Test Definition: THYRO

Thyrotropin Receptor Antibody, Serum

Overview

Useful For

Recommended first-line test for detection of thyrotropin receptor antibodies

Differential diagnosis of etiology of thyrotoxicosis in patients with ambiguous clinical findings and/or contraindicated (eg, pregnant or breast-feeding) or nondiagnostic thyroid radioisotope scans

Diagnosing clinically suspected Graves disease (GD) (eg, extrathyroidal manifestation of GD include endocrine exophthalmos, pretibial myxedema, thyroid acropachy) in patients with normal thyroid function tests

Determining the risk of neonatal thyrotoxicosis in a fetus of a pregnant female with active or past active GD

Differential diagnosis of gestational thyrotoxicosis versus first trimester manifestation or recurrence of GD

Assessing the risk of GD relapse after antithyroid drug treatment

Method Name

Electrochemiluminescence Immunoassay

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Required

Patient Preparation:

1. For 12 hours before specimen collection. patient **should not** take multivitamins or dietary supplements (eg, hair, skin, and nail supplements) containing biotin (vitamin B7).
2. Patient **should not** be receiving heparin treatment.

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)

Collection Container/Tube:

Preferred: Serum gel

Acceptable: Red top

Submission Container/Tube: Plastic vial

Specimen Volume: 1 mL

Collection Instructions: Centrifuge and aliquot serum into a plastic vial.

Forms

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

Specimen Minimum Volume

0.75 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	OK
Gross icterus	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	7 days	
	Frozen	90 days	

Clinical & Interpretive

Clinical Information

Autoimmune thyroid disease is characterized by the presence of autoantibodies against various thyroid components, namely the thyrotropin receptor, thyroid peroxidase, and thyroglobulin, as well as by an inflammatory cellular infiltrate of variable severity within the gland.

Among the autoantibodies found in autoimmune thyroid disease, thyrotropin receptor autoantibodies (TRAb) are most closely associated with disease pathogenesis. All forms of autoimmune thyrotoxicosis (Graves disease [GD], Hashitoxicosis, neonatal thyrotoxicosis) are caused by the production of stimulating TRAb. These autoantibodies, also known as long-acting-thyroid-stimulators or thyroid-stimulating immunoglobulins (TSI), bind to the receptor and transactivate it, leading to stimulation of the thyroid gland independent of the normal feedback-regulated thyrotropin stimulation.

Some patients with GD also have TRAb that do not transactivate the thyrotropin receptor. The balance between stimulating and blocking antibodies, as well as their individual titers, is felt to be a determinant of GD severity. Some patients with autoimmune hypothyroidism also have evidence of either blocking TRAb or, rarely, TSI.

Thyrotropin receptor autoantibodies may be detected before autoimmune thyrotoxicosis becomes biochemically or clinically manifest. Since none of the treatments for GD are aimed at the underlying disease process but rather ablate thyroid tissue or block thyroid hormone synthesis, TSI may persist after apparent clinical cure. This is of particular relevance for pregnant women with a history of GD treated with thyroid-ablative therapy. Some of these women may continue to produce TSI. Since TSI are IgG antibodies, they can cross the placental barrier causing neonatal thyrotoxicosis.

While the gold standard for thyroid-stimulating immunoglobulins is the bioassay (see TSI / Thyroid-Stimulating Immunoglobulin, Serum), the TRAb test has a shorter turnaround time, less analytical variability, and is less expensive.

Reference Values

< or =1.75 IU/L

Interpretation

The sensitivity and specificity of an elevated thyrotropin receptor antibody (TRAb) test for Graves disease (GD) diagnosis depends on whether patients have disease treated with antithyroid drugs or clinically active, untreated disease. Based on a study that included specimens from 436 apparently healthy individuals, 210 patients with thyroid diseases without diagnosis of GD, and 102 patients with untreated GD, a decision limit of 1.75 IU/L showed a sensitivity of 97% and a specificity of 99% for detection of GD.(1) In healthy individuals and in patients with thyroid disease without diagnosis of GD, the upper limit of antithyrotropin receptor values are 1.22 IU/L and 1.58 IU/L, respectively (97.5th percentiles). A Mayo study of 115 patients, including 42 patients with GD, showed a sensitivity of 95% and a specificity of 97% for detection of GD at a decision limit of 1.75 IU/L.

Assessment of TRAb status is particularly relevant in women who have undergone thyroid ablative therapy or are on active antithyroid treatment and, therefore, no longer display biochemical or clinical evidence of thyrotoxicosis. Significant neonatal thyrotoxicosis is likely if a pregnant woman with a history of GD has TRAb concentrations of more than 3.25 IU/L during the last trimester, regardless of her clinical remission status. Lesser elevations are only occasionally associated with neonatal thyrotoxicosis.

Gestational thyrotoxicosis, which is believed to be due to a combination of human chorionic gonadotropin cross-reactivity on the thyrotropin receptor and transient changes in thyroid hormone protein binding, is only very rarely associated with an elevated TRAb test. Finding an elevated test result in this setting usually suggests underlying GD.

An elevated TRAb test at the conclusion of a course of antithyroid drug treatment is highly predictive of relapse of GD. However, the converse, a normal TRAb test, is not predictive of prolonged remission.

Cautions

In rare cases, some individuals can develop antibodies to mouse or other animal antibodies (often referred to as human anti-mouse antibodies [HAMA] or heterophile antibodies), which may cause interference in some immunoassays. The presence of antibodies to streptavidin or ruthenium can also rarely occur and may also interfere in this assay. Caution should be used in interpretation of results, and the laboratory should be alerted if the result does not correlate with the clinical presentation.

Supportive Data

A Mayo method comparison study between this assay and the Kronus TSH Receptor Antibody binding inhibition assay showed an overall agreement between the assays of 96.5% and a calculated Kappa statistic of 0.93.

Clinical Reference

1. Schott M, Hermsen D, Broecker-Preuss M, et al. Clinical value of the first automated TSH receptor autoantibody assay for the diagnosis of Graves disease: an international multicentre trial. Clin Endocrinol (Oxf). 2009;71(4):566-573
2. Hermsen D, Broecker-Preuss M, Casati M, et al. Technical evaluation of the first fully automated assay for the detection of TSH receptor autoantibodies. Clin Chim Acta. 2009;401(1-2):84-89
3. Diana T, Olivo PD, Kahaly GJ. Thyrotropin receptor blocking antibodies. Horm Metab Res. 2018;50(12):853-862

4. Kotwal A, Stan M. Thyrotropin receptor antibodies-an overview. Ophthalmic Plast Reconstr Surg. 2018; 34(4S Supple 1)S20-S27

Performance

Method Description

The Roche TSHR (thyrotropin receptor antibody [TRAb]) assay is a competitive assay using electrochemiluminescence detection. Patient sample is treated with a reagent buffer consisting of a pre-formed immunocomplex of solubilized porcine thyrotropin (TSH) receptor and biotinylated anti-porcine TSH receptor mouse monoclonal antibody. TRAb in the patient's sample are allowed to interact with the TSH receptor complex. After addition of streptavidin-coated microparticles and a human thyroid-stimulating monoclonal autoantibody (M22) labeled with a ruthenium complex, bound TRAb are detected by their ability to inhibit the binding of labeled M22. The entire complex becomes bound to the solid phase via interaction of biotin and streptavidin. This reaction mixture is aspirated into a measuring cell where the bound microparticles are captured onto the electrode surface and unbound substances are removed. Voltage is applied to the electrode inducing a chemiluminescent emission, which is then measured against a calibration curve to determine the amount of thyrotropin receptor antibody in the patient specimen.(Package insert: Elecsys Anti-TSHR. Roche Diagnostics; V 3.0, 09/2023)

PDF Report

No

Day(s) Performed

Monday through Saturday

Report Available

1 to 3 days

Specimen Retention Time

2 weeks

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Superior Drive

Fees & 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 account representative. For assistance, contact Customer Service.

Test Classification

This test has been cleared, approved, or is exempt by the US 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

83520

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
THYRO	Thyrotropin Receptor Ab, S	5385-0

Result ID	Test Result Name	Result LOINC® Value
THYRO	Thyrotropin Receptor Ab, S	5385-0