connected with the fetus.

Genetic illnesses of newborns.
Hemolytic disease of newborns.
Congenital defects of the cardiovascular system.
Pre-natal infection.
Intracranial trauma.

IV group.

Partial or complete obstruction of the respiratory tract (characteristic only for distress of newborns).

Clinical picture

Main displays of fetal distress: heart rate abnormalities (at first tachycardia, then bradycardia), muffled heart sounds (in the beginning little increase, then muffled); arrhythmia, decrease in the intensity of fetal movements, excretion of meconium, change in the indicators of the acid-base balance of the amniotic fluid and blood.

Diagnostics

Diagnostics of fetal distress can only be complex. Registration of cardiac activity is one of the most simple and widespread methods of monitoring the functional condition of the fetus during pregnancy and delivery. In clinical practice, CTG is used.

Test with functional loads (diagnostics of chronic fetal distress). The pregnant woman for 3-4 min. steps up and down on 2 steps. Before and after the workout register the fetal cardiac activity. During a normal course of pregnancy, the heart rate remains within the physiological borders 116-160 b.p.m. When the fetus is in distress, monotony of the rhythm of the heart is marked, tachycardia or bradycardia.

Test with oxytocin. Under the influence of oxytocin, the blood circulation decreases in the intervillous lacuna, appearing as change in the fetal heart rate. To perform the test, 1 unit of oxytocin is dissolved into 100 ml of 5% glucose. 1 ml of this solution contains 0,01 units of oxytocin. 5 ml of the solution is put into a syringe, and introduced by i\v with a speed of 1 ml per minute. Normally, the fetal heart rate does not change. When the fetus is in distress tachycardia or bradycardia is observed.

Test with holding of breath during inhalation and during exhalation. Normally, when breath is held, the fetal heart rate changes on average 7 b.p.m. Holding of breath during inhalation causes a decrease, and on exhalation - increase in fetal heart rate. When the fetus is in distress, there is no change in fetal heart rate.

Cold test gives a decrease in fetal heart rate by 10 b.p.m. When the fetus is in distress, the rhythm does not change.

There are tests with the introduction of atropine sulphate, aminophylline, etc. Atropine easily passes through the placenta and causes tachycardia, so it is not recommended.

Modern methods of evaluating the condition of the fetus include US (fotometry, placentography, "biophysical profile"), Doppler flowmetry, amniocentesis (pH of the amniotic fluid, delta Oe450, level of hormones, phospholipids), chordocentesis (blood indicators), cardiomonitoring with computer evaluation of the received data, pH of the blood from the skin of the fetus's head (during labor).

Treatment

Treatment plan for fetal distress.

Treatment of the mother's basic disease, regulation of tone of the uterus, correction of placental dysfunction.

Treatment of the mother's basic disease (pathology of pregnancy or extragenital pathologies).

Observation in the hospital (mainly on the left side to prevent inferior vena cava syndrome).

Oxygen therapy.

I\v introduction of glucose (500 ml - 10% solution) +10 units of insulin + cocarboxilase 100 mg + ascorbic acid (10 ml - 5%). Infusion for 5-8 days.

I\v introduction of preparations improving the uterine – placental circulation: aminophylline (10 ml - 2,4%), sigentin (2 ml -1%), ATP (2 ml-1%) or curants (2 ml-0,5%). Reopolyglucin 200 ml i\v droplet.

Use of tocolytics (especially with preterm pregnancy and increased irritability of the uterus): magnesium (10 ml - 25% in 5% solution of glucose - 100 ml i\v droplet) or alupent (0,5 mg) in 5% solution of glucose for 2-6 days with further use of pills and i\m introduction.

Treatment plan for acute fetal distress.

Position on left side.

Long inhalation of pure humidified O2 by mask.

I\v introduction of 10% solution of 100 ml glucose + 4 units of insulin + 50 mg of cocarboxilase and 5 ml of solution of ascorbic acid 5%.

10 ml of 2,4% solution of aminophylline i\v gradually + 2 ml of 1% sigetin + ATP (2 ml-1%).

I\v droplep introduction of sodium hydrocarbonate (60-80 ml - 5%).

I\v introduction of 10% solution of 10 ml of calcium gluconate.

If the fetus suddenly develops bradycardia - introduce 0,3% ml i\v or 0,7 ml under the skin 0,1% solution of atropine sulphate. If the presented fetal part is accessible, introduce atropine sulphate hypodermically (0.1 ml - 0,1%).

If there is no effect from treatment of acute and chronic fetal distress - deliver.

Retardation, hypotrophy of the fetus.

In literature you meet a large quantity of terms: "intrauterine development delay", "intrauterine growth retardation ", "hypotrophy of the fetus", "fetal retardation", "small gestational age", etc. In the ICD-10 all terms specified above are united into one concept "Delay in growth and lack of nutrition for the fetus".

The term " intrauterine growth retardation " - pathology of the fetus resulting from the influence of harmful factors. IUGR is diagnosed in infants who have insufficient body weight at birth in relation to their gestational age, when the body weight is 10% less than for that pregnancy term, and\or the morphological index of maturity of the fetus is behind by 2 or more weeks from the valid gestational age.

Fetal development delay is one of the most frequent reasons for a decrease in the adaptation of newborns in the neonatal period, high disease rate, psychological disorders. Perinatal death rate for IUGR reaches 80-100%.

The mortality rate for low-weight infants is 35-37 times more than in mature infants with physiological body weight. The death rate for many depends on the body weight at birth. So, with a weight of 500-700 gr the death rate is 56%, with a weight of 751-999 gr - 48%, and with a weight of 1000 gr - 40%. The maximum death rate for low-weight infants is evident in the 1st week of life.

According to recommendations of WHO, infants born with a body weight less than 2500 gr are called infants with small weight at birth. Thus, infants with small weight at birth are divided into three groups:

1) Newborns before 37 weeks of gestational age with corresponding gestation growth to the given term – immature newborns with growth and body weight, corresponding to the gestation term;

2) Newborns before 37 weeks of gestational age and small for the given term – immature newborns with IUGR;

3) Newborns after 37 weeks gestation and small for the given term – mature newborns with IUGR.

Prenatal infections also lead to IUGR and make up about 10% of the reasons for this pathology. Rubella leads to IUGR in 60% of cases.

Retardation (from lat. - delay) (biological), late rudiment of organs and their slow development in descendants in comparison with ancestors. It depends on the beginning of the organ's functioning and also on the conditions of environment in which individual development of the organism occurs - ontogenesis.

Retardation - delay (in medicine) - delay of sexual development of an organism. In girls – delay of first menstruation, delay in breast development. In boys – delay of first ejaculation.

Retardation (in literature) – delay in literary and art development, lyrical digressions, different mistakes (interior, characteristic).

Hypotrophy of the fetus

This term doctor's use for delay in the rate of physical growth of a fetus; it includes: the physical parameters of the fetus do not correspond with the size for given term of pregnancy. Today, very often, the term hypotrophy is replaced by intrauterine growth retardation.

Intrauterine growth retardation (IUGR) in infants who have insufficient body weight at birth in relation to their gestational age, when the body weight is 10% less than for that pregnancy term, and\or the morphological index of maturity of the fetus is behind by 2 or more weeks from the valid gestational age. Evaluation is performed during the first hours of life.

There are two forms of this syndrome: symmetrical and asymmetrical. The symmetric form develops at early terms of pregnancy. All the fetus's organs are evenly small; upon US the size parameters of the fetus are less than what is characteristic for the given term of pregnancy. The reasons for symmetric form of hypotrophy are intrauterine fetal infection, chromosomal pathology, developmental anomalies of the fetus, and also insufficient nutrition of mother and smoking.

The asymmetrical form develops later, after 28 weeks of pregnancy and is characterized by non-uniform development of different organs; the brain, skeleton, extremities are developed according to pregnancy term, but the development of the organs (liver, kidneys) is delayed. In this case, during US, the sizes of the fetal head and extremities correspond to the pregnancy term, but the size of the circumference of the abdomen is smaller.

Hypotrophy of the fetus is divided into three degrees according to the severity level:

First degree - situation when the fetus is delayed in development by two weeks.
Second degree – delayed by 2 to 4 weeks.
Third degree – delayed by more than 4 weeks.

The reasons for asymmetrical hypotrophy are. They are divided into the following basic groups:

I. Social factors:

a) the mother's age (17 years or younger, 30 years or older)

b) professional harm (difficult physical work, emotional overstrain, work with chemicals)

c) bad habits (smoking, alcohol)

II. Condition of the mother's organism:

a). chronic infections (chronic tonsillitis, chronic tracheobronchitis)

b) general diseases (diseases of the kidneys, cardiovascular system, endocrine system)

III. Gynecologic diseases of the pregnant woman and features of the course of previous pregnancies:

a) hormonal imbalance – menstrual dysfunction, infertility

b) miscarriages in anamnesis

c) uterus pathology (scar on the uterus after an operation, myoma of the uterus, endometriosis)

IV. Complicated course of the given pregnancy

a) risk of miscarriage

b) anemia

c) multiple pregnancy

d) hypotonia

e) acute attack of chronic infections during the pregnancy.

All these reasons lead to infringement of the so-called uterine-placental-fetal circulation, because then there is a efect in the blood supply to the uterus, placenta and fetus. And, accordingly, the fetus starts to receive insufficient amounts of food and oxygen, resulting in the development of oxygen starvation and delay in growth.

The diagnosis hypotrophy can be diagnosed at the doctor during external obstetrical examination: measuring the height of the uterine fundus and circumference of the abdomen. No increase in the circumference of the abdomen by 2 cm in 2-3 weeks and lack in height of the uterine fundus by 2 cm from the target date testifies of delay in intrauterine growth.

Nevertheless, an accurate diagnosis can be made with US, where photometry and measurements of all the fetus's parameters. Also the condition of the placenta, where metabolism and oxygen exchange between the mother's blood and the fetus's blood, is evaluated. During one US, especially when primary signs are seen, it is difficult to make a definitive diagnosis about a delay in the development of the fetus. Therefore, it is important to perform an US in dynamic, and repeat the US 3 weeks after the first one.

Other methods of examination are Dopplermetry, during which the blood flow in the uterine vessels, arteries of the umbilical cord and arteries of the brain of fetus, are determined with ultrasound. By means of the given method, it is possible to judge the sufficiency of the blood supply to the uterus and fetus. For hypotrophy of the fetus, not only is a delay in physical sizes from normal important, but also the functional condition of the fetus. Therefore, for hypotrophy of the fetus, it is necessary to evaluate the cardiovascular activity of the fetus with ultrasonic cardiotocography, which is performed after 30 weeks of pregnancy.

Prevention of fetal hypotrophy consists of planning and preparing for the pregnancy. It is necessary to treat all infections before becoming pregnant; if chronic sites of infection (for example, chronic tonsillitis) exist then prevention of an acute attack of this infection during pregnancy should be taken. If other diseases of the kidneys, lungs, liver, cardiovascular system exist, it is necessary to consult with experts about possible complications during the pregnancy, and also about what actions need to be made so that these complications do not occur. Early registration at the female consultation is important so that your doctor from the beginning can evaluation your condition and make a prognosis for the course of the pregnancy. It should not have to be said, that after becoming pregnant and during the pregnancy, it is necessary to conduct a healthy lifestyle and lose all harmful habits: smoking, alcohol, drugs. Correct high-grade food during pregnancy, the use of special, balanced vitamin complexes for pregnant women, and also following all the recommendations of the doctor is important. Treatment of fetal hypotrophy depends on the severity, and can be done in out-patient conditions or in the hospital (in the department for pathology of pregnancy) with obligatory evaluation of the functional condition of the fetus.

MATERIALS FOR ACTIVATION OF STUDENTS DURING THE LECTURE: QUESTIONS, SITUATIONAL TASKS, ETC.

QUESTIONS:

- Fundamentals of reproduction: gametogenesis, ovulation, fertilization, implantation.
- Principal events in embryonic and fetal development.
- Development, structure and function of the placenta and fetal membranes.
- Placenta dysfunction, classification, etiology.
- Fetal distress syndrome.
- Intrauterine growth restriction, classification, management.
- Methods of estimation of a baby's wellbeing at antenatal period.
- Dopplerometry and fetometry.
- Methods of obstetrical abdominal examination: inspection, palpation, auscultation, measurement of the woman's abdomen

TEST TASKS

Direction: For each of the multiple-choice questions select the lettered answer that is the one best response in each case.

1. A 23-year-old woman (gravida 1) at about 12 weeks' gestation develops persistent nausea and vomiting that progresses from an occasional episode to a constant retching. She has no fever or diarrhea but lost 3 kg in 1 week and appears dehydrated. What is your diagnosis?

A. Ptyalism
B. Gastroenteritis
C. Hyperemesis gravidarum
D. Anorexia nervosa
E. Morning sickness

2. A 28-years-old woman complains of nausea and vomiting about 10 times per day. She has been found to have body weight loss and xerodermia. The pulse is 100 bpm. Body temperature is 37,2oC. Diuresis is low. USI shows 5-6 weeks of pregnancy. What is the most likely diagnosis?

A. Premature abortion
B. Food poisoning
C. Moderate vomiting of pregnancy
D. Mild vomiting of pregnancy

3. A patient develops excessive salivation during pregnancy. What is this called?

A. Eructation
B. Ptyalism
C. Deglutition
D. Pruritus
E. Emesis

4. In Primagravida, at 15-16 weeks of gestation, was determined that level of α-fetoprotein in serum significantly higher than normal. Pregnancy occurred against the backdrop klostylbehitom stimulate ovulation. When ultrasound revealed twins. How should treat elevated levels □-fetoprotein in this case?

A. liver necrosis of fetus.
B. Disorders of osteogenesis of the fetus .
C. Symptom of multiple pregnancy
D. Defect neural tube.
E. Underestimation of gestational period.

5. A 17-year-old G2P0 woman with no prenatal care at 29 weeks' gestation presents with painful contractions and pressure. Her cervix is 2 cm dilated, 60% effaced, and breech at –2 station. There is no evidence of ruptured membranes. Her contractions are every 3 minutes. FHT are 150 with accelerations. Maternal vital signs are temperature 36.8 degrees, pulse 96, BP 110/72. What should you do?

A. Prepare for a cesarean delivery
B. Observe to look for cervical change
C. Give IV sedation
D. Begin tocolytic agents
E. Start antibiotics

6. A child was born at a gestational age of 34 weeks. The leading symptoms were respiratory distress symptoms, namely sonorous and prolonged expiration, involving additional muscles into respiratory process. The Silverman score at birth was 0 points, in 3 hours it was 3 points with clinical findings. Which diagnostic study will allow to diagnose the form of pneumopathy?

A. X-ray of chest
B. Clinical blood test
C. Determination of blood gas composition
D. Proteinogram
E. Immunoassay

7. A multipara woman was admitted to hospital with a diagnosis of multiple pregnancy. Possible complications of pregnancy and childbirth:

A. Premature detachment of normally situated placenta
B. Occipital fetal presentation
C. Acute fetal distress
D. Polyhydramnios
E. Preterm labor

8. A patient has entered spontaneous premature labor at 28 weeks' gestation. During the vertex delivery, one should do which of the following?

A. Use prophylactic forceps
B. Use vacuum extraction
C. Recommend epidural anesthesia to control delivery
D. Allow spontaneous vaginal birth
E. Perform an episiotomy

9. A patient presents at 30 weeks' gestation in labor that cannot be stopped. Lung maturity is unlikely. Fetal lung surfactant production may be increased by a number of factors. Which of the following is proven clinically useful?

A. Glucocorticosteroids
B. Prolactin
C. Thyroxine
D. Estrogen
E. Alpha-fetoprotein

Answer key

1.	C
2.	C
3.	B
4.	C
5.	D
6.	A
7.	E
8.	D
9.	A

EQUIPMENT AND EDUCATIONAL AND METHODOLOGICAL SUPPORT OF THE LECTURE:

- Obstetric models and obstetric instruments (pelvimeter, obstetric stethoscope, centimeter tape).
- Professional algorithms, structural-logical schemes, tables, videos.
- Results of laboratory and instrumental researches, situational tasks, patients, medical histories.
- Multimedia equipment (computer, projector, screen), TV.

RECOMMENDED LITERATURE

Basic:

1. Gladchuk I.Z. Obstetrics: student`s book / Gladchuk I.Z., Ancheva I.A. . – Vinnitsia: Nova Knyha, 2021. – 288 p.
2. Obstetrics and Gynecology: in 2 volumes. Volume 1. Obstetrics: textbook / V.I. Gryshchenko, M.O. Shcherbina, B.M. Ventskivskyi et al. (2nd edition). – «Medicina», 2018. – 392 p.
3. Hiralal Konar DC Dutta's Textbook of Obstetrics (9th Ed.) / Hiralal Konar (Ed.). – Jp Medical Ltd, 2018. – 700 p.
4. F. Gary Cunningham Williams Obstetrics (26th Edition) / F. Gary Cunningham, Kenneth Leveno, Jodi Dashe, Barbara Hoffman, Catherine Spong, Brian Casey. – McGraw Hill / Medical, 2022. – 1328 p.
5. Jeremy Oats, Suzanne Abraham Llewellyn-Jones Fundamentals of Obstetrics and Gynaecology (10th Ed) / Jeremy Oats, Suzanne Abraham. – Elsevier, 2016. – 384 p.

Additional:

1. The PROMPT-CIPP Editorial Team. (2019). PROMPT-CIPP Course Participant's Handbook: Care of the Critically Ill Pregnant or Postpartum Woman (Critical Car Prompt Practical Obstetric Multi-professional Training). – Cambridge University Press; 1st edition, 2019. – 136 p.
2. L. A. Magee The FIGO Textbook of Pregnancy Hypertension. An evidence-based guide to monitoring, prevention and management. / L. A. Magee, P. Dadelszen, W. Stones, M. Mathai (Eds). – The Global Library of Women’s Medicine, 2016. – 456 p.
3. Edwin Chandraharan Handbook of CTG Interpretation: From Patterns to Physiology / Edwin Chandraharan. – Cambridge University Press; 1st edition, 2017. – 256 p.
4. Louise C. Kenny, Jenny E. Myers Obstetrics by Ten Teachers (20th ed) / Louise C. Kenny, Jenny E. Myers. – CRC Press, 2017. – 342 p.
5. J. Studd Current Progress in Obstetrics and Gynaecology. Vol 4. / J. Studd, Seang Lin Tan, F. Chervenak. – TreeLife Media (A Div of Kothari Medical), 2017. – 419 p.

6. J. Studd Current Progress in Obstetrics and Gynaecology. Vol 5. / J. Studd, Seang Lin Tan, F. Chervenak. – TreeLife Media (A Div of Kothari Medical), 2019. – 403 p.
7. J. Studd Current Progress in Obstetrics and Gynaecology. Vol 6. / J. Studd, Seang Lin Tan, F. Chervenak. – TreeLife Media (A Div of Kothari Medical), 2022. – 309 p.
8. Mark Landon Obstetrics: Normal and Problem Pregnancies, 8th Edition / Mark Landon, Henry Galan, Eric Jauniaux, Deborah Driscoll, Vincenzo Berghella, William Grobman, et al. – Elsevier, 2021. – 1280 pp.
9. Mark B. Landon Gabbe's Obstetrics Essentials: Normal & Problem Pregnancies, 1st Edition / Mark B. Landon, Deborah A. Driscoll, Eric R. M. Jauniaux, Henry L. Galan, William A. Grobman, Vincenzo Berghella. – Elsevier, 2019. – 496 pp.
10. Ian M. Symonds, Sabaratnam Arulkumaran Essential Obstetrics and Gynaecology, 6th Edition / Ian M. Symonds, Sabaratnam Arulkumaran. – Elsevier, 2020. – 480 pp.
11. Myra J. Wick Mayo Clinic Guide to a Healthy Pregnancy, 2nd Edition / Myra J. Wick. – Mayo Clinic Press, 2018. – 520 p.

INTERNET SOURCES:

- https://www.cochrane.org/
- https://www.ebcog.org/
- https://www.acog.org/
- https://www.uptodate.com
- https://online.lexi.com/
- https://www.ncbi.nlm.nih.gov/
- https://pubmed.ncbi.nlm.nih.gov/
- https://www.thelancet.com/
- https://www.rcog.org.uk/
- https://www.npwh.org/