

Patient: **SAMPLE PATIENT**

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Completed:

Age: 86

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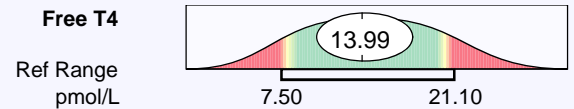
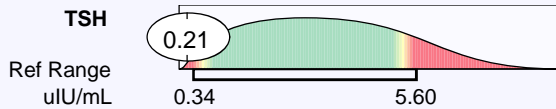
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MRN:

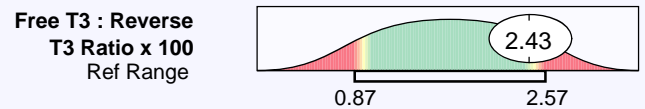
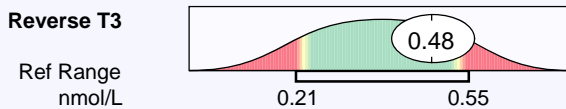
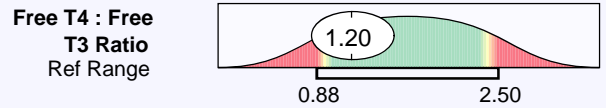
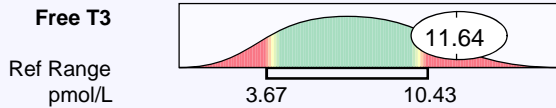
SAMPLE REPORT

Central Thyroid Regulation & Activity



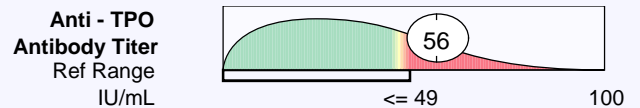
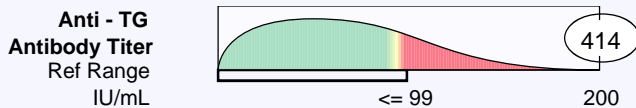
Histograms represent idealized data based upon large populations

Peripheral Thyroid Function



Histograms represent idealized data based upon large populations

Thyroid Auto Immunity



Histograms represent idealized data based upon large populations

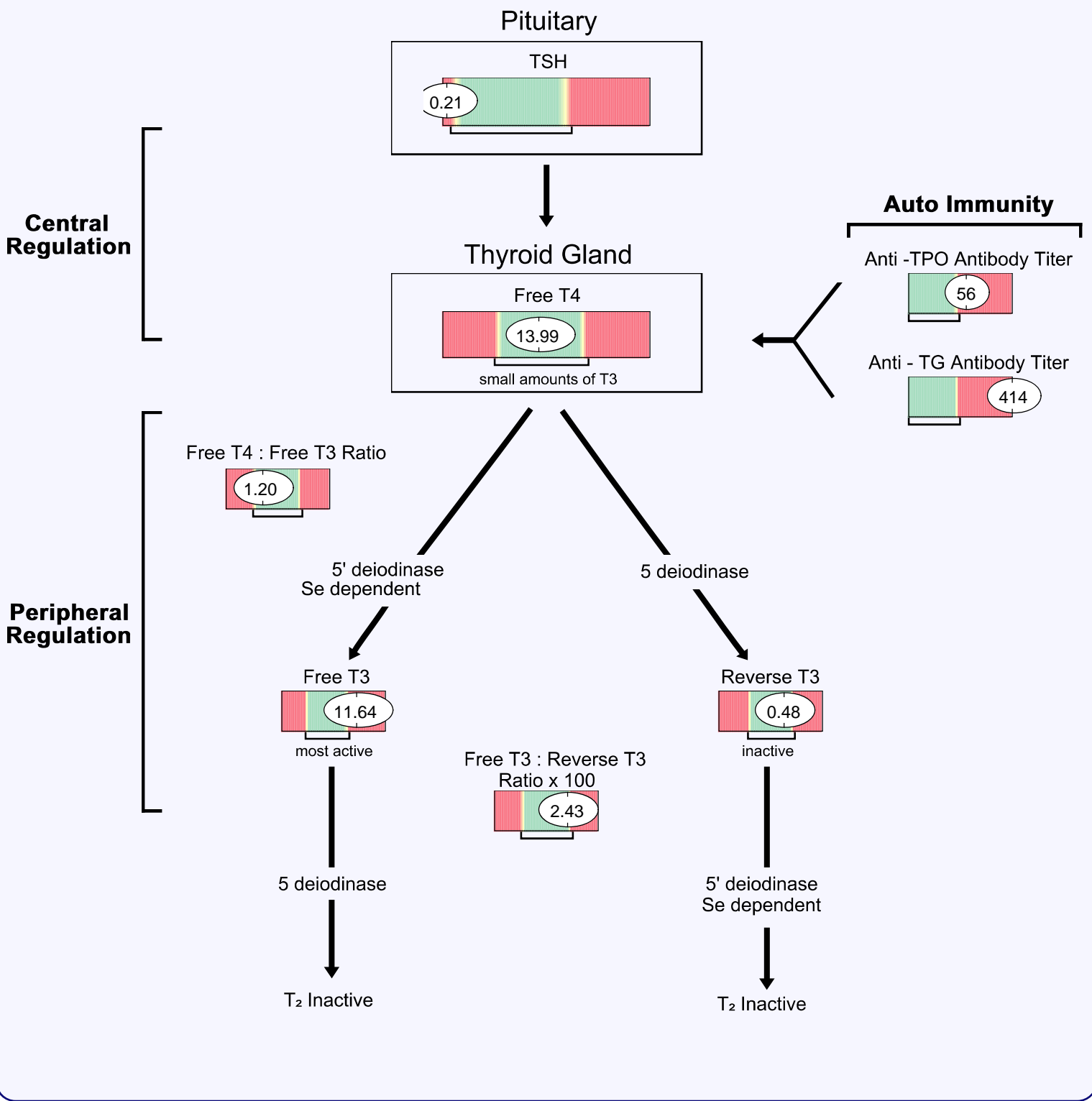
This test has been developed and its performance characteristics determined by GSDL, Inc. It has not been cleared or approved by the U.S. Food and Drug Administration.

Thyroid Metabolism Summary

Thyroid hormone production is centrally regulated (hypothalamus-pituitary-thyroid axis) but thyroxine (T4) from the thyroid gland is peripherally transformed in liver and kidney cells into T3 and reverse T3 (rT3). Ultimately, the site of action for thyroid hormones is at cell nuclei throughout the body, where T3 is five times as potent as T4, and rT3 is completely inert. Thyroid dysfunction may occur even when the hypothalamus-pituitary-thyroid axis is operating adequately. Problems with peripheral conversion (reflected by T3 and rT3 levels) and/or with immune system interference in the form of auto-antibodies (reflected by anti-thyroglobulin and anti-thyroidal peroxidase antibodies) may still affect thyroid hormone production or its action at the cellular level. Thus to achieve a comprehensive assessment of thyroid adequacy, central regulation, peripheral conversion, and auto-immune involvement must be thoroughly evaluated.

SAMPLE REPORT

Thyroid Metabolism at a Glance



Commentary

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.

Commentary

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

Free T3 (FT3) is measured to be above 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.

In most cases, FT3 is elevated only when FT4 is also elevated. In these cases, the increased T3 production is merely a consequence of increased T4 production, and indicates a hyperthyroid state. A few exceptions to this general rule exist.

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

In toxic adenoma of the thyroid gland (Plummer's disease), FT3 may be sharply elevated while TSH is markedly depressed, and FT4 may be normal or high normal. Almost invariably, a unilateral nodule ("hot nodule") is palpable on physical examination.

Exogenous supplementation of T3 (e.g., Cytomel) or of desiccated thyroid (Armour) could result in elevated levels of FT3.

Reverse T3 is measured to be within the reference range.

The free T4: free T3 ratio has been determined by the Department of Medical Science and is based upon current scientific literature and consensus medical opinion. The FT4: FT3 ratio is within the reference range.

The free T3: reverse T3 ratio has been determined by the Department of Medical Science and is based upon current scientific literature and consensus medical opinion. The FT3: rT3 ratio is within the reference range.

Abnormal levels of anti-thyroglobulin antibodies were found in this patient. 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.

Antibodies to thyroglobulin can form any time there is significant leakage of thyroid cellular contents, stimulating an autoimmune response. Any variant of thyroiditis can initiate such cellular leakage. Typically, anti-Tg antibodies form more quickly in thyroiditis than anti-TPO antibodies, but anti-Tg antibody levels also tend to normalize over time, especially in chronic thyroiditis.

Anti-Tg antibody levels may be elevated in Grave's disease or in Hashimoto's thyroiditis. In either case, antibody

Commentary

levels alone are insufficient markers to predict hyper- or hypothyroidism. 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.

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.

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