Thyroid lab tests

Dr sepideh nazemi

- Secretion of the thyroid hormones ***T4 (thyroxine) and T3*** (triiodothyronine) is regulated by ***pituitary thyroid-stimulating hormone*** (TSH) .

- ***TSH secretion***, in turn, is controlled through ***negative feedback by thyroid hormones.***

- There is a negative log-linear relationship between serum free T4 and TSH concentrations.

- This means that ***very small changes in serum free T4 concentrations induce very large reciprocal changes in serum TSH concentrations***.

- As a result, ***thyroid function is best assessed by measuring serum TSH,*** assuming steady-state conditions and the ***absence of pituitary or hypothalamic disease.***

- Nevertheless, direct measurement of serum thyroid hormone levels is still important since it may be difficult in some patients to be certain about the state of pituitary and hypothalamic function.

LABORATORY TESTS USED TO ASSESS THYROID FUNCTION

- Thyroid function is assessed by one or more of the following tests:

- ●Serum TSH concentration

- ●Serum total T4 and T3 concentrations

- ●Serum free T4 and T3 concentrations

- There is considerable controversy as to the appropriate ***upper limit of normal for serum TSH.***
- Most laboratories have used values of approximately ***4.5 to 5.0 mU/L.***
- The distribution of TSH values in the population ***differs by age.***
- Third-generation TSH chemiluminometric assays, currently in wide use, have ***detection limits of approximately 0.01 mU/L.***
- They can therefore provide detectable TSH measurements even in mild hyperthyroidism .

- ***Normal ranges*** vary among laboratories; a typical reference range for total ***T4 is 4.6 to 11.2 mcg/dL*** (60 to 145 nmol/L).

- The normal range for total ***T3 is even more variable*** among laboratories than that for total T4; a typical range is approximately ***75 to 195 ng/dL*** (1.1 to 3 nmol/L).

- ***Serum free T4 and T3*** – The free hormone hypothesis states that the unbound or free hormone is the fraction that is ***available for uptake into cells and interaction with nuclear receptors*** .

- The bound hormone, on the other hand, represents a circulating storage pool that is not immediately available for uptake into cells.

- ***Since drugs and illness can alter concentrations of binding proteins or interaction of the binding proteins with T4 or T3*** , the free and total hormone concentrations may not be concordant.

- An example is estrogen-induced ***TBG excess***, in which ***total T4 concentrations are high due to increased TBG-bound hormone***, but the physiologically important free T4 concentrations are normal.
- It is therefore necessary to estimate free hormone concentrations.

- ***Reverse T3 —*** Reverse T3 (rT3) is an ***inactive metabolite of thyroxine***.
- It is widely measured by alternative health practitioners to justify the use of T3 therapy and supplements thought to enhance the conversion of T4 to T3.

Drugs that cause hypothyroidism, hyperthyroidism, or changes in thyroid function tests

Drugs causing hypothyroidism
Inhibition of thyroid hormone synthesis and/or release – thionamides, lithium, perchlorate, aminoglutethimide, thalidomide, and iodine and iodine-containing drugs including amiodarone, radiographic agents, expectorants (eg, guaifenesin), kelp tablets, potassium iodine solutions (SSKI), Betadine douches, topical antiseptics
Decreased absorption of T4 – cholestyramine, colestipol, colesevelam, aluminum hydroxide, calcium carbonate, sucralfate, iron sulfate, raloxifene, omeprazole, lansoprazole, and possibly other medications that impair acid secretion, sevelemer, lanthanum carbonate, and chromium; malabsorption syndromes can also diminish T4 absorption
Immune dysregulation – interferon alfa, interleukin-2, ipilimumab, alemtuzumab, pembrolizumab, nivolumab
Suppression of TSH – dopamine
Destructive thyroiditis – TKIs (eg, sunitinib, sorafenib); checkpoint inhibitors (eg, nivolumab, pembrolizumab, and ipilimumab)
Increased type 3 deiodination – TKIs (eg, sorafenib)
Increased T4 clearance and suppression of TSH – bexarotene
Drugs causing hyperthyroidism
Stimulation of thyroid hormone synthesis and/or release – iodine, amiodarone
Immune dysregulation – interferon alfa, interleukin-2, ipilimumab, alemtuzumab, pembrolizumab
Drugs causing abnormal thyroid function tests without thyroid dysfunction
Low serum TBG – androgens, danazol, glucocorticoids, slow-release niacin (nicotinic acid), L-asparaginase
High serum TBG – estrogens, tamoxifen, raloxifene, methadone, 5-fluouracil, clofibrate, heroin, mitotane
Decreased T4 binding to TBG – salicylates, salsalate, furosemide, heparin (via free fatty acids), certain NSAIDs
Increased T4 clearance – phenytoin, carbamazepine, rifampin, phenobarbital
Suppression of TSH secretion – dobutamine, glucocorticoids, octreotide
Impaired conversion of T4 to T3 – amiodarone, glucocorticoids, contrast agents for oral cholecystography (eg, iopanoic acid), propylthiouracil, propanolol, nadolol

SSKI: saturated solution of potassium iodide; T4: thyroxine; TSH: thyroid-stimulating hormone; TKIs: tyrosine kinase inhibitors; TBG: thyroxine-binding globulin; NSAIDs: nonsteroidal anti-inflammatory drugs; T3: triiodothyronine.

Patterns of thyroid function tests during assessment of thyroid function

Serum TSH	Serum free T4	Serum T3	Assessment
Normal hypothalamic-pituitary function			
Normal	Normal	Normal	Euthyroid
Normal	Normal or high	Normal or high	Euthyroid hyperthyroxinemia
Normal	Normal or low	Normal or low	Euthyroid hypothyroxinema
Normal	Low	Normal or high	Euthyroid: T3 therapy
Normal	Low-normal or low	Normal or high	Euthyroid: thyroid extract therapy
High	Low	Normal or low	Primary hypothyroidism
High	Normal	Normal	Subclinical hypothyroidism
Low	High or normal	High	Hyperthyroidism
Low	Normal	Normal	Subclinical hyperthyroidism
Abnormal hypothalamic-pituitary function			
Normal or high	High	High	TSH-mediated hyperthyroidism
Normal or low*	Low or low-normal	Low or normal	Central hypothyroidism

T3: triiodothyronine; T4: thyroxine; TSH: thyroid-stimulating hormone.
* In central hypothyroidism, serum TSH may be low, normal, or slightly high.

- ***Monitoring levothyroxine therapy*** — One of the more common reasons for assessing thyroid function is to assess the adequacy of levothyroxine therapy.

- ●***Primary hypothyroidism*** – Patients with primary hypothyroidism who are ***taking levothyroxine replacement therapy*** can be ***monitored*** by assessing the serum ***TSH only.*** In general, serum free T4 measurements are very insensitive for assessing the appropriateness of the levothyroxine dose.

- ***Liothyronine*** (T3, Cytomel) is generally ***not recommended for treating hypothyroidism***.

- However, in patients with ***persistent hypothyroid symptoms on levothyroxine*** monotherapy, ***T3 is sometimes added***.

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- ***Secondary hypothyroidism*** – The one setting in which the ***serum free T4 value should be used to titrate the thyroid hormone dose*** is in patients with secondary hypothyroidism due to pituitary or hypothalamic disease who have absent or impaired TSH release.

ANTITHYROID ANTIBODIES

- Thyroglobulin

- Thyroid peroxidase (TPO, formerly known as the microsomal antigen)

Nearly all patients with Hashimoto's thyroiditis have high serum concentrations of TPO antibodies. Serum anti-TPO antibodies ***need not be measured in patients with overt primary hypothyroidism, because almost all have chronic autoimmune thyroiditis***. However, a test for anti-TPO antibodies may be useful to predict the likelihood of ***progression to permanent overt hypothyroidism in patients with subclinical hypothyroidism***.

- The TSH receptor – Thyrotropin receptor antibodies (TRAbs) are classified as stimulating, blocking, or neutral.