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Review Article

Endocrine System in Embryogenesis

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Abstract

New experimental methods that made it possible to perform surgical operations on embryos, extirpation of endocrine glands with their subsequent implantation, destruction of endocrine glands by ionizing radiation, blocking of one or another gland by chemical means, introduction of hormones, transplantation of gland rudiments, made it possible to clarify some of the established issues of endocrinology of the antenatal period of development. The results obtained gave grounds to talk about endocrinopathies of intrauterine development. During these periods, the processes of development, formation, differentiation occur with particular intensity, and violation of morphogenesis, maturation of endocrine glands have significant disturbances in the fetus.

Kew Words: embryos; endocrine gland

Introduction

New experimental methods that made it possible to perform surgical operations on embryos, extirpation of endocrine glands with their subsequent implantation, destruction of endocrine glands by ionizing radiation, blocking of one or another gland by chemical means, introduction of hormones, transplantation of gland rudiments, made it possible to clarify some of the established issues of endocrinology of the antenatal period of development. The results obtained gave grounds to talk about endocrinopathies of intrauterine development. During these periods, the processes of development, formation, differentiation occur with particular intensity, and violation of morphogenesis, maturation of endocrine glands have significant disturbances in the fetus. [3]

Any disorders of the endocrine system function in a developing organism led to severe changes due to a wide range of physiological effects of hormones. In addition to the specific influence of one or another hormonal principle, all hormones have metabolic, morphogenetic, kinetic and corrective effects. Interacting with enzyme systems, hormones affect metabolic processes, finely regulating the simultaneous course of synthesis and decay processes. In the early stages of ontogenesis, at a certain level of differentiation of cellular structures, hormones act as regulators of this complex process, influencing the activity of the gene apparatus of cells. Therefore, a violation of the formation of the endocrine system in the antenatal period - a delay in the development of any endocrine gland and in subsequent periods can significantly slow down or distort the growth and development of the body The rapid development of endocrinology has significantly changed the understanding of the role of endocrine glands in regulatory processes, helped to more deeply illuminate the pathogenesis of a number of endocrine diseases, but the features of the physiology and pathology of the endocrine glands in children require further study, and in this brief review we are not able to consider all the features of the pathology of the endocrine system of childhood and will focus only on some, in our opinion, more important issues. [1]

Both adults and children may develop endocrine diseases due to a variety of causes: hereditary factors, embryopathies, injuries, including mental ones, infectious diseases, local circulatory disorders, tumors, and poor nutrition. Of particular importance are protein deficiency and lack of microelements such as iodine, zinc, magnesium, copper, etc. Currently, autoimmune processes play a large role in the etiology of endocrinopathies, in particular, derepression of prohibited clones of lymphoid cells, leading to the formation of autoantibodies. There are numerous observations that acute childhood diseases of a viral nature often precede the development of endocrine diseases. It is assumed that the development of an endocrine disease requires a set of factors that can act both in the embryonic and postembryonic periods. Among these factors, an important role is given to genetic disorders of embryogenesis. In the pathogenesis of endocrine diseases, disturbances in the regulatory relationships between the hypothalamus, higher bulbar centers, peripheral parts of the nervous system, and effector organs are important. Pathological impulses to the hypothalamus will lead to a disruption of the neurosecretory function and a change in the activity of pituitary cells. [2]

The anterior pituitary gland. Pituitary diseases in children are rare. In childhood and adolescence, gigantism, acromegaly, pituitary dwarfism, adiposogenital dystrophy, and diabetes insipidus may occur. Pituitary cachexia does not occur in children. The anterior pituitary gland secretes a number of tropic hormones: adrenocorticotropic (ACTH), thyroidstimulating (TSH), somatotropic (STH), lactotropic (LTH), and gonadotropic hormones (GTH), which regulate the activity of other endocrine glands by the feedback principle. The secretion of hormones by

the anterior pituitary gland is stimulated by neurosecretion formed in the nuclei of the hypothalamus under the influence of nerve impulses. If the hypothalamus is damaged or its function is changed, the production of neurosecretion is limited or stopped, which disrupts the transmission of impulses to the effector organs both through the hypothalamus and the parahypophyseal pathway. The consequence will be a dysfunction of one or more endocrine glands. [6]

The concentration of somatotropic hormone in the blood of a newborn can be 100 times higher than in the blood of an adult. Eosinophilic adenoma of the anterior pituitary gland causes hypersecretion of STH, and if this occurs before the completion of growth processes, gigantism occurs (a mouth above 190 cm is considered pathological). In the absence of a tumor, gigantism is explained by increased reactivity of the epiphyseal cartilages to a normal amount of STH. Acromegaly in children is very rare. It is assumed that in its pathogenesis, different tissue sensitivity to STH is important. Pituitary dwarfism develops as a result of decreased secretion of STH. It is possible, however, that it may be caused by a genetically determined or antenatal lesion of the central nervous system, namely the pituitary-hypothalamic region. Growth retardation usually begins at 2-3 years of age; bone development is delayed. The growth zones remain open for a long time. Childish body proportions are maintained throughout life; the reproductive system does not develop. Intelligence is not impaired. Cushing's disease occurs when the diencephalon and pituitary gland are affected with secondary hyperplasia of the adrenal cortex. The disease often begins after encephalitis, cranial trauma, or mental trauma. The pathogenesis of the disease is unclear. It is assumed that under the influence of increased secretion of ACTH, the ratio of corticosteroids secreted by the adrenal cortex is disrupted. It is believed that a change in the daily rhythm of ACTH secretion is important in the pathogenesis of the disease. [4]

Under normal conditions, a decrease in the number of corticosteroids in the blood, according to the law of feedback, will cause excitation of basophilic cells of the anterior pituitary gland, resulting in increased secretion of ACTH into the blood. In a stressful situation, other mechanisms for regulating the synthesis and excretion of ACTH into the blood come into effect, and an increase in its content in the blood occurs even with a high level of corticosteroids in the blood.

Studies have shown that in Itsenko-Cushing's disease, the binding capacity of transcortin is very low and therefore there is a large amount of free cortisol in the blood, which can explain the development of the disease. Itsenko-Cushing's disease is characterized by delayed growth and development, obesity, hypertension, decreased total bone mass, trophic skin disorders, and carbohydrate metabolism disorders. Obesity is explained by hypersecretion of glucocorticoids that stimulate neoglucogenesis. One of the possible mechanisms for increased fat deposition in Itsenko-Cushing's disease can be considered the stimulation of the pentose cycle of carbohydrate conversion, as well as the direct formation of fatty acids from glucose.

Hypertension in Itsenko-Cushing's disease has a complex pathogenesis, regarding which there is no consensus. It is explained by an excess of adrenal hormones that regulate electrolyte metabolism, others do not distinguish between essential hypertension and hypertension in Itsenko-Cushing's disease. There may be excessive secretion of aldosterone, leading to sodium retention in the body, and as a consequence to its deposition in the vascular wall, swelling of the endothelium. Under the influence of sodium, actomyosin threads shorten, the sensitivity of the vascular wall to catecholamines increases, and the secretion of ADH increases. In children, insufficiently formed regulation of vascular tone contributes to an increase in arterial pressure.

The posterior lobe of the pituitary gland (neurohypophysis) contains a large number of nerve fibers of neurons, the bodies of which are located in the supraoptic and paraventricular nuclei of the posterior region of the hypothalamus. Oxytocin and vasopressin (antidiuretic hormone) are secreted in these nuclei. Through the hypothalamic-pituitary tract, the neurosecretion, which is oxytocin and vasopressin, moves along the axons to the posterior lobe of the pituitary gland, where it is stored. It is possible that some transformation occurs there. The posterior nuclei of the hypothalamus, the hypothalamic-pituitary tract and the neurohypophysis are functionally a single whole. With degeneration, destruction of the supraoptic-pituitary system, diabetes insipidus develops. According to some data, the disease manifests itself clinically when more than 80% of the tissue secreting the neurosecretion is lost. Causes of damage to the hypothalamic-pituitary system may be head trauma, including birth trauma, tumors, meningitis, neurotropic viral infections. The first signs of the disease are thirst, polyuria, weakness. Sick children can drink from 5 to 12 liters of water per day in the absence of sweating. The specific gravity of urine is usually low (1.000-1.005). [5]

Oxytocin is secreted mainly in the paraventricular nuclei of the hypothalamus. This hormone causes contraction of smooth muscles, especially of the pregnant uterus, and inhibits the activity of cholinesterase, increasing the sensitivity of the uterus to acetylcholine. Probably, the violation of oxytocin secretion and the intensity of its breakdown by oxytocinase - an enzyme contained in the blood, myometrium and placenta of pregnant women, are important in the pathogenesis of delayed labor or its premature onset. Hypothalamic-pituitary disorders can lead to a symptom complex called adiposogenital dystrophy, characterized by obesity, delayed sexual development, growth, and sometimes decreased intelligence. The pathogenesis of the disease remains unclear. [6]

Adrenal cortex. The secretion of various corticosteroid metabolites occurs differently in boys and girls, starting from the age of 3-5 years. During puberty, the appearance of secondary sexual characteristics in boys occurs under the influence of androsterone, secreted by the testes, and in girls, the same process is stimulated by androsterone, formed in the reticular zone of the adrenal cortex. In newborns, the total excretion of corticosteroids in the urine usually reflects their content in the blood serum, with the exception of the first day after birth. At this time, the child has very low diuresis and, accordingly, a small number of corticosteroids is excreted, since the kidneys of the newborn are not able to concentrate urine. [17]

It is believed that newborns have instability of the glucocorticoid function of the adrenal cortex, which they associate with the reverse development of the fetal zone of the cortex, which occurs at this time, and the lack of formation of feedback with the pituitary gland. [19]

Hypercorticism in the development of a hormonally active tumor in the adrenal cortex in children is rare and usually leads to supragenital syndrome, manifested in the activation of heterosexual characteristics and the suppression of isosexual ones.

Hypofunction of the adrenal cortex can manifest itself acutely and chronically. Acute adrenal insufficiency is most often a consequence of birth trauma, asphyxia of newborns, intrauterine asphyxia. Difficult births using forceps often result in hemorrhages in the adrenal glands. Severe infectious diseases (typhus, diphtheria, measles, etc.) can also lead to adrenal insufficiency. Acute adrenal insufficiency is characterized by a fulminant course, convulsions, sepsis and ends in collapse.[20]

Birth injury causing minor hemorrhages in the adrenal cortex gives a picture of chronic hypocorticism. Chronic hypocorticism in children is observed with an adenoma of the adrenal cortex originating from the reticular layer. Excessive production of androgens causes depletion of the fascicular and glomerular zones. In these cases, boys experience premature puberty, and

girls experience pseudohermaphroditism, combined with insufficiency of glucocorticoid function. [18]

With insufficiency of the glomerular zone of the adrenal cortex, the synthesis of mineralocorticoids is impaired. Deficiency of aldosterone disrupts the balance between sodium and potassium ions. Sodium penetrates and is retained in the cells; potassium is removed in excess. This is due to a disruption of the cell membrane system and membrane potential, which entails the impossibility of maintaining the difference in osmotic pressure in intracellular and extracellular fluids and the transition of a substance against the concentration gradient. The same disorders occur in the membranes of the organelles of the mitochondrial apparatus, ribosomes, lysosomes, which will manifest itself in a disorder of cell function. Deficiency of aldosterone is characterized by hypotension, physical inactivity, impaired absorption of carbohydrates in the intestine, which is impossible without sodium and potassium ions. [21] [22]

Pineal gland. The function of the pineal gland, or epiphysis, is poorly understood and controversial; there is no clarity on the issue of whether the pineal gland is an endocrine gland, what its function is, and what disorders cause disruption of its activity. It has long been noted that with tumors of the pineal gland in boys (under 10 years old), premature puberty (macrogenitosomia) develops. It was assumed that a normally functioning gland inhibits the secretion of gonadotropins and sexual development, delaying the onset of puberty. As the pineal gland involution occurs with age, inhibition is eliminated, and under the influence of secreted gonadotropic hormones, the activity of the sex glands begins. A tumor of the pineal gland, destroying it, prematurely removes the inhibitory effect on the secretion of gonadotropins. According to a number of other authors, the cause of macrogenitosomia is inflammation or destructive changes in the wall of the 3rd ventricle, in the hypothalamus, therefore, along with premature sexual development, water-salt metabolism disorders, polyuria, polydipsia, etc. are often observed. According to the data, macrogenitosomia is not associated with endocrine disorders, but is hereditary, probably its cause is a chromosomal aberration.

Based on comparative anatomical studies, it was established that the pineal gland belongs to the organs that undergo reverse development in phylogenesis. He suggested that the pineal gland is a remnant of the proximal part of the parietal eye, a highly differentiated receptive organ of ancient amphibians. Through this eye, animals received signals about the brightness of lighting. The pineal gland is closely connected with the diencephalon, therefore, in case of pathological processes affecting the pineal gland, it is very difficult to decide whether the observed disorders are a consequence of the pineal gland lesion or the result of the spread of the pathological process to neighboring areas of the brain. [7] [8]

Thyroid gland. This gland occupies an important place in the child's endocrine gland system. Its hormones affect morphogenetic processes, growth, tissue differentiation, and metabolism. In a newborn child, the thyroigland has signs of incomplete development; this is indicated by the insufficiency of the follicular structure of the gland, the almost complete absence of colloid in them, and the low iodine content. In early postnatal ontogenesis, there is a rapid accumulation of iodine in the thyroid gland tissue, and in a child of 4-5 years, the iodine content in the gland reaches the same values as in an adult, 300 times exceeding its amount in the blood plasma. High activity of metabolic processes - oxidative, plastic, at an early age requires large amounts of thyroid hormone, which is ensured by its intensive secretion. This explains the faster replacement of iodine in the gland. In an adult, iodine is replaced after 1 - 1.5 months, in a child almost twice as fast. [10]

Dysfunction of the thyroid gland in a child is a common phenomenon, and at an early age, hypothyroidism occurs somewhat more often than hyperthyroidism. Complete functional insufficiency of the thyroid gland in newborns is called cretinism and most often it is based on aplasia of the gland caused by an embryonic developmental defect. The causes of thyroid aplasia can be poor nutrition of a woman during pregnancy, inadequate nutrition of plant proteins that do not contain the necessary amino acids, in particular tyrosine, needed for the synthesis of thyroid hormones, or iodine deficiency; severe infectious diseases, the effect of various toxic substances. It is believed that iodine deficiency during pregnancy, which is aggravated by the above factors, plays an important role in the mechanism of athyroidism development in a child. Hypothyroidism can be hereditary; low hormonal activity of the gland is transmitted by an autosomal recessive type of inheritance. Congenital hypothyroidism occurs as a result of damaging factors during the sensitive period of formation of the fetal thyroid gland, and this form of gland deficiency is detected after breastfeeding, i.e. after the thyroid hormones stop entering the child's body with mother's milk.

In a young child with hypothyroidism, as a result of insufficient oxidative processes, heat production (chemical thermoregulation) decreases. Taking into account the immaturity of physical thermoregulation, characteristic of this age period, the manifestations of poikilothermia in a child become understandable. With hypothyroidism, the basal metabolic rate drops by 25-35%, hypercholesterolemia develops, and the content of iodine-bound protein in the blood decreases. As a rule, bradycardia develops, pulse pressure drops, peripheral vessels narrow, limiting heat transfer, and, accordingly, the volume of circulating blood decreases due to a decrease in the volume of the vascular system; hypovolemia develops, caused by both hypoplasmy and a decrease in globular volume. Hypothyroidism is always accompanied by hypoplastic normochromic anemia.

The child's growth and development are delayed, which is especially pronounced in congenital hypothyroidism. In this case, all signs of the disease appear in the first 6 months of life, as breastfeeding is limited. The development of cartilaginous tissue of the epiphysis, ossification is impaired, and teething slows down. Very characteristic of hypothyroidism is the development of ossification from irregular foci scattered throughout the area of the altered cartilage. The large fontanelle and cranial sutures do not close for a long time. Early hypothyroidism delays brain development, but hypothyroidism that occurs at a later age inevitably entails a delay in the development of both mental and motor activity. Skin changes (dryness, peeling), so characteristic of hypothyroidism in adults, are not always expressed in childhood. Thyroid insufficiency in childhood and adolescence is referred to as childhood or adolescent hypothyroidism, and in cases of severe insufficiency - as childhood or adolescent myxedema. [11] Removal of the thyroid gland in young animals produces a picture similar to cretinism in children. Growth retardation is explained by a violation of the correlation between the pituitary gland and the thyroid gland, since the introduction of growth hormone (STH) to such animals has no effect.

It is known that most of those suffering from endemic goiter are children. Endemic goiter occurs in certain geographical areas, the so-called biogeochemical provinces, poor in iodine. In coastal areas, if they are not separated from the sea by high mountains, endemic goiter does not occur, since the iodine in sea water evaporates and enters the atmosphere. In addition to the iodine content, the concentration of some trace elements is important. Thus, copper and zinc weaken the manifestations of iodine deficiency, lead and fluorine - increase it. Hard water with a high content of calcium ions contributes to the development of hypothyroidism due to the fact that calcium hinders the absorption of iodine in the gastrointestinal tract.

Deficiency of thyroid hormone synthesis causes increased secretion of thyroid stimulating hormone (TSH), which leads to the formation of goiter without hyperthyroidism. Although such goiter is considered euthyroid, it is accompanied by a number of painful phenomena - hypochromic anemia,

leukopenia, dystrophic changes in the myocardium. Hyperthyroid endemic goiter is rare and usually occurs without an increase in basal metabolism. In the pathogenesis of thyroid hypofunction, the main role is played by the insufficiency of the synthesis of thyroid hormones: triiodothyronine and thyroxine. Hyposecretion is based on a violation of enzymatic reactions involving iodine oxidase and peroxidase. The following mechanisms of disorders are possible: insufficient accumulation of iodine by the gland and its conversion into an organic form, the inclusion of iodine in tyrosine, the conversion of monoiodotyrosine into diiodotyrosine may be disrupted.

Hypothyroidism reduces oxidative processes in cell mitochondria, thereby undermining the energy supply of cells; the synthesis of DNA, messenger RNA, protein - cell-specific antigens - decreases, which leads to insufficient differentiation of cellular formations. Thyroid hormones activate respiratory enzymes, and with hypofunction of the gland, oxidative processes decrease, in particular, fat oxidation is disrupted.

Diffuse toxic goiter (Graves' disease, hyperthyroidism, thyrotoxicosis) occurs in childhood. The disease can be caused by various reasons (mental and physical trauma, infectious diseases). According to the data, toxic goiter occurs mainly in girls in the prepubertal and pubertal period, and the main significance is the disruption of the interaction of the endocrine glands at the time when the sex glands begin to function. A congenital form of diffuse toxic goiter is known. In these cases, as a rule, the mother has a similar disease. In the pathogenesis of the disease, the penetration of the maternal thyroid hormone through the placenta or stimulation of the thyroid gland of the fetus by excess TSH of the mother's body, also penetrating through the placenta, are important. In hyperthyroidism, thyroid hormones have a high catabolic effect, increasing the basal metabolic rate by 100 - 150% and increasing oxygen consumption by 2 times or more, which makes the child's body highly sensitive to oxygen deficiency. The experiment established that the rate of oxygen consumption by the myocardium, kidneys, liver, and skeletal muscles increases sharply with hyperthyroidism. Thyroid enlargement in children develops earlier than in adults and is also accompanied by cardiovascular changes, which primarily include tachycardia (from 90 to 200 heartbeats per minute, an increase in the heart border to the left, caused by dilation of the left ventricle). Dilation is based on an increase in the volume of circulating blood and the cardiac output. Vascular peripheral resistance is usually reduced. In hyperthyroidism, a regular increase in the volume of circulating blood is established, which is explained by an increase in the capacity of the vascular system - the expansion of cutaneous vessels, providing heat transfer with increased heat production. As indicated, excess thyroid hormones increase the myocardium's need for oxygen and cause oxygen debt and hypoxia. Therefore, myocardial hypertrophy does not develop, but only dilation is observed, initially tonogenic, and later often myogenic. [13]

One of the important manifestations of diffuse toxic goiter in children is increased nervous excitability, emotional and motor instability. Thyroid hormones exert their effect at the cellular level, being included in the phospholipids of cell membranes and mitochondrial membranes, they change the permeability of the latter. Excessive amounts of thyroid hormones damage highly dynamic structures such as mitochondria, they swell, increase in size, the number of cristae decreases, which reduces the overall surface area of mitochondrial membranes, the electron density of the matrix changes, which leads to disruption of the energy-producing and genetic functions of the mitochondria of somatic cells. All electron carriers of the coupled respiration and phosphorylation chain are located on the mitochondrial membranes - pyridine nucleotides, flavoproteins, cytochromes, enzymes of the Krebs cycle. This is the central place in the system of enzymes of amino acid deamination, beta-oxidation of fatty acids. Excessive amounts of thyroid hormones disrupt the complex system of the respiratory chain. When the coupling of oxidative phosphorylation is dissociated, the accumulation of energy-rich phosphorus compounds in the cell (ATP, creatine phosphate) decreases, and the function of the mitochondria is directed not at providing energy for complex functional functions and plastic processes of a growing, developing organism, but at excess heat generation. Iodine, contained in thyroxine and triiodothyronine, imparts mobility to metabolic processes by activating sulfhydryl groups in the protein molecule, enhances protein breakdown, as evidenced by the increased content of amino acids in the blood, increased excretion of nitrogen, potassium, and phosphorus in the urine. This state of protein metabolism leads to a decrease in immunogenesis and disrupts immunological reactions. The catabolic effect of thyroid hormones extends to carbohydrate, fat, and lipid metabolism. The process of glycogenolysis is increased, as a result of which the amount of glycogen in the liver, kidneys, striated muscles, and myocardium is reduced. [12]

Children have hyperglycemia due to active glycogenolysis, increased absorption of carbohydrates in the intestine and high tone of the sympathoadrenal system. This condition leads to tension and overstrain of the cells of the insular apparatus of the pancreas, which can result in its failure and diabetes mellitus. With hyperfunction of the thyroid gland, diabetes mellitus occurs 2-3 times more often. Under the influence of excess thyroid hormones, there is an increased mobilization of fatty acids, cholesterol from their depots, which is accompanied by emaciation and growth retardation. Such pronounced catabolic processes, the formation of a large number of metabolic products causes the loss of intracellular water, which is a serious damaging factor for the cell. Hypoalbuminemia enhances the phenomena of hyperthyroidism, since the hormone in the blood binds to albumin, and with a deficiency of the latter, the bond is fragile and the flow of the hormone into the tissues accelerates. [14]

In hypothyroidism and hyperthyroidism, the adaptive role of the hormones of this gland is disrupted. As adaptive hormones, they participate in the regulation of metabolism, and depending on the conditions, either anabolic or catabolic effect prevails. The anabolic effect of thyroid hormones is expressed during the period of growth of the body, even if the child is on a low-protein diet, during the recovery period after an illness. Under the influence of thyroid hormones, wound healing is accelerated, as they stimulate cell division, accelerate the synthesis of mRNA, thereby promoting the formation of protein in the body. Under these conditions, catabolic processes are reduced and anabolic ones prevail. Thyroid hormones affect the adrenal glands. An experiment on dogs showed a decrease in the activity of the adrenal cortex with hypothyroidism. With unilateral adrenalectomy, the thyroid gland affects the process of vicarious hyperplasia of the remaining adrenal gland. Patients with hyperthyroidism often have signs of adrenal cortex insufficiency in the form of general weakness, hypotension, lymphocytosis, skin pigmentation and other manifestations. [9] [11]

Parathyroid glands. The main function is to regulate the level of calcium and phosphorus in the blood, and their action in this regard is so closely related to vitamin D that it is impossible to consider the effect of parathyroid hormone and vitamin D on the body in isolation. [24]

Removal of the parathyroid glands leads to the death of the animal within 1-3 days due to convulsions. In this case, blood calcium drops and phosphorus increases. The level of calcium in the blood determines the excitability of the neuromuscular apparatus and is regulated very precisely, but the regulatory mechanism remains not fully understood. It is only known that the following take part in the regulation: parathyroid hormone - parathyroid hormone, vitamin D and thyroid hormone - thyrocalcitonin. Their points of application are the intestines, bones and kidneys. With a deficiency of parathyroid hormone, calcium absorption in the intestine decreases, phosphorus reabsorption in the renal tubules increases and calcium and phosphorus are not mobilized from the bones. In bone cells, calcium is combined with phosphorus in the form of oxyapatite. Under the influence of parathyroid

hormone, glucose metabolism in bones switches to the formation of citric acid and, due to the shift to the acidic side, osteoclasts are activated, the activity of osteoblasts is inhibited - apatite dissolves. Apparently, under the influence of parathyroid hormone, which inhibits metabolism in cells, some osteoblasts are converted into osteoclasts. The released calcium combines with citric acid, and in the kidneys this compound is oxidized, is destroyed, and calcium returns to the blood. Thyrocalcitonin stops the formation of citric acid, thereby stopping the mobilization of calcium from the bones and, conversely, promoting its fixation in the bones. In this regard, the effect of thyrocalcitonin is opposite to the effect of parathyroid hormone. Thyrocalcitonin is apparently formed in the parafollicular cells of the thyroid gland, arising from the so-called ultimobranchial bodies. With a lack of vitamin D, the absorption of calcium and phosphorus from the intestines decreases, since a poorly soluble calcium-phosphorus compound is formed there. A decrease in the level of calcium in the blood stimulates the secretion of the parathyroid glands, and blood calcium is restored by mobilizing it from the bones. [25]

The most common form of phosphorus-calcium metabolism disorder in childhood is rickets. It is caused by a lack of vitamin D, the need for which is especially great during the period of intensive growth in the first 2 years of life. Hypovitaminosis D can be a consequence of low vitamin B content in breast and cow's milk, with insufficient ultraviolet insolation in the winter months, due to which the conversion of provitamin 7-dehydrocholesterol into vitamin B3 does not occur. The insufficiency of ultraviolet insolation is especially great in cities, where air pollution contributes to the absorption of ultraviolet rays by smoke particles. [15]

Rickets is characterized by insufficient calcium deposition in the bones, as a result of which the cartilaginous substances between the epiphysis and diaphysis expand, since the cartilaginous cells do not degenerate and do not calcify. The formation of bone tissue slows down. The load caused by crawling, lying, sitting, walking leads to the deformation of wide rickety metaphyses, and disturbances in the formation of the spine, ribs, and pelvic extremities occur. Already calcified bones are poor in calcium, which leads to further disturbances in their shape. [22]

In addition to bone changes, a child with rickets is characterized by a lag in physical and often mental development, impaired emotional tone, slow formation and instability of conditioned reflexes, rapid onset of inhibition, and hypotension. These changes indicate that although the main factor in the pathogenesis of rickets is a lack of vitamin D, metabolic processes can also be affected by a disturbance in the activity of the subcortical centers In the first weeks of life, newborns sometimes experience tetany caused by hypofunction of the parathyroid glands, the cause of which is hyperparathyroidism in the mother. If this condition is combined with hyperventilation, i.e. with sharply increased breathing, then a significant drop in the concentration of ionized calcium in the blood can pose a threat to the child's life. In latent tetany, an attack of convulsions can be caused by any, even moderate irritation, including hyperventilation. [16]

Excessive dosage of vitamin D, especially in combination with irradiation of food products, can lead to chronic hypercalcemia, when the calcium level exceeds 15 mg. Calcium absorption in the intestine increases, the phosphorus content in the blood decreases, the acidbase balance is disturbed, and the excretion of ammonium salts by the kidneys increases. Calcium is deposited in the walls of the stomach, in the lungs, in the kidneys, in the walls of blood vessels. Osteoblast activity decreases. High calcium levels suppress the secretion of the parathyroid glands. A picture of calciphylaxis is created. The clinical picture is characterized by anorexia, vomiting, thirst with polydipsia. In severe cases, intelligence is impaired.[15]

Reference

1. Vankelecom H. (2016). “Pituitary stem cells: Quest for hidden functions. In: Research and Perspectives in Endocrine Interactions. Cham, Switzerland: *Springer Verlag*.
2. Willems C, Fu Q, Roose H, Mertens F, Cox B, Chen J, et al. (2016). Regeneration in the pituitary after cell-ablation injury: time-related aspects and molecular analysis. Endocrinology
3. Guillou A, Romanò N, Steyn F, Abitbol K, Le Tissier P, Bonnefont X, et al. Assessment of lactotroph axis functionality in mice: Longitudinal monitoring of PRL secretion by ultrasensitive-ELISA. Endocrinology (2015)
4. Edwards W, Raetzman LT. Complex integration of intrinsic and peripheral signaling is required for pituitary gland development. *Biol Reprod*
5. Cox B, Roose H, Vennekens A, Vankelecom H. Pituitary stem cell regulation: Who is pulling the strings? J Endocrinol (2017)
6. Davis SW, Keisler JL, Pérez-Millán MI, Schade V, Camper SA. All hormoneproducing cell types of the pituitary intermediate and anterior lobes derive from prop1-expressing progenitors. Endocrinology (2016)
7. KOPÁNI M, VRANÍKOVÁ B, KOSNÁČ D, ZEMAN M, ŠIŠOVSKÝ V, POLAKOVIČOVÁ S, BIRÓ C: (2019). Pineal gland calcification under hypoxic conditions. *Physiol Res* 68 (Suppl 4): S405-S413.
8. (2019) FIPAT (The Federative International Programme for Anatomical Terminology). Terminologia Anatomica. 2nd ed. FIPAT.library.dal.ca
9. BATH SC, RAYMAN MP. (2015). A review of the iodine status of UK pregnant women and its implications for the offspring. *Environ Geochem Health;*619–629.
10. BÍLEK R, DVOŘÁKOVÁ M. (2018). Thyroglobulin and other laboratory diagnosis parameters in treating hypothyroidism in children. (In Czech) *Ces-slov Pediat.*
11. BILEK R, CEROVSKA J, ZAMRAZIL V. (2015). The relationship between iodine intake and serum thyroglobulin in the general population. Physiol Res.
12. BILEK R, KANOVA N, MINDZAKOVA V, NEUMANN D, JISKRA J, et all., (2016). Iodine supply of pregnant women in the Czech Republic. (In Czech) *Vnitr Lek.*
13. EUTHYROID CONSORTIUM. The Krakow Declaration on Iodine: tasks and responsibilities for prevention programs targeting iodine deficiency disorders. Eur Thyroid J. 2018
14. Bagley AM. Roman children in the early empire: a distinct epidemiologic and therapeutic category. PhD Thesis. UK: University of Birmingham; 2016
15. Jones G. 100 years of vitamin D: Historical aspects of vitamin D. *Endocr Connect*. 2022
16. Mays S. (2018). The epidemiology of rickets in the 17th–19th centuries: Some contributions from documentary sources and their value to palaeopathologists. *Int J Paleopathol*.
17. Bandiera, R., Sacco, S., Vidal, V. P. I., Chaboissier, M. C. & Schedl, A. (2015). Steroidogenic organ development and homeostasis: a WT1-centric view. *Mol. Cell. Endocrinol.* **408**, 145–155

18. Grabek, A. et al. (2019). The adult adrenal cortex undergoes rapid tissue renewal in a sexspecific manner. *Cell Stem Cell* **25**, 290–296.e2
19. Basham, K. J. et al. A ZNRF3-dependent Wnt/β-catenin signaling gradient is required for adrenal homeostasis. *Genes Dev.* **33**, 209–220 (2019).
20. Finco, I., Lerario, A. M. & Hammer, G. D. Sonic hedgehog and WNT signaling promote adrenal gland regeneration in male mice. *Endocrinology* **159**, 579–596 (2018).
21. Steenblock, C. et al. Isolation and characterization of adrenocortical progenitors involved in the adaptation to stress. *Proc. Natl Acad. Sci. USA* **115**, 12997–13002 (2018)
22. Steenblock, C. et al. Adrenal cortical and chromaffin stem cells: is there a common progeny related to stress adaptation? *Mol. Cell. Endocrinol.* **441**, 156–163 (2017).
23. Mallik S, Aggarwal P, Singh I, et al. (2017). A study on development and morphogenesis of parathyroid gland in the developing human embryo. *J Med Soc*
24. Elgazzar A, Alenezi S, Asa'ad S. (2015). Scintigraphic parathyroid imaging: concepts and new developments. Res *Rep Nucl Med*
25. Silva BC, Cusano NE, Bilezikian JP. (2018). Primary hyperparathyroidism. Best Pract Res *Clin Endocrinol Metab*

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