MAYO CLINIC LABORATORIES

Test Definition: TGQN

Thyroglobulin, Tumor Marker, Serum

Overview

Useful For

Quantitative thyroglobulin measurement as a part of evaluating suspected interference from heterophile antibodies causing a falsely elevated thyroglobulin result

Method Name

Only orderable as part of profile. For more information see IETG / Interference Evaluation Heterophile, Thyroglobulin Tumor Marker, Serum.

Immunoenzymatic Assay

NY State Available

Yes

Specimen

Specimen Type

Serum Red

Specimen Required

Only orderable as part of profile. For more information see IETG / Interference Evaluation Heterophile, Thyroglobulin Tumor Marker, Serum.

Patient Preparation: For 12 hours before specimen collection, patient **should not** take multivitamins or dietary supplements (eg, hair, skin, and nail supplements) containing biotin (vitamin B7)
Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube:
Preferred: Red top
Acceptable: None (serum gel/SST are **not** acceptable)
Submission Container/Tube: Plastic vial
Specimen Volume: 2.5 mL
Collection Instructions: Centrifuge and aliquot serum into a plastic vial.

Specimen Minimum Volume

2 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	OK

Gross icterus	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum Red	Ambient	7 days	
	Refrigerated (preferred)	14 days	
	Frozen	90 days	

Clinical & Interpretive

Clinical Information

Serum thyroglobulin (Tg) measurements are used 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.

Most often Tg is measured by immunometric assays as they are widely available in automated high-throughput instruments, have shorter turnaround times, and have functional sensitivities of 0.1 mcg/L or less. However, these immunoassays may be affected by the presence of both anti-thyroglobulin antibody (TgAb) and heterophile antibody interferences. The presence of TgAb might cause falsely low/undetectable Tg that can mask disease; whereas heterophile antibodies might cause falsely high Tg that can be mistaken for residual or recurrent disease.

Some patients, due to exposure to animal antigens, have developed heterophile antibodies, such as human anti-mouse antibodies, that can interfere with immunoassay testing by binding to the animal antibodies used in immunoassays. In some sandwich immunoassays, including those for Tg, the presence of heterophile antibodies in the patient's sample might lead to a false-positive result.

Although rare, false-negative assay results due to heterophile interference have also been reported in the literature. Manufacturers often add blocking agents to their reagents, but occasionally, patient samples containing heterophile antibodies are incompletely blocked and exhibit heterophile antibody interference. Subsequent reporting of erroneous results can have adverse effects on patient management, especially with tumor marker assays.

Dilution of the specimen prior to assay performance often yields unexpected nonlinear results in the presence of interfering substances such as heterophile antibodies and/or TgAb. Heterophile blocking tube treatment is also utilized for troubleshooting samples that exhibit potential heterophile interference. Finally, assessment of an analyte such as Tg with an alternative assay will often lead to apparent discrepant results in the presence of heterophile antibodies and/or TgAb interference.

Measurement of Tg by liquid chromatography tandem mass spectrometry (Tg-MS) has been introduced as a method for accurate Tg quantitation in the presence of TgAb and heterophile antibodies. Tg-MS assays are based on peptide quantitation after tryptic digestion and immunocapture of Tg-specific peptides. The advantage of trypsin digestion is that all proteins are cleaved, including both TgAb and heterophile antibodies, thus eliminating them as interferences.

Reference Values

Only orderable as part of profile. For more information see IETG / Interference Evaluation Heterophile, Thyroglobulin Tumor Marker, Serum.

< or =33 ng/mL

Interpretation

Specimens are evaluated for the presence of potential interfering anti-thyroglobulin (TgAb) and heterophile antibody interference in the Beckman Access thyroglobulin (Tg) immunoassay. While the presence of TgAb can result in falsely low Tg concentrations in the Beckman immunoassay, the presence of heterophile antibodies can result in falsely elevated Tg concentrations in the Beckman immunoassay. Following investigation of the presence of TgAb, heterophile antibody evaluation consists of pretreatment with commercial heterophile antibody blocking reagents, serial dilutions of the sample and testing on an alternate platform generally unaffected by the presence of heterophile antibodies or TgAb (ie, Tg liquid chromatography tandem mass spectrometry [Tg-MS]). The presence of heterophile antibody interference in the Beckman Access Tg immunoassay is not suspected when the results from the pretreatment, serial dilutions and the alternative platform (Tg-MS) agree with the original result.

The presence of heterophile antibody interference in the Beckman Access Tg immunoassay is suspected when 1 or more of the following are observed: a significant decrease in Tg concentration (>20%) upon treatment of the sample with heterophile antibody blocking reagents, lack of linearity upon serial dilutions, or a significant difference in Tg concentration on the alternate platform (Tg-MS). When a heterophile antibody interference affecting the Beckman Access immunoassay is suspected, the Tg result from this assay is considered false-positive and should not be used in clinical management.

Cautions

This heterophile antibody interference evaluation does not rule out the presence of other types interfering substances such as biotin.

There may be some samples with extremely strong heterophile interference. In such cases heterophile blocking reagents may not be able to block all the assay interference.

Specimens with thyroglobulin (Tg) concentrations greater than 250,000 ng/mL may "hook" and appear to have markedly lower levels.

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

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.

Clinical Reference

1. Barbesino G, Algeciras-Schimnich A, Bornhorst JA. False positives in thyroglobulin determinations due to the presence of heterophile antibodies: an underrecognized and consequential clinical problem. Endocr Pract. 2021;27(5):396-400. doi:10.1016/j.eprac.2020.10.011
2. American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer, Cooper DS, Doherty GM, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid. 2009;19(11):1167-1214
3. Netzel BC, Grebe SKG, Algeciras-Schimnich A. Usefulness of a thyroglobulin liquid chromatography-tandem mass spectrometry assay for evaluation of suspected heterophile interference. Clin Chem. 2014;60(7):1016-1018
4. Algeciras-Schimnich A. Thyroglobulin measurement in the management of patients with differentiated thyroid cancer. Crit Rev Clin Lab Sci. 2018;55(3):205-218
5. Ward G, Simpson A, Boscato L, Hickman PE. The investigation of interferences in immunoassay. Clin Biochem. 2017;50(18):1306-1311

Performance

Method Description

The Beckman Coulter UniCel DxI 800 is the instrument used for thyroglobulin tumor marker testing. The Access Thyroglobulin (2) assay is a simultaneous one-step immunoenzymatic (sandwich) assay. The sample is added to a reaction vessel, along with a biotinylated mixture of four monoclonal anti- thyroglobulin (Tg) antibodies, streptavidin-coated paramagnetic particles, and monoclonal anti-Tg antibody-alkaline phosphatase conjugate. The biotinylated antibodies and the serum thyroglobulin bind to the solid phase, while the conjugate antibody reacts with a different antigenic site on the thyroglobulin 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 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 thyroglobulin in the sample. The amount of analyte in the sample is determined from a stored, multi-point calibration curve (Package insert: Access Thyroglobulin. Beckman Coulter Inc; 09/2024).

PDF Report

No

Day(s) Performed

Monday through Saturday

Report Available

3 to 5 days

Specimen Retention Time

6 months

Performing Laboratory Location

Rochester

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 has been cleared, approved, or is exempt by the US 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

84432

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
TGQN	Thyroglobulin, Tumor Marker, S	96460-1

Result ID	Test Result Name	Result LOINC® Value
TGQN	Thyroglobulin, Tumor Marker, S	96460-1