

MODERN LABORATORY DIAGNOSTICS OF THE THYROID GLAND

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Relevance of the Issue: The thyroid gland plays a crucial role in regulating metabolism and energy balance in the body. Disorders of the thyroid, such as hypothyroidism and hyperthyroidism, can significantly affect a patient's quality of life. Modern laboratory diagnostic methods allow for timely detection and management of these conditions, which is essential for successful treatment and prevention of complications. This article examines the main contemporary methods of thyroid laboratory diagnostics, their principles, and clinical significance.

Thyroid-Stimulating Hormone (TSH): TSH, produced by the pituitary gland, is the primary regulator of thyroid function. Measuring TSH levels in the blood serum is the first and most informative test when thyroid dysfunction

is suspected. Elevated TSH levels indicate hypothyroidism, whereas decreased levels suggest hyperthyroidism.

The sensitivity and specificity of TSH measurements make them the cornerstone of thyroid function testing. In primary hypothyroidism, the pituitary responds to low thyroid hormone levels by producing more TSH.

Conversely, in primary hyperthyroidism, excessive thyroid hormone production suppresses TSH secretion. TSH assays are typically conducted using immunoassay techniques, which have evolved to become highly sensitive, capable of detecting minute changes in hormone levels.

Free Thyroxine (FT4) and Free Triiodothyronine (FT3): FT4 and FT3 are the active hormones of the thyroid gland. Measuring their free forms is more informative than total levels, as free forms are biologically active and not influenced by changes in binding protein levels. In hypothyroidism, FT4 levels are typically low, and TSH levels are elevated, whereas in hyperthyroidism, the opposite pattern is observed.

FT4 is usually measured using direct equilibrium dialysis or ultrafiltration followed by immunoassay. FT3 measurements are especially useful in diagnosing and managing hyperthyroidism, where FT3 levels may be disproportionately elevated. The accurate assessment of FT3 is crucial in cases where TSH suppression is present, but FT4 remains within the normal range, a condition known as T3 toxicosis.

Autoimmune Markers. Antibodies to Thyroid Peroxidase (TPOAb) and Thyroglobulin (TgAb). Autoimmune thyroid diseases, such as autoimmune thyroiditis (Hashimoto's thyroiditis) and Graves' disease, are characterized by the presence of specific antibodies. TPOAb and TgAb are markers of autoimmune thyroid damage and are used for diagnosis and monitoring of these diseases. High levels of TPOAb and TgAb are often observed in Hashimoto's thyroiditis and may indicate an increased risk of developing hypothyroidism.

TPOAb is directed against thyroid peroxidase, an enzyme crucial for the synthesis of thyroid hormones. The presence of TPOAb in serum is indicative of autoimmune activity against the thyroid gland. Similarly, TgAb targets thyroglobulin, a precursor in thyroid hormone synthesis. Both antibodies are typically measured using chemiluminescent immunoassays (CLIA) or enzyme-linked immunosorbent assays (ELISA), which provide high sensitivity and specificity.

Thyroid-Stimulating Immunoglobulins (TSI). TSI are key diagnostic markers of Graves' disease, an autoimmune condition characterized by hyperthyroidism. These antibodies stimulate the thyroid gland, causing excessive production of thyroid hormones. Determining TSI levels is used for the diagnosis and monitoring the efficacy of treatment in Graves' disease.

The bioassays for TSI involve measuring the ability of patient serum to stimulate cyclic AMP production in cells expressing the TSH receptor. High levels of TSI are indicative of active Graves' disease and can also be useful in predicting the likelihood of disease relapse after antithyroid drug therapy.

Other Diagnostic Tests. Thyroglobulin (Tg). Tg is a protein produced by thyroid cells and used as a precursor for thyroid hormone synthesis. Measuring Tg levels in blood serum is mainly used for monitoring patients with differentiated thyroid cancer after surgical treatment. Elevated Tg levels may indicate tumor recurrence or metastasis.

In clinical practice, Tg measurements are performed using immunoassays, which can detect even low levels of the protein in the blood. The interpretation of Tg levels is complex and requires consideration of antithyroglobulin antibodies (TgAb), as these can interfere with Tg measurements, leading to falsely low results. Thus, concurrent measurement of TgAb is recommended to ensure accurate Tg monitoring.

Calcitonin is a hormone produced by parafollicular cells (C-cells) of the thyroid gland. Its level is measured for the diagnosis and monitoring of

medullary thyroid carcinoma, which is characterized by excessive secretion of this hormone. Elevated calcitonin levels may indicate the presence or progression of medullary thyroid carcinoma.

Calcitonin assays are typically conducted using two-site (sandwich) immunoassays. These assays are highly sensitive and can detect early stages of medullary thyroid carcinoma. Additionally, calcitonin levels can be used to monitor the efficacy of treatment and detect recurrences post-surgery.

Genetic Studies. Modern technologies allow for genetic testing to identify mutations associated with hereditary forms of thyroid cancer, such as familial medullary thyroid carcinoma and multiple endocrine neoplasia (MEN) syndrome. Genetic tests can be useful for early diagnosis and prevention in relatives of patients with these conditions.

Next-generation sequencing (NGS) and polymerase chain reaction (PCR)-based methods are commonly used for genetic testing. These methods can identify mutations in the RET proto-oncogene, which are implicated in MEN 2 and familial medullary thyroid carcinoma. Genetic counseling and testing are recommended for family members of affected individuals to guide surveillance and management strategies.

Imaging and Functional Tests

Thyroid Ultrasound: Thyroid ultrasound is a non-invasive imaging technique used to evaluate the thyroid gland's size, structure, and presence of nodules. It is particularly useful for guiding fine-needle aspiration biopsies of suspicious nodules. Ultrasound can differentiate between solid and cystic lesions and assess features suggestive of malignancy, such as microcalcifications and irregular borders.

Radioactive Iodine Uptake (RAIU) and Scanning: RAIU measures the thyroid gland's ability to take up iodine from the bloodstream, which is crucial for thyroid hormone production. This test involves administering a small amount of radioactive iodine and measuring its uptake by the thyroid gland.

using a gamma camera. RAIU is particularly useful in evaluating hyperthyroidism, distinguishing between Graves' disease, toxic multinodular goiter, and thyroiditis.

Fine-Needle Aspiration Biopsy (FNAB):FNAB is a minimally invasive procedure used to sample cells from thyroid nodules for cytological examination. It is the gold standard for evaluating thyroid nodules and distinguishing between benign and malignant lesions. FNAB is performed under ultrasound guidance to increase accuracy and reduce complications.

Conclusion. Modern laboratory diagnostics of the thyroid gland encompass a wide range of tests that not only detect thyroid dysfunction but also elucidate its etiology and predict outcomes. The combination of hormonal studies, autoimmune markers, specific proteins, genetic tests, imaging, and functional tests provides a comprehensive approach to diagnosing and treating thyroid diseases. The introduction of new technologies and the improvement of existing diagnostic methods continue to expand clinicians' capabilities in managing these conditions, thereby improving patients' quality of life and reducing the risk of complications.

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