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Understanding Thyroid Tests (for Practitioners)

Advances in thyroid testing are emerging and have the potential to help clinicians better identify and treat patients with thyroid dysfunction. These changes include a more thorough look at biomarkers of thyroid status and closer consideration of what is needed for the optimal function of an individual patient. This evolution is similar to recent improvements in other areas of laboratory evaluation.

ABBREVIATIONS

- TSH = thyroid-stimulating hormone
- T3 = triiodothyronine
- T4 = thyroxine or tetraiodothyronine
- FT3 and FT4 = free (active, unbound) thyroid hormone
- RT3 = reverse T3
- TPO-Ab = thyroid peroxidase antibodies
- TG-Ab = thyroglobulin antibodies

Inadequacy of TSH Alone

For decades, the TSH test has been viewed as the gold standard for evaluating thyroid function. It has long been assumed that this single biomarker could accurately distinguish normal thyroid status (euthyroidism) from hypothyroidism and hyperthyroidism.

That assumption was based on the notion that elevated levels of the active forms of thyroid hormones (FT3 and FT4) suppress TSH secretion in a predictable negative feedback loop. Newer evidence shows that the control of thyroid function is far more complex.[1-3]

Overreliance on TSH as the primary measure of thyroid function has failed to relieve symptoms or significantly improve quality of life in many hypothyroid patients.[4] In addition, a systematic review of observational studies revealed that thyroid hormone levels are more strongly associated with clinical indicators of physiological health (such as cardiac or bone health) than TSH levels.[5]

TSH Reference Range

Controversy surrounds the reference range for TSH itself, especially the upper limit of the range.[6] The width of the standard range was determined by calculating the statistical mean (average) of TSH drawn from populations thought to be healthy.[7]

The challenge is that using a population-based reference interval overlooks some physiological factors (such as age and sex) and health conditions that may alter the optimal or "functional" range for an individual patient in the clinical setting. These other factors should be taken into consideration.[8,9]

Conversion Considerations

FT3 and FT4 can enter the body's cells to exert their actions, but FT3 is far more potent. When the body needs to reduce thyroid hormone activity, it creates more RT3, a biologically "inactive" form of thyroid hormone.[10] In some cases, an elevated RT3 level may signal an issue converting T4 to T3.[11]

A growing body of evidence indicates that the conversion of T4 to T3 (or to RT3) is quite variable under different physiological and environmental conditions. For example, certain genetics, nutritional deficiencies, stress (physical or psychological), and environmental toxins could lead to the inadequate conversion of T4 to T3.[10-15] The long-term use of some medications, such as beta-blockers and proton pump inhibitors, may also decrease conversion to T3.[16-21]

Thyroid Antibodies

Testing thyroid antibody levels, including TPO-Ab and TG-Ab, can help identify Hashimoto's thyroiditis. In this autoimmune condition, white blood cells make antibodies against thyroid peroxidase and/or thyroglobulin.[22] Those are two enzymes involved in producing thyroid hormones in the thyroid gland. Reduced levels of these enzymes can contribute to hypothyroidism.

Evolving Practice

Clinicians should be aware of the limitations of TSH tests and factors affecting thyroid hormone conversion when interpreting lab results. There are cases when a TSH value that falls within the population-based reference range may still warrant testing of T4 and T3 species and thyroid antibodies. Practitioners should also evaluate the full history and symptoms of the patient during clinical assessment.[23]

Although these principles and practices are not yet widespread, substantial evidence supports them. This more nuanced and advanced model of thyroid function and testing is well-aligned with the principles of personalized, precision, and preventive medicine, as well as systems-based thinking.

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