

Overview

Useful For

Second-order testing for autoimmune thyroid disease, including:

-Differential diagnosis of etiology of thyrotoxicosis in patients with ambiguous clinical signs or contraindicated (eg, pregnant or breast-feeding) or indeterminate thyroid radioisotope scans

-Diagnosis of clinically suspected Graves disease (eg, extrathyroidal manifestations of Graves disease: endocrine ophthalmos, pretibial myxedema, thyroid acropachy) but normal thyroid function tests

-Determining the risk of neonatal thyrotoxicosis in a fetus of a pregnant female with active or past Graves disease

-Differential diagnosis of gestational thyrotoxicosis versus first-trimester manifestation or recurrence of Graves disease

-Assessing the risk of Graves disease relapse after antithyroid drug treatment

A combination of TSI / Thyroid-Stimulating Immunoglobulin (TSI), Serum and THYRO / Thyrotropin Receptor Antibody, Serum is useful as an adjunct in the diagnosis of unusual cases of hypothyroidism (eg, Hashitoxicosis).

Method Name

RecombinantBioassay

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Required

Container/Tube:

Preferred: Red top

Acceptable: Serum gel

Specimen Volume:0.5 mL

Forms

If not ordering electronically, complete, print, and send a [General Request](#) (T239) with the specimen.

Specimen Minimum Volume

0.1 mL

Reject Due To

Gross hemolysis	Reject
-----------------	--------

Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Frozen (preferred)	60 days	
	Refrigerated	7 days	
	Ambient	24 hours	

Clinical and Interpretive

Clinical Information

Autoimmune thyroid disease is characterized by the presence of autoantibodies against various thyroid components, namely the thyrotropin receptor (thyroid-stimulating hormone receptor: TSHR), thyroid-peroxidase (TPO), and thyroglobulin (Tg), as well as an inflammatory cellular infiltrate of variable severity within the gland. Among the autoantibodies found in autoimmune thyroid disease, TSHR autoantibodies are most closely associated with disease pathogenesis. All forms of autoimmune thyrotoxicosis (Graves disease, Hashitoxicosis, neonatal thyrotoxicosis) are caused by the production of TSHR-stimulating autoantibodies. The role of the TPO and Tg autoantibodies in either autoimmune thyrotoxicosis or autoimmune hypothyroidism is less well established; they may merely represent epiphenomena. Detectable concentrations of anti-TPO antibodies are observed in most patients with autoimmune thyroid disease (eg, Hashimoto thyroiditis, idiopathic myxedema, and Graves disease).

Autoantibodies that bind and transactivate the TSHR lead to stimulation of the thyroid gland independent of the normal feedback-regulated thyroid-stimulating hormone (TSH) stimulation. These TSHR autoantibodies also are known as long-acting-thyroid-stimulator or thyroid-stimulating immunoglobulins (TSI). Some patients with Graves disease also have TSHR-blocking antibodies, which do not transactivate the TSHR. The balance between TSI and TSHR-blocking antibodies, as well as their individual titers, are felt to be determinants of Graves disease severity. At least 20% of patients with autoimmune hypothyroidism also have evidence either of TSHR-blocking antibodies or, less commonly, TSI.

TSHR autoantibodies may be found before autoimmune thyrotoxicosis becomes biochemically or clinically manifest. Since none of the treatments for Graves disease are aimed at the underlying disease process, but rather ablate thyroid tissue or block thyroid hormone synthesis, TSI may persist after apparent cure.

TSI are IgG antibodies and can, therefore, cross the placental barrier, causing neonatal thyrotoxicosis.

First-order tests for autoimmune thyroid disease include TPO / Thyroperoxidase (TPO) Antibodies, Serum (most suited for suspected cases of autoimmune hypothyroidism) and THYRO / Thyrotropin Receptor Antibody, Serum. Thyrotropin receptor antibody (TSHR-antibody) is a binding assay that detects both TSI and TSHR-blocking autoantibodies; it can be used instead of this TSI assay for most applications, as long as the results are interpreted in the clinical context. The TSHR-antibody test has a shorter turnaround time than the TSI assay, is less expensive, and if interpreted within the clinical context, has excellent correlation with the TSI assay. Specific detection of TSI is accomplished by this second-order bioassay.

Reference Values

< or =1.3 TSI index

Reference values apply to all ages.

Interpretation

The sensitivity and specificity of an elevated thyroid-stimulating immunoglobulins (TSI) index for Graves disease diagnosis depends on whether patients have clinically active, untreated disease or disease treated with antithyroid drugs. Using a TSI index of 1.3 as the cutoff level in newly diagnosed, untreated patients, the sensitivity and specificity are higher than 90%. For a higher cutoff of 1.8, specificity approaches 100%, but sensitivity decreases somewhat. In patients with inactive or treated Graves disease the specificity is similar, while sensitivity is lower, ranging from 50% to 80%.

Significant neonatal thyrotoxicosis is likely if a pregnant woman with a history of Graves disease has a TSI index above 3.9 during the last trimester, regardless of her remission status. Lesser elevations are only occasionally associated with neonatal thyrotoxicosis. This is particularly relevant for women who have previously undergone thyroid-ablative therapy or are on active antithyroid drug treatment and, therefore, no longer display biochemical or clinical evidence of thyrotoxicosis.

Gestational thyrotoxicosis, which is believed to be due to a combination of human chorionic gonadotropin cross-reactivity on the thyroid-stimulating hormone receptor (TSHR) and transient changes in thyroid hormone protein binding, is not associated with an elevated TSI index. Finding an elevated TSI index in this setting suggests underlying Graves disease.

An elevated TSI index at the conclusion of a course of anti-thyroid drug treatment is highly predictive of relapse of Graves disease. However, the converse, a normal TSI index, is not predictive of prolonged remission.

In patients with thyroid function tests that fluctuate between hypo- and hyperthyroidism or vice versa, a clearly elevated TSHR-antibody level (>25%) and a simultaneous TSI index that is normal or only minimally elevated (1.3-1.8) suggest a diagnosis of possible Hashitoxicosis.

Cautions

Positive results are strongly indicative of Graves disease, but do not always correlate with the presence and severity of hyperthyroidism.

Patients with Hashimoto disease may have an elevated thyroid-stimulating immunoglobulins (TSI) index, which can be above 1.8. A TSI index of above 1.3 and less than or equal to 1.8 also is occasionally observed in various other thyroid disorders, including nodular goiter, and subacute thyroiditis.

Supportive Data

Pediatric data is based on a Mayo study of 50 male and 50 female children between the ages of 10 days and 18 years.

Clinical Reference

1. Morris JC III, Hay ID, Nelson RE, Jiang NS: Clinical utility of thyrotropin-receptor antibody assays: comparison of radio-receptor and bioassay methods. *Mayo Clin Proc* 1988;63:707-717
2. Volpe R: Rational use of thyroid function tests. *Crit Rev Clin Lab Sci* 1997;34:405-438
3. Saravanan P, Dayan CM: Thyroid autoantibodies. *Endocrinol Metab Clin North Am* 2001;30(2):315-335
4. Grebe SKG: Thyroid disease. In *The Genetic Basis of Common Diseases*. Second edition. Edited by RA King, JI Rotter, AG Motulsky. New York, Oxford University Press, 2002, pp 397-430

Performance

Method Description

This bioassay compares the cyclic adenosine monophosphate (cAMP) production of thyroid-stimulating hormone (TSH)-responsive cells upon exposure to patient serum with that obtained in the same cells after exposure to normal control serum.

The assay uses Chinese hamster ovary cells that have been permanently transfected with the human thyroid-stimulating hormone receptor (TSHR) and a luciferase expression construct under the control of a cAMP responsive promoter. Luciferase transcription in these cells is proportional to the concentration of intracellular cAMP.

The cells are grown to near-confluence. An aliquot of cells is then incubated with each diluted patient serum. Cells are lysed at the end of incubation, luciferase substrate is added and chemiluminescence is measured in a luminometer. The ratio of the light-units produced in the cell-lysate exposed to patient serum divided by a control cell-lysate light-signal is the TSI index. (Preissner CM, Wolhuter PJ, Sistrunk JW, et al: Comparison of thyrotropin-receptor antibodies measured by four commercially available methods with a bioassay that uses Fisher-rat thyroid cells. Clin Chem 2003;49:1402-1404; package insert: Thyroid Stimulating Immunoglobulin Assay. Diagnostic Hybrids)

PDF Report

No

Day(s) and Time(s) Test Performed

Monday through Friday; 10 a.m.

Analytic Time

2 days when specimen is received Sunday through Thursday; 4 days when specimen is received Friday and Saturday

Maximum Laboratory Time

6 days

Specimen Retention Time

3 months

Performing Laboratory Location

Rochester

Fees and Codes

Fees

- Authorized users can sign in to [Test Prices](#) for detailed fee information.
- Clients without access to Test Prices can contact [Customer Service](#) 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact [Customer Service](#).

Test Classification

This test has been cleared or approved by the U.S. Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information

84445

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
TSI	Thyroid-Stimulating Immunoglob, S	30567-2

Result ID	Test Result Name	Result LOINC Value
8634	Thyroid-Stimulating Immunoglob, S	30567-2