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Review Article

Body Reactivity in Early Postnatally

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Abstract

The reactivity of the child depends to a large extent on the state of the nervous system. A child is born with incomplete morphological and physiological development of the nervous system. The cortex of the cerebral hemispheres in the newborn is much thinner than in older children, nerve cells are incompletely differentiated, the formation of cortical centers is not complete, as well as myelination of nerve fibers of the brain, underdeveloped pyramidal pathways, striated body. Both morphologically and functionally, the formation of the nervous system is discrete, on the basis of continuous and discontinuous development. In other words, the uniform and gradual development of the nervous system is periodically interrupted by a discontinuous movement. Incompleteness of the morphological structure of the nervous system of the newborn corresponds to its limited functional capabilities. Excitability of the cerebral cortex is low, easily comes fatigue. All vital processes are carried out under the prevailing influence of subcortical centers. Various unconditional stimuli cause a wide irradiation of the nervous process - excitation or inhibition, in result of which the body always responds with a generalized reaction. Characteristic is the weakness of internal inhibition, concentration process and differentiation. Incomplete formation of the brain in the newborn causes less sensitivity of the cerebral cortex to changes in the chemical composition of the blood.

Key words: body reactivity; early postnatally

Introduction

Some data on morphophysiological features of children, which determine their reaction to environmental factors, preface the presentation of the material devoted to nonspecific and specific reactivity in early childhood.[4] Reactivity of the organism is considered as a form of biological reflection, as a property of the organism to respond to irritation, to a pathogenic factor by an act of counteraction, a complex of protective and adaptive reactions.

Both in phylogenesis and ontogenesis reactivity becomes more complex, the range between the upper and lower thresholds of reactivity of a cell, tissue, organ, system, organism increases, the reason for this is the increasing lability of regulatory systems. The nature of reactivity of a child's organism, the breadth of its protective-adaptive and compensatory reactions, their intensity and speed of activation, duration of action are determined primarily by heredity (the law of hereditary determination applies), the conditions of intrauterine development and the conditions of the child's existence after birth.[1]

The reactivity of the child depends to a large extent on the state of the nervous system. A child is born with incomplete morphological and physiological development of the nervous system. The cortex of the cerebral hemispheres in the newborn is much thinner than in older children, nerve cells are incompletely differentiated, the formation of cortical centers is not complete, as well as myelination of nerve fibers of the brain, underdeveloped pyramidal pathways, striated body. Both morphologically and functionally, the formation of the nervous system is discrete, on the basis of continuous and discontinuous development. In other words, the uniform and gradual development of the nervous system is periodically interrupted by a discontinuous movement. Incompleteness of the morphological structure of the nervous system of the newborn corresponds to its limited functional capabilities. Excitability of the cerebral cortex is low, easily comes fatigue. All vital processes are carried out under the prevailing influence of subcortical centers. Various unconditional stimuli cause a wide irradiation of the nervous process - excitation or inhibition, in result of which the body always responds with a generalized reaction. Characteristic is the weakness of internal inhibition, concentration process and differentiation. Incomplete formation of the brain in the newborn causes less sensitivity of the cerebral cortex to changes in the chemical composition of the blood.

Due to underdevelopment of the pain centers of the optic tubercle, irritation of sensitive nerves in early animals (puppies) does not cause a reaction characteristic of adult animals.[14] At early stages of ontogenesis, pain sensation does not have a local sign, i.e. it is not localized, because during this period there is no functional unification of the hypothalamic region, reticular formation of the brain stem, optic tubercle and cerebral cortex, which occurs in a child at the age of not earlier than 4 weeks. Pediatricians have long noticed that pain sensitivity in newborn children is weakly expressed. Peter-1, producing irritation by electric current or needle pricks, found the threshold of pain irritation in newborns much higher than in older children. High pain threshold is maintained in children up to 1 year of age and even up to the beginning of the second year. Clinical assessment of the degree of pain sensation in an adult are: pupil dilation, spasm of peripheral

vessels, cutaneous galvanic reflexes. In the early postnatal age, these reactions are absent.

The stability of a living system depends on the level of its lability: the higher the lability, the wider the possibilities of adaptation.[5] In the early stages of ontogenesis, the lability of the nervous system is low, which in turn determines the limited possibilities of adaptation to fluctuations in environmental conditions. The younger the organism, the less mature are its compensatory functions.

B. D. Rozanova established the adaptive significance of the initial bradycardic phase of heart rhythm changes when the organism is exposed to bacterial toxins (dysentery, diphtheria, typhoid, staphylococcal). This phase of cholinergic nature has anabolic significance - it leads to a decrease in oxygen consumption (on average by 24.9%). In the bradycardic phase, the lability of the nervous system increases and energy is accumulated for the tachycardic phase. Early puppies do not have an initial bradycardic phase in heart function. Only tachycardia is formed in them.

When environmental conditions are constant or when they deviate minimally from the optimal level for an early childhood child, its regulatory mechanisms and ability to adapt are quite sufficient to maintain homeostasis. Significant deviations of environmental factors from the optimal value, and even more so pathological conditions reveal the limitations of compensatory-adaptive reactions, the consequence of which are functional and morphological shifts in the child's body. Therefore, children of early age more easily fall ill. This depends on the fact that the formation of somatic, sexual and mental in the child's body is not simultaneous (heterochronous). The development of various functional systems and their regulators is uneven, which makes the child's reaction to a pathogenic factor less perfect.

[3] The peculiarity of the manifestation of adaptation in a child during early postnatal ontogenesis is the easy occurrence of hyperplastic process, while in an adult adaptation is carried out by changing the energy of biochemical processes in cells, increasing the rate of enzymatic reactions. Pathological processes that develop in a child under the influence of pathogenic factors are characterized by manifestations with little specificity, and therefore these manifestations have less diagnostic and differential-diagnostic value. However, this does not mean that early childhood diseases with a certain etiology are completely devoid of specific features. A number of diseases are manifested by symptoms with marked specificity, such as urine composition in phenylketonuria, blood composition in sickle cell anemia, and others.

[8] Perinatal morbidity and mortality in children is often a consequence of fetal abnormalities in the antenatal period. Changes that occurred in the fetus in the antenatal period, in the future entail somatic and mental disorders, contributing to the manifestation of pathological reactivity in the child and developmental anomalies. In this regard, the observance of the child's regime, nutrition, sanitary and hygienic conditions, cultural level of the family are of great importance.

The hypothalamic-pituitary-adrenal system (HGNS) plays a major role in the mechanism of reactivity. The degree of involvement of the hypothalamic-pituitary-adrenal system in the newborn period in reactions to various stressors is still unclear. [11]Some authors believe that the GHNS matures after birth, and in newborns and even more so in the fetus it does not function, although N. V. Mikhaylova and I. V. Mikhailova and I. A. Eskin have established the presence of ACTH in the pituitary gland of newborn rats, but they believe that the ability to respond to GHNS appears gradually and to different stimuli non-simultaneously, depending on the formation of nerve pathways that carry out the reflex. Thus, in rats the GHNS reaction to adrenaline appears on the 3-4th day of life, to trauma on the 8-9th day, to temperature effects - on the 16-18th day, to electric current - on the 20-21st day. L. Badalyan, V.A. Tabolin, Y.E. Veltischev believe that despite the early laying of the adrenal glands, they do not show their hormonal activity, entirely under the influence and control of maternal homeostatic mechanisms. Maternal corticoids easily penetrate through the placenta into the fetus.

[4] P. D. Horizontov and T. N. Protasova explain the absence of adrenal cortex reaction to stressors in the first days after birth by the immaturity of the hypothalamic region, its nuclei regulating the hormonal activity of the pituitary gland. This statement, it seems to us, cannot be regarded as evidence of inactivity of the hypothalamus. In a newborn and a child of the first weeks of life, the hypothalamic area is one of the active areas, representing an integrative department of the nervous system in the regulation of autonomic functions.

There are many data, discussed below, proving the functioning of the adrenal glands in newborns. It is known that the adrenal glands are laid down early, on day 28, at an embryonic length of 9 mm. In the fourth month of embryonic life, they reach their maximum size and are equal to or greater than the kidneys. At this time 80% of the mass of the adrenal glands is the germinal or fetal zone and 20% is the outer zone, which is the rudiment of the tubular and fascicular zones.[2] In the second half of pregnancy, the fetal zone begins to decrease in size, and from the outer zone gradually differentiate the tubular and fascicular zones. After birth, the fetal zone rapidly disintegrates, but its remnants finally disappear only by the end of the first year of life.

Both zones of the fetal adrenal cortex are capable of synthesizing corticosteroids of the same intensity as in the adult. The large weight of the adrenal glands, hyperplasia of their parenchyma, and richness in ascorbic acid and cholesterol are evidence that fetal adrenal glands can synthesize corticosteroids. T. C. Sakhatskaya found that a 17-day-old rat embryo is able to secrete corticosteroids under the influence of injected ACTH, and the ability of the adrenal glands to respond with increased hormone formation to ACTH injection occurs on the 17th day, while the presence of ACTH in the pituitary gland is detected on the 18th day.

[9] M. L. Zhukovsky believes that already from the 25th week of the antenatal period, corticosteroids are synthesized and a functional connection between the pituitary gland and the adrenal cortex is established. By the time of birth, the GHNS reaches significant functional activity.

Hyperplasia of fetal adrenal glands in maternal diseases has been proved. L. I. Lukina, E. 3. Yusfina, T. G. Sofienko, established lengthening of life of adrenalectomized females in pregnancy. Signs of adrenal response to stressors were observed in the fetus of M. M. Sokolov. The functional activity of the adrenal cortex in the fetus is confirmed by the data obtained during the study of adrenal function in premature infants.[7] In case of a favorable course of the disease they have an increased synthesis of corticosteroids. N. A. Punchenok, L. E. Pototskaya, I. Yu. Podolskaya noted increased content of 17- oxycorticosteroids and eosinopenia in the blood of newborn children, especially those born in asphyxia. Rats of the first day of life show high sensitivity to glucocorticoids.

The hypothalamic-pituitary-adrenal system plays an important role in the adaptation mechanisms unfolding during the transition of the child to extrauterine existence: the act of childbirth, the need for temperature adaptation, the inclusion of the lungs in the act of breathing, switching the liver to a new type of blood supply. After birth, the child's liver mainly receives venous blood through the portal vein, and only 30% of all blood flowing to it is arterial - all this requires the tension of adaptive mechanisms.

[10] Hyperplasia and fullness of the adrenal cortex in newborns testify to its high activity. Weight loss of the adrenal glands, their delipoidization, occurring after birth and associated with resorption of the fetal zone, in the opinion of J. I. Lashene, indicate an extremely high functional stress of the adrenal cortex with some lag in hormone synthesis. V. A. Tabolin et al., determining the ratio of different forms of corticosteroids and their breakdown products in the urine, established the ability of the adrenal cortex in children of early age to synthesize cortisone and corticosterone; excretion of hormones reflects the dynamics of their content in the blood. From the 2nd-4th day after birth, the reaction of the adrenal glands to ACTH is inhibited, which can be regarded as a consequence of their reorganization and some functional exhaustion. At this time, the action of an additional stressor, such as hemorrhage occurring during labor, infection can cause acute adrenal insufficiency. Therefore, in cases of threat of adrenal insufficiency is advisable prophylactic administration of corticosteroids to newborns. V. P. Geraskina, based on her own experience, recommends the administration of glucocorticoids to premature infants at the beginning of their pneumonia.

[13] In hemolytic disease of newborns, the function of the adrenal cortex is always reduced, because liposoluble indirect bilirubin accumulates in the cells of the adrenal cortex and dissociates the associated processes of oxidation and phosphorylation. Synthesis of corticosteroids, so necessary for the newborn during labor and for adaptation during the transition to the conditions of extrauterine existence, is disturbed.

JI. Badalyan et al. believe that the ratio of secreted corticosteroids is important. Thus, the ratio of hydrocortisone and corticosterone content in blood plasma in adults is 13:1, and in newborns 1:1. Obviously, this ratio is biologically appropriate: high corticosterone content in the blood of a newborn contributes to anabolic processes actively occurring in the growing organism. Thus, most of the available data allow us to conclude about the functioning of the adrenal glands in the antenatal and newborn period.

On the basis of experiments proving the immaturity of the pituitary gland in the fetus and newborn, a parahypophyseal pathway of inclusion in the adrenal reaction at early stages of ontogenesis should be assumed. Under the action of strong stimuli, the hypothalamic-pituitary-adrenal reaction does not develop in early puppies (up to the 18th-20th day of life). [15] In this case, according to E. A. Arshavsky, the animals fall into a state of portrait collapse. The concept introduced by I. A. Arshavsky characterizes the state of reduced vital activity. In pups, oxygen consumption drops, bradycardia develops, respiration is shortened and body temperature decreases. I. A. Arshavskii believes that these reactions are achieved due to the reversible shutdown of the diencephalic area and subordinating function of the cerebral cortex, which enables the bulbar centers to continue their activity for a long time, although at a reduced level.

Immediately after birth, the child is confronted with various infectious agents. Insufficient development of defense mechanisms in children at this age and the peculiarities of their immunological reactivity led to a high incidence of disease. The adult body has a number of formed protective barriers: skin, mucous membranes, lymph nodes, which protect the body from the penetration of microbes in the internal environment. In a newborn baby, protective barriers are not sufficiently developed and differentiated. [17] The structure of the skin of a newborn determines its lower resistance. Thus, the epidermis layer is thin, the stratum corneum consists of only 2-3 rows of cells instead of 7 rows in an adult. Connective tissue and elastic elements of the skin are underdeveloped. The epidermis is easily separated from the skin proper. Until the 7th day of postnatal life, the pH value of the skin is greater than in adults, which, according to P. Popkhristov, favors the penetration of infection and contributes to high vulnerability of the skin, especially in premature infants. The bactericidal capacity of the body's liquid media is lower the younger the organism. [16] In the first 2 days after birth, blood lysozyme - an enzyme that lyses mucopolysaccharides of microorganisms, is absent, the complement titer in the blood is low, so, despite the existence of a barrier function of the skin, the multiplication of microorganisms in the newborn is faster than in an adult. Comparatively low content of lysozyme, complement in the blood and incompleteness of phagocytosis persist in the following weeks of postnatal life. One of the factors of organism resistance is the property of tissues to produce interferon - low molecular weight protein formed in cells when exposed to the virus and provides immunity to it. Up to 2 years of age, interferon is synthesized in the body in insignificant amounts.

Immunologic reactivity is formed in the process of phylo- and ontogenesis. The formation of the immunologic system begins in ante- and early perinatal ontogenesis and is associated with the function of the thymus and lymphoid system. A specific immunologic reaction to an antigenic stimulus is formed after the appearance of small lymphocytes - immunocompetent cells. They differentiate into plasma cells that form antibodies. In the blood of tadpoles until the 40-50th day after hatching from eggs contains all leukocytes except lymphocytes. At this time, tadpoles do not react to antigen and do not reject the homograft. With the appearance of lymphocytes, the ability to reject the homotransplant appears. A. K. Lebedev studied the dynamics of development of globulin producing plasma cells in the lymph nodes of guinea pigs during ontogenesis. He found that by the 10th day of life only single plasma cells can be seen, and by the 3rd month their number increases sharply. During embryogenesis, immunity is predominantly cellular in nature. The first signs of it appear in the fetus after the 3rd month of intrauterine development. Only gradually, with the development and complexity of the organism, the ability to antibody formation is acquired and increases.

[19] The baby is born with antibodies in the blood that are transplacental from the mother's body. Their content corresponds to the titer of antibodies in the mother's blood or even exceeds it. On this basis, Bleek, Nightapp, Flamm believe that the villi of the placenta have selective properties, due to which the blood of the child is enriched with antibodies. Based on this, they believed that a newborn child, and even more so a fetus, is immunologically inert, i.e. not capable of producing antibodies. Subsequent studies have shown that this is not the case. In 1969, examining the content of immunoglobulins in the blood of the mother and in the umbilical cord of the newborn, it was found that the child receives immunoglobulin IgO from the mother, and some of the immunoglobulins are synthesized in the body of the newborn. There are known 5 types of immunoglobulins: IgC, IgM, IgE, IgA, Ig0, differing in antigenic properties of heavy polypeptide chains. The characteristics of different classes of immunoglobulins (ability to fix complement, sensitize the skin or other tissues, cytophilicity, opsonizing effect, passage through the placenta and penetration into external secretions) are associated with these structural differences. [12] For example, the ability to sensitize the skin is associated with the presence of immunoglobulin IgE in the immune serum. According to P. F. Zdrodovsky, antibodies produced during the first two months of postnatal life have a slightly different structure (195-macroglobulins) instead of 75-gamma-globulins, which are characterized by a wider range of protective antibodies (5 - Sweiberg sedimentation unit). Maternally derived antibodies function for a relatively short time, and their content in the baby's blood gradually decreases, reaching a minimum value by the 3rd month. Meippeg Beppagh et al. found that the content of maternal gamma globulin in the baby's blood falls by half within 20-35 days. In premature infants, low gamma globulin levels persist in the blood until 6 months of age.

[18] In the light of current data, immunologic inertness in the early postnatal period should be considered relative. Children of 21-42 days of age produce gamma-globulins. According to P. F. Zdrodovsky, antibodies against viruses can be synthesized even in the antenatal period. In the neonatal period, the child's body is able to produce antibodies not to all antigens, but only to some and at a certain dose. The antibodies formed do not have a high titer, are not strictly specific and function for a short time. With the development of the lymphoid system increases the ability to antibody formation. [20] The development of lymph nodes in a child occurs during the first year and is completed only by puberty.

In the neonatal period, along with low immunologic reactivity, there is high resistance to a number of bacterial toxins, such as typhoid, typhoid toxin, yellow fever toxin. Resistance depends on the insensitivity of cells to the toxin. With age, passive resistance gives way to active defense reactions, adaptation. Along with resistance to some toxins there is high sensitivity to others, for example, to toxins of festering microbes, to diphtheria toxin, to the toxin of tubercle bacilli, measles virus, pertussis.

The use of modern treatments has changed the nature of many diseases. The role of Staphylococcus aureus has increased significantly, as treatment measures are mainly directed against Streptococcus aureus.

[17] Early massive introduction of antibiotics stimulates the production of humoral antibodies, but shortening the period of contact of the organism with the infectious factor, resulting from the use of antibiotics, prevents the deployment of other defense mechanisms: there is insufficient antibacterial function of RPS or lymphoid-macrophage system, weakened absorptive and digestive function of leukocytes, which was proved by B. N. Smirnov in the infection with salmonellae in rabbits and mice.

As a result, the number of recurrences of the disease increases and creates conditions for the transition of the disease into a chronic form.

The state of the maternal organism is of exceptional importance in the development of neonatal sepsis. As shown in the studies of L. G. Kvasnaya, plays a role in the duration of the anhydrous period in labor, in addition, the

main importance in the infection of the newborn has the microflora of the nipples and not the vagina. [21] This is evidenced by the coincidence of the nature of the bacterial flora; nipples of the mother and the skin of the newborn baby. Staphylococcus aureus is isolated from the mother's pharynx and nipples; similar microflora is found on the skin and navel of the child.

In the formation of immunologic reactivity, the thymus and the lymphoid system play a leading role. Msheg's studies initiated a broad study of the influence of the thymus on the immunologic reactivity of the organism. Subsequent studies confirmed the idea of the thymus as the largest lymphoid organ that determines the initial formation of immunologic reactivity, forming immunologic reactions in response to antigenic stimulus.

[23] The thymus rudiment appears in the human fetus in the 6th week and by the time of birth the thymus weighs 10-15 g, making up the bulk of the body's lymphoid tissue. It reaches its maximum weight during puberty (30-40 g), after which the process of slow, gradual involution begins, but the remnants of the thymus are found in old people. The relatively large size of the thymus in the fetus and in the early postnatal periods, high mitotic index and richness in nucleic acids show that this organ plays a major role in providing the body with lymphocytes, immunocompetent cells. Formation of immunological reactivity, formation of immunological systems, synthesis of a set of unique, species-specific proteins antigens, enzymes, antibodies occur in antenatal and early postnatal ontogenesis with the participation of thymus. [22] It is established that immunologically competent cells are polypotent small lymphocytes, with the emergence of their generation immunologic reactions, specific response to antigenic stimulus. Small lymphocytes differentiate into plasma cells - antibody producers.

As a result of antigenic action, an immunological "memory" is formed in the organism, the morphological substrate of which is the small lymphocyte. Unlike antibody formation, immunological "memory" has a generalized character. It is preserved due to the population of lymphoid cells carrying a trace of the received immunologic information. The secondary response is realized by lymphocytes that have been in contact with a given antigen or their descendants, as well as by cells that have never encountered a given antigen but have received specific information from sensitized lymphocytes. [15] The mechanism of this transmissible function of lymphocytes still requires further investigation. The capacity for a specific immunologic response is formed during phylo- and ontogenesis under specific and nonspecific stimulation. Neonatal removal of the thymus in animals in the first 24-48 h after birth is characterized by immunological and trophic disorders. In 2 72 months, 57% of neonatally thymectomized animals develop exhaustion syndrome with subsequent death.

Neonatal thymectomy causes impaired formation and development of cellular and humoral immunity, which is expressed in the absence of formation of transplantation immunity, as a result of which not only homograft but also heterograft engraftment is possible. [24] Delayed-type hypersensitivity does not develop; there is no response to antigenic stimulus.

Neonatal thymectomy is accompanied by atrophic changes in peripheral lymphoid organs: spleen, lymph nodes, decrease in the number of lymphocytes in peripheral blood (by 80-90% of the initial one), tissues and organs. The number of recirculating lymphocytes decreases sharply. Thus, 1 million lymphocytes can be obtained from the common lymphatic duct in 3 h, while in intact and falsely thymectomized animals - 5 million. Even more significant difference in the number of recirculating lymphocytes in 24 h, when in neonatal thymectomized animals it is possible to obtain only 5 million lymphocytes, and in intact and falsely thymectomized animals - 100 million.

[19] Neonatal thymectomy inhibits cellular mechanisms of reactivity and impairs the function of phagocytes in processing antigenic information. Both absorptive and digestive capacity of phagocytes were found to be suppressed, and the phagocytic activity of macrophages was more severely impaired. At the same time, a decrease in the intensity of the inflammatory response and impaired barrier function of lymphoid organs was found, which contributes to the generalization of infection. At primary antigen administration to neonatally thymectomized animals a decrease in antibody formation was found both due to a decrease in the number of antibody-forming cells in the spleen and lymph nodes, and due to a decrease in antibody synthesis by a single cell, which is established by the method of local hemolysis in liquid medium according to the method of Erne. But, as it was established by I. S. Podosinnikov, antibody formation is not completely inhibited and increases with the age of neonatally thymectomized animals. To some antigens antibody formation does not change, which, apparently, also indicates the primary dependence of humoral immunity reactions on thymus function and is due to the fact that the time of formation of immune reactions to different antigens is different.

The decrease in the functional activity of small lymphocytes at neonatal thymectomy is expressed in a sharp inhibition of blasttransformation reaction both spontaneous and on FGA (phytohemagglutinin) at change of antigenic environment.

Disturbances of cellular humoral immunity in neonatal thymectomy allows us to consider that the thymus at early stages of ontogenesis determines the development of both thymus-dependent and thymus-independent immunologic systems of the organism. [25] The thymus-dependent immunologic system determines cellular immunity reactions: transplantation immunity, delayed-type hypersensitivity reactions, tuberculin-type reactions. Its morphological basis is the population of small lymphocytes of periarteriolar zones of spleen follicles and paracortical zones of lymph nodes.

The thymus-independent immunologic system causes the formation of reactions of humoral immunity, the morphologic substrate of which are plasma cells of spleen follicles and lymph nodes. Proof of the relative independence of the thymus-dependent system is the 01 Spote syndrome, which develops in congenital aplasia of the thymus and perithyroid glands and is manifested by disorders of transplantation immunity, delayed-type hypersensitivity with relatively sufficient formation of humoral antibodies.

[17] The relative independence of the thymus-independent immunologic system is confirmed by the existence of hypogamma-globulinemia. Hypogamma-globulinemia occurs only in boys, is transmitted with the sex chromosome and is caused by impaired formation of the plasma cell system, which limits the formation of humoral antibodies while preserving cellular immunity reactions. Hypogamma-globulinemia is characterized by frequently recurrent infectious processes in boys.

Trophic disorders occurring in an animal after neonatal thymectomy are characterized by lagging growth, development, progressive emaciation, thinning of the skin, disappearance of fat in the subcutaneous tissue, hemorrhages, liver abscesses, diarrhea and death of the animal in 2.5-3 months after the operation. There are reasons to connect trophic disorders with atrophic phenomena in lymphoid tissue and a sharp decrease in the fund of recirculation of small lymphocytes. Small lymphocytes are part of a very large in physiological conditions fund of amoeboid, migrating cells, diverse in immunologic properties, life span, with diverse functions and different activity. They accumulate DNA and RNA in their nucleus, transport nucleic acids to tissues and organs, transfer morphogenetic, morphostatic and plastic material to other cells. Small lymphocytes are involved in maintaining the level of differentiation of various cell populations. Approaching the sites of mitotic cell division, they stimulate mitoses of somatic cells, thus participating in the control of growth, restoration of cell systems in the process of regeneration. [21] The phenomenon of reutilization of small lymphocytes by epithelial, reticular cells of the body (which is not their elimination) attracts attention - this is the use of small lymphocytes substance for proliferation, regenerative processes in various tissues. Rosette shapes in blasttransformation, in which a large blast cell is surrounded on all sides by small lymphocytes - a special case of lymphocyte reutilization. Involution of the lymphoid system that develops after neonatal thymectomy, a sharp decrease in the production of lymphocytes, immunocompetent cells, the number of which is not restored in the absence of thymus, their qualitative changes explain the origin of immunologic and trophic disorders, antigenic aggression in the animal.

The role of the thymus gland in the pathogenesis of a number of human diseases is still very unclear, largely controversial. Aplasia of the thymus in children characterized by lymphopenia, agammaglobulinemia and lack of transplantation immunity has been described. Autopsy usually reveals

aplasia of lymphoid tissue with almost complete absence of small lymphocytes and plasma cells, and a very underdeveloped thymus.

For a long time, the sudden death of children was explained by mechanical pressure of the enlarged thymus on the mediastinal organs. Later, hyperplasia began to be regarded as a constitutional factor, expressed in hyperplasia of the entire lymphoid system of the child and combined with its high vulnerability. Such children often have inflammatory processes in the tonsils, lymph nodes, mucosa of the upper respiratory tract, hypoplasia of the cardiovascular system, hypotonia, decreased turgor, pastosity associated with impaired water-salt metabolism. Children are lethargic, their reactions are slow, they often have allergic diseases. M. S. Maslov defines this condition as lymphatic-hypoplastic diathesis.

[22] It is now considered established that a variety of stressors that do not lead to immediate death cause rapid shriveling (involution) of the organ, so the section usually shows a small thymus gland, and in cases of sudden death of children and young people, when thymus involution does not have time to occur, a large thymus gland is found.

It is known that increased function of the adrenal cortex leads to involution of the thymus and hypoplasia of lymphoid tissue. Cases of sudden death of children when the organism is exposed to a pathogenic factor of small force should be considered as a consequence of acute adrenal insufficiency, developed when the body's need for corticosteroids increases. In hypocorticism potassium content in the body, in particular in the myocardium, falls, which reduces its contractility and predisposes to collapse. At the section is found (against the background of generalized hyperplasia of lymphoid tissue) decrease in the weight of the adrenal glands 2-3 times. E. Yusfina believes that there is a suppression of the function of the adrenal cortex by hyperplasive thymus. Yules and Hollo believe that the increase in hormone production in thymus hyperplasia leads to a decrease in glycogen content in the liver and myocardium, which is the direct cause of sudden death.

Functional insufficiency of the lymphoid system in children with lymphatic-hypoplastic diathesis and the associated predisposition to allergic diseases are manifested during antigenic load, for example, after vaccination, infection, and determine the severity of the disease, its outcomes. The organism lives in the external environment and, as shown above, in the process of ontogenesis adapts to it, acquiring resistance to pathogenic factors.[14] Isolation of the organism of the early age period from external influences prevents the development of protective adaptations and weakens its resistance. Under the influence of environmental factors develop and improve afferent systems. Widespread and often unjustified use of antibiotics in the recent past has reduced the sensitivity of microflora to these valuable therapeutic drugs and changed the reactivity of the child who has lost the ability to actively fight infectious agents. Obviously, at the same time the resistance of the organism to other unfavorable environmental factors is also reduced. This position is very illustratively proved by experiments in which animals (guinea pigs, rabbits, mice, chickens) for a number of generations were grown and reproduced in special sterile containers. The arrangement of the containers allowed to supply sterile air, water, and food to the animals. Special manipulators cleaned the room. It turned out that life in sterile conditions led to a lag in the development of experimental animals. They had smaller liver, spleen, reduced amount of gamma-globulins in blood.

Animals raised under sterile conditions were immunologically inert. Proliferative activity in lymphoid organs, including thymus, was completely absent. The resistance of animals to blood loss, overheating, infection and other factors was much lower than that of animals raised under normal conditions.

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