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Current Concepts of the Pathological Physiology of Congenital Hypothyroidism

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Abstract: Congenital hypothyroidism (CH) is the most common endocrine disorder in newborns, preventable through early diagnosis, newborn screening, and treatment. CH is characterized by a deficiency of thyroid hormones at birth and is one of the most common causes of preventable mental retardation worldwide. It occurs as a result of underdevelopment of the thyroid gland, insufficient hormone synthesis, or thyroid hormone intolerance. This article discusses congenital hypothyroidism: its main causes, incidence, the effect of thyroid hormone, genetic predisposition, and the possibility of gene linkage.

Keywords: congenital hypothyroidism, etiology, incidence, thyroid hormone, thyroid gland.

Relevance. Congenital hypothyroidism (CH) is the most common endocrine disorder in newborns, preventable through early diagnosis, newborn screening, and treatment [2]. CH is characterized by a deficiency of thyroid hormones at birth and is one of the most common causes of preventable intellectual disability worldwide [4]. It results from underdevelopment of the thyroid gland, insufficient hormone synthesis, or thyroid hormone resistance [5].

Hypothyroidism is a disorder characterized by low levels of circulating thyroid hormones (TH), which are insufficient to exert their metabolic and neurological effects at the cellular level. It is caused by a defect at any level of the hypothalamic-pituitary-thyroid axis, resulting in the inability to produce TH in sufficient quantities [6]. The thyroid gland is a bilobed gland located in the neck. It is composed of two types of cells: follicular cells, which produce thyroxine, and parafollicular cells, which produce calcitonin. Follicular cells constitute the predominant cell population and are organized into thyroid follicles [3].

Congenital hypothyroidism is the most common endocrine disorder in newborns. The incidence of CH has varied over the years. Before newborn screening for this disorder began in 1974, the incidence of CH was estimated at 1:7000; subsequently, it gradually doubled, reaching 1:3500 live births in regions with adequate iodine availability [1]. Clinical signs and symptoms of chronic hyperthyroidism result from the lack of effects of TH. At the cardiovascular level, TH decreases systemic vascular resistance and increases heart rate, contractility, and output; Promotes the excretion of salts and water by the kidneys, stimulates gastrointestinal motility, increases basal metabolic rate and body temperature, and ultimately regulates growth and neurological development.[11] The exact etiology of thyroid dysgenesis is unknown. It may be associated with mutations in the thyroid stimulating hormone (TSH) gene or mutations in the genes encoding transcription factors that regulate thyroid development.[7] The most common cause of primary thyroiditis is thyroid dysgenesis, which includes athyroidism due to the complete absence of thyroid tissue, ectopic thyroid gland due to abnormal migration of the embryonic thyroid gland, and thyroid hypoplasia or hemithyroiditis/one lobe due to defective

growth of the gland after complete migration.[9] In most patients with ectopic thyroid gland, the gland is located on the dorsum of the tongue or, less commonly, sublingually.[10] Genetic predisposition to thyroid dysgenesis is detected in less than 5–10% of cases, while familial status is present in approximately 2% of cases [8].

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