

Pathological Mechanisms of Human Embryonic Development and the Role of the Medical Genetic Counseling System in Their Prevention

Патологические механизмы эмбрионального развития человека и значение системы медико-генетического консультирования в их профилактике

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Аннотация. В данной статье анализируются медико-биологические механизмы патологических изменений, возникающих в критические периоды эмбрионального развития человека, а также современные стратегии их профилактики. В ходе исследования освещена роль генетических и экзогенных факторов в возникновении тератогенеза, а также морфологические последствия нарушений фундаментальных клеточных процессов (пролиферации, миграции, апоптоза). Основное внимание в статье уделено приоритетному значению центров медико-генетического консультирования, созданных по инициативе Президента Республики Узбекистан, в раннем выявлении врожденных дефектов и обеспечении рождения здорового поколения.

Abstract. This article analyzes the medical-biological mechanisms of pathological changes occurring during critical periods of human embryonic development, as well as modern strategies for their prevention. The study highlights the role of genetic and exogenous factors in the occurrence of teratogenesis, along with the morphological consequences of disturbances in fundamental cellular processes (proliferation, migration, apoptosis). Particular emphasis is placed on the priority importance of medical-genetic counseling centers, established at the initiative of the

President of the Republic of Uzbekistan, in the early detection of congenital defects and ensuring the birth of a healthy generation.

Ключевые слова: эмбрион, тератогенез, критические периоды, апоптоз, Нох-гены, пренатальная диагностика, врожденные пороки развития, медико-генетическое консультирование, постановление ПП-46, здоровое поколение.

Keywords: embryo, teratogenesis, critical periods, apoptosis, Hox-genes, prenatal diagnosis, congenital malformations, medical-genetic counseling, Resolution PP-46, healthy generation.

Introduction. The embryonic period of human ontogenesis is one of the most complex and delicate stages of organism development, during which the foundations of all organs and organ systems are established. The theory of “critical periods” proposed by P.G. Svetlov demonstrated that, at certain stages of development, the embryo is particularly sensitive to various external and internal factors [1]. Today, the occurrence of congenital developmental anomalies (CDAs) in approximately 3–5% of newborns worldwide has elevated this issue to the level of a global medical and social concern [5].

Embryonic pathologies are not merely the result of morphological abnormalities but also arise from disruptions in complex molecular processes at the cellular level. However, modern medical biology is not limited to the study of pathological conditions; it also focuses on developing measures for their prevention. In our country, the protection of maternal and child health, particularly the establishment and development of genetic centers, has been identified as a priority area of state policy. This article analyzes not only the pathological mechanisms underlying embryonic development but also the scientific and practical prospects of prenatal screening and the medical-genetic counseling system currently being implemented in Uzbekistan.

Main Causes of Pathologies (Etiology). Pathological changes and congenital developmental anomalies (CDAs) occurring during embryonic development result from the complex interaction of genetic and environmental factors. From the perspective of medical biology, these processes can be regarded as a disruption of the balance between the embryo’s genetic program and external exogenous signals. According to the modern classification, the causes of pathologies can be divided into three main groups:

Endogenous (Hereditary) Factors. Hereditary factors account for approximately **20–25%** of all congenital anomalies [3,4,6]. These processes are directly associated with abnormalities in the genetic material of germ cells (gametopathies) or the fertilized egg cell.

Chromosomal mutations: Changes in the number or structure of chromosomes (chromosomal aberrations). For example, trisomy of chromosome 21 causes **Down syndrome**, trisomy of chromosome 13 causes **Patau syndrome**, and trisomy of chromosome 18 causes **Edwards syndrome** [7].

Gene mutations: Molecular-level alterations in individual genes (point mutations). These genes often encode proteins that regulate embryonic induction and organogenesis. Mutations in developmental regulatory genes may result in lethality or severe morphological abnormalities [2,6].

Exogenous (Teratogenic) Factors: Factors originating from the external environment that affect the embryo and disrupt normal developmental processes are known as **teratogens**. At the cellular level, they can cause cytotoxic, mutagenic, or metabolic disturbances.

Biological factors: These include maternal infectious diseases, particularly the **TORCH complex** (Toxoplasma, Rubella, Cytomegalovirus, and Herpes). For example, the rubella virus slows the mitotic cycle of embryonic cells. As a result, cells fail to proliferate adequately, which may lead to the development of microcephaly, cataracts, and congenital heart defects, collectively referred to as the **Gregg triad** [7].

Chemical factors: These include certain medications, heavy metals such as mercury and lead, and household toxins. One of the most well-known historical examples is **thalidomide**, which caused underdevelopment of the limbs (phocomelia). In addition, **Fetal Alcohol Syndrome (FAS)** is particularly dangerous because ethanol disrupts neuronal migration, potentially resulting in intellectual disability [7].

Physical factors: These include ionizing radiation (X-rays and other forms of radiation) and high temperatures (hyperthermia). Radiation can directly damage DNA and generate free radicals, potentially causing extensive cellular death (necrosis) [6].

Multifactorial Factors: The largest proportion of congenital anomalies (**60–70%**) is considered to have a multifactorial etiology. This means that the development of a pathological condition generally requires the simultaneous presence of both a genetic predisposition and an unfavorable environmental factor [6,7].

Examples include **cleft lip** and **cleft palate**. In such cases, the embryo may have a genetic predisposition, while maternal factors during pregnancy—such as severe stress, nutritional deficiencies (particularly folic acid deficiency), or smoking—may contribute to the manifestation of the developmental defect.

Pathologies in this group are difficult to predict because they do not result from a single gene but rather from complex interactions between multiple genes (polygenic factors) and environmental influences.

Molecular mechanisms of pathological processes: Pathological changes occurring during embryonic development are not merely external defects but are also the consequences of complex biological abnormalities at the cellular and molecular levels. For the formation of each organ, cells must divide, migrate, and differentiate at specific times and in specific locations. If this sequence is disrupted by abnormalities in the genetic program or by environmental influences, the process of **teratogenesis** is initiated [10].

The development of pathologies is based on several major cellular mechanisms:

- **Disruption of proliferation:** A decrease in the rate of cell division may lead to insufficient organ development (**hypoplasia**), whereas uncontrolled cell proliferation may result in cystic changes.
- **Migration and differentiation:** During organogenesis, cells must migrate to their designated locations and differentiate into specific tissue types. If these molecular “guidance signals” are disrupted, abnormal positioning of organs or tissues (**ectopia**) may occur.
- **Apoptosis (programmed cell death):** During normal development, certain cells must undergo programmed cell death; for example, the tissue between the developing fingers must be eliminated. Impaired apoptosis may result in developmental anomalies such as **syndactyly**, in which the fingers are fused together.
- **Regulatory genes (Hox genes):** These “master genes,” which determine the overall body architecture, play a crucial role in embryonic development. Mutations in Hox genes may cause abnormalities in the number and positioning of body structures, such as **polydactyly**.

Critical periods of development and stages of organogenesis: The severity of pathological processes depends not only on the type of causative factor but also on the developmental stage at which it acts. In this regard, the theory of “**critical periods**” proposed by P.G. Svetlov plays a central role [1]. According to this theory, the period of rapid organ formation (**organogenesis**) is the stage when the embryo is most susceptible to external influences.

Developmental period	Nature of the Process	Pathological Consequences
Blastogenesis (Days 0-15)	Fertilization, cleavage, and blastocyst formation.	The “all-or-none” principle: Since the cells are totipotent, severe

		damage may result in embryonic death, whereas minor damage may be followed by complete regeneration and normal development without congenital anomalies.
Embryogenesis (weeks 3-8)	Formation of the foundations of the organs (the most critical period).	Severe anomalies, including anencephaly, congenital heart defects, and limb aplasia.
Fetogenesis (From week 9 to birth)	Growth and functional maturation of organs.	Functional disorders, including intellectual disability, hearing and visual impairments, and growth retardation

Prevention and modern diagnostic approaches: The prevention and early detection of embryonic pathologies represent strategic priorities in modern perinatology and medical biology. In the Republic of Uzbekistan, the protection of maternal and child health and the prevention of births affected by hereditary diseases have become priority areas of state policy.

In particular, **Resolution No. PQ-46 of the President of the Republic of Uzbekistan, dated December 15, 2021, “On Measures to Further Develop Hematology and Oncology Services in the Republic and Establish Genetic Counseling Centers,”** marked a significant turning point in this area. Based on this initiative, modern **Medical Genetic Counseling Centers** have been established in all regions of the country [9].

Within this system, the following measures are being implemented:

- **Medical Genetic Counseling (MGC):** This is one of the most effective approaches to preventing hereditary and congenital disorders. It involves providing evidence-based counseling to families belonging to high-risk groups, including consanguineous couples and families with a history of congenital developmental anomalies (CDAs). Advanced cytogenetic and molecular genetic laboratories have been established at MGC centers.
- **State Screening Programs:** At the initiative of the President, universal prenatal screening for pregnant women has been established as a free and

mandatory service. This represents a practical implementation of the national principle of “**Healthy Mother – Healthy Child.**”

- **Preconception Care:** Research indicates that taking folic acid (vitamin B9) beginning three months before conception and continuing throughout the first trimester can reduce the risk of neural tube defects in the embryo by up to 80%. The government has also established programs to provide women with vitamins and iodine preparations free of charge.

Conclusion. Analysis of pathological changes in human embryonic development demonstrates that this process is not merely a biological problem but also an issue of social and demographic importance. Although the cellular and molecular abnormalities identified in this study—including disturbances in proliferation, migration, and apoptosis—form the basis of teratogenesis, modern medicine provides opportunities for their prevention, early detection, and management.

In conclusion, the reforms being implemented in Uzbekistan at the initiative of the President, particularly the establishment of regional genetic centers and the improvement of the prenatal screening system, contribute to reducing the incidence of congenital anomalies. Further expansion of medical genetic counseling services and improvement of public health literacy are important measures for strengthening the foundation of a healthy future generation.

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