Biochemical Testing in Thyroid Disorders

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KEYWORDS

• Biochemical testing • Thyroid • TSH • Thyroglobulin • Calcitonin

KEY POINTS

- Serum thyroid-stimulating hormone (TSH) remains the primary screening test for thyroid dysfunction. Current guidelines recommend that serum TSH is used as the first-line test for detecting thyroid dysfunction.
- Thyroid autoantibodies are present in autoimmune thyroid disorders. Measurement is recommended in evaluating subclinical hypothyroidism; antibodies directed against the TSH receptor can be used in Graves' disease.
- Thyroglobulin (Tg) is primarily used as a tumor marker to evaluate the effectiveness of treatment and to monitor for recurrence of well-differentiated thyroid cancers.
- When measuring a Tg level, Tg antibodies should always be measured concurrently to allow for accurate interpretation of the Tg level.
- Calcitonin is mainly used as a tumor marker to monitor for the recurrence of medullary thyroid cancer.

INTRODUCTION

This review summarizes the main principles for the appropriate use of laboratory testing in the diagnosis and management of thyroid disorders, as well as controversies that have arisen in association with some of these biochemical tests. To place a test in perspective, the sensitivity and accuracy of the test should be taken into account. Ordering the correct laboratory tests facilitates the early diagnosis of a thyroid disorder and institutes timely and appropriate treatment. This review will focus on a comprehensive update regarding thyroid-stimulating hormone (TSH),

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thyroxine (T4)/triiodothyronine (T3), thyroid autoantibodies, thyroglobulin (Tg), and calcitonin. The clinical uses of these biochemical tests are outlined in **Table 1**.

THYROID-STIMULATING HORMONE

Overview

TSH or thyrotropin is a glycoprotein secreted by the anterior pituitary gland and is regulated by negative feedback from the serum free thyroid hormones (T4 and T3). TSH exhibits diurnal variation, with the lowest value in the late afternoon and highest value between midnight and 4 AM.[1–3] Therefore, variations of serum TSH values within the normal range of up to 50% do not necessarily reflect a change in thyroid status.[3] TSH secretion is extremely sensitive to minor changes in serum free T4, and abnormal TSH levels occur while developing hypothyroidism and hyperthyroidism before free T4 abnormalities are detectable.[4]

Available Assays and Functional Sensitivity

Several advances have been made in the last few decades in the development of sensitive assays for TSH measurement. The first-generation of TSH assays were based on radioimmunoassay methodology that had limited functional sensitivity (~1.0 mIU/L).[5–7] Second-generation assays were developed in the 1970s by using modified radioimmunoassay procedures and had a functional sensitivity of 0.1 mIU/L.[8–11]

Currently, the most widely used assays are third-generation immunometric assays (also called "sandwich" or "noncompetitive" assays), which became available in the

Table 1
Clinical uses of biochemical tests for thyroid disorders

Biochemical Test	Clinical Uses
TSH	• Primary screening test for thyroid dysfunction • Evaluation of thyroid hormone replacement therapy in patients with primary hypothyroidism • Evaluation of suppressive therapy in patients with follicular cell-derived thyroid cancer
T4	• Detection of thyroid dysfunction in conjunction with TSH • Evaluation of thyroid hormone replacement therapy in patients with secondary hypothyroidism (free T4) • Evaluation of thyroid dysfunction in pregnancy (total T4)
T3	• Detection of hyperthyroidism • No usefulness in the management of hypothyroidism • May be useful in diagnosis of nonthyroidal illness
Thyroid autoantibodies	• Positive in autoimmune thyroid disease • TPOAb – evaluation of patients with subclinical hypothyroidism and women with recurrent miscarriages • TRAb – diagnosis of Graves' disease; help to predict which Graves' patients can be weaned from antithyroid medications
Thyroglobulin	• Evaluation of effectiveness of treatment for differentiated thyroid cancer and monitoring for residual or recurrent disease • Diagnosis of thyrotoxicosis factitia
Calcitonin	• To diagnose medullary thyroid cancer and monitor for recurrence, progression, and response to treatment

Abbreviations: T3, triiodothyronine; T4, thyroxine; TPOAb, antibodies to thyroid peroxidase; TRAb, antibodies directed against the thyroid-stimulating hormone receptor; TSH, thyroid-stimulating hormone.