How useful are autoantibodies in diagnosing thyroid disorders?

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Evidence-based answer

They're useful in diagnosing Graves' disease and, to a lesser extent, autoimmune thyroid disease; they can also help predict hypothyroidism. Thyrotropin receptor antibodies (TRAb) may be mildly elevated in a variety of thyroid disorders, but a TRAb level >10 U/L increases the probability of Graves' disease by a moderate to large degree (strength of recommendation [SOR]: **B**, cross-sectional study). A positive or negative thyroid peroxidase antibody (TPOAb) test increases or decreases the probability of autoimmune thyroid disease by only a small to moderate degree (SOR: **B**, 3 cross-sectional studies).

Thyroid-stimulating hormone (TSH) levels >2 mU/L, although still in the normal range, can be followed up with TPOAb testing to determine whether the patient has an increased probability of developing hypothyroidism (SOR: **B**, cohort study with a vague hypothyroidism reference standard).

Clinical commentary

In equivocal situations and pregnancy, antibodies may help

Under most circumstances, hypo- and hyperthyroid disorders can be diagnosed by testing TSH and free T_4, without thyroid antibody testing. Radionuclide uptake and scan provide diagnostic information for hyperthyroid states.

Thyroid antibody tests may help in equivocal situations, such as a normal radioiodine study in hyperthyroidism or evaluating the cause of hypothyroidism when infiltrative disorders, Reidel's thyroiditis, or subacute granulomatous thyroiditis are suspected. TPOAb may help predict the development of clinical hypothyroidism in patients with TSH in the range of 5-10 mU/L.

Pregnancy-related hyperthyroidism requires antibody testing because radioiodine scans are contraindicated. Antibody titers also may estimate the risk of pregnancy-related adverse outcomes.

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FAST TRACK

Thyroid autoantibodies can help diagnose Graves' disease and autoimmune thyroid disease; they can also help predict hypothyroidism

Evidence summary

Although TSH followed by free T_4 remain the initial screening tests for thyroid disorders, adding thyroid autoantibodies may refine the diagnosis. Three principal thyroid antibodies—TPOAb, thyroglobulin, and TRAb—can be positive in a variety of autoimmune thyroid disorders. TPOAb represents a specific antigen of antimicrosomal antibody (AMA). It has largely replaced AMA testing in most laboratories and clinical settings.

Antibodies point to Graves', autoimmune disorders

A cross-sectional study of 267 Singa-

TABLE

Autoimmune markers in thyroid disorders

THYROID DISORDERS	% OF STUDY PATIENTS	% TRAb >3.4 U/L		% TRAb >10 U/L		% AMA POSITIVE		% THYROGLOBULIN POSITIVE	
		LR+	LR-	LR+	LR-	LR+	LR-	LR+	LR-
Graves' disease	68	4.6	0.1	13	0.2	1.3	0.6	1.1	0.9
CAHT	20	0.2	4.7	0.1	2.8	1.4	0.2	1.4	0.6
Subacute thyroiditis	4	0.2	3.0	0	2.4	0.1	3.6	0.5	1.5
Thyroid nodules	6	0.2	3.4	0	2.4	0.1	4.1	0.1	2.0
Others	2	0.8	1.4	0	2.3	0	2.8	0	2.0

AMA, antimicrosomal antibodies; CAHT, chronic autoimmune (Hashimoto's) thyroiditis; LR+, positive likelihood ratio; LR-, negative likelihood ratio; TRAb, thyrotropin receptor antibodies

Source: Khoo DHC, et al.[1]

FAST TRACK

Pregnancy-related hyperthyroidism requires antibody testing because radioiodine scans are contraindicated

porean patients with previously diagnosed thyroid disorders measured TRAb, AMA, and thyroglobulin (**TABLE**). TRAb levels >10 U/L were found to have a positive likelihood ratio (LR+) of 13 and a negative likelihood ratio (LR–) of 0.2 for Graves' disease.[1]

Two cross-sectional studies compared AMA to TPOAb in healthy patients and those with autoimmune thyroid and nonthyroid disorders. One study of 235 people in a university endocrinology department found that a TPOAb level >190 U/mL yielded an LR+ of 10.75 and an LR– of 0.15 for chronic autoimmune (Hashimoto's) thyroiditis [CAHT]; the AMA-positive sera yielded an LR+ of 13.67 and an LR– of 0.19. Both TPOAb and AMA test characteristics were highly associated with CAHT (P<.001).

TPOAb is more sensitive than AMA and thyroglobulin

In the second study comparing AMA to TPOAb, the thyroid antibody test results of 32 healthy patients were compared with those of 262 clinic patients. In those with known thyroid dysfunction, TPOAb was found to be a more sensitive assay than AMA for autoimmune thyroid disorders. The sensitivity of TPOAb levels >3.1 U/mL was 88.1%; AMA sensitivity was 70.2% (P<.001).[2,3]

A cross-sectional study (National Health and Nutrition Examination Survey [NHANES III]) evaluated the presence of thyroid antibodies in 17,353 people representing the geographic and ethnic distribution of the United States, 95% of whom were categorized as free of thyroid disease.[4] The study found that TPOAb was more sensitive than thyroglobulin for diagnosing nonspecific thyroid disease. The diagnosis of thyroid disease was based on abnormal TSH and free T_4 levels. Abnormally high levels of TPOAb had an LR+ of 4.3 and LR– of 0.6 (P<.0001) for thyroid disease, compared with an LR+ of 3.4 and LR– of 0.7 (P<.01) for abnormally elevated thyroglobulin.

TSH + TPOAb more accurate than TSH in women

In the early 1970s, a cohort study of 2779 adults from Great Britain attempted to establish the incidence of thyroid disease in the general population by measuring TSH and TPOAb. Twenty years later, investigators restudied 1708 people from the original sample to determine the incidence of hypothyroidism and the prognostic value of these 2 biochemical markers for its development. At follow-up, the definition of a new case of hypothyroidism was based on an "intention to treat by the general practitioner by meeting clear biochemical criteria and/or symptoms."

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The initial presence of abnormally high serum TPOAb levels and TSH >2.0 mU/L predicted a 4.3% annual risk of developing hypothyroidism compared with a 2.6% annual risk with serum TSH >6.0 mU/L alone in women. This risk was not estimated for men because of the small number of cases.[5]

Recommendations

The American Association of Clinical Endocrinologists (AACE) makes no specific recommendations about laboratory testing of thyroid antibodies. Based on clinical judgment, the AACE states that antibodies may be considered in the workup of hyperthyroidism and hypothyroidism and to determine potential risk to the fetus in pregnant women diagnosed with Graves' disease.[6]

The National Academy of Clinical Biochemistry (NACB) recommends TPOAb measurements in patients who have Down syndrome, are pregnant, or have miscarried or failed in vitro fertilization. The NACB also advocates measuring TPOAb before treatment with amiodarone, lithium, interferon-α, or interleukin-2.[7] ■

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