Overview

Useful For

Reporting of accurate thyroglobulin results, depending on the antithyroglobulin antibodies status of the patient

Accurate measurement of serum thyroglobulin in patients with known or suspected antithyroglobulin autoantibodies or possible heterophile antibodies

Reflex Tests

Test ID	Reporting Name	Available Separately	Always Performed
HTGT	Thyroglobulin, Tumor Marker, IA, S	No	No
TGMS	Thyroglobulin, Mass Spec., S	Yes	No

Testing Algorithm

This test begins with the analysis of thyroglobulin antibody by immunoassay. If the thyroglobulin antibody result is negative (<1.8 IU/mL), then thyroglobulin testing will be performed by immunoassay.

If the thyroglobulin antibody result is positive (> or =1.8 IU/mL), then thyroglobulin testing will be performed by mass spectrometry.

Method Name

Immunoenzymatic Assay

NY State Available

Yes

Specimen

Specimen Type

Serum Red

Specimen Required

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

Collection Container/Tube: Red top

Submission Container/Tube: Plastic vial

Specimen Volume: 1 mL

Forms

If not ordering electronically, complete, print, and send an Oncology Test Request (T729) with the specimen.

Specimen Minimum Volume

See Specimen Required

Reject Due To

Gross hemolysis	Reject
Gross lipemia	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum Red	Refrigerated (preferred)	7 days	
	Frozen	30 days	

Clinical and Interpretive

Clinical Information

Thyroglobulin (Tg) is a thyroid-specific glycoprotein (approximately 660 KDa) that serves as the source for thyroxine (T4) and triiodothyronine (T3) production within the lumen of thyroid follicles. For T4 and T3 release, Tg is reabsorbed into thyrocytes and proteolytically degraded, liberating T4 and T3 for secretion. Small amounts of intact Tg are secreted alongside T4 and T3 and are detectable in the serum of healthy individuals, with levels roughly paralleling thyroid size (0.5-1.0 ng/mL Tg per gram thyroid tissue, depending on thyroid-stimulating hormone [TSH] level). In situations of disordered thyroid growth (eg, goiter), increased thyroid activity (eg, Graves disease), or glandular destruction (eg, thyroiditis) larger amounts of Tg may be released into the circulation.

Clinically, the main use of serum Tg measurements is in the follow-up of differentiated follicular cell-derived thyroid carcinoma. Because Tg is thyroid-specific, serum Tg concentrations should be undetectable, or very low, after the thyroid gland is removed during treatment for thyroid cancer.

Current clinical guidelines consider a serum Tg of more than1 ng/mL in an athyrotic individual as suspicious of possible residual or recurrent disease. To improve diagnostic accuracy, it is recommended that at least initially this measurement is obtained after TSH stimulation, either following thyroid hormone withdrawal, or after injection of recombinant human TSH. Most patients will have a relatively low risk of recurrence, and will thereafter only require unstimulated Tg measurement. If unstimulated (on thyroxine) serum Tg measurements are less than 0.1 to 0.2 ng/mL, the risk of disease is below 1%. Patients with higher Tg levels, who have no demonstrable remnant of thyroid tissue, might require additional testing, such as further stimulated Tg measurements, neck ultrasound, or isotope imaging. A stimulated Tg above 2 ng/mL is considered suspicious.

The presence of anti-thyroglobulin autoantibodies (TgAb), which occur in 15% to 30% of thyroid cancer patients, could lead to misleading Tg results. In immunometric assays, the presence of TgAb can lead to false low measurement; whereas it might lead to false high results in competitive assays. Traditionally, there have been no reliable means to obtain accurate Tg measurements in patients with TgAb. However, recently, trypsin digestion of serum proteins, which cuts both antibodies and Tg into predictable fragments, has allowed accurate quantification of Tg in samples with antibody interferences through measurement of Tg-specific tryptic peptides by mass spectrometry.

Reference Values

Thyroglobulin Antibody: <1.8 IU/mL

Interpretation

Current guidelines recommend measurement of thyroglobulin (Tg) with a sensitive immunoassay - limit of quantification less than 1 ng/mL; for measurements of unstimulated Tg, the detection limit should be in the 0.1 to 0.2 ng/mL range.

In all cases, serum anti-thyroglobulin autoantibodies (TgAb) should also be measured, preferably with a method that allows detection of low concentrations of TgAb. If TgAb are detected, the laboratory report should alert the ordering provider to the possibility of false-low Tg results. If the apparent Tg concentration is less than 1.0 ng/mL, the sample should be remeasured by liquid chromatography-tandem mass spectrometry (LC-MS/MS). This will allow confident detection of Tg in the presence of TgAb down to 0.5 ng/mL (risk of residual/recurrent disease <1%-3%).

Samples from patients with Tg concentrations greater than 1.0 ng/mL might not require Tg measurement by mass spectrometry, because current guidelines suggest further work-up might be necessary above this threshold. However the positive predictive value for residual/recurrent disease is modest when Tg is just above this threshold (3%-25%) in athyrotic patients. Above 10 ng/mL, the risk of residual/recurrent disease is at least 25%, with many studies showing 60% to greater than 90% risks. In selected patients, it might therefore also be useful to test TgAb positive samples by mass spectrometry, even if the Tg concentration is greater than 1.0 ng/mL, but has not yet passed the 10 ng/mL threshold. These considerations are even more relevant in patients with a known thyroid remnant of a few grams, who may always have serum Tg concentrations of 1.0 to 10 ng/mL, owing to remnant Tg secretion, regardless of the presence or absence of residual/recurrent cancer.

It has been determined that the presence of anti-thyroglobulin autoantibodies (TgAb) in serum can lead to underestimation of Tg concentration by immunometric methods. When TgAb are present in samples with detectable Tg, the Tg values may be underestimated by up to 60% in immunoassays. In addition, some specimens containing TgAb which are negative for Tg by immunoassay tested positive by LC-MS/MS. Therefore, measuring of Tg by LC-MS/MS is the preferred method in TgAb positive patients. The listed decision levels are for thyroid cancer follow-up of athyrotic patients and apply to unstimulated and stimulated thyroglobulin measurements. Decision levels are based on best practice guidelines and the literature, which includes Mayo Clinic studies.

Decision levels for thyroid cancer patients, who are not completely athyrotic (ie, patient has some remnant normal thyroid tissue), have not been established, but are likely to be somewhat higher: remnant normal thyroid tissue contributes to serum Tg concentrations 0.2 to 1.0 ng/mL per gram of remnant tissue, depending on the TSH level.

Thyroglobulin by Mass Spectrometry:

Tg <0.2 ng/mL: Tg levels must be interpreted in the context of TSH levels, serial Tg measurements, and radioiodine ablation status. Undetectable Tg levels in athyrotic individuals on suppression therapy indicate a minimal risk (<1%-2%) of clinically detectable recurrent papillary/follicular thyroid cancer.

Tg > or =0.2 ng/mL to 2.0 ng/mL: Tg levels must be interpreted in the context of TSH levels, serial Tg measurements, and radioiodine ablation status. Tg levels of 0.2-2.0 ng/mL in athyrotic individuals on suppressive therapy indicate a low risk of clinically detectable recurrent papillary/follicular thyroid cancer.

Tg 2.1 ng/mL to 9.9 ng/mL: Tg levels must be interpreted in the context of TSH levels, serial Tg measurements and radioiodine ablation status. Tg levels of 2.1-9.9 ng/mL in athyrotic individuals on suppression therapy indicate an increased risk of clinically detectable recurrent papillary/follicular thyroid cancer.

Tg > or =10 ng/mL: Tg levels must be interpreted in the context of TSH levels, serial Tg measurements and radioiodine ablation status. Tg levels of > or =10 ng/mL in athyrotic individuals on suppressive therapy indicate a significant (>25%) risk of clinically detectable recurrent papillary/follicular thyroid cancer.

Thyroglobulin by Immunoassay:

Tg <0.1 ng/mL: Tg levels must be interpreted in the context of TSH levels, serial Tg measurements and radioiodine ablation status. Tg levels <0.1 ng/mL in athyrotic individuals on suppressive therapy indicate a minimal risk (<1%-2%) of clinically detectable recurrent papillary/follicular thyroid cancer.

Tg > or =0.1 to 2.0 ng/mL: Tg levels must be interpreted in the context of TSH levels, serial Tg measurements and radioiodine ablation status. Tg levels 0.1 to 2.0 ng/mL in athyrotic individuals on suppressive therapy indicate a low risk of clinically detectable recurrent papillary/follicular thyroid cancer.

Tg 2.1 ng/mL to 9.9 ng/mL: Tg levels must be interpreted in the context of TSH levels, serial Tg measurements and radioiodine ablation status. Tg levels 2.1 to 9.9 ng/mL in athyrotic individuals on suppressive therapy indicate an increased risk of clinically detectable recurrent papillary/follicular thyroid cancer.

Tg > or =10 ng/mL: Tg levels must be interpreted in the context of TSH levels, serial Tg measurements and radioiodine ablation status. Tg levels > or =10 ng/mL in athyrotic individuals on suppressive therapy indicate a significant risk (>25%) of clinically detectable recurrent papillary/follicular thyroid cancer.

Cautions

Thyroglobulin Antibody:

Antithyroglobulin 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 values from different methods might lead to erroneous clinical interpretation.

Thyroglobulin by Mass Spectrometry:

Rare normal amino acid sequence variations within thyroglobulin (Tg) can cause a false-low result in the Tg mass spectrometry assay, if they happen to be present in the Tg proteotypic peptides that are used for Tg quantification.

While the exact prevalence of such changes is unknown, the validation data on large sample numbers indicate that this affects less than 1% of samples. In the heterozygote state, the result would be an apparent reduction in Tg concentration by about 50%, while the homozygous state (<0.01%) is predicted to result in total loss of signal. Therefore, if the results of the mass spectrometry measurement are much lower than those obtained previously (within 3-6 months) with an immunometric immunoassay, this possibility should be considered. In this event, alert Mayo Clinic Laboratories as soon as possible, and an attempt will be made to resolve the discrepancy.

Thyroglobulin by Immunoassay:

Thyroid autoantibodies may interfere with the measurement of Tg by immunometric methods leading to an underestimation of the Tg present. Heterophile antibodies may also interfere. Specimens with thyroglobulin concentrations greater than 250,000 ng/mL may "hook" and appear to have markedly lower levels when assayed by immunoassay.

Clinical Reference

1. Grebe SKG: Diagnosis and management of thyroid carcinoma: A focus on serum thyroglobulin. Expert Rev Endocrinol Metab. 2009;4:25-43

2. Cooper DS, Doherty GM, Haugen BR, et al: Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid. 2009;19:1167-1214

3. Pacini F, Catagana MG, Brilli L, Pentheroudakis G, on behalf of the ESMO Guidelines Working Group: Thyroid cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2010 May;21 Suppl 5:v214-v219

4. National Comprehensive Cancer Network (NCCN) guidelines for treatment of cancer by site: version 2.2013: Thyroid Carcinoma. Accessed August 25, 2020. Available at: https://www.uptodate.com/contents/differentiated-thyroid-cancer-role-of-serum-thyroglobulin

Performance

Method Description

The Access Thyroglobulin Antibody II assay (TgAb) is a sequential 2-step immunoenzymatic (sandwich) assay, performed on a Beckman Coulter Unicel DxI 800 system. A sample is added to a reaction vessel with paramagnetic particles coated with the thyroglobulin protein. The serum TgAb binds to the thyroglobulin. After incubation in a reaction vessel, materials bound to the solid phase are held in place by a magnetic field, while unbound materials are washed away. The thyroglobulin-alkaline phosphatase conjugate is added and binds to the TgAb. After the second incubation, materials bound to the solid phase are held in place by a magnetic field, while unbound materials are washed away. Then, the chemiluminescent substrate, Lumi-Phos 530 is added to the reaction vessel and light generated by the reaction is measured with a luminometer. The light production is directly proportional to the concentration of thyroglobulin antibody in the sample.(Instruction Manual: Thyroglobulin Antibody II Assay. Beckman Coulter, Inc; 2011)

Thyroglobulin by immunoassay is performed using a Beckman Coulter Unicel DxI 800 system. The Access Thyroglobulin (Tg) assay is a simultaneous 1-step immunoenzymatic (sandwich) assay. A sample is added to a reaction vessel, along with a biotinylated mixture of 4 monoclonal anti-Tg antibodies, streptavidin-coated paramagnetic particles, and monoclonal anti-Tg antibody alkaline phosphatase conjugate. The biotinylated antibodies and the serum Tg binds to the solid phase, while the conjugate antibody reacts with a different antigenic site on the Tg molecule. After incubation in a reaction vessel, materials bound to the solid phase are held in a magnetic field while unbound materials are washed away. Then, the chemiluminescent substrate Lumi-Phos 530 is added to the vessel and light generated by the reaction is measured with a luminometer. The light production is directly proportional to the concentration of Tg in the sample.(Instruction manual: Beckman Coulter Assay Manual. Beckamn-Coulter, Inc; 2010)

Thyroglobulin by mass spectrometry is performed as follows: serum is fractionated by a salting out method. Fractionated serum is then reduced, alkylated, and digested with trypsin. Tryptic fragments are further purified by immunocapture with antibodies specific to the individual fragments. Finally, these fragments are analyzed by liquid chromatography-tandem mass spectrometry (LC-MS/MS).(Unpublished Mayo method)

PDF Report

No

Day(s) and Time(s) Test Performed

TGABR and HTGT:

Monday through Friday; 6 a.m.-12 a.m.

Saturday; 6 a.m.-6 p.m.

TGMS:

Monday through Friday; 4 p.m.

Analytic Time

1 day if thyroglobulin antibody result is negative or 2 to 3 days if positive

Maximum Laboratory Time

6 days

Specimen Retention Time

12 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, approved or is exempt 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

86800

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
HTGR	Thyroglobulin Reflex to MS or IA	56536-6

Result ID	Test Result Name	Result LOINC Value
TGABR	Thyroglobulin Antibody, S	56536-6