

Discussion Thyroglobulin

Thyroglobulin (Tg) is a glycoprotein produced only by thyroid follicular cells and is therefore used as a tumor marker to monitor for the recurrence of differentiated thyroid cancer. However, antibodies to thyroglobulin are often produced in patients with thyroid cancer and can interfere with Tg immunoassays. Consequently, numerous guidelines include recommendations to test every Tg sample for anti-Tg antibodies when performing immunoassay Tg measurements.¹⁻⁴ The College of American Pathologists included Supplemental Questions in the TM-A 2020 mailing on how different laboratories approach anti-Tg antibody testing.

Of laboratories that responded, 26% performed Tg testing in-house, 40% sent the test to a reference laboratory, and 35% did not offer Tg testing. Of those labs that performed Tg testing in-house, 83% test anti-Tg consistent with recommendations (68% test both anti-Tg and Tg on every sample, 15% test Tg only after resulting a negative anti-Tg). The remaining laboratories (18%) that offer Tg testing either do not test anti-Tg (10%), or anti-Tg testing is performed only for specimens with abnormal or unexpected Tg levels (8%). The practices of these 18% of laboratories are not consistent with current guidelines.⁴

Laboratories also report anti-Tg results differently. Most laboratories (75%) report both anti-Tg and Tg together. A smaller group only reports anti-Tg if any is detected (16%) or if anti-Tg is above a threshold determined to cause interference (9%). While there are no clear guidelines on this issue, if both anti-Tg and Tg are reported, there should be a qualifying comment as to the likelihood of interference given different levels of anti-Tg detected. Similar comments are often included for potassium measurements in samples with various levels of hemolysis.

Tandem mass spectrometry testing for Tg is not susceptible to anti-Tg interference, and recent improvements have increased the sensitivity of these assays.^{5,6} It is therefore a useful test, particularly for samples with anti-Tg antibodies present. In this survey, 43% of laboratories reported offering reflex testing to mass spectrometry if anti-Tg is detected (3% in-house, 41% send-out). It should be noted that clinical guidelines support following anti-Tg levels for surveillance of thyroid cancer,^{1,3} which may be clinical practice when mass spectrometry testing is unavailable.

Anti-Tg antibody interference is an important analytic source of error in Tg monitoring by immunoassay. Each laboratory performing Tg testing by immunoassay should ensure appropriate implementation of an anti-Tg antibody testing and reporting strategy. Thyroid cancer patients with anti-thyroglobulin antibodies may need to be monitored using either the antibody levels alone (as these seem to correlate with tumor burden) or sensitive LC-MS/MS methodologies, traceable to the thyroglobulin standard reference material,⁶ if available.

Q: How does your laboratory incorporate anti-thyroglobulin antibody testing for patient testing?

Number (%) of responses	
37 (15%)	Specimen is first tested for anti-thyroglobulin antibodies and if negative thyroglobulin is tested and resultud
172 (68%)	Specimen is tested for both thyroglobulin and anti-thyroglobulin antibodies at the same time
19 (8%)	Anti-thyroglobulin antibody testing is performed only for specimens with abnormal or unexpected thyroglobulin levels
25 (10%)	We do not test for anti-thyroglobulin antibodies for any patient

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