Overview

Useful For
Recommended first-line test for detection of thyrotropin receptor (TSHR) antibodies, and used in the following situations:

- 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

- Diagnosis of clinically suspected Graves disease (eg, extrathyroidal manifestation of Graves disease 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 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

Method Name
Electrochemiluminescence Immunoassay

NY State Available
Yes

Specimen
Specimen Type
Serum

Specimen Required

Patient Preparation; For 12 hours before this test do not take multivitamins or dietary supplements containing biotin (vitamin B7), which is commonly found in hair, skin, and nail supplements and multivitamins.

Container/Tube:
Preferred: Red top
Acceptable: Serum gel

Specimen Volume: 1 mL

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

<table>
<thead>
<tr>
<th>Condition</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gross hemolysis</td>
<td>Reject</td>
</tr>
<tr>
<td>Gross lipemia</td>
<td>OK</td>
</tr>
</tbody>
</table>

Specimen Stability Information

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum</td>
<td>Refrigerated (preferred)</td>
<td>7 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Frozen</td>
<td>30 days</td>
<td></td>
</tr>
</tbody>
</table>

Clinical and Interpretive

Clinical Information

Autoimmune thyroid disease is characterized by the presence of autoantibodies against various thyroid components, namely the thyrotropin receptor (TSHR), thyroid peroxidase (TPO), and thyroglobulin (Tg), as well as by 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. These autoantibodies, also known as long-acting-thyroid-stimulator (LATS) 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 (TSH) stimulation.

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. Some patients with autoimmune hypothyroidism also have evidence of either TSHR-blocking antibodies or, rarely, TSI.

TSHR autoantibodies may be detected 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 clinical cure. This is of particular relevance for pregnant women with a history of Graves disease that was 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 [TSI], Serum), the thyrotropin receptor antibody 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 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 Graves disease, and 102 patients with untreated Graves disease, a decision limit of 1.75 IU/L showed a sensitivity of 97% and a specificity of 99% for detection of Graves disease.(1) In healthy individuals and in patients with thyroid disease without diagnosis of Graves disease, the upper limit of antithyrotropin receptor (anti-TSHR) values are 1.22 IU/L and 1.58 IU/L, respectively (97.5th percentiles).(1) A Mayo study of 115 patients, including 42 patients with Graves disease, showed a sensitivity of 95% and a specificity of 97% for detection of Graves disease 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 Graves disease has TRAb concentrations of >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 TSHR and transient changes in thyroid hormone protein binding, is only very rarely associated with an elevated TRAb test. Finding an elevated TRAb test in this setting suggests usually underlying Graves disease.

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

Cautions
Do not use specimens from patients receiving heparin treatment.

In rare cases, interference due to extremely high titers of antibodies to streptavidin and ruthenium can occur.

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


Performance

Method Description
Testing is performed on a Roche Cobas. The Roche TSH/thyrotropin receptor antibody (TSHR Ab) assay is a competitive assay using electrochemiluminescence detection. Patient specimen is treated with a reagent buffer consisting of a preformed immunocomplex of solubilized porcine TSH receptor and biotinylated antiporcine TSH receptor mouse monoclonal antibody. TSHR Ab in patient's serum 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 TSHR Ab 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 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: Roche Cobas. Roche Diagnostics, Indianapolis, IN 2010-09, V4)

PDF Report
No

Day(s) and Time(s) Test Performed
Monday through Friday 5 a.m. - 12 a.m.
Saturday 6 a.m. - 6 p.m.

Analytic Time
Same day/1 day

Maximum Laboratory Time
3 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
83520

LOINC® Information

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Test Order Name</th>
<th>Order LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>THYRO</td>
<td>Thyrotropin Receptor Ab, S</td>
<td>5385-0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Result ID</th>
<th>Test Result Name</th>
<th>Result LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>THYRO</td>
<td>Thyrotropin Receptor Ab, S</td>
<td>5385-0</td>
</tr>
</tbody>
</table>