THYROID TESTING

ASSESSING THYROID DISEASE IN YOUR PATIENTS

LabCorp

THYROID FUNCTION

LabCorp's expertise in thyroid testing provides clinicians with a comprehensive portfolio for their thyroid needs.

SCREENING FOR THYROID FUNCTION IS IMPORTANT.

- It is estimated that 20 million Americans suffer from some form of thyroid disease.[1]
- More than 70% of hyperthyroid cases are caused by overproduction of thyroid hormone by the thyroid gland (Graves' disease).[2]
- Hypothyroidism accounts for approximately 80% of patients with thyroid disorders.[3]

Diagnosing whether hyper- or hypothyroidism is caused by an autoimmune disease is critical for patient care and treatment.

- Graves' disease is the most common form of hyperthyroidism, and diagnostic testing indicators show a presence of thyroid-stimulating immunoglobulin (TSI) and TSH receptor antibodies (TRAb/TBII).[4]
- Hashimoto's thyroiditis is one of the most common forms of hypothyroidism,[5] and it is usually characterized by the development of antithyroid peroxidase (anti-TPO) and/or antithyroglobulin (anti-Tg) autoantibodies.[6]

LabCorp Offers Tests That Can Assist

in the diagnosis of thyroid disorders, including hyperthyroidism, hypothyroidism, and autoimmune diseases such as Graves' disease and Hashimoto's thyroiditis.

Clients also have direct access to specialized offerings and services through LabCorp's Specialty Testing Group, including Endocrine Sciences and Dianon Pathology. Endocrine Sciences is a research-quality laboratory specializing in highly specific and sensitive endocrine testing services. Dianon Pathology is a leader in providing anatomic pathology services.

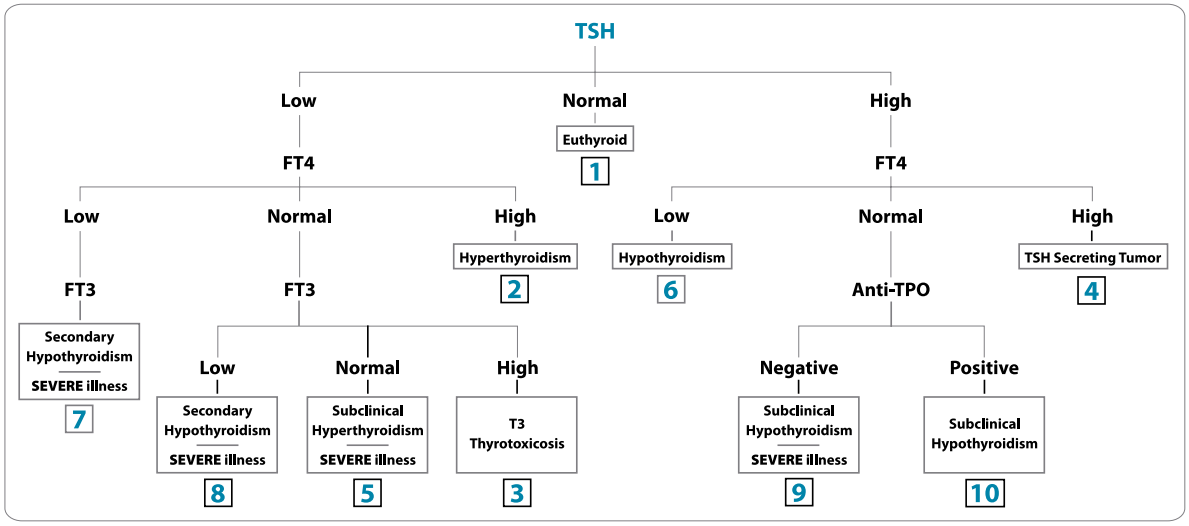
Clinical Application

LabCorp offers several test options to assist with your diagnosis, including:

- Thyroid cascade testing to assist with the diagnosis of thyroid dysfunction.
- A full menu of thyroid tests for diagnosis of thyroid function and autoimmune disease.
- Free thyroxine (T4) and free triiodothyronine (T3) assays by dialysis and HPLC/MS-MS, which provides enhanced accuracy over commonly used analog (automated) methods.[7-10] Dialysis and HPLC/MS-MS may be preferred for evaluating patients who have conditions that impact protein binding capacity, including those who:
  - Have congenital absence of thyroxine-binding protein (TBG).[7]
  - Are pregnant.[11]
  - Are taking oral contraceptives or undergoing hormone therapy.[12]
  - Are taking antipsychotic medications.[13]
  - Have been diagnosed with a malignancy or other critical illness.[14]

LabCorp Thyroid Cascade

The panel is based on a cascade algorithm that selects specific assays based on the results of previously performed tests, which are necessary to arrive at the most appropriate laboratory diagnosis.



Note: Please refer to LabCorp's Thyroid Cascade Technical Review (L964) for additional information regarding interpretation and references for thyroid cascade testing.

Thyroid Cancer Testing

LabCorp offers comprehensive testing for the diagnosis and monitoring of thyroid cancer.

Detection and diagnosis of thyroid cancer is important.

- Thyroid nodules are common, particularly in older adults. While fewer than 1 in 10 adults have palpable thyroid nodules, when thyroid ultrasonography is performed up to half of adults examined are found to have nodules.[15] About 1 in 20 thyroid nodules is cancerous.[16]
- A thyroid biopsy using fine needle aspiration can differentiate between malignant and benign nodules.
- When diagnosed and treated, common thyroid tumors present an 80% to 90% survival rate at 10 years, with survival rates of greater than 97% for younger patients who are treated appropriately.[16]

LabCorp offers serum calcitonin testing for patients with suspected medullary thyroid carcinoma (MTC)[17]

- Serum calcitonin testing is useful for the detection and confirmation of C-cell hyperplasia (the precursor of MTC) as well as a tumor marker for diagnosis and management of MTC.
- Preoperative serum calcitonin is reported to roughly correlate with tumor weight or extent of disease; therefore, postoperative levels also have prognostic application.

LabCorp also offers molecular blood testing for RET gene mutations.

- Testing includes mutation analysis by sequencing of exons 10, 11, 13, 14, 15, and 16 of the RET proto-oncogene.
- Mutations found in these exons have been associated with patients that develop multiple endocrine neoplasia type 2 (MEN 2) and/or familial medullary thyroid carcinoma (FMTC). Testing for RET germline mutations is recommended in patients with a family or personal history consistent with MEN 2 or FMTC.[17]
- Known mutation testing of RET mutations is also available for patients with family members who have previously identified mutations.

LabCorp and Dianon Pathology, a member of the LabCorp Specialty Testing Group, offer several test options for detecting and diagnosing thyroid cancer using fine needle aspiration (FNA) biopsies.

Fine Needle Aspirate Collection Kits

LabCorp and Dianon Pathology both offer fine needle aspirate collection kits that employ a space-saving design to assist with efficient biopsy collection. The collection kits include:

- 8 slides with fixative containers and 1 CytoLyt® vial.
- Convenient design to hold specimen containers in place during the aspiration procedure.
- Specialized thyroid FNA kits with an option that includes a vial of RNARetain® for molecular testing

Dianon Test Kit

Dianon Thyroid FNA Kit with RNARetain®

If FNA results are indeterminate, LabCorp and Dianon Pathology offer ThyGenX® with reflex to ThyraMIR™. These laboratories also offer an option for the Thyroid FNA test with indeterminate reflex to ThyGenX® only, and utilize the Bethesda system nomenclature for thyroid FNA cytology results.

Dianon Pathology also provides the following cytopathology services, including:

- Specialized endocrine pathology requisition
- Full-color reports with photomicrographs
- Dedicated cytopathology staff with expertise that includes thyroid biopsies

ThyGenX® and ThyGenX® with reflex to ThyraMIR™ are performed by Interpace Diagnostics as a send-out from LabCorp.

- ThyGenX® includes markers for BRAF, KRAS, HRAS, NRAS, PIK3CA, RET/PTC1, RET/PTC3, and PAX8/PPARgamma
- ThyraMIR™ includes 10 miRNA markers and occurs if ThyGenX® is negative or not fully indicative of malignancy
- Combined negative predictive value (likelihood negative result is truly benign) found to be 94%[22]
- Combined positive predictive value (likelihood positive result is malignant) found to be 74%[22]
- Predicted to result in up to 85% reduction in unnecessary diagnostic surgeries[22]

Thyroid Cancer Monitoring

Once thyroid cancer has been diagnosed and treated, patients must be closely monitored for cancer recurrence.

- Thyroglobulin is a protein secreted only by thyroid tissue.
- After thyroidectomy, thyroglobulin levels are commonly used to detect recurrence of thyroid cancer.[18]
- Patients with MTC are also monitored with calcitonin and CEA testing as recommended by American Thyroid Association guidelines.[17]

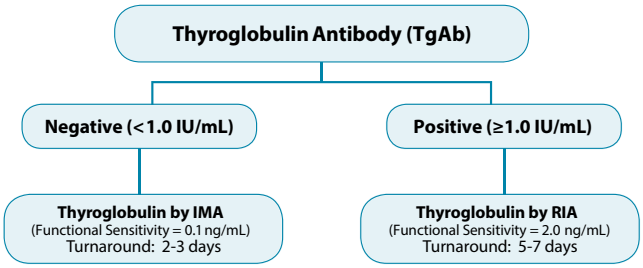
LabCorp offers enhanced sensitivity for thyroglobulin and antithyroglobulin testing to monitor for thyroid cancer recurrence.

- Serum thyroglobulin (Tg) is primarily used in the postoperative management of differentiated thyroid cancer (DTC).
- Thyroglobulin antibody (TgAb) is detected in an estimated 25% of patients with DCT.[19] In those patients, there is a risk of interference with Tg measurement using immunometric (IMA) methods that can lead to false-negative (inappropriately low or undetectable) Tg results.[4,19,20] Even low antibody concentrations can interfere with Tg measurements.[4]
- LabCorp's Thyroglobulin With Antithyroglobulin Antibody test offers a dual assay strategy for Tg in an effort to minimize the potential effect of TgAb interference.
  - Specimens are tested for TgAb using a sensitive IMA.
  - Specimens with TgAb below the detectable limit (<1.0 IU/mL) are tested for Tg by sensitive second-generation IMA.
  - Specimens with any measurable TgAb levels (≥1.0 IU/mL) are tested for Tg by radioimmunoassay (RIA), which is less prone to interference by TgAb.[4]
- Clinicians who require extended (I year) specimen storage may order LabCorp's Comprehensive Thyroglobulin Profile, which is performed by Endocrine Sciences, a member of the LabCorp Specialty Testing Group.

LabCorp offers thyroglobulin testing for lymph node aspirate diluted in saline.

- Aspirate material from lymph nodes can be tested for the presence of thyroglobulin if there is suspicion that thyroid cancer has spread to the lymphatic system.[21]
- The lymph node aspirate is collected and washed into a 1 mL saline solution, and the saline solution is tested for the presence of thyroglobulin.

Thyroglobulin With Antithyroid Antibody Test



Lymph Node Aspirate Collection Kit

A convenient lymph node aspirate collection kit is available that includes instructions and a vial containing 1 mL of saline solution.

Thyroid Testing Services

Thyroid Function: Testing for Hyper- and Hypothyroidism

Test Name	Number	Methodology	Specimen	Container	Storage
Thyroid Cascade Profile: TSH with automatic reflex (as diagnostically warranted) to FT_4, FT_3, and/or TPO antibodies	**330015**	ECLIA	2.0 mL serum Minimum: 1.0 mL	Red-top tube or gel-barrier tube	Refrigerate
Thyroxine (T_4)	**001149**	CEDIA	Serum: 1 mL (adult), 0.8 mL (pediatric) Minimum: 0.5 mL (adult), 0.3 mL (pediatric)	Red-top tube or gel-barrier tube	Refrigerate
Thyroid-stimulating Hormone (TSH)	**004259**	ECLIA	0.8 mL serum Minimum: 0.3 mL	Red-top tube or gel-barrier tube	Refrigerate
Thyroxine (T_4) Free, Dialysis/Mass Spectrometry++	**501902***	Direct dialysis mass spectrometry; HPLC/MS	1.0 mL serum **or** plasma Minimum: 0.5 mL	Red-top tube or lavender-top (EDTA) tube	**Freeze**
Thyroxine (T_4), Free, Direct, Serum	**001974**	ECLIA	0.8 mL serum Minimum: 0.3 mL	Red-top tube or gel-barrier tube	Refrigerate
Thyroxine-binding Globulin (TBG), Serum	**001735**	ICMA	0.5 mL serum Minimum: 0.3 mL	Red-top tube or gel-barrier tube	Refrigerate
Triiodothyronine (T_3)	**002188**	ECLIA	0.8 mL serum Minimum: 0.3 mL	Red-top or gel-barrier tube	Refrigerate
Triiodothyronine (T_3), Free, Serum	**010389**	ECLIA	0.8 mL serum Minimum: 0.3 mL	Red-top tube or gel-barrier tube	Refrigerate
Triiodothyronine, Free (FT_3), Dialysis and LC-MS/MS++	**503600***	Equilibrium dialysis and HPLC/MS-MS	1.0 mL serum Minimum: 0.3 mL	Red-top tube, gel-barrier tube, lavender-top (EDTA) tube, or green-top (sodium heparin) tube	**Freeze** (preferred) or refrigerate

General Autoimmune Screen: Testing for Hyper- and Hypothyroidism

Thyroglobulin Antibody	**006685**	ICMA	1.0 mL serum	Red-top tube or gel-barrier tube	Room Temperature
Thyroid Antibodies	**006684**	See individual test descriptions	1.0 mL serum	Red-top tube or gel-barrier tube	Refrigerate
Thyroid Peroxidase (TPO) Antibodies	**006676**	ECLIA	0.8 mL serum Minimum: 0.3 mL	Red-top tube or gel-barrier tube	Refrigerate

Graves' Disease Autoimmune Screen

Thyroid-Stimulating Immunoglobulin (TSI)	**140749**	Chinese hamster ovary cell line transfected with thyrotropin receptor and a luciferase reporter gene	3.0 mL serum Minimum: 0.3 mL	Red-top tube or gel-barrier tube	Refrigerate
TSH Receptor Antibody (TRAb/TBII)	**500538***	Binding inhibition assay	1.0 mL serum Minimum: 0.3 mL	Red-top tube or gel-barrier tube	Ambient (same day) or **freeze**

Visit the online Test Menu at **www.LabCorp.com** for full test information, including CPT codes and current specimen collection requirements.

* Testing performed at Endocrine Sciences.
++ Free T_4 and free T_3 by dialysis and HPLC/MS-MS should be used for patients known to have abnormal binding proteins due to pregnancy, hormone replacement, or critical illnesses.

Thyroid Cancer Screen: Testing for Diagnosis of Thyroid Cancer

Test Name	Number	Methodology	Specimen	Container	Storage
Calcitonin (Thyrocalcitonin)	**004895**	ICMA	1.0 mL serum Minimum: 0.4 mL	Red-top tube or gel-barrier tube	**Freeze**
Fine Needle Aspiration Cytology	**009001**	Morphologic analysis	Aspirated material Recommend using LabCorp Collection kit: Catalog N° FNAK10	Slide(s); Coplin jar(s)	Refrigerate
MEN2: RET Gene Sequencing (for hereditary thyroid cancer)	**504008***	PCR, sequencing	4.0 mL whole blood Minimum: 1.0 mL	Lavender-top (EDTA) tube	Ambient or refrigerate

Thyroid Cancer Monitoring: Testing for Recurrence of Thyroid Cancer

Calcitonin (Thyrocalcitonin)	**004895**	ICMA	1.0 mL serum Minimum: 0.4 mL	Red-top tube or gel-barrier tube	**Freeze**
Carcinoembryonic Antigen (CEA)	**002139**	ECLIA	0.8 mL serum Minimum: 0.3 mL	Red-top tube or gel-barrier tube	Refrigerate
Thyroglobulin Antibody and Thyroglobulin, IMA or LC/MS-MS	**042045**	IMA or LC/MS-MS	3 mL serum Minimum: 2 mL	Red-top tube or gel-barrier tube	Room temperature
Thyroglobulin Antibody and Thyroglobulin, IMA or RIA	**042060**	IMA or RIA	3 mL serum Minimum: 2 mL	Red-top tube or gel-barrier tube	Room temperature
Thyroglobulin, Lymph Node Aspirate	**502380***	ICMA	Lymph node aspirate in 1.0 mL saline Recommend using LabCorp Collection kit: Catalog N° 38621G	Lymph Node Collection Kit and saline vial	**Freeze**

Visit the online test menu at **www.LabCorp.com** for full test information, including CPT codes and current specimen collection requirements.

***** Testing performed at Endocrine Sciences.
++ Free T_4 and free T_3 by dialysis and HPLC/MS-MS should be used for patients known to have abnormal binding proteins due to pregnancy, hormone replacement, or critical illnesses.

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