

Patient: **SAMPLE  
PATIENT**

**Order Number:**

Completed:

Age: 51

Received:

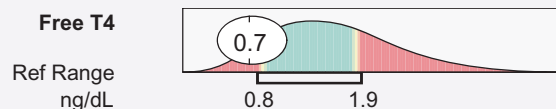
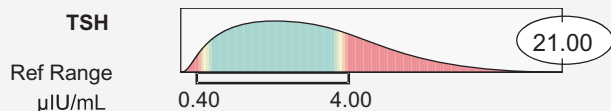
Sex: M

Collected:

MRN:

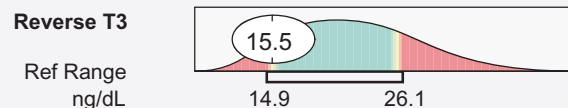
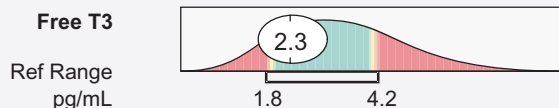
## SAMPLE REPORT

### Central Thyroid Regulation & Activity



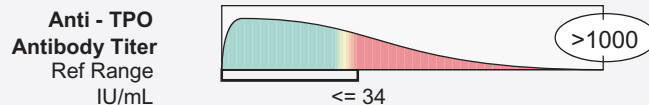
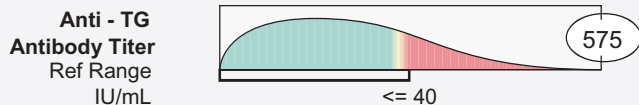
Histograms represent idealized data based upon large populations

### Peripheral Thyroid Function



Histograms represent idealized data based upon large populations

### Thyroid Auto Immunity



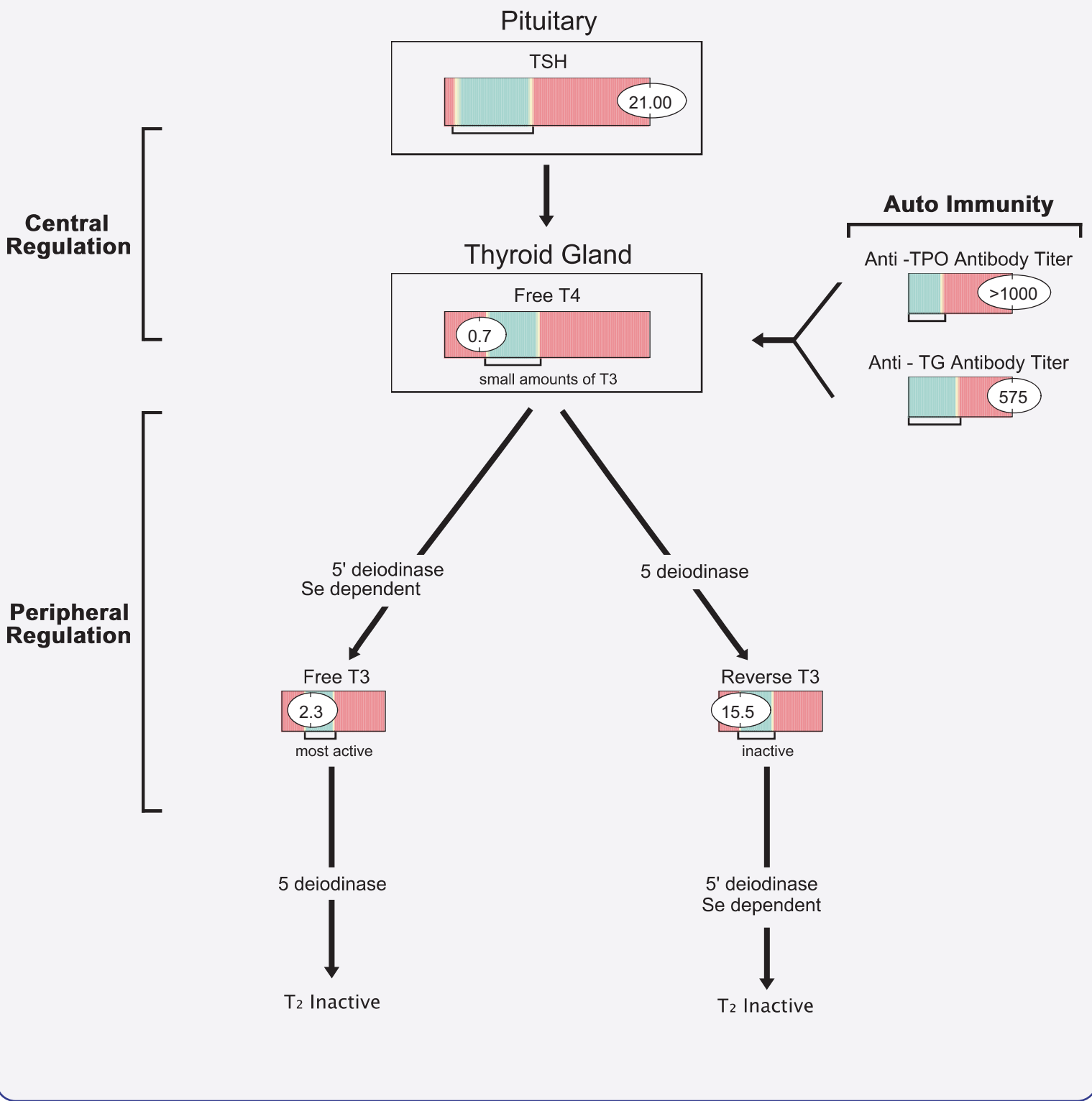
Histograms represent idealized data based upon large populations

The test for Reverse T3 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.

### Thyroid Metabolism at a Glance



## Commentary

Free T4: ng/dL x 12.87 = pmol/L

Free T3: pg/mL x 1.54 = pmol/L

Reverse T3: ng/dL x 0.0154 = nmol/L

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

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	$\alpha$ -TPO	$\alpha$ -Tg
Early Hashimoto's	nl	nl	nl	nl	$\pm$	$\uparrow$
Late Hashimoto's	$\uparrow$	$\downarrow$	$\downarrow$	$\pm$	$\uparrow$	$\pm$
Early Graves'	$\downarrow$	nl	$\uparrow$	$\pm$	$\uparrow$	$\uparrow$
Late Graves'	$\downarrow$	$\uparrow$	$\uparrow$	$\uparrow$	$\uparrow$	$\pm$
Wilson's Syndrome, Low T3, or ESS	nl	nl	$\downarrow$	$\uparrow$	–	–
Early DeQuervain's	$\downarrow$	$\uparrow$	$\uparrow$	$\pm$	–	–
Late DeQuervain's	$\uparrow$	$\downarrow$	$\downarrow$	$\pm$	$\pm$	$\pm$
Plummer's Disease	$\downarrow$	$\uparrow$	$\uparrow\uparrow$	$\pm$	–	–

nl = normal

$\pm$  = indeterminate

### Laboratory Results

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

If free T4 (FT4) is low or low normal, this is indicative of primary hypothyroidism, usually requiring thyroid replacement therapy. In cases of non-toxic, endemic goiter, low FT4 with an elevated TSH would also be found, but the physical presence of goiter would be unmistakable, indicating an iodine deficiency. Happily, endemic goiter is currently extremely rare in North America with the ongoing fortification of table salt with iodine.

In subacute (De Quervain's) thyroiditis, initially, TSH is low while FT4 and free T3 (FT3) may be quite elevated; elevated autoantibodies are usually not detected 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

### Commentary

implicated. As this thyroiditis progresses, TSH levels can rise above the reference range and both FT3 and FT4 levels can fall, eventually settling into a clinical picture of hypothyroidism.

If FT4 is also elevated, this is indicative of secondary (or, in very rare cases, tertiary) hyperthyroidism. A TSH-secreting pituitary tumor or pituitary resistance to T4 and T3 inhibitory feedback may be causal.

High normal or slightly elevated TSH, even in the presence of normal free T4, may be indicative of subclinical hypothyroidism. If such a condition exists, future repeat testing may be warranted.

Free T4 (FT4) is measured below the reference range, indicating a hypothyroid state, although multiple causes for decreased FT4 are possible. 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.

In primary hypothyroidism, TSH values will be high, indicating a lack of responsiveness of the thyroid gland to TSH stimulation. Generally in such cases, free T3 (FT3) and reverse T3 will also be low or low normal. The ratio of FT4 to FT3 may be depressed since the body will preferentially make relatively more T3 in an attempt to compensate partially for low total thyroid hormone production.

Thyroiditis can also present a laboratory picture of primary hypothyroidism. In addition to low FT4, low FT3, and elevated TSH, anti-thyroglobulin, anti-thyroid peroxidase, or anti-TSH antibodies may be elevated, blocking the production and release of thyroid hormone.

If TSH is also below the reference range, pituitary involvement must be suspected. In classic secondary hypothyroidism, TSH production from the pituitary is low and thus T4 production is low. In extremely rare cases, thyrotropin-stimulating hormone production is low indicating tertiary hypothyroidism.

Prescription drugs like corticosteroids (e.g., prednisone) and dopamine can suppress TSH production, leading to reduced T4 production. Phenytoin (dilantin) therapy can lower T4 and T3 levels, but TSH levels are usually unaffected.

Cushing's syndrome can also lead to low TSH and FT4 levels.

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.

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 levels alone are insufficient markers to predict hyper- or hypothyroidism. FT4, FT3 and TSH levels are necessary to

### *Commentary*

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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