GENOVA DIAGNOSTICS EUROPE

46-50 Coombe Road
New Malden
Surrey KT3 4QF

63 Zillicoa Street
Asheville, NC 28801

Patient: **SAMPLE PATIENT**
DOB:
Sex:
MRN:

4402 Thyroid Plus - Serum

Methodology: Chemiluminescent, RIA

Comprehensive Thyroid Assessment

Central Regulation

		Reference Range			Reference Range
Thyroid Stimulating Hormone (TSH)	<0.01	0.40-2.50 microIU/mL	Free Thyroxine (FT4)	24.58	7.86-14.41 pmol/L

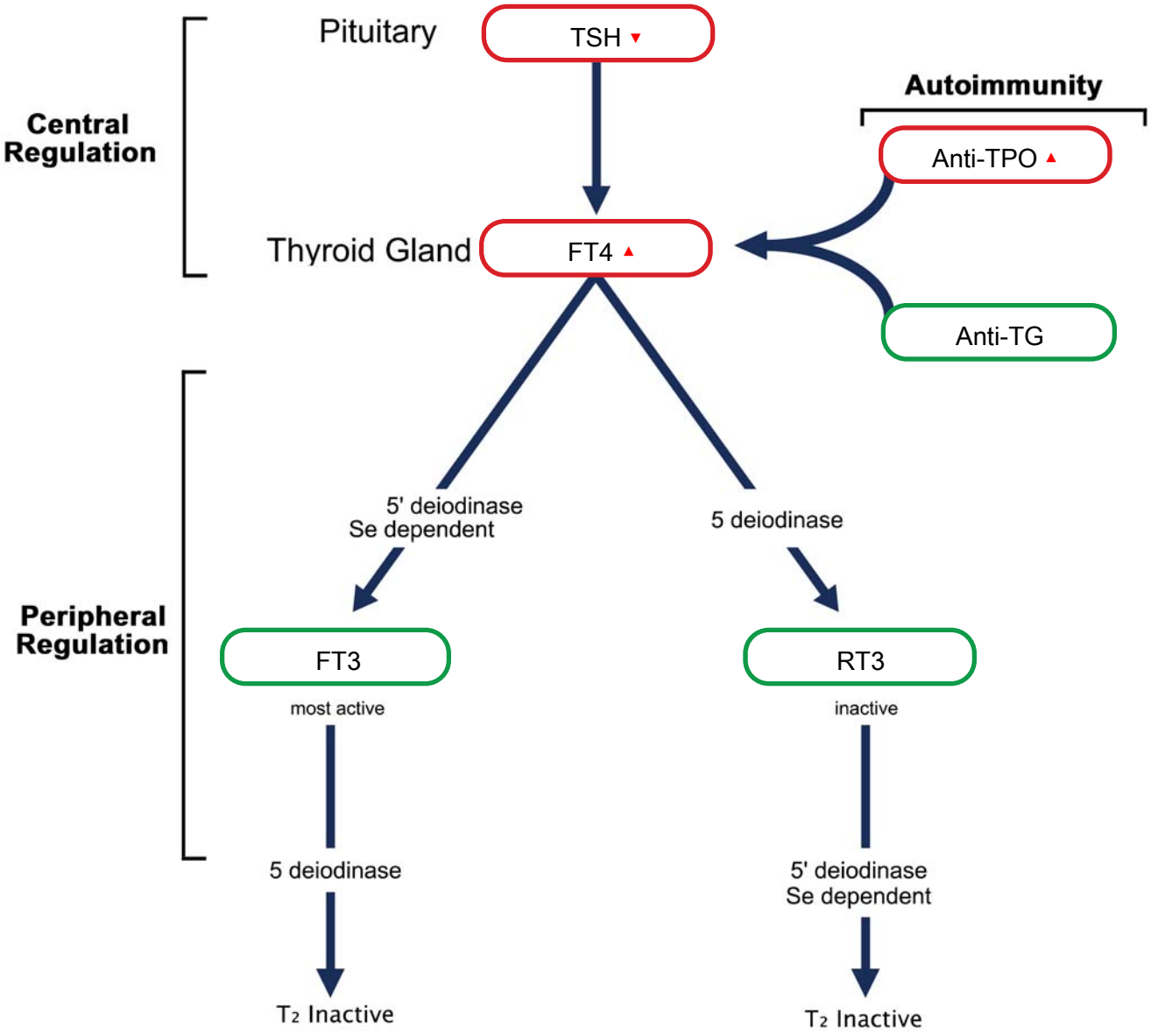
Peripheral Regulation

		Reference Range			Reference Range
Free Triiodothyronine (FT3)	4.3	3.8-6.0 pmol/L	Reverse T3 (RT3) ♦	0.45	0.14-0.54 nmol/L
Total Thyroxine (TT4)	127.00	78.38-157.40 nmol/L	FT4:FT3 Ratio :	5.7	

Thyroid Antibodies

		Reference Range			Reference Range
Anti-Thyroglobulin Antibody (Anti-TG)	<0.9	<4.0 IU/mL	Anti-Thyroid Peroxidase (Anti-TPO)	12	<9 IU/mL

Thyroid Metabolism-At-A-Glance



Commentary

Please note the reference ranges for Total Thyroxine (TT4), Thyroid Stimulating Hormone (TSH), Free Thyroxine (FT4), Free Triiodothyronine(FT3), Thyroglobulin (TG), and Peroxidase (TPO) have been updated.

Commentary is provided to the practitioner for educational purposes, and should not be interpreted as diagnostic or as treatment recommendations. Diagnosis and treatment decisions are the practitioner's responsibility.

Thyroid hormones play an integral role in regulating the body's temperature and production of energy. In addition, thyroid hormones regulate protein synthesis and enzyme production at the cellular level. Thyroid hormone deficiencies may be suspected clinically whenever an insidious slowing of the metabolism is observed as might be the case with protracted fatigue, low energy, depression, mental asthenia, coldness or cold extremities, fluid retention, or diffuse hair loss. Conversely, thyroid hormone excess may be suspected when the opposite clinical picture is observed: excess energy, palpitations, anxiety, nervousness ("like I'm going to jump out of my skin"), short sleep, or feeling like "everything is moving too fast". Physically, such thyroid excess may present as heat intolerance, diarrhea, idiopathic weight loss without loss of appetite, fine tremor of the extremities, and in prolonged cases, exophthalmia.

Common Laboratory Patterns in Thyroidal Illness

	TSH	FT4	FT3	rT3	α-TPO	α-Tg
Early Hashimoto's	nl	nl	nl	nl	±	↑
Late Hashimoto's	↑	↓	↓	±	↑	±
Early Graves'	↓	nl	↑	±	↑	↑
Late Graves'	↓	↑	↑	↑	↑	±
Wilson's Syndrome, Low T3, or ESS	nl	nl	↓	↑	–	–
Early DeQuervain's	↓	↑	↑	±	–	–
Late DeQuervain's	↑	↓	↓	±	±	±
Plummer's Disease	↓	↑	↑↑	±	–	–

nl = normal
± = indeterminate

Laboratory Results

Thyroid-stimulating hormone (TSH) is measured to be below the reference range, indicating decreased production and release of TSH from the pituitary gland.

If Free T4 (FT4) is elevated, this may be indicative of primary hyperthyroidism, Graves' disease, toxic nodular goiter, or exogenous thyroid hormone therapy. In patients undergoing thyroid replacement therapy, severely depressed levels of TSH may indicate excessive thyroid hormone supplementation.

In early and recurrent Graves' disease, Free T3 (FT3) may be elevated while FT4 may be normal. Elevated thyroid autoantibodies are a common finding in all variants of Graves' disease.

Similarly, in toxic adenoma of the thyroid gland (Plummer's disease), FT3 is sharply elevated while TSH is markedly depressed. Almost invariably, a unilateral nodule ("hot nodule") is palpable on physical examination.

In sub-acute (De Quervain's) thyroiditis, initially TSH is low while FT4 and FT3 may be quite elevated; autoantibodies are usually not detectable in the serum. Fever, malaise, and soreness in the neck on palpation belie the suspected etiology: viral infection. The mumps virus, coxsackievirus and adenoviruses have all been implicated in sub-acute thyroiditis. Erythrocyte sedimentation rate values are usually elevated at this stage. As sub-acute thyroiditis progresses, TSH levels will rise and both FT3 and FT4 levels will fall, eventually settling into a clinical picture of hypothyroidism.

If FT4 is also depressed, this could indicate secondary hypothyroidism with dysfunction at the level of the

Commentary

pituitary, or possibly (though extremely rare) tertiary hypothyroidism with inadequate production and release of thyrotropin-releasing hormone (TRH) from the hypothalamus. A TRH-stimulation test can confirm this rare disorder. A pituitary adenoma or pituitary destruction may cause secondary hypothyroidism.

Prescription drugs like corticosteroids (e.g., prednisone) and dopamine can suppress TSH production, leading to reduced T4 production. Endogenous hypersecretion of corticosteroids (Cushing's syndrome) can also lead to low TSH and FT4 values, mimicking secondary hypothyroidism.

Free T4 (FT4) is measured above the reference range indicating a hyperthyroid state. FT4 measures the biologically active fraction of total T4, the majority of which is bound by protein carriers in the serum and is therefore inactive. If TSH is depressed, this is typical of a primary hyperthyroidism and may be indicative of Graves' disease, toxic nodular goiter, or exogenous thyroid hormone therapy. In patients undergoing thyroid replacement therapy, severely depressed levels of TSH may indicate excessive thyroid hormone supplementation.

In any thyroiditis, FT4 may be elevated, especially in the early stages of such conditions. Elevated thyroidal autoantibodies (anti-thyroglobulin, anti-thyroid peroxidase, or anti-TSH) are a common but by no means necessary finding in such conditions.

In subacute (De Quervain's) thyroiditis, initially TSH is low while FT4 and free T3 (FT3) may be quite elevated; autoantibodies are usually not detectable in the serum. Fever, malaise, and soreness in the neck on palpation belie the suspected etiology: viral infection. The mumps virus, coxsackievirus and adenoviruses have all been implicated. Erythrocyte sedimentation rate values are usually elevated in early stages. As sub-acute thyroiditis progresses, TSH levels will rise and both FT3 and FT4 levels will fall, eventually settling into a clinical picture of hypothyroidism.

Free T3 (FT3) is measured to be within the reference range. FT3 measures the biologically active fraction of total T3, the majority of which is bound by protein carriers in the serum and is therefore inactive. T3 is 3-5 times as physiologically active as T4, and 80% of the circulating T3 is from the peripheral conversion of T4 predominately in liver and kidney.

Reverse T3 is measured to be within the reference range.

Levels of anti-thyroglobulin antibodies are within the reference range. Thyroglobulin (Tg) is a large glycoprotein synthesized in response to TSH stimulation. T4 and, to a limited extent, T3 are produced when tyrosine residues in Tg are iodinated and coupled together under the action of thyroid peroxidase (TPO). Subsequent proteolysis of Tg in cellular lysosomes allows for the release of T4 and T3 from the thyroid gland into the systemic circulation.

Abnormal levels of anti-thyroid peroxidase (TPO) antibodies were found in this patient. Thyroid peroxidase is a heme-containing enzyme that is necessary for the oxidation of iodide ions and for using hydrogen peroxide for the incorporation of these iodide ions into the tyrosine residues of thyroglobulin. Antibodies to TPO can form whenever there is leakage of thyroid cellular contents, stimulating an autoimmune response. Any variant of thyroiditis can initiate such cellular leakage.

In any thyroiditis with autoimmune antibodies, antibody levels alone are insufficient markers to predict hyper- or hypo-thyroidism. FT4, FT3 and TSH levels are necessary to make this diagnosis.

In Hashimoto's thyroiditis, the most common cause of hypothyroidism in the U.S., lymphocytes become sensitized to thyroidal antigens and autoantibodies are formed that react with these antigens. In early stages, anti-Tg antibodies are markedly elevated whereas anti-TPO antibodies are only slightly elevated. In later stages, anti-Tg antibodies may decrease, but anti-TPO antibodies will remain elevated, often for many years. As Hashimoto's thyroiditis progresses, lymphocyte infiltration can destroy normal thyroid architecture, and the destruction of the gland can result in falling FT4 and FT3 levels and rising TSH levels. In early stages, secondary to the effect of TSH stimulation and lymphocyte infiltration, the thyroid gland is usually painlessly enlarged and palpable.

Commentary

The performance characteristics of all assays have been verified by Genova Diagnostics Inc. Assays are cleared by the U.S. Food and Drug Administration,
unless otherwise noted with ♦.