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Hypothyroidism: Current Approaches to Diagnosis and Therapy

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Abstract: Hypothyroidism is among the most common endocrine disorders. This article presents data on its prevalence, causes, and clinical manifestations. The main approaches to diagnosing thyroid hormone deficiency and the principles of levothyroxine replacement therapy are discussed. Factors influencing the effectiveness of hypothyroidism compensation and key reasons for its decompensation are also analyzed.

Keywords: hypothyroidism, autoimmune thyroiditis, sodium levothyroxine, replacement therapy.

Hypothyroidism is a condition characterized by insufficient thyroid hormone levels in the body. By pathogenesis, primary hypothyroidism—caused by thyroid gland pathology—is distinguished from secondary hypothyroidism, which is associated with thyroid-stimulating hormone deficiency. In adults, the overwhelming majority of cases (approximately 99%) are primary, most often due to chronic autoimmune thyroiditis (AIT). Less commonly, causes include thyroid resection, radioactive iodine therapy, and other factors that generally result in persistent and irreversible reduction of thyroid hormone levels. In some situations—such as subacute, postpartum, or cytokine-induced thyroiditis, or the use of certain medications (excessive iodine intake, antithyroid drugs)—transient hypothyroidism may occur, usually resolving spontaneously or after removal of the provoking factor.

Secondary hypothyroidism is rare (about 1% of cases) and is usually caused by destructive changes in the hypothalamic–pituitary region. The most common causes are pituitary macroadenomas or suprasellar lesions, as well as surgery or radiation therapy performed for these conditions. The prevalence of overt hypothyroidism in the general population is estimated at about 2%, but in specific age groups this figure can reach 6–8%, with the highest rates observed in elderly women.

According to a large population study, hypothyroidism was detected in 4% of women aged 18–24, compared to 21% in women over 74 years. A similar trend is observed in men: from 3% in the 18–24 age group to 16% among men older than 74 [1].

Clinical Presentation. The manifestations of hypothyroidism are highly variable, and their severity depends on the patient's age, the rate of hormone deficiency development, and the underlying cause. Common symptoms include decreased sweating, hoarseness, paresthesia, dry skin, constipation, hearing loss, weight gain, psychomotor slowing, skin coarsening, periorbital edema, and cold skin. The main diagnostic challenge is the nonspecific nature of these signs and the absence of pathognomonic symptoms, which complicates timely recognition. Various clinical scoring systems for hypothyroidism have been proposed, but none are widely used in daily practice.

In a population-based study using a questionnaire covering 14 typical symptoms, patients with overt hypothyroidism reported them more frequently than those with subclinical disease, and both groups reported symptoms more often than healthy controls. Notably, about 30% of patients with overt hypothyroidism reported no complaints, whereas about 20% of euthyroid individuals had four or more symptoms [1].

Diagnosis. Laboratory confirmation is based on measuring thyroid-stimulating hormone (TSH) and free thyroxine (fT4) in blood. TSH level is the key marker; fT4 provides supplementary information, while triiodothyronine (T3) measurement is not recommended. Isolated TSH elevation with normal fT4 indicates subclinical hypothyroidism, whereas elevated TSH with low fT4 confirms overt

hypothyroidism. In secondary hypothyroidism, both TSH and fT4 are reduced. Total T4 determination is less informative due to binding protein fluctuations.

Replacement Therapy. Overt hypothyroidism is an absolute indication for replacement therapy. Levothyroxine (L-T4) is the drug of choice due to its efficacy, safety, bioavailability, long half-life (~7 days), ease of use, and low cost [2]. Historically, thyroid extracts from animals were used until the 1960s, but their variable potency and risk of immunogenic reactions were major drawbacks. Synthetic L-T4 later replaced these preparations. Early dosing practices (200–400 μg/day) sometimes caused iatrogenic thyrotoxicosis [3]. Studies in the 1970s demonstrated the efficacy of lower doses (100–150 μg/day) [4–6], which are now standard.

The recommended dose of L-T4 for overt hypothyroidism is 1.6–1.8 μg/kg/day. Dosing depends on age, body weight, disease severity and duration, and comorbid cardiovascular conditions. Elderly patients may require about 20% less. Therapy is usually initiated at a low dose and titrated upward to avoid cardiac stress, except in younger patients without heart disease, where full doses may be started immediately.

Treatment of subclinical hypothyroidism remains controversial. In pregnant women or those planning pregnancy, therapy should start immediately. In other adults, the decision is individualized. L-T4 should be taken daily, in the morning, on an empty stomach, 30–40 minutes before breakfast, with water. Food or drinks like milk or coffee can impair absorption [2].

Therapy effectiveness is evaluated by TSH levels, which should be maintained within 0.4–4.0 mIU/L. TSH is checked 2–3 months after reaching a full dose, then every 6–12 months once stable. Although monitoring T4 and T3 may occasionally be necessary, TSH measurement is usually sufficient. Small dose changes of 12.5–25 μg can significantly affect TSH, so precise titration is crucial.

Decompensation may occur due to drug interactions (e.g., cholestyramine, sucralfate, aluminum hydroxide, iron sulfate, dietary fiber, calcium carbonate), enzyme inducers (e.g., phenobarbital, carbamazepine, phenytoin, sertraline, chloroquine), or poor adherence. For example, co-administration of calcium carbonate increased mean TSH from 1.6 to 2.7 mIU/L, which returned to baseline after discontinuation [4]. Multivitamins containing calcium or iron may also reduce absorption [5]. In refractory cases, evaluation for H. pylori gastritis, atrophic gastritis, or celiac disease is recommended [2]. Expired medication or improper storage can also reduce effectiveness.

Modern thyroid hormone preparations allow effective hypothyroidism compensation, improving symptoms and patients' quality of life.

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