

Autoimmune Thyroid Disease

Indications for Ordering

- Differentiate autoimmune-mediated thyroid disease (eg, Hashimoto thyroiditis, Graves disease [GD]) from other etiologies for hypo- or hyperthyroidism
- Predict risk of fetal thyroid dysfunction in mothers with history of GD
- Establish an autoimmune cause for recurrent miscarriage

Test Description

Thyroid Stimulating Immunoglobulin (TSI)

- Semiquantitative bioassay – TSHR-expressing cell line with a modified G protein (GNAS)
 - Improves sensitivity by increasing cAMP levels following receptor stimulation
- Quantitative chemiluminescent immunoassay – detects cAMP

Thyroid Stimulating Hormone Receptor Antibody (TRAb)

- Quantitative electrochemiluminescent immunoassay

Thyroid Peroxidase (TPO) Antibody

- Quantitative chemiluminescent immunoassay

Thyroglobulin (TG) Antibody

- Quantitative chemiluminescent immunoassay

Tests to Consider

Typical testing strategy

Autoimmune thyroid testing performed when hypo- or hyperthyroidism or subclinical hypo- or hyperthyroidism is suspected based on clinical signs/symptoms and thyroid function testing (TSH and free T4) (see guidelines below)

Primary tests

[Thyroid Stimulating Immunoglobulin 0099430](#)

- Acceptable testing for autoimmune thyroid disease
- Prognostic marker for relapse of GD or remission following drug therapy
- Support GD diagnosis in difficult (euthyroid) cases
- Predict risk of thyroid dysfunction in newborns of mothers with GD

[Thyroid Stimulating Hormone Receptor Antibody \(TRAb\) 2002734](#)

- Acceptable test for autoimmune thyroid disease
- Aids in the differentiation of GD from factitious thyrotoxicosis, postpartum thyroiditis, or toxic nodular goiter
- Prognostic marker for relapse of GD or remission following drug therapy
- Predict risk of thyroid dysfunction in newborns of mothers with GD
- Evaluate for the presence of euthyroid GD ophthalmopathy

[Thyroid Peroxidase \(TPO\) Antibody 0050075](#)

- Primary test for Hashimoto thyroiditis
- Secondary testing for GD
 - Aids in the differentiation of GD from factitious thyrotoxicosis, postpartum thyroiditis, or toxic nodular goiter
- Predict progression to hypothyroidism in individuals with subclinical hypothyroidism
- Evaluate individuals with recurrent miscarriage, with or without infertility issues

Related tests

[Thyroglobulin Antibody 0050105](#)

- Diagnose autoimmune thyroid disease when TPO antibody measurements are negative and a high clinical suspicion exists for autoimmune thyroid disease
- Predict progression to hypothyroidism in individuals with subclinical hypothyroidism (eg, Hashimoto thyroiditis)

[Thyroid Antibodies 0050645](#)

- Test panel composed of TPO and TG antibody tests

Disease Overview

Prevalence

- GD – <1%
 - Most common cause of hyperthyroidism in U.S.
- Hashimoto thyroiditis-associated hypothyroidism – 1-2%
- Both diseases affect women more than men

Age of onset

- GD – 20-40 years
- Hashimoto thyroiditis-associated hypothyroidism – 40-60 years

Symptoms

Hypothyroidism

- Fatigue, weakness
- Weight gain
- Cold intolerance
- Constipation
- Dry, brittle skin and nails
- Depression

Hyperthyroidism

- Hyperactivity
- Weight loss
- Heat intolerance
- Anxiety
- Hair loss
- Irritability
- Pretibial myxedema (GD)
- Exophthalmos (GD)

Physiology

GD

- Anti-TSH receptor IgG autoantibodies bind to the TSH receptor
 - Activation and subsequent secretion of thyroxine (T4) and triiodothyronine (T3)
 - Hyperthyroidism develops
- TSH levels fall due to T3/T4 feedback to the hypothalamus and pituitary

Hashimoto thyroiditis

- Autoimmune destruction of thyrocytes
 - Autoantibodies against TPO, TG, and TSHR antibodies likely contribute to the destruction of thyroid tissue
 - Hypothyroidism develops

Prognostic issues

GD and pregnancy

- Women with GD treated with radioactive iodine or thyroidectomy prior to pregnancy
 - Test for anti-TRAb antibodies
 - During the first trimester and at 20-26 weeks (if initially elevated) OR
 - Only at 20-26 weeks
- Antibody-positive mothers – at risk for fetal/infant hypothyroidism

Test Interpretation

Sensitivity/specificity

Thyroid Stimulating Hormone Receptor Antibody (TRAb)

- Analytical sensitivity – 0.9 IU/L limit of detection
- Analytical specificity – 88.9%

Thyroid Peroxidase (TPO) Antibody

- Analytical sensitivity – 0.25 IU/mL limit of detection
- Clinical sensitivity
 - GD – ~75%
 - Hashimoto thyroiditis – >90%

Results

GD

- Positive – elevated TSI antibodies and/or TRAb
 - Consistent with autoimmune thyroid disease
 - GD likely if individual has signs/symptoms and biochemical evidence of hyperthyroidism
- Negative – no evidence of TSI antibodies and/or TRAb
 - NOT consistent with GD

Hashimoto thyroiditis

- Positive – elevated TPO and/or TG antibodies
 - Consistent with autoimmune thyroid disease
 - Hashimoto thyroiditis likely if individual has signs/symptoms and biochemical evidence of hypothyroidism
 - Elevated TPO antibodies in individual with subclinical hypothyroidism
 - Associated with an increased risk of developing hypothyroidism versus those without elevated TPO antibody titers
- Negative – no evidence of TPO and/or thyroglobulin antibodies
 - NOT consistent with Hashimoto disease

Limitations

Thyroid Stimulating Immunoglobulin (TSI)

- Blocking antibodies specific to TSHR may decrease TSI antibody levels
 - Net response is most likely physiologic
- TSH serum levels ≥ 6 mU/L may cause a false-positive result

Thyroglobulin Antibody

Presence of other nonthyroid autoimmune diseases may cause a false-positive result

References

- Hyperthyroidism and Other Causes of Thyrotoxicosis: Management Guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists (May/June 2011)
- Clinical Practice Guidelines for Hypothyroidism in Adults: Cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association (Nov/Dec 2012)