Thyroglobulin Mass Spectrometry, Serum

**Useful For**
- An adjunct to anti-thyroid peroxidase (anti-TPO) autoantibody (TPO / Thyroperoxidase [TPO] Antibodies, Serum), antithyrotropin-receptor autoantibody (THYRO / Thyrotropin Receptor Antibody, Serum), and thyroid-stimulating immunoglobulin (TSI / Thyroid-Stimulating Immunoglobulin [TSI], Serum) measurements in the diagnosis of autoimmune thyroid diseases: Hashimoto disease, postpartum thyroiditis, neonatal hypothyroidism, and Graves disease
- Identification of potentially unreliable serum thyroglobulin measurements in the follow-up of patients with differentiated follicular-cell derived thyroid carcinomas

**Clinical Information**
Thyroglobulin autoantibodies bind thyroglobulin (Tg), a major thyroid-specific protein. Tg plays a crucial role in thyroid hormone synthesis, storage, and release. Noniodinated Tg is actively transported from thyrocyte cytosol to the thyroid follicular lumen. At the extracellular apical villae-follicular luminal interface, thyroid peroxidase (TPO) catalyzes the iodination of tyrosine and thyrone residues of Tg. This is followed by intramolecular coupling of pairs of mono- and diiodotyrosines to form thyroid hormones, predominately thyroxine (T4) or, to lesser degree, triiodothyronine (T3). The iodinated Tg is stored in the follicular lumen, forming the colloid. For thyroid hormone release, colloid is reabsorbed at the apical membrane and proteolyzed. Iodinated tyrosine residues are deiodinated and recycled for synthesis of new Tg molecules, while the bulk of T3 and T4 residues are secreted from the basal membrane into the systemic circulation.

Tg is not secreted into the systemic circulation under normal circumstances. However, follicular destruction through inflammation (thyroiditis and autoimmune hypothyroidism), hemorrhage (nodular goiter), or rapid disordered growth of thyroid tissue, as may be observed in Graves disease or follicular cell-derived thyroid neoplasms, can result in leakage of Tg into the blood stream. This results in the formation of autoantibodies to Tg in some individuals. The same processes also may result in exposure of other "hidden" thyroid antigens to the immune system, resulting in the formation of autoantibodies to other thyroid antigens, in particular TPO. Since anti-Tg and anti-TPO autoantibodies are observed most frequently in autoimmune thyroiditis (Hashimoto's disease), they were originally considered to be of possible pathogenic significance in this disorder. However, the consensus opinion today is that they are merely disease markers. It is felt that the presence of competent immune cells at the site of thyroid tissue destruction in autoimmune thyroiditis simply predisposes the patient to form autoantibodies to hidden thyroid antigens.

Of individuals with autoimmune hypothyroidism, 30% to 50% will have detectable anti-Tg autoantibodies, while 50% to 90% will have detectable anti-TPO autoantibodies. In Graves disease, both types of autoantibodies are observed at approximately half these rates, while in papillary and follicular thyroid cancer, mainly anti-Tg autoantibodies are detected at rates of 10% to 20%. In this latter case, the main importance of anti-Tg measurement is identification of individuals in whom measurement of circulating Tg cannot be relied upon as a tumor marker during follow-up. The presence of anti-Tg autoantibodies may lead to false-low, or less commonly, false-high serum Tg measurements.

Thyroglobulin antibody is used as both a strand-alone marker for autoimmune thyroiditis and related diseases, and as part of the thyroglobulin tumor marker profile.

**Analytic Time**
Same day/1 day

**Reference Values**
<116 IU/mL
Reference values apply to all ages.
Interpretation

Diagnosis of Autoimmune Thyroid Disease:
Measurements of anti-thyroid peroxidase (anti-TPO) autoantibodies have higher sensitivity and equal specificity to anti-thyroglobulin (anti-Tg) autoantibody measurements in the diagnosis of autoimmune thyroid disease. Anti-Tg autoantibody levels should, therefore, only be measured if anti-TPO autoantibody measurements are negative, but clinical suspicion of autoimmune thyroid disease is high.

Positive thyroid autoantibody levels in patients with high-normal or slightly elevated serum thyrotropin levels predict the future development of more profound hypothyroidism.

Patients with postpartum thyroiditis with persistently elevated thyroid autoantibody levels have an increased likelihood of permanent hypothyroidism.

In cases of neonatal hypothyroidism, the detection of anti-TPO or anti-Tg autoantibodies in the infant suggests transplacental antibody transfer, particularly if the mother has a history of autoimmune thyroiditis or detectable thyroid autoantibodies. The neonatal hypothyroidism is likely to be transient in these cases.

Thyroid Cancer Follow-Up:
Following therapy of differentiated follicular-cell derived thyroid cancer, all patients who have no, or only trivial, amounts of normal residual thyroid tissue and no persistent or recurrent cancer will have undetectable or very low serum Tg levels. Persistently elevated or rising serum Tg levels, either on or off thyroxine replacement therapy, suggest possible tumor persistence or recurrence. However, if a patient also has measurable anti-Tg autoantibody levels, the results of serum Tg measurements are unreliable.

Anti-Tg autoantibodies may result in both falsely-low and, less commonly, falsely-high serum Tg measurements. Therefore, in anti-Tg-positive patients, serum Tg measurements should either not be used in thyroid cancer follow-up or be interpreted with extreme caution. A thyroglobulin antibody result of <22 IU/mL is unlikely to cause clinically significant thyroglobulin assay interference. It is recommended that the thyroglobulin result be reviewed for concordance with clinical presentation.

Cautions

Low titers of thyroid autoantibodies may be observed in the absence of autoimmune or other thyroid diseases and are considered a nonspecific finding. The population prevalence of such nonspecific low-level anti-thyroglobulin (anti-Tg) positivity is higher in females than in males and increases with age in both genders.

Detection of significant titers of anti-Tg or anti-thyroid peroxidase (anti-TPO) autoantibodies is supportive evidence for a diagnosis of Graves disease in patients with thyrotoxicosis. However, measurement of the pathogenic anti-TSH receptor antibodies by binding assay (THYRO / Thyrotropin Receptor Antibody, Serum) or bioassay (TSI / Thyroid-Stimulating Immunoglobulin [TSI], Serum) is the preferred method of confirming Graves disease in atypical cases and under special clinical circumstances.

Patients with nodular thyroid disease who are anti-thyroid autoantibody positive may have coexisting Hashimoto disease, which can result in a suspicious fine-needle aspiration biopsy diagnosis of follicular or Hurthle cell neoplasia.

Anti-Tg values determined by different methodologies might vary significantly and cannot be directly compared with one another. Some patients might show to be antibody-positive by some methods and antibody-negative by others. Comparing anti-Tg antibodies values from different methods might lead to erroneous clinical interpretation.

In patients receiving therapy with high biotin doses (ie, >5 mg/day), no specimen should be drawn until at least 8 hours after the last biotin administration.

Tg concentrations >2,000 ng/mL may lead to falsely elevated anti-Tg concentrations. In this case, anti-Tg concentrations might be unreliable.

Clinical References


For additional interpretation information and clinical references, please visit the following website: