Test Definition: TGMS

Thyroglobulin Mass Spectrometry, Serum

Overview

Useful For

Accurate measurement of serum thyroglobulin (Tg) in patients with known or suspected antithyroglobulin autoantibodies (TgAb) or heterophile antibodies (HAb)

Reflex testing of samples with previously unknown TgAb status that prove TgAb positive during immunoassay testing

Assisting in the differential diagnosis of early phase silent thyroiditis versus Graves disease in patients without thyroid cancer (the mass spectrometry-based method would only be required if these patients have TgAb or HAb)

Method Name

Tryptic Protein Fragmentation, purified with Immunocapture, Analysis by Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)

Testing is performed pursuant to an agreement with SISCAPA Assay Technologies Inc. covering US Patent 7,632,686.

NY State Available

Yes

Specimen

Specimen Type

Serum Red

Specimen Required

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube: Red top (serum gel/SST are **not** acceptable)
Submission Container/Tube: Plastic vial
Specimen Volume: 1.25 mL Serum
Collection Instructions: Centrifuge and aliquot serum into a plastic vial.

Forms

If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:
-Oncology Test Request (T729)
-Renal Diagnostics Test Request (T830)

Specimen Minimum Volume

Serum: 0.75 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	Reject
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum Red	Refrigerated (preferred)	7 days	
	Ambient	72 hours	
	Frozen	416 days	

Clinical & Interpretive

Clinical Information

Thyroglobulin (Tg) is a highly thyroid-specific large homodimeric glycoprotein (approximately 660 kDa). It contains 8% to 10% of carbohydrates and iodine. Thyroxine (T4) and triiodothyronine (T3) are synthesized on Tg 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 thyrotropin [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 highly organ-specific, serum Tg concentrations should be undetectable, or very low, after the thyroid gland is removed during primary treatment for thyroid cancer.

Current clinical guidelines consider a serum Tg of more than 1 ng/mL in an athyrotic individual as suspicious of possible residual or recurrent disease. To improve diagnostic accuracy, it is recommended this measurement be initially 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 thereafter, will 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 additional stimulated Tg measurements, neck ultrasound, or isotope imaging. A stimulated Tg above 2 ng/mL is considered suspicious.

There are 3 situations when serum Tg measurement may be misleading:
1. Remnant thyroid tissue (see above, 0.5-1 ng/mL Tg per gram)
2. Antithyroglobulin autoantibodies (TgAb), which occur in 15% to 30% of thyroid cancer patients, can lead to false-low measurement in immunometric assays (most commonly used); in competitive assays they may cause false-high results.
3. Heterophile antibodies (HAb), which are antibodies that can interact with the antibodies used in immunoassays, usually resulting in false-high measurements. Depending on the assay and the patient population, this can lead to

erroneously high results in 0.1% to 3.0% of patients.

Traditionally, there have been no reliable means to obtain accurate Tg measurements in patients with TgAb or HAb. However, 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

Healthy individuals with intact, functioning thyroid: < or =33 ng/mL

Interpretation

Current guidelines recommend measurement of thyroglobulin (Tg) with a sensitive immunoassay limit of quantification below 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 antithyroglobulin autoantibodies (TgAb) should also be measured, preferably with a method that allows detection of low concentrations of TgAb (< or =20 kIU/L). 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 below 1 ng/mL, the sample should be remeasured by mass spectrometry. This will allow confident detection of Tg in the presence of TgAb down to 0.2 ng/mL (risk of residual/recurrent disease <1-3%).

Samples from patients with Tg concentrations above 1 ng/mL (or 2 ng/mL; there is some discussion in the literature) might not require Tg measurement by mass spectrometry, because current guidelines suggest further work-up may be necessary above this threshold. However, the positive predictive value for residual/recurrent disease is modest at best when Tg is just above this threshold (3%-20%, rising in parallel with Tg concentrations up to 10 ng/mL) in athyrotic patients. Above 10 ng/mL, the risk of residual/recurrent disease is at least 25%, with many studies showing 60% to >90% risks. In selected patients, it might also be useful to test TgAb positive samples by mass spectrometry, even if the Tg concentration is above 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 between 1.0 and 10 ng/mL, owing to remnant Tg secretion, regardless of the presence or absence of residual/recurrent cancer.

There are no routine tests that can detect heterophile antibodies in patient samples. An unexpected high result is usually the tip-off in this case and should prompt remeasurement by mass spectrometry, which will provide a reliable result.

It has been determined that the presence of TgAb in serum can lead to underestimation of Tg concentration by immunoassay methods. When antibodies are present in samples with detectable Tg, the Tg values may be underestimated by up to 60% in immunoassays. In addition, 20% of specimens containing antibodies that are negative for Tg by immunoassay tested positive by liquid chromatography tandem mass spectrometry (LC-MS/MS); no results over 3 ng/mL by LC-MS/MS were observed.

In rare cases, when Tg is measured in patients with an intact thyroid gland who do not have thyroid cancer, substantial elevations will primarily be observed in very large goiters, highly active Graves disease, and, most pronounced, in the early phase of acute thyroiditis when follicular destruction releases massive amounts of stored Tg into the circulation. Levels are often well above 100 ng/mL.

Cautions

The test is most sensitive for detection of thyroid cancer recurrence when patients are off thyroid replacement long enough to have an elevated thyrotropin (TSH) prior to collecting the specimen. This test can also be used to follow patients with normal TSH; however, thyroglobulin (Tg) values from specimens with high TSH should not be compared with values with normal TSH, because TSH stimulation may change the baseline determinations, if any residual benign thyroid tissue is still present.

Rare normal amino acid sequence variations within 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, 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, the recommendation is to alert the lab as soon as possible, and they will attempt to resolve the discrepancy.

Clinical Reference

1. Grebe SKG. Diagnosis and management of thyroid carcinoma: a focus on serum thyroglobulin. Exp Rev Endocrinol Metab. 2009;4(1):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(11):1167-1214
3. Pacini F, Castagna MG, Brilli L, Pehteroudakis G, ESMO Guidelines Working Group. Thyroid cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2010;21Suppl 5:v214-v219
4. Haddad RI, Bischoff L, Applewhite M, et al. NCCN Guidelines Insights: Thyroid Carcinoma, Version 1.2025. J Natl Compr Canc Netw. 2025;23(7):e250033. doi:10.6004/jnccn.2025.0033
5. Tuttle RM. Differentiated thyroid cancer: Role of serum thyroglobulin. In: Cooper DS, Ross DS, Mulder JE, eds UpToDate. Updated August 5, 2025. Accessed January 6, 2026. Available at www.uptodate.com/contents/differentiated-thyroid-cancer-role-of-serum-thyroglobulin
6. Haugen BR, Alexander EK, Bible KC, et al. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid. 2016;26(1):1-133. doi:10.1089/thy.2015.0020

Performance

Method Description

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.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available
3 to 10 days

Specimen Retention Time
14 months

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 was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
84432

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
TGMS	Thyroglobulin, Mass Spec., S	3013-0

Result ID	Test Result Name	Result LOINC® Value
62749	Thyroglobulin, Mass Spec., S	3013-0
35998	Interpretation	59462-2