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Physiological Processes During Intrauterine Development.

Mal GS[1]*, Zavalishina S Yu[2], Grishan MA[2], Vorobyeva NV[3], Glagoleva TI[4], and Mironova D Yu[1].

[1]Kursk State Medical University, st. K. Marx, 3, Kursk, Russia, 305000
[2]RussianStateSocialUniversity, st.V. Pika, 4, Moscow, Russia, 129226
[3]South-West State University, st. 50 years of October, 94, Kursk, Russia, 305040
[4]All-Russian Research Institute of Physiology, Biochemistry and Nutrition of Animals, Institute of Village, Borovsk, Russia, 249013

ABSTRACT

Intrauterine development is an important stage of ontogenesis, at which the initiation and formation of all internal organs takes place. In all periods of antenatal development, the embryo and fetus are sensitive to the action of adverse factors. However, in the process of prenatal development, periods of increased sensitivity of the developing organism to the action of damaging factors can be distinguished. These periods are called critical periods. It is customary to distinguish several such critical periods: fertilization, implantation period (6-7 days) and period of placentation and organogenesis (3-8 weeks), since at this time there is a separation of embryonic rudiments of tissues and organs (3 weeks), differentiation of mesoderm (3 -5 weeks), placenta development (6-8 weeks), initial stages of organogenesis (4-8 weeks). At the same time, developmental disruption of the embryo at the pre-implantation stage proceeds according to the principle "all or nothing". At this stage, the action of adverse factors, as a rule, ends with the death of the embryo. However, if the embryo survives, organ-specific anomalies do not develop, since the repair or replacement of damaging cells ensures further normal development. In this regard, a seriously ill woman gives birth to a healthy child, and with a relatively mild pathological process a physiologically immature child with developmental defects is sometimes born to the mother.

Keywords: physiology, development, embryogenesis, fetus, vital activity.

Corresponding author

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INTRODUCTION

Numerous studies have found that the normal development of fetal development requires dynamic constancy of conditions of prenatal development (specific homeostasis), which is regulated by neuroendocrine and neurohumoral mechanisms of both the maternal organism and the fetus and is carried out within the functional system mother-placenta-fetus [1]. Disorders of fetal development occur, as a rule, in the process of interaction of the organism with inadequate conditions of the external and internal environment, causing disturbances of fetal homeostasis [2].

In the early periods of antenatal development in the embryo, due to the immaturity of vital organs and systems, adaptation mechanisms in response to the action of pathogenic agents are almost completely absent [3]. Therefore, changes in the conditions of intrauterine development at this time lead to serious violations of the development of the embryo, up to its death. Later, the fetus undergoes maturation of the most important organs and systems, that is, morphological and functional prerequisites arise for the formation of adequate compensatory reactions aimed at maintaining homeostasis. These primarily include an increase in the rhythm of heart contractions and an increase in musculoskeletal generalized motor reactions, resulting in an increase in the amount of blood flowing through the capillaries of the placenta per unit of time, and, consequently, oxygenation of the fetal blood increases and the metabolism between the two organisms increases [4,5].

However, the range of adaptive reactions in the fetus is limited. In this regard, the effect of various extraordinary on the strength and duration of damaging factors even at the end of pregnancy adversely affects the development of offspring [6].

The science of congenital malformations - teratology, currently attracts the close attention of researchers of various specialties and, above all, embryologists. This is due to the fact that, thanks to the achievements of embryology, including experimental, and genetics, teratology began to learn the causes of congenital malformations. It is important that congenital malformations occupy one of the first places, both in the structure of childhood morbidity and in perinatal and early infant mortality [7]. Thanks to the achievements of teratology, experts today offer a number of effective measures to prevent congenital malformations. So, at present, in all large medical centers, medical genetic counseling and perinatal diagnostics are carried out, allowing to determine the progeny prognosis, recommendations to parents and the attending physician [8].

Objective: to consider issues of intrauterine development disorders.

Congenital defects are very diverse. To date, the number of nosological forms of congenital malformations in the thousands. In this regard, there is no single recognized classification of disorders of intrauterine development. They are distinguished by etiological basis, localization, time and object of exposure to the teratogenic factor, the sequence of occurrence [9].

According to the etiological principle, hereditary disorders of intrauterine development, caused by changes in hereditary structures in germ cells, are distinguished. In addition, there are exogenous disorders of antenatal development resulting from the action of various teratogenic factors on the fetus [10].

In clinical practice, most often use the classification of developmental anomalies on a temporary basis. According to this classification, gametopathies, blastopathies, embryopathies and fetopathies are distinguished [11].

Gametopathies are disorders of intrauterine development, which are based on damage to the germ cells, associated either with mutations of hereditary structures, a change in the number of chromosomes, or with the maturation of male and female germ cells. These malformations are very serious and, as a rule, do not combine with the viability of the fetus. Mutations are changes in the genetic apparatus of cells. Since in this case hereditary mechanisms are affected, these violations are transmitted to all descendants of the mutant cell, unless, of course, the mutation that occurred does not immediately lead to its death. It is believed that germ cell mutations are one of the most common causes of congenital malformations (about 40%). Mutations can occur in both somatic and germ cells at all levels of hereditary structures: genes, chromosomes and the genome. In this regard, there are gene, chromosomal and genomic mutations [12,13].

Gene mutations are new molecular states of a gene that arise due to the replacement of bases or rearrangement of nucleotides within a gene. In most cases, hereditary congenital malformations are the result of gene mutations [14].

Chromosomal mutations unite all types of changes in the structure of chromosomes: translocations, deletions, duplications and inversions. Translocations are the exchange of segments between chromosomes: reciprocal (two chromosomes mutually exchange their segments), non-reciprocal (segments of one chromosome are transferred to another chromosome) and Robertsonian (two acrocentric chromosomes are connected by their centromeric regions). A deletion is a chromosome breakdown with a loss of part of its short or long shoulder. Duplication is a duplication of a chromosome region. Inversion occurs as a result of two breakdowns in one chromosome, followed by rotation of the section between breakdowns by 180. The share of chromosomal mutations in the origin of congenital malformations is approximately 7% of all chromosomal diseases. With all the diversity of chromosome structural changes, all the chromosomal diseases associated with these rearrangements are clinically reduced to the consequences of either partial trisomy or partial monosomy [15].

Genomic mutations are a change in the number of chromosomes. Trisomy (increase in the number of chromosomes by one) or monosomy (the absence of one of the chromosomes) is most often observed. The most common genomic disorder is Down syndrome (trisomy of the 21st pair of autosomes), in which the karyotype contains not 47 chromosomes, but 47 chromosomes, that is, there is a third chromosome N21. In such children there is a violation of the development of the central nervous system, which causes a sharp lag in mental and physical development. Another example of trisomy is Klinefelter syndrome, in which the karyotype contains 47 chromosomes, that is, there is an additional third sex chromosome (XXY). These children are characterized by male gender, mental retardation and infertility. Triploidy and tetraploidy, the presence of one or two additional haploid sets of chromosomes, are relatively rare forms of genomic mutations. Genomic mutations are usually accompanied by changes in the phenotype and lead to spontaneous abortion or chromosomal disease. They arise as a result of nondisjunction, lag or elimination of chromosomes in the process of cell division [16].

According to the sequence of occurrence of developmental anomalies are divided into primary and secondary. Primary defects arise as a result of direct exposure to the teratogenic factor (genetic or exogenous), and secondary defects are a complication or consequence of the primary and are always associated with them causally. For example, congenital clubfoot (secondary defect) is caused by the occurrence of spinal hernia, which is the primary defect [17].

Even from a simple enumeration of congenital malformations of organs and systems, it can be concluded that there are no “privileged” parts of the body in which structure errors would never occur. Any organ or system in its development can go the wrong way. At the same time, various anomalies affect the viability of the developing organism in different ways. For example, with anencephaly, that is, in the absence of large cerebral hemispheres, bones of the cranial vault and soft tissues, the fetus is viable only during the prenatal period, and the transition to an independent existence after birth is almost impossible. At the same time, dextrocardia or polydactyly have practically no effect on the viability of the fetus and child [18].

All congenital malformations are formed as a result of a delay in the formation of organs, the disturbance of the primordia of organs, or even the complete suppression of their development. For example, during the formation of the brain, the edges of the neural groove first close at the head end of the embryo, as a result of which the brain germ is formed here — the brain bladder. In some cases, there is no complete closure of the edges of the neural plate, so this area does not develop further and the cerebral hemispheres cannot form from it, which leads to the formation of anencephaly [19].

In other cases, the laying of an organ is partially suppressed (not completely), which leads to underdevelopment or the formation of another tissue of the organ. This is accompanied by a decrease or increase in the size and mass of the organ. What causes the violation of the functions of the body. For example, a fairly common cerebellar underdevelopment leads to impaired coordination of movement and muscle tone. Another example is macrocephaly, that is, an increase in the mass and size of the brain, which is accompanied by dementia [20].

Congenital malformations are also manifested by an increase and decrease in certain parts of the organs or the organs themselves: a decrease or increase in the number of fingers, the appearance of additional organs (adrenal glands, uterus, ureters).

A special group of anomalies is made up of conserved embryonic (temporary) structural features of a number of organs. For example, in the antenatal period between the right and left ventricles of the heart there is a batall duct, due to which the fetus's blood from the right ventricle does not enter the small circulation (into the lungs), but returns to the large, that is, the fetus has no pulmonary respiration. At the first inhalation of a child, the battalls duct contracts and gradually grows. In this case, blood is directed from the pulmonary circulation to the lungs (and not through the placenta), where it is enriched with oxygen. When the batallov duct is not clogged, blood from the small circle (rich in carbon dioxide, but poor in oxygen) returns to the tissues and organs [21].

Congenital anomalies are quite common: their frequency ranges from 1% to 5%. At the same time, it is important to remember that most of the defects in newborns are not clinically manifested: many defects, including defects of the sense organs, nervous system, endocrine glands, and genital organs are found much later. Therefore, the actual incidence of congenital malformations is more than 10%. According to embryologists, a number of features of a person's character, impaired mental abilities, low vitality of the body, poor adaptation to environmental conditions, susceptibility to a number of diseases very often congenital malformations.

Among the damaging factors that may have an adverse effect on the intrauterine developing organism, it is customary to secrete exogenous and endogenous factors.

The endogenous factors responsible for impaired intrauterine development are, first of all, mutations of germ cells. Altering factors (cosmic radiation, neutrons and high-energy particles, ultraviolet rays, gamma rays, x-rays, various chemical substances such as mustard, caffeine, formaldehyde, colchicine, pesticides, food preservatives) can cause mutation. Depending on the level of damage to hereditary structures, gene, chromosomal and genomic mutations are distinguished [22].

There are numerous data indicating that the pathology of the cardiovascular, hepatobiliary, endocrine, excretory systems of the maternal organism can adversely affect the fetus. Clinical observations have established that the above-mentioned diseases of the mother can lead to the birth of children with reduced resistance and viability, with developmental disabilities, often leading to their death. Such children, as a rule, have an altered weight, they show signs of impaired hormonal homeostasis, the cardiovascular system, and neurological changes [23].

Important is the age of parents, especially mothers. For example, a correlation is found between the age of a woman and the frequency of birth of children with Down syndrome, as well as trisomy. It is established that if the mother is at the age of 35-36 years, the risk of trisomy in the fetus is 0.9%. At the same time, in women aged 43-44 years, the risk of this pathology increases to 7.8%. These disorders of intrauterine development are primarily due to an increase in the age of mutations of germ cells. However, the human chromosomal pathology depends not only on the intensity of the mutation process, but also on the effectiveness of the "selection of the natural". The fact is that in humans more than 95% of mutations that occur are eliminated in utero, that is, they are absorbed or removed by spontaneous miscarriage. In this regard, many embryologists believe that an increase in the frequency of birth of older anomalies of fetal development in parents is associated with both an increase in chromosomal aberrations and a weakening of the "selection". That is why in the early stages of pregnancy, spontaneous miscarriage is considered as a defensive reaction developed in evolution aimed at preventing the birth of handicapped children [24].

Exogenous factors include physical, chemical and biological. Biological factors include viruses, chlamydia, bacteria, fungi and protozoa. For example, the rubella virus can lead to stillbirths, congenital defects: eye cataracts, heart defects, and disturbances in the development of the central nervous system.

The physical factors that violate fetal development, first of all, include temperature and mechanical effects, as well as ionizing radiation. Thus, the explosion of the atomic bomb in Japan led in the overwhelming

number of cases (over 70%) to intrauterine development disorders: miscarriages, skeletal malformations, and stillbirth [25].

The most numerous are the chemical factors, which include malnutrition, avitaminosis, various drugs, toxic compounds, alcohol, drugs, nicotine [26].

At the end of the 60s of the last century, the whole world spread around a sensational tragic message of scientists. The fact is that one West German pharmaceutical company for several years produced the drug thalidomide, advertised as a sedative. This drug was widely used by pregnant women to stop nausea, vomiting, and insomnia in the early stages of pregnancy. The consequences of the use of this drug were tragic: children were born with deformities of the limbs or lack of.

Disorders of fetal development can be caused by such widespread drugs as antibiotics, sulfonamides, aspirin, narcotic drugs. So, there is every reason to believe that "harmless" aspirin can lead to heart defects, the antibiotic streptomycin can cause disorders of the vestibular and cochlear apparatus, and, consequently, hearing loss. Penetrating through the placental barrier, these drugs affect the proliferation and differentiation processes of embryonic bookmarks of various organs, which ultimately leads to impaired organogenesis, and, as a result, developmental abnormalities [27].

One of the “topical” embryotoxic factors today is alcohol, which easily passes through the placental barrier and has a direct impact on the processes of morphogenesis. Most scientists believe that it is impossible to calculate the minimum level of alcohol in the blood of the mother, which would be harmless to the fetus. At the clinic, obstetricians are often confronted with fetal alcohol syndrome born in female alcoholics. Such children may have congenital deformities of bones, heart defects, and small brain volume. These children are lagging behind in physical and mental development, have a predisposition to various diseases. In recent years, alcohol has been shown to cause impaired stem germ cell formation [20].

Currently, the problem associated with the influence of maternal smoking on the fetus is of not only medical, but also social importance, as in a number of studies about 50% of women of childbearing age smoke. It is established that nicotine has an embryotoxic effect on the fetus. In children whose mothers smoke, suppression of behavioral reactions is observed, their viability decreases, the diameter of the blood vessels of the microvasculature decreases in organs and tissues, which cannot but affect the intensity of metabolic processes.

There is convincing evidence indicating a decrease in the number of primordial follicles and increased oocyte degeneration at the pachyenema stage in the ovary of fetuses in smoking females. At the same time, some authors point to smoking as a causal factor contributing to the development of developmental abnormalities in children, such as splitting of the upper palate and lips. The risk of miscarriages in women smokers is 30-35% higher.

In recent years, embryologists have paid attention to the negative effect of passive smoking, that is, tobacco smoke, under the influence of which nicotine and carboxyhemoglobin also accumulate in fetal blood at a concentration substantially higher than that of a woman’s blood, which causes fetal hypoxia. A feature of the embryos of all living beings is their exceptionally high damageability, especially in the early stages of embryogenesis. It is a postulate that to obtain any teratogenic effect it is necessary that the damaging factor act on the organism (organ) before its formation is completed [5].

CONCLUSION

In all periods of antenatal development, the embryo and fetus are sensitive to the action of adverse factors. However, in the process of prenatal development, periods of increased sensitivity of the developing organism to the action of damaging factors can be distinguished. These periods were called critical periods, the concept of which was first formulated by P.G.Svetlov. It is customary to distinguish several such critical periods: fertilization, implantation period (6-7 days) and period of placentation and organogenesis (3-8 weeks), since at this time there is a separation of embryonic rudiments of tissues and organs (3 weeks), differentiation of mesoderm (3 -5 weeks), placenta development (6-8 weeks), initial stages of organogenesis (4-8 weeks). At the same time, developmental disruption of the embryo at the pre-implantation stage proceeds according to

the principle “all or nothing”. In other words, at this stage the action of unfavorable factors, as a rule, ends with the death of the embryo. However, if the embryo survives, organ-specific anomalies do not develop, since the repair or replacement of damaging cells ensures further normal development. On this basis, it becomes clear why the damaging effect of the mother’s disease on the fetus does not always correspond to the severity of the latter, why in some cases a seriously ill woman is born to a seriously ill woman, and a relatively mild pathological process sometimes causes a physiologically immature child with developmental defects.

REFERENCES

[1] Lenchenko E, Lozovoy D, Strizhakov A, Vatnikov Y, Byakhova V, Kulikov E, Sturov N, Kuznetsov V, Avdotin V, Grishin V (2019) Features of formation of Yersinia enterocolitica biofilms. VeterinaryWorld. 12(1): 136-140.

[2] Suleymanov SM, Usha BV, Vatnikov YA, Sotnikova ED, Kulikov EV, Parshina VI, Bolshakova MV, Lyshko MU, Romanova EV (2018) Structural uterine changes in postpartum endometritis in cows. Veterinary World. 11(10): 1473-1478.

[3] Yousefi M, Hoseini SM, Vatnikov YA, Nikishov AA, Kulikov EV. (2018b) Thymol as a new anesthetic in common carp (Cyprinuscarpio): Efficacy and physiological effects in comparison with eugenol. Aquaculture.495 :376-383.

[4] Makhov AS, Medvedev IN. (2019) The Physiological Response Of The Body To The Practice Of Physical Therapy After Spinal Cord Injuries. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 10(1) : 118-124.

[5] Makhov AS, Medvedev IN. (2019) The Functional State Of Human Sensory Systems On The Background Of Regular Exercise. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 10(1) : 183-188.

[6] Mal GS, Vorobyeva NV, Medvedev IN. (2019) Physiological Significance Of The Active Muscle Activity Of The Body. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 10(1) : 366-371.

[7] Makhov AS, Medvedev IN. (2019) The Functional State Of The Joints In Conditions Of Regular Ordered Muscle Activity. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 10(1) : 594-599.

[8] Makhov AS, Medvedev IN. (2019) Regular Muscular Activity In Maintaining The Optimum Of Human Physiological Parameters In Conditions Of Increased Mental Stress. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 10(1) : 625-629.

[9] Makhov AS, Medvedev IN. (2019) Dynamics Of Functional Parameters In The Post-Stroke Period On The Background Of Active Muscular Activity. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 10(1) : 650-654.

[10] Makhov AS, Medvedev IN. (2019) The Physiological Significance Of The Formation And Maintenance Of Correct Posture. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 10(1) : 685-688.

[11] Makhov AS, Medvedev IN. (2019) Physiological Changes In The Locomotor System During Massage Effects. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 10(1) : 755-760.

[12] Makhov AS, Medvedev IN. (2019) Basics Of Physiotherapy In Diseases Of The Musculoskeletal System. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 10(1) : 801-805.

[13] Makhov AS, Medvedev IN. (2019) The Functional State Of The Body With Vascular Dysfunction On The Background Of Regular Physical Exertion. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 10(1) : 869-873.

[14] Makhov AS, Medvedev IN.(2019)The Problem Of Flatfoot And Approaches To Its Solution. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 10(1) : 905-910.

[15] Makhov AS, Medvedev IN. (2019) Functional Features Of The Nervous System In The Context Of Regular Physical Education. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 10(1) : 961-966.

[16] Medvedev IN. (2019) Weakening Of Platelet Activity In Patients With A High Degree Of Arterial Hypertension In The Metabolic Syndrome Who Received Complex Treatment. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 10(1) : 1000-1006.

[17] Medvedev IN.(2019)Functional Readiness Of Platelets In Young People Who Regularly Visited The Section Of Unarmed Combat In Their Youth. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 10(1) : 1381-1385.

[18] Medvedev IN. (2019) Functional Activity Of Platelet Hemostasis Of Amateur Soccer Players Aged 26-35, Who Regularly Trained In Adolescence. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 10(1) : 1426-1430.
[19] Medvedev IN.(2019)Physical Features Of Platelet Activity During Low Physical Activity. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 10(1) : 1468-1473.
[20] Medvedev IN. (2019) Physiological Response Of Intravascular Platelet Activity In Adolescents With High Normal Blood Pressure To Regular Exercise. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 10(1) : 1516-1520.
[21] Medvedev IN.(2019)Platelet Functionality Of Candidates And Masters Of Sports In Athletics Of Youth And First Adulthood. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 10(1) : 1543-1548.
[22] Medvedev IN. (2019) Functional Features Of Erythrocytes In Calves Of Vegetable Nutrition. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 10(1) : 1848-1852.
[23] Lenchenko EM, VatnikovYuA, Kulikov EV, Lozovoy DA, Gavrilov VA, Gnezdilova LA, Zimina VN, Kuznetsov VI, Annikov VV, Medvedev IN, Petryaeva AV, Glagoleva TI. (2019) Aspects of Salmonellosis pathogenesis using chicken models.Bali Medical Journal. 8(1): 206-210. DOI:10.15562/bmj.v8i1.920
[24] Skoryatina IA, Medvedev IN. (2019) Correction of aggregation level of basic regular blood elements in patients with hypertension and dyslipidemia receiving rosuvastatin and non-medicinal treatment. Bali Medical Journal. 8(1) : 194-200. DOI:10.15562/bmj.v8i1.648
[25] Makhov AS, Medvedev IN. (2018) Functional Mechanisms To Ensure The Reactivity Of The Organism. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 9(6) : 924-929.
[26] Alifirov AI, Mikhaylova IV, Fomina SN, Seselkin AI, Zhalilov AV. (2019) Methods Of Training Chess Players Of Higher Sportsmanship. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 10(1) : 45-51.
[27] Alifirov AI, Chepik VD, Baymurzin AR, Zhalilov AV. (2019) Features Of Psychophysical Training In The Cadet Cossack Corps. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 10(1) : 442-448.