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## CONGENITAL ANOMALIES IN CHILDREN REVALENCE AND RISK FACTORS

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### ABSTRACT

Congenital malformations have been in the focus of physicians since ancient times, but despite their centuries-old history, many aspects of the etiology and pathogenesis of congenital malformations in humans have not been adequately studied even today. Congenital deficiencies of development are defined as stable morphological changes that go beyond the limits of structural variations of members or parts of organs and disrupt their function. Apply the term "sporadic the defect

of birth", meaning unknown cause, accidental appearance and low risk appearance have future children. For 20-25% of anomalies more likely "multi-factor" reason - complex interaction many small genetic defects and risk factors environmental environment. The rest 10-13% of anomalies associated with the influence environment. Only 12-25% of anomalies have purely genetic causes.

**Key words:** congenital anomalies, congenital malformation, congenital heart defects, perinatal causes



## РЕЗЮМЕ

Врожденные пороки развития находятся в центре внимания врачей с древних времен, но, несмотря на их многовековую историю, многие аспекты этиологии и патогенеза врожденных пороков развития человека до сих пор недостаточно изучены. Врожденные пороки развития определяются как стойкие морфологические изменения, которые выходят за пределы структурных изменений членов или частей органов и нарушают их функцию. К ним применяют термин «спорадические дефекты рождения», обозначающий неизвестную причину, случайное возникновение и низкий риск повторного возникновения у будущих детей. Для 20-25% аномалий более вероятна «многофакторная» причина - комплексное взаимодействие многих небольших генетических дефектов и факторов риска окружающей среды. Остальные 10-13% аномалий связаны с воздействием среды. Только 12-25% аномалий имеют чисто генетические причины.

**Ключевые слова:** врожденные аномалии, врожденные порок, врожденные пороки сердца, перинатальные причины

Congenital malformations have been in the focus of physicians since ancient times, but despite their centuries-old history, many aspects of the etiology and pathogenesis of congenital malformations in humans have not been adequately studied even today. Congenital deficiencies of development are defined as stable morphological changes that go beyond the limits of structural variations of members or parts of organs and disrupt their function [1,7].

Significant achievements in the prevention and treatment of infectious parasitic and foodborne diseases in our country in recent decades, as well as modest success in preventing the birth of children with congenital malformations, have led to the prevalence of this common pathology in childhood morbidity, disability and mortality. An average of 20% of infant deaths occur due to the presence of congenital malformations in the child [4,8]. Chronic diseases in up to 20% of children are associated with congenital malformations of organs and systems [17].

Congenital malformations have been in the focus of physicians since ancient times, but despite their centuries-old history, many aspects of the etiology and pathogenesis of congenital malformations in humans have not been adequately studied even today. Congenital deficiencies of development are defined as stable morphological changes that go beyond the limits of structural variations of members or parts of organs and disrupt their function [12].

According to many authors, congenital heart defects are the leading cause of congenital malformations. According to the latest statistics, the prevalence of congenital circulatory defects tends to increase, from

499.1 in 2007 to 547.4 in 2019 per 100,000 eligible population.

However, the variability in the frequency of congenital malformations and congenital malformations of the face and neck in certain years, neural tube defects, and multiple congenital malformations.

Class XVII according to ICT-10 (congenital anomalies of development, deformities and chromosomal abnormalities), belongs to the junior class Q20-Q28 (congenital malformations of the circulatory system). [11,16]

Heart congenital deficiency sometimes occurs in conjunction with defects of other systems. In clinical practice, the occurrence of congenital heart defects in combination with defects of other organs is observed in about 10% of cases. Defects of the cardiovascular system are a constant companion of chromosome and gene-related syndromes. Chromosomal diseases in congenital heart disease can occur in 3-4% of cases, and in congenital syndromes in 26% of cases, congenital heart disease [29].

Congenital heart defects (Heart congenital deficiency) are the leading cause of all congenital malformations (30%), are one of the leading causes of the most common developmental defects, contribute significantly to perinatal and infant mortality, lead to disability, and lead to blindness, implementation and significant social costs are required to provide social assistance to children with disabilities.

Therefore, preventive measures aimed at preventing the birth of children with congenital heart defects, early detection of this pathology and surgical correction are very relevant [1,28]. Monitoring of congenital malformations (congenital malformations of development) is one of the prophylactic measures, which allows to determine the population frequency of congenital heart defects, including congenital heart defects, the impact of mass programs of primary and secondary prevention on them.

However, according to various researchers, the frequency of congenital heart disease is 4-17 per 1000 newborns, which may be due to the lack of a holistic approach to data collection and recording, diagnosis [19,21,32].

The clinical manifestations of congenital heart defects are diverse: they may be the main cause of infant mortality, an aggravating factor in the accompanying disease, or a random finding that does not affect the course of the underlying pathology and may be asymptomatic [9, 20, 17, 22].

The fetal age of 23-25 days is a critical period for the formation of major heart defects. Acute and teratogenic terminological periods are of particular importance in identifying and preventing the causes of congenital heart disease.



The significant role of fetal period infections (HDI) in the development of developmental defects in children has been confirmed [12]. A significant proportion of congenital heart defects, brain and other organ defects are associated with HDI (17). XDI is characterized by joint damage of several members of the same system, as well as joint occurrence of defects in the development of different systems, which indicates evidence of polyorganic tropism of pathogens.

TORCH-infections are particularly dangerous for the fetus, among which the measles virus poses the greatest risk for the development of congenital heart disease [21]. Only 15-25% of children born to mothers with measles during pregnancy had congenital measles symptoms, however, in 85-90% of these children, congenital, slow, predominantly cardiac pathology was confirmed [17].

It has been shown that the occurrence of defects in 23.3% is directly related to genetic factors, 50.8% to the multifactorial group, and only 2% to the influence of teratogenic factors (59). The causes of other deficiencies remain unclear.

In addition to risk factors for the development of congenital heart disease, there are also factors that play the role of protectors. In particular, the use of multivitamins for 3 months before and after pregnancy can prevent about 1 in 4 major heart defects. The intake of multivitamins is highly effective in preventing the development of major vascular anomalies and interventricular barrier defects [7,15].

It should be noted that the antimutagenic properties of tocopherol acetate, adenosine, and dimethosphones are known [27]. In a number of cases, the effectiveness of antimutagenesis is so high that individual antimutagens have the property of completely preventing the mutagenic effects of xenobiotics. Data from animal experiments suggest that the biomass of pink rhodiola cells has the property of inhibiting gene and chromosomal mutations. [7,12]. The use of antimutagens is promising for genetic integrity and prevention of diseases occurring in humans under mutagenic influences. However, the use of pharmacological antimutagens is difficult due to the formal problems of prescribing drugs for prophylactic purposes to healthy people [8]. Congenital disorders of development. Ways are being sought to perform surgical correction during pregnancy.

Antenatal detection of congenital heart defects is important in principle. Currently, a triad of research methods for laboratory assessment of fetal status: evaluation of «-fetoprotein, chorionic gonadotropin, and free estriol in the blood of women in the second half of pregnancy is widely used [21]. However, none of the methods mentioned are considered specific for the detection of congenital heart defects.

The diagnostic possibilities of fetal ultrasound for the detection of congenital heart defects are currently limited: such tests can detect only 30% of congenital heart defects, including developmental anomalies of the cardiovascular system [4,21]. Left ventricular hypoplasia, a three-chambered heart, a common atrioventricular nucleus, and marked obstruction of the aorta and pulmonary artery are better diagnosed [3,4,19].

In recent years, examination of the fetus using NMR-tomography has been widely used, which allows to detect structural abnormalities that can not be detected by UTT: small abnormalities of the brain, tuberculous sclerosis, polycystic kidney disease [21]. NMR tomography is a promising non-invasive method in the diagnosis of congenital heart disease and other cardiovascular diseases [2,14]. However, this method is not yet widely used in practice.

A certain tendency to increase the frequency of detection of B 40 antigens in the group of children with urinary tract pathology (renal aplasia and hesitation, ureterocele) and A2 antigens in the group of children with congenital heart defects (oval valve insufficiency, halo tetrad) was detected [7,9]. These data suggest that genetic determinants in the pathogenesis of congenital malformations are multigenetic in nature.

There are now grounds for an increase in the birth rate of children with congenital heart disease in relation to environmental pressure. Pollution of the environment with substances with mutagenic and teratogenic effects is increasing [21,31].

To date, strict control over the teratogenic properties of new chemicals, including those widely used in the national economy, has not been sufficiently established in many countries. The population's exposure to ionizing radiation and chemical mutagens is increasing.

It should be noted as a paradoxical fact that there are always unjustified attempts to save any pregnancy that is at risk of termination in the event of an increase in the number of birth defects. The above example strongly demonstrates that birth defects are not only a medical but also a social problem. [12,31]

Thus, congenital heart defects are a topical and unresolved problem. Numerous data on risk factors for congenital heart disease do not give an idea of the role of each factor in the emergence and development of this pathology. This situation requires that the mentioned factors need to be evaluated not only qualitatively but also quantitatively.

Influence of socio-hygienic factors on the formation of congenital defects

Health, including the health of the fetus and child, is an integral quantity, determined by a number of objective factors that are not dependent on human influence and are related to its activities. The first unrelated factors are the genetic code of the developing





organism, which determines the following vital parameters: sex, growth and physical development rates and levels, "binding" periods and activity of key enzyme processes in the body, morphological and functional functions of tissues, organs and systems. The rate and level of maturation, the level and quality of the interdependence of the body's control mechanisms, the basis of the fetus's response to external traumatic influences, as well as metabolic and adaptive to extraterrestrial life in the first hours, days and weeks of life and adaptive mechanisms, later pathological conditions and genetically related conditions that lead to disease, and so on. [6,8,17]

The second group of factors relates to factors whose impact is related to human activity and can be conditionally divided into non-medical and, in particular, medical types.

Non-medical factors include social, societal, social, religious, spiritual, and environmental factors that affect the developing fetal organism and the newborn organism. Their influence is realized through the body, psyche, perception, lifestyle and activities of the woman.

Depending on the situation, this condition can mitigate and even flatten the negative impact on the fetus and child, as well as increase and significantly increase its impact. It should be noted that in addition to environmental influences, these factors, which have nothing to do with biology and medicine, still have a large biological effect, because the child undergoes processes of high intensity: growth, development and perfection, a new form of human existence as well as cases of reconstruction, which are very important in terms of their level and importance, and so on. Therefore, their medical and non-biological nature is characterized by impaired growth and development of the fetus, impaired organ and tissue maturation, normal management processes in the body, the formation of adaptive mechanisms for survival outside of pregnancy and their effects. Thus, non-medical adverse factors affecting the health of the fetus and newborn are considered to have genetic and, in particular, biological effects no less than medical factors. Understanding this situation by each individual, the whole society and the state creates new opportunities to improve the quality of health not only of fetuses and newborns, but also of the population of the whole country. This problem is undoubtedly of independent political and state importance.[22,27,30]

Second, medical factors include women - maternal pathology, pregnancy, obstetric pathology, diseases acquired during pregnancy (fetal diseases), neonatal diseases, and the quality of medical care for women, fetuses, newborns. All these factors primarily affect the growth, development and improvement of the fetal organism in order to realize one of the most important

functions of the human body - an independent and full life outside of pregnancy. [4]

Obviously, the health of the fetus and newborn does not depend solely on any cause or factor, so it cannot be the sole concern of the parents, only the family, only medicine or society or the state. Their mutual harmony is necessary for the normal development and health of a person.

Nowadays, the importance of fetal pathology leading to impaired or impossible adaptation of the child to life outside of pregnancy is clearly increasing. These problems include immunosuppressive pregnancies, congenital infections, respiratory distress syndrome, and developmental defects. The nervous, endocrine, and immune systems of the fetus and newborn are immature and, accordingly, the most inefficient in the implementation of adaptive mechanisms. It is their functional deficiency that sometimes serves as a starting point in the formation of pathology. These deviations are the basis for the formation of functional disorders and diseases. There is a fairly clear link between the physical development of the fetus and genetically related factors and the risk of developing various pathological conditions. [1,2,4,7,9,21].

For example, chromosomal aberrations in children with delayed gestational development occur in 7% of cases (2 times more than in healthy newborns), while developmental defects occur in 11% and 5% in healthy newborns, respectively. These data require attention to be paid to human development during pregnancy. At the present time, there is a need to create a State National Program aimed at building and assessing the quality of fetal and child health in the new millennium. This situation can be a serious basis for predicting the formation of the nation's health, determining the priorities for the development of science and applied medicine. [8,12]

An analysis of the domestic and foreign literature shows that changes in the chemical composition of the human environment are one of the main causes of birth defects in children.

There are currently more than 500 substances that have a teratogenic effect. These include substances with different chemical composition: ethanol, testosterone, lead, chloroprene, mercury, ethyleneamine, benzene, most pesticides, sulfur carbon, poor quality tumors, and even some of the anti-diabetic drugs, even vitamin D. Hybridization of representatives of one species belonging to populations adapted to different natural conditions has been proven to lead to high mortality of the offspring, its high incidence of malignant tumors and other undesirable complications, including developmental anomalies. Such effects can often be explained by the adaptive nature of organisms in different environmental conditions.[2,7]

Identifying the causes of developmental anomalies and the emergence of various diseases at this or that



stage of human life has led to the conclusion that there are sensitive periods in human life to various factors and substances: The first and most important period is the period before egg fertilization. For at least 3 months (depending on the dose under the influence of ionizing radiation - several years) it is necessary to prevent the entry of substances with teratogenic properties into the body of the mother and father of the future child. The second period is the period of embryogenic development. During this period, especially in the 2-3rd week of pregnancy (when organogenesis is active, ie the period when the foundation is laid for various organs and systems of the body), the fetus becomes very sensitive). For example, 300,000 nerve cells are formed per minute. Naturally, the organ most active in cell division during exposure to a teratogenic substance is more likely to develop anomalies.

Congenital malformations include serious changes in children's health that significantly affect their morbidity and mortality. In recent years, there has been an increase in the incidence of this type of pathology among children and adolescents. In this case, despite the development and improvement of medical science, the number of primarily detected congenital anomalies among the population over 17 years of age, i.e. in the group of adolescents and adults, did not decrease, but increased by 1.1%. There is a tendency to increase infant mortality from congenital anomalies. Areas with low rates of frequency of this pathology are bordered by regions with high rates of them. Questions arise about the reasons for these discrepancies, the completeness and quality of the diagnosis, and the primary accounting and collection of data. In addition, given the diversity of natural and socio-economic characteristics of the regions, the influence of environmental factors on the formation of congenital malformations is of interest.

Congenital and inherited diseases occupy one of the leading positions in the structure of perinatal and infant mortality.). Unfortunately, the CIS countries are not yet involved in the International System of Defects, which was established in 1974 and covers 27 countries. The form of state registration, introduced by the former union Ministry of Health in 1989, directs health authorities to only the total number of congenital anomalies. However, in recent years, the epidemiology of congenital malformations has become increasingly important. This situation is due to a number of reasons. First, information on the frequency and composition of congenital malformations of development is used in the development of organizational measures to provide specialized medical care to children with this pathology. Second, the prevention of congenital malformations is not considered effective enough without data on the epidemiology of congenital malformations as one of the ways to reduce perinatal and infant mortality. Third, the dynamic accounting

of the frequency of congenital malformations allows us to assess the environmental situation in the region.

It has been proven that the frequency of congenital malformations increases with the age of the mother. According to the in Lipetsk region, 3% of children born to underage mothers with congenital malformations were observed for 2 years, the mothers of children with congenital malformations of 20% were over 30 years old, including 7.1% were 35 years old. The younger the marriage age of a woman, the greater the number of births. The earlier young people start having sex, the more likely it is that it will not be related to marriage, as well as the risk of unplanned pregnancies, abortions or unwanted births in adolescents with biological, mental and social disabilities. For adolescents and women under 20 years of age, pregnancy and childbirth itself can also be a risk factor: pathological course of childbirth, cesarean section and subsequent complications, frequent, pronounced vegetative-vascular dystonia syndrome, increased number of gestoses (30-40 %).

It is known that alcohol serves as a direct cause of every tenth embryonic pathology. For every 10 mentally immature children, 5 were born to pianist parents. Analysis of the questionnaires showed that 5.3% of mothers and about 50% of fathers smoked alcohol, 6.6% of mothers and 61.7% of fathers smoked. Mothers of children with congenital malformations were more likely to have anemia, pyelonephritis, cardiovascular disease, as well as pathology of the thyroid gland, measles and venereal diseases. 53% of women had a history of somatic diseases, 26.3% had gynecological diseases, and in this regard, 50% of women used drugs, including several drugs at the same time. Prior to pregnancy, 37.4% of women and 33.4% of women during pregnancy were exposed to harmful occupational conditions.

Based on an analysis of 207 birth histories of children with congenital and inherited diseases, G.M. Saveleva and coauthors noted that MAT developmental defects (22%) and congenital heart defects (19%) predominated in the pathology. Defects in the development of the gastrointestinal tract and urogenital system were observed with almost the same frequency (9.8% and 9.7%). Numerous developmental anomalies have been identified in 2% of newborns. Among the risk factors, the risk of early termination of pregnancy (34%), spontaneous abortion in the anamnesis (17%), occupational hazards and environmentally unfavorable living conditions (17%) were more frequent. Examination of alpha-fetoprotein in the serum of pregnant women showed that in 10 of them, including 2, an increase in its dynamics (18 and 22 weeks of gestation) was observed, which was an indication for the implementation of amniocentesis. Medical-genetic counseling is of great importance in screening pregnant women at risk, as they set



guidelines for detailed screening. Chromosomal abnormalities detected during karyotyping in 12% of pregnant women served as guidelines for fetal karyotyping. In this case, 2/3 of the fetus has different chromosomal abnormalities (balanced and unbalanced anomalies, Patau syndrome). The authors conclude that the pathological karyotype in the mother can be a risk factor in the formation of a similar pathology in the fetus and requires mandatory karyotyping. The data obtained are consistent with the results of other studies (Kozlova VI and co-authors), which also included women at risk for the successful implementation of the program for the prevention of congenital and hereditary diseases from the first trimester of pregnancy (medical-genetic), counseling, karyotyping of pregnant women if necessary, determination of serum alpha-fetoprotein levels, diagnosis of intrauterine infection, ultrasound examination in the I and II trimesters of pregnancy, strict adherence to the algorithm of examination of invasive prenatal procedures (chorionic biopsy, amniocentesis) which should be done without.

The lack of a single methodological approach to the consideration of developmental birth defects is one of the significant shortcomings in the study of the dynamics of their prevalence. This makes it more difficult to compare data obtained by different researchers. This situation can be explained by the breadth of the prevalence of congenital malformations, which are covered in the local press in relation to foreign scientific work. All of this does not allow for real reasoning to think about situations in which environmentally unfavorable areas arise.

According to IP Bochkov and coauthors, retrospective analysis of medical records in different regions does not provide accurate data on the frequency of congenital malformations. This may be due to hyper- and hypodiagnosis, inaccuracy in the registration of passport data (possible changes in the surname in the near future after delivery), incomplete storage of medical documents (possibility of transferring a medical document to a children's hospital to continue treatment, loss of documents).

In Kazakhstan, they have studied the resources to reduce infant mortality. Analysis of perinatal causes of death showed that congenital malformations in the structure of causes of death accounted for 10.5%.

According to the authors, infant mortality and stillbirths are affected by relatively constant background factors that are difficult to correct (socio-economic conditions), conditionally variable (natural-climatic conditions) and a complex of compensatory mechanisms (health system). If these factors are categorized according to their importance and manageability, the first two groups of factors belong to a group that is important but conditional or unmanageable. In that case, the threatening burden falls on the health care system, the existing compensatory mechanisms, despite their diversity, they are not very well developed and can not ensure the stability of infant mortality rates to the negative impact of factors. However, the most compensatory option is unconditional primary prevention, which in turn has insufficiently developed theoretical and managerial aspects, which ultimately leads to a decrease in the quality and effectiveness of medical and social measures to prevent infant mortality and stillbirth.

The prevalence of congenital malformations, perinatal morbidity and mortality were studied in Tashkent. Congenital malformations were observed in 2.5% of children, of which 93.9% were found alive and 6.1% were stillborn. The rate of perinatal morbidity associated with congenital anomalies averaged 2.2-2.6% among live births. The perinatal mortality rate associated with congenital malformations was 7.1%. Among the developmental defects, neural tube defects (21.3%), skeletal system developmental defects (21.3%) and multiple developmental defects (16.1%) took the leading place. The majority of women (90.9%) who gave birth to children with congenital malformations were indigenous. Women aged 17-21 accounted for 31.3% and those aged 35 and over for 26.7%.

Hereditary and congenital diseases and heart defects are serious problems not only in the health system but also in the whole country, as their treatment, as well as, unfortunately, the disability of children, requires large material costs and is one of the causes of birth defects - many married couples and do not want to have third children. Although the relative proportion of these diseases is small, the correction and treatment of these diseases subsequently results not only in the incidence rate but also in the disability of the population.

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## СОВРЕМЕННЫЕ МЕТОДЫ МОНИТОРИНГА ОСТЕОИНТЕГРАЦИИ

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Мониторинг остеointegrации имеет принципиальное значение не только в период

приживления имплантата и определения критериев для передачи пациента на ортопедический этап лечения, но необходим и в динамике наблюдения при дальнейшей эксплуатации ортопедической конструкции. Суммируя многочисленные обоснования и практики, С.С. Серегин (2016) [1] указывает, что наиболее рациональным является трехкратное наблюдение за пациентами с ортопедическими конструкциями с опорой на внутрикостные имплантаты в течение первого года после их установки (например, через 3, 6 и 12 мес.), а в дальнейшем - ежегодная диспансеризация. Эти осмотры должны включать элементы клинко-гигиенического и рентгенологического контроля, а также, по возможности, сеансы профессиональной гигиены полости рта. В то же время, автор не отрицает, что сроки и методики обследования могут зависеть от состояния органов полости рта и уровня гигиены, а также от общего состояния здоровья пациента, и это вносит индивидуальные коррективы в план обследования. Следовательно, элементами наблюдения за пациентами с несъемными зубными протезами с опорой на внутрикостные имплантаты во время периодических осмотров должны стать, прежде всего, оценки состояния самого протеза, имплантата и окружающей его костной ткани. Практически все авторы, затрагивающие

в своих исследованиях вопросы гигиенического ухода за полостью рта, подтверждают необходимость периодических сеансов профессиональной гигиены полости рта для ухода за зубами, имплантатами и супраконструкциями, что положительно отражается на сроках использования протезов [2].

### РЕЗОНАНСНЫЙ ЧАСТОТНЫЙ АНАЛИЗ

RFA является широко используемым методом оценки первичной стабильности дентальных имплантатов. Результаты RFA количественно отображаются в виде коэффициента стабильности имплантата (ISQ), значения которого могут варьировать от 1 (предельно низкая стабильность) до 100 (высокая стабильность) [3].

Наиболее распространенной в отечественной практике системой для RFA является

«Osstell mentor», в котором используются магнитные штифты типа «Smartpeg», имеющие самые различные винтовые соединения, так что исследование можно проводить со всеми основными системами имплантатов различного производства. Штифт можно обратимо присоединять к имплантату на любом этапе его приживления вплоть до установки ортопедической конструкции, используя обычный динамометрический ключ [4]. Стабильность первичного имплантата является ключевым фактором, влияющим на выживаемость этих имплантатов [5]. Она определяется как оцен-