VEGETATIVE NERVOUS SYSTEM DISTURBANCE
IN CONGENITAL HEART DISEASES

In the patients with congenital heart defects the various circulatory disorders are connected with their association in the pathogenesis of the primary manifestations being malformations of the cardiovascular system and secondary (chronic insufficiency of the cerebral circulation) mechanisms realized in the postnatal period.

Evidently, in time diagnosis and appropriate tactics and management of the patients with congenital heart defects in the preoperative period allow reducing the percentage of complications and enhance of the process of rehabilitation in the postoperative period.

Keywords: Heart defects, congenital, vegetative nervous system, circulation disorder, pathogenesis.

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The human congenital malformations (CM) have been attracting the attention of physicians from the ancient times, and in spite of the centuries-old history of mankind many aspects of etiology and pathogenesis of the congenital heart defects remain to be studied insufficiently at present. The notion of the congenital malformations includes persistent morphological changes in the organs or in parts of them beyond the variations in their structure and damaging their function.

In the structure of congenital malformations the significant specific gravity is related to the congenital heart defects (CHD) which occupy the second place after the anomalies of the nervous system and account for 16 to 40% (Babajanov et al., 1996; Katin, 2000; Pariyskay and Gikaviy, 1989; Scvortcov and Ermolenko, 2003), presenting 6.6 per 1000 live births in Europe, 5.7 - in Canada, 11.5 - in the Lebanon (Panteleeva et al., 2001; Pariyskay and Gikaviy, 1989; Popov, 2004; Vasilenco et al., 1993).

According to Tyler the 14 (22%) newborns die in the first week of life, 19 (27%) - during the first month of life, and 30(80%) do not live by the first year of life. Insufficient supplying with the modern diagnostic equipment of the children clinics also results in reduced evaluation of the frequency of congenital heart defect incidence. The increase in incidence rates over the past decade is rather connected with increase in the level and quality of diagnosis, introducing beginning from 90s new medical technologies into clinical practice, when such modern methods of investigations as echocardiography, drug and loading tests, Holter monitoring, electrocardiography were introduced into the pediatric practice. Only the use of echocardiographic apparatuses allows 82% increase in identification of the defect of interventricular septum and open arterial duct (Pariyskay and Gikaviy, 1989). It is known about more than 90 variants of congenital heart defects and a great number of their combinations. Classification of the Bakulev Institute of Cardiovascular surgery (1982) divides the CHD according to anatomical specificities of the malformation and disorders of intracardiac and general hemodynamics:

1. Pale type congenital heart defects with arteriovenous shunt: defect of interventricular septum (IVSD), defect of interatrial septum (IASD), open arterial duct (OAD); open atroventricular canal (AVC);

2. Congenital heart defects, cyanotic, with venoarterial shunt: transposition of the great vessels (GVT), Fallot’s tetralogy, Fallot’s trilogy, tricuspid valve atresia (TCVA) and others;

3. Congenital heart defects without blood outflow, but with obstacle to blood flow from the ventricles (stenosis of pulmonary artery and aorta). This division covers 9 most common congenital heart diseases.
The frequency of different nosological forms of CHD varies in different age periods, which indicates the low rate of CHD identification. Besides, the frequency of the defect varies in relation to the sex. Thus, the ratio boys/girls accounts 1.09 : 1 (Babajanov et al., 1996; Pariyskay and Gikaviy, 1989; Vasilenco et al., 1993). The beginning of the study of CHD etiology was in the 60s of the last century. In the first monograph “Congenital aorta ostium closing” devoted to the congenital heart defects Raukhfus (1869) wrote, that the cause of unclosing or narrowing of the aorta entrance is endocarditis previously having by the fetus of the 3-6 intrauterine month, and confirming this condition by pathological anatomic findings (Pariyskay and Gikaviy, 1989). The congenital heart defects have no unique etiology, they occur as a result of complex interactions between multifactor genetic system and external effects (Babajanov et al., 1996; Belacon and Podzaicov, 1991; Vein, 2003). Belakon, Vasilenko, Feldman, Campbell and Polani present the following principles resulting in CHF: chromosome abnormalities - 5%; mutation of one gene - 2-3%; environmental factor (alcoholism of the parents, rubella, ARVD, drugs and others) - 1-2%; polygenic-multifocal inheritance - 90% (Vein, 2003; Katin, 2000; Scvortcov and Ermolenko, 2003).

Quantitative and structural chromosome mutations occur in the process of different chromosome aberrations. In the majority of cases, aberrations of large and middle chromosomes are not compatible with life. Aberrations, that are compatible with life, are manifested by various clinical syndromes of multiple anomalies of chromosomes which include the congenital heart defects. The heart defects associated with chromosome anomalies are always a part of syndrome of poly-system malformations, but not of isolated defects. Screening of the patients with congenital heart defects for chromosome anomalies is not important if heart lesion is not associated with other abnormalities (Babajanov et al., 1996; Kurbanov, 2000; Vasilenco et al., 1993; Troshin et al., 2004; Zhu et al., 2009).

About 2% of CHDs are connected with mutations of the single genes. As in the cases of chromosome anomalies the majority of CHD, connected with mutation of single genes, associate with malformations of other organs. In many forms of inherited pathology, according to simple Mendeleev’s regularities, the malformations of the cardiovascular system are the part of the syndrome of autosome-dominant (syndromes Holt-Oram, Nunan, Krous, Marfan and others), autosome-recessive (syndrome of Gurler, cartagener, Karpenter, Ellise-van-Kreveld, Robertson and others) types of inheritance. Also these defects could be connected with X-chromosome (syndrome of Aase, Elers-Danlo V type, Golte, mucopolisacharide 2 type Gunter and others). It is necessary to notice a number of common principles for these syndromes. Firstly, the majority of syndromes are characterized by variable expressiveness: lesion of cardio-vascular system in patients with this syndrome may vary from light to sever. As a rule, variability of the gene expression in the individuals of one family is less marked than of interfamil. Secondly, in some individuals, evidently having appropriate genotype, some marked phenotype anomalies may be absent (nonpenetrance). The degree of penetrance of mutating gene depends on criteria of the signs of this gene presence (Vasilenco et al., 1993; Troshin et al., 2004; Zhu et al., 2009; Minich et al., 2010).

The harmful environmental factors, contributed to the formation of the CHD, include effect of the roentgen irradiation on woman’s body in the first trimester of pregnancy, ionization, some therapeutic agents, infectious and viral agents, alcohol and others. According to the main principles of the teratology the evaluation of the teratogenic effect of different harmful factors is performed considering mechanisms of effect, time of coincidence of teratogenic effect with periods of intensive formation of the fetal organs and systems. It is necessary also to take into consideration the effect of the dose, genetic predisposition of the individuals to adverse reactions to the launch impact of the environment (sometimes particularly to a specific drug), to the malformation development in general, and the cardiovascular system in particular (Vasilenco et al., 1993; Troshin et al., 2004; Zhu et al., 2009).

The problem of cardio-vascular system damage in the newborns due to intrauterine, intranatal of perinatal hypoxia has induced great interest over the last time. The research
(Shvarkov, 2003; Tabolin et al., 2000) for making a virological “picture”, and evaluation of the effect of congenital viral infections on the severity of cardiovascular system damage in newborns and infants, establish that the great majority of patients (98% of newborn and 92% of infants) with different heart pathology (CHD, cardiomyopathies, myocarditis, posthypoxic syndrome of disadaptation) had mixed poly-viral infection. Virological examination of children in a representative group of viruses has revealed the predominance of enteroviruses (91% of newborns and 83.3% of infants) with lower frequency of viruses of influenza, cytomegalia, simple herpes virus and rubella. In comparison with findings of the parallel virological study of mothers and their newborns a transplacentary transmission of absolute majority of viruses found in infants with congenital heart pathology was confirmed. Direct correlation was revealed between severity of heart lesions and activity of viral infection, as measured by morphometric indices of active viral replication in the epithelial cells of the urine and the amount of viral associations found in the body of sick children. The catamnestic observation during the first year of life has established persistence of the majority of viruses, detected in children in the neonatal period including cardiotropic coxsackieviruses type 1-5 and coxsackievirus A13 (Ulitskiy and Chukhovina, 2001).

According to the data (Pariyskay and Gikaviy, 1989) the presence rubella infection during pregnancy is one of the environmental factors resulting in birth of a newborn with CHD. The frequency of congenital rubella as cause of CHD accounts 2.4%, classic syndrome of congenital rubella includes trilogy of the most frequent malformations- cataract or glaucoma, heart defects and hearing loss. Besides, there are anomalies of the nervous system (microcephaly); disorders of skeleton and skull development, many children fall behind in the physical and mental development (Djordjikiya et al., 2005; Tabolin et al., 2000). CHD children with congenital rubella infection may have open arterial duct, transposition of great vessels, common arterial trunk, atresia or malformations of atrioventricular and semilunar valve, open atrioventricular canal, Fallot’s tetralogy (5-10% of all CHD), IVSD (5%), stenosis of pulmonary artery (Babajanov et al., 1996; Belacon and Podzaicov, 1991; Popov, 2004; Ulitskiy and Chukhovina, 2001).

Significant risk of organogenesis breach and formation of congenital malformations is proved only for a few numbers of drugs. Teratogenic effect on the cardiovascular system has: alcohol (leads to more frequent formation of IVSD, open arterial duct, IASD), amfetamines (condition IVSD, transposition of great vessels), anticonvulsive preparations - hydantoin (conditions IVSD, transposition of pulmonary artery and aorta, aorta coarctation, open arterial duct) and trimethadione (transposition of great vessels, Fallot’s tetralogy, hypoplasia of heart left side), lithium (Ebshtein anomaly, tricuspid valve atresia, IASD), progestogens (Fallot’s teratology, complex CHD) (Belacon and Podzaicov, 1991; Djordjikiya et al., 2005). According to report of Voroncova (2000) the deficit of folic acid in the ration of pregnant women may induce CHD in a newborn. Some authors give the prime importance to folic acid in the development of CHD (Kurbanov, 2000; Pariyskay and Gikaviy, 1989; Minich et al., 2010).

Among the toxic substances contributing to the occurrence of CHD, ethyl alcohol has a leading role. The effect of ethyl alcohol on the fetus results in birth of newborn with embryofetal alcohol syndrome. Over the last years the interest for studying of this syndrome has increased due to rising frequency of cases of chronic alcoholism among women. In the USA one newborn out of 800-2400 newborns has embryofetal alcohol syndrome, and in some European countries - one of 200-600 newborns. According to Tabolina and Urivchikova (1990) in mothers, suffering from alcoholism, 305 newborns are damaged and in 30-49% of these cases the CHD occurs. Alcohol is the cause of CHD in 1% of cases (Kramer et al., 1990). Especially marked teratogenic effects on cardiovascular system alcohol has in the period of intensive formation of organs (critical period of development) - during the first 3 months of pregnancy (Tabolin et al., 2000).

The most common explanation of the type of inheritance in CHD is mainly related to the polygenic/multifactorial model, the main signs of which suppose:
1. Risk of the repeated lesion increases with the increase in the number of patients among the relatives of the first degree;
2. If the population data show sexual differences in frequency of disorders, the relatives of the patients of the same gender having less frequent diseases appeared to have this lesion more often;
3. The more severe defect the higher risk of its repeating;
4. The risk of repeating anomaly in relatives of the first degree of the individual ill is equal approximately to the square root of the frequency of pathology in the population (Ulitskiy and Chukhovina, 2001; Scully et al., 2010; Nakajima, 2009).

Besides etiological factors it is important to isolate risk factors of having a child born with CHD. They include mother’s age, endocrine disorders in the couple, toxicosis in the first trimester of pregnancy and threat of pregnancy interruption, still-birth in the anamnesis, presence of other congenital malformations.

In the occurrence of congenital malformations of heart in children, evidently, the occupational risk factors of mother and father have some significance. In 15% of children with CHD mother during pregnancy had contact with lacquer, paints, benzene and other chemical substances at work. Kochergina (1990) and other authors reported that CHD observed in 30% of children whose fathers had contacts with toxic substances, and in 30% of children fathers were professional drivers of the auto motors (Vasilenco et al., 1993). Thus, the findings of Babadjanov (1996) showed that from 500 fathers, the children of which had CHD, 29.3±2.6% worked as drivers of vehicles for a along time (Babajanov et al., 1996).

The views reported in literature on the impact of maternal age on a newborn with CHD are rather contradictory. A number of authors suggest that the danger of birth of child with CHD increases if mothers are older than 35 years old, others do not attach much importance to this factor. Up to 17 clinical-amnestic risk factors of prenatal CHD are described in literature, and the specific gravity of each risk factor has not been established yet (Babajanov et al., 1996).

Thus, among suggested risk factors of CHD the leading ones are severe toxicosis, threat of pregnancy interruption, viral infection at the early stage of pregnancy, occupational risk factors of the parents. The prophylaxis of children with CHD should be complex, beginning with protection of mother's health, study of anamnesis, hereditary and genetic characteristics of the parents, occupational risk factors, ecological disorders, appropriate pregnancy management and others.

The famous Russian clinicians Botkin, Ostroumov, Lang and Badolyan showed the important role of nervous system in the pathogenesis of diseases of cardio-vascular system. The activities of the organism are associated with the functional state of the cardiovascular system, which has great importance in maintaining homeostasis and adapting to constantly changing environmental conditions (Belacon and Podzaicov, 1991; Vasilenco et al., 1993). Changes in the nervous system in congenital heart defects are caused, first of all, by the growing disparity of brain blood supply. Continuous arterial under-saturation of blood with oxygen can lead to chronic disorder in supplying brain tissue with oxygen. The decrease in volume of circulating blood in the large and small circle, and the associated reduction in cerebral blood flow, even without hypoxemia, results in chronic insufficiency of cerebral circulation, enhancing the severity of brain dyscirculatory. These changes underlie in the formation of sever pathological background providing development of neurological syndromes (Belacon and Podzaicov, 1991; Vasilenco et al., 1993; Nakajima, 2009; Zhu et al., 2009).

Since the end of the last century our knowledge about the role of vegetative nervous system (VNS) in the clinical pathology has considerably increased. According to findings of Vein (2003) the role of vegetative nervous system is considered in two aspects. The first is the maintenance of the integrity of internal body condition. Investigation of this problem is connected with the names of Bernard, Cannon, Barcroft (Vein, 2003). Disturbed homeostasis is not only manifested by a variety of autonomic disorders, but
significantly alters human behavior. The second aspect is to ensure various forms of mental and physical activity by the function of autonomic nervous system. In the works of Badolyan (1976) is shown a special role of nervous system in the homeostasis maintenance. With high sensitivity to different changes in the external and internal environment it constantly “alignments” occurring changes, prevents crude deviations in circulation activity. Found that, in addition to the hypothalamus, in the regulation of its functions an important role belongs to other structures of limbic- reticular complex, and the stimulation of almost any area of the central nervous system leads to some vegetal dysfunctions. In accordance with this conception was created a new concept of pathogenesis of autonomic pathology with suprasegmental and segmental systems of the brain. According to Vein, the number of neurons included into segmentary apparatus, prevails the number of neurons of the brain, which emphasizes the important role of segmentary system. Autonomic neurons are mainly located in spinal cord: in the thoracic - sympathetic and in sacral - parasympathetic neurons. Segmentary apparatus are incorporated in the brain trunk. Segmentary system consists of sympathetic and parasympathetic parts. Dominant structures devoid of segmental structures are developed in the brain stem, even more developed in the overlying parts of the brain. The most important element of this system is the reticular formation of the brain trunk, hypothalamus, thalamus, amygdale, hippocampus, septum, which together with their ducts form functional systems called limbic- reticular complex.

Prior to the current classification of autonomic disorders of Wayne there were no detailed and complete classification of autonomic disorders in literature. The topic type dominated: cortical, subcortical, trunk, spinal, sympathetic chain lesions, lesions of plexuses, peripheral nerves. According to the Vein classification (1991) the vegetative disorders are divided into: suprasegmentary (cerebral) vegetative disorders (primary and secondary); segmentary (peripheral) vegetative disorders (primary, secondary); Combination of suprasegmentary and segmentary vegetative disorders (primary and secondary).

The principles of VNS research must be based on clinical-experimental approach, the main role of which belongs to the vegetative tone and reactivity to evaluate the homeostatic body capacity; the vegetative maintenance is also studied for evaluation of adaptation mechanisms. In presence of vegetative disorders in every and each case it is necessary to identify etiology and nature of damage, to determine the level of damage of VNS (Vein, 2003).

The studies of the syndrome of vegetative dysfunction in children with CHD are very few and they are contradictory. Some authors (Djordjikija et al., 2005; Panteleeva et al., 2001; Sidikhodjaeva and Pakhomova, 2003; Scully et al., 2010) emphasize the syndrome of vegetative dystonia in CHD: the disturbance of heart rhythm, hyperventilation syndrome, disorder of thermoregulation, disorders in the gastrointestinal tract (abdominal pains, nausea, eructation), vascular disturbances in the extremities (paleness, mottled picture, cyanotic skin), vegetative crises, damage of pain sensitivity in the extremities by dyseaesthesia type (sensation of tingling and burning in the distal parts of extremities, increased when touching skin integuments), cardialgia syndrome with vegetative expressions (Sidikhodjaeva and Pakhomova, 2003; Shvarkov, 2003). In patients with CHD the presence of various circulatory disorders occur with great regularity (Vein, 2003). The majority of native and foreign researchers assign a leading role in the pathogenesis of dyscirculatory disorders in CHD to the dysfunction of vegetative nervous system, providing various clinical symptoms in these patients (Vein, 2003; Popov, 2004; Sidikhodjaeva and Pakhomova, 2003). The complex set of etiological factors contributing development of CHD may effect the delayed development of VNS in the prenatal period. The degree of damage of the vegetative nucleus in the patients with CHD prevailed in the hypothalamus and medulla oblongata; however it very seldom achieves high level (Vein, 2003; Scully et al., 2010). The damage of vegetative centers is comparable with disturbances in other parts of CNS. Besides, in patients with CHD the damage of embryogenesis and segmentary part of VHS is registered, characterized by immaturity of
nervous conductor, formation of neuroplastic accumulation along the flow of nervous elements of sympathetic and parasympathetic innervation. These changes of innervation apparatuses do not provide stable hemodynamics and, according to several authors, are one of the causes of development of cardio-vascular system insufficiency with disturbance of microhemocirculation (Popov, 2004; Sidikhodjaeva and Pakhomova, 2003; Shvarkov, 2003).

Thus, in CHD patients various circulatory disorders are connected with their association in the pathogenesis of the primary manifestations being malformations of the cardiovascular system, and secondary (chronic insufficiency of the cerebral circulation) mechanisms realized in the postnatal period. In spite of significant importance of the problem, the aspects of vegetative dysregulation in patients with CHD remain to be studied insufficiently. The questions of early prevention and principles of non-medicamentous and medicamentous correction of vegetative disorders in CHD remain to be not resolved. Evidently, in time diagnosis, appropriate tactics and management of the patients with CHD in the preoperative period allow reducing the percentage of complications and enhance the process of rehabilitation in the postoperative period.

**References**


Nakajima, Y., 2009. The second lineage of heart forming region provides new understanding of conotruncal heart defects, Congenit Anom (Kyoto).


