

# Tests Regarding the Thyroid Gland Functioning

## Plasma total thyroxine (T4)

- Normal plasma concentration: 60 - 150 nmol/l
- Was widely used in the past as a test of thyroid function
- Disadvantage: dependent on concentration of binding protein (TBG), therefore increased e.g. in pregnancy and on anticonceptive drugs.

## Plasma total triiodothyronine (T3)

- Normal plasma concentration 1.0 - 2.9nmol/l
- Concentration nearly always raised in hyperthyroidism (to greater extent than t4)
- May be normal in hypothyroidism due to preference in production of T3 in thyroid and then peripherally converted to T4
- Disadvantage: dependent on concentration of binding protein (TBG)

## Free T4 test

- Normal plasma concentration 10 - 25 pmol/l
- Measure only unbound, active thyroxine
- Routine clinical use in laboratories
- Measures thyroxine-binding globulin (TBG) too

## Free T3 test

- Normal plasma concentration 3.5 - 7.5 pmol/l

## Thyroid Stimulating Hormone (TSH) measurement

- Normal plasma concentration 0.3 - 3.5 mU/L (reducing the upper limit to 2.5 mU/L is currently subject of discussion).
- Levels of TSH can differentiate between hypothyroidism, hyperthyroidism, and euthyroidism.
- Eg. In case suspicion of primary thyroid disease; but if plasma TSH concentration is normal, patient is euthyroid. To diagnose primary hypothyroidism, TSH concentrations should be greatly increased
- TSH measurement is most sensitive as they increase above normal range before T4 fall below
- Accurate diagnosis however requires at least 2 tests, eg. TSH with free T4 / T3
- For diagnosis of secondary thyroid dysfunctions simultaneous determinations of TSH and FT4 are required.

		Plasma free T4		
		Low	Normal	High
Plasma TSH	Low	Hypopituitarism (other pituitary hormones decreased); sick euthyroid (severe, with decrease of free T3 too)	T3 thyrotoxicosis (free T3 increased); early in treatment of hyperthyroidism; subclinical hyperthyroidism (T3 normal or increased)	Hyperthyroidism (free T3 increased)
	Normal	Sick euthyroid (free T3 decreased); hypopituitarism (other pituitary hormones decreased)	euthyroid	Euthyroid with T4 autoantibodies (uncommon), thyroid hormone resistance
	High	Hypothyroidism (primary); recovery from sick euthyroid state	Borderline / compensated hypothyroidism	TSH - secreting tumor (rare) (free t3 increased, TSH may be high-normal)

## Thyrotrophin-Releasing Hormone (TRH) test

- Obsolete as modern sensitive basal TSH immunoassays preferred, except for investigation of hypothalamic-pituitary dysfunction.
- To test: plasma TSH measured before, 20 min, and 60 min after giving the patient 200 µg of TRH i.v. Normally, TSH concentration increases by 2 - 20 mu/l in 20 min, then reverts to basal level at 60 min.
- Delayed (higher concentration at 60 min than at 20 min) TSH response to TRH is characteristic for hypothalamic disease.

Sick euthyroid syndrome in patients with non-thyroidal illness but other systemic diseases (eg infections, malignancy, myocardial infarction, post-surgery) can have an apparently low total and free T4 and T3 with a normal or low basal TSH. Levels are usually only mildly below normal and are thought to be mediated by interleukins IL-1 and IL-6.

**They are caused by:**

- reduced concentration and affinity of binding proteins.
- decreased peripheral conversion of T4 to T3 with more rT3 (reverse T3 blocks action of normal T3).
- non-thyroidal influences on the hypothalamic-pituitary-thyroid axis (eg by cortisol) to inhibit TSH production.
- increased plasma free fatty acids displacing thyroid hormones from their binding sites.

Today, structure parameters have advantages also in diagnosing non-thyroidal illness syndrome (see below).

## Structure parameters

For special purposes, e.g. in diagnosis of nonthyroidal illness syndrome or central hypothyroidism, derived structure parameters that describe constant properties of the overall feedback control system, may add useful information<sup>[1]</sup>. Compared with TRH test, calculating these parameters is fast and easily performed and it may reduce patient strain.

### Secretory capacity (GT)

Thyroid's secretory capacity (GT, also referred to as SPINA-GT, if calculated from equilibrium levels of TSH and FT4) is the maximum stimulated amount of thyroxine the thyroid can produce in one second. GT is elevated in hyperthyroidism and reduced in hypothyroidism.

GT is calculated with

$$\hat{G}_T = \frac{\beta_T(D_T + [TSH])(1 + K_{41}[TBG] + K_{42}[TBPA])[FT_4]}{\alpha_T[TSH]}$$

or

$$\hat{G}_T = \frac{\beta_T(D_T + [TSH])[TT_4]}{\alpha_T[TSH]}$$

$\alpha_T$ : Dilution factor for T4 (reciprocal of apparent volume of distribution, 0.1 l<sup>-1</sup>)

$\beta_T$ : Clearance exponent for T4 (1.1e-6 sec<sup>-1</sup>)

$K_{41}$ : Dissociation constant T4-TBG (2e10 l/mol)

$K_{42}$ : Dissociation constant T4-TBPA (2e8 l/mol)

$D_T$ : EC<sub>50</sub> for TSH (2.75 mU/l)

**Reference range:**

Lower limit	Upper limit	Unit
1.41	8.67	pmol/s/70 kg

### Sum activity of peripheral deiodinases (GD)

Calculated sum activity of peripheral deiodinases (GD, SPINA-GD (if calculated from levels of thyroid hormones) or estimated total deiodinase activity) is reduced in nonthyroidal illness with hypodeiodination and increased in rare states of hyperdeiodination.

GD is obtained with

$$\hat{G}_D = \frac{\beta_{31}(K_{M1} + [FT_4])(1 + K_{30}[TBG])[FT_3]}{\alpha_{31}[FT_4]}$$

or

$$\hat{G}_D = \frac{\beta_{31}(K_{M1} + [FT_4])[TT_3]}{\alpha_{31}[FT_4]}$$

$\alpha_{31}$  : Dilution factor for T3 (reciprocal of apparent volume of distribution, 0.026 l<sup>-1</sup>)

$\beta_{31}$  : Clearance exponent for T3 (8e-6 sec<sup>-1</sup>)

$K_{M1}$ : Dissociation constant of type-1-deiodinase (5e-7 mol/l)

$K_{30}$ : Dissociation constant T3-TBG (2e9 l/mol)

#### Reference range:

Lower limit	Upper limit	Unit
20	40	nmol/s/70 kg

## TSH index

TSH index (TSHI or Jostel's index) helps to determine thyrotropic function of anterior pituitary on a quantitative level.

It is calculated with

$$TSHI = LN(TSH) + 0.1345 * FT4 .$$

Additionally, a standardized form of TSH index (sTSHI) may be calculated with

$$sTSHI = (TSHI - 2.7)/0.676 .$$

#### Reference ranges:

Parameter	Lower limit	Upper limit	Unit
TSHI	1.3	4.1	
sTSHI	-2	2	

## Carrier proteins

### Thyroxine-binding globulin

Increased levels of thyroxine-binding globulin result in increased total thyroxine and total triiodothyronine concentrations without an actual increase in hormonal activity of biologically active thyroid hormones.

#### Reference range:

Lower limit	Upper limit	Unit
12	30	mg/L

#### Reasons for abnormal concentrations of thyroxine-binding globulin (TBG)

Decrease	Increase
Genetic, protein-losing states (nephrotic syndrome), malnutrition, malabsorption, acromegaly, Cushing's syndrome, high dosage of corticosteroids, androgens	Genetic, pregnancy, oestrogens (including oestrogen containing oral contraceptives)

## Thyroglobulin

#### Reference ranges:

Lower limit	Upper limit	Unit
1.5	30	pmol/L
1	20	µg/L

## Other binding hormones

- Transthyretin (prealbumin)
- Albumin

## References

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## Additional references

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