THE TSH THYROID FUNCTION TEST

When Thyrotropin Isn't The Gold Standard

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The TSH test result is an excellent tool for screening new patients for thyroid disease. But in some cases of autoimmune thyroid disease, the results can be misleading.

TSH

The hormone thyrotropin, which is also known as thyroid stimulating hormone or TSH, is produced by the pituitary gland. The pituitary gland regulates thyroid hormone levels by secreting more or less TSH. Consequently, low levels of TSH are seen in hyperthyroidism, and high levels are seen in hypothyroidism. Usually, blood levels of TSH can detect abnormal thyroid function.

The Hypothalamic-Pituitary-Thyroid Axis

The hypothalamus at the base of the skull is considered the true master gland since it controls the other endocrine glands, including the pituitary gland. The hypothalamus monitors all of the body’s hormone levels. When slight abnormalities occur, the hypothalamus engages other organs to correct matters.

Normally, the pituitary gland secretes TSH in small pulses throughout the day. TSH orders follicular thyroid cells to grow and produce thyroid hormone. Without adequate TSH (due to a pituitary or hypothalamic malfunction as is seen in central hypothyroidism) the thyroid gland normally couldn’t produce adequate thyroid hormone.

The hypothalamus secretes a hormone known as thyrotropin-releasing-hormone or TRH. TRH directs the pituitary gland to secrete TSH. When the hypothalamus notes a rise in thyroid hormone levels it secretes less TRH, causing the pituitary to secrete less TSH. When the hypothalamus sees that thyroid hormone levels are falling, it releases more TRH, which raises TSH levels and, in turn, thyroid hormone levels.

The Axis Has Its Limits

In thyroid disease, the axis can’t fully correct thyroid hormone levels. In Graves’ disease, stimulating TSH receptor antibodies (also known as thyroid stimulating immunoglobulins or TSI) stimulate the thyroid receptor to produce more thyroid hormone. Acting in place of TSH, TSI antibodies order thyroid hormone production even when TSH falls to non-detectable levels. In Graves’ disease, thyroid function falls under immune system control rather than hypothalamic regulation.
In hypothyroidism, damaged or defective thyroid cells can’t produce adequate thyroid hormone. Even with a steadily rising TSH, thyroid hormone levels remain low.

Benefits of TSH Testing

As soon as the pituitary gland is alerted that thyroid hormone levels are changing, it adjusts secretion of TSH accordingly. Normally, TSH levels rise to abnormally high levels before thyroid hormone (FT4 and FT3) levels fall below the normal range. Similarly, TSH levels fall below the reference range before thyroid hormone levels rise above the normal range.

Thus, in screening for thyroid disease, the TSH test is the best early indicator of thyroid dysfunction. If the TSH level is normal, thyroid function and levels of FT4 and FT3 are usually also normal. In screening new patients, the TSH test is considered a cost-effective gold standard for evaluating thyroid function.

If the TSH result is abnormal, the FT4 level is tested. If FT4 is normal, the FT3 level is tested. In some thyroid disorders, particularly Graves’ disease and toxic multinodular goiter, T3 is released from thyroid cells at a high rate, and levels of FT3/T3 become elevated before FT4 levels rise. Because T3 is nearly 5 times as potent as T4, even a slight rise in FT3 levels can cause symptoms of hyperthyroidism requiring treatment.

Subclinical Thyroid Disorders

In subclinical hypothyroidism and subclinical hyperthyroidism, thyroid hormone levels remain within the normal range while TSH is abnormal. Presumably, thyroid hormone levels may have changed slightly and been corrected by the pituitary. In subclinical disorders, thyroid function remains normal, but the abnormal TSH level suggests that a problem may be developing.

Because TSH only affects thyroid hormone production, an abnormal TSH doesn’t cause physiological changes related to hyperthyroidism or hypothyroidism. Symptoms of thyroid disease are caused by low or high thyroid hormone levels. However, if the levels are within range but too high or low for the individual’s bodily needs, symptoms of hyperthyroidism or hypothyroidism can occur.

Subclinical disorders are difficult to confirm. Changes in temperature, diet, altitude, general health, medications and stress influence TSH secretion. TSH also falls in illness (euthyroid sick syndrome, endogenous depression) and during treatment with corticosteroids or dexamethasone. And, as mentioned, TSH can fall when the pituitary gland or the hypothalamus aren’t functioning properly.

False Decreases in TSH

In autoimmune thyroid disease, TSH levels also fall in people with TSH receptor antibodies (TRAb). Both the stimulating TRAb seen in Graves’ disease and
Hashitoxicosis, and the blocking TRAb seen in atrophic hypothyroidism are recognized by the pituitary gland as if they were TSH. Erroneously thinking that blood levels of TSH are adequate, the pituitary gland secretes less TSH. For this reason, patients with Graves’ disease may have low TSH levels even after they become euthyroid (normal thyroid function). Patients with Graves’ disease are considered euthyroid as soon as FT4 falls within range.

Reference Ranges

Controversy surrounds the normal TSH range. Early ranges based on results of female hospital workers were much too high. Since, the range has been lowered several times.

The current recommendations are for a TSH reference range of 0.3-3.0 μu/L with levels below 0.3 suggesting hyperthyroidism and levels above 3.0 suggesting hypothyroidism. However, as with any clinical laboratory test, correlation must be made with other laboratory results, clinical signs and symptoms, and a careful medical history.

Resources:

GJ Canaris, NR Manowitz, G Mayor, EC Ridway, The Colorado Thyroid Disease Prevalence Study, Archives of Internal medicine;160: 526-534.


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