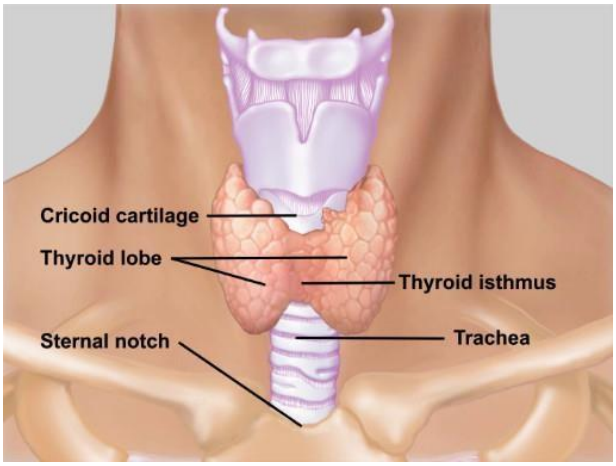
Thyroid hormones

- Thyroxine (T4), tri-iodothyronine(T3) and calcitonin are secreted by the thyroid gland.
  - T4 and T3 are products of the follicular cells and influence the rate of all metabolic processe.
  - Calcitonin is produced by the specialized C cells and influences calcium metabolism.



PHYSIOLOGY

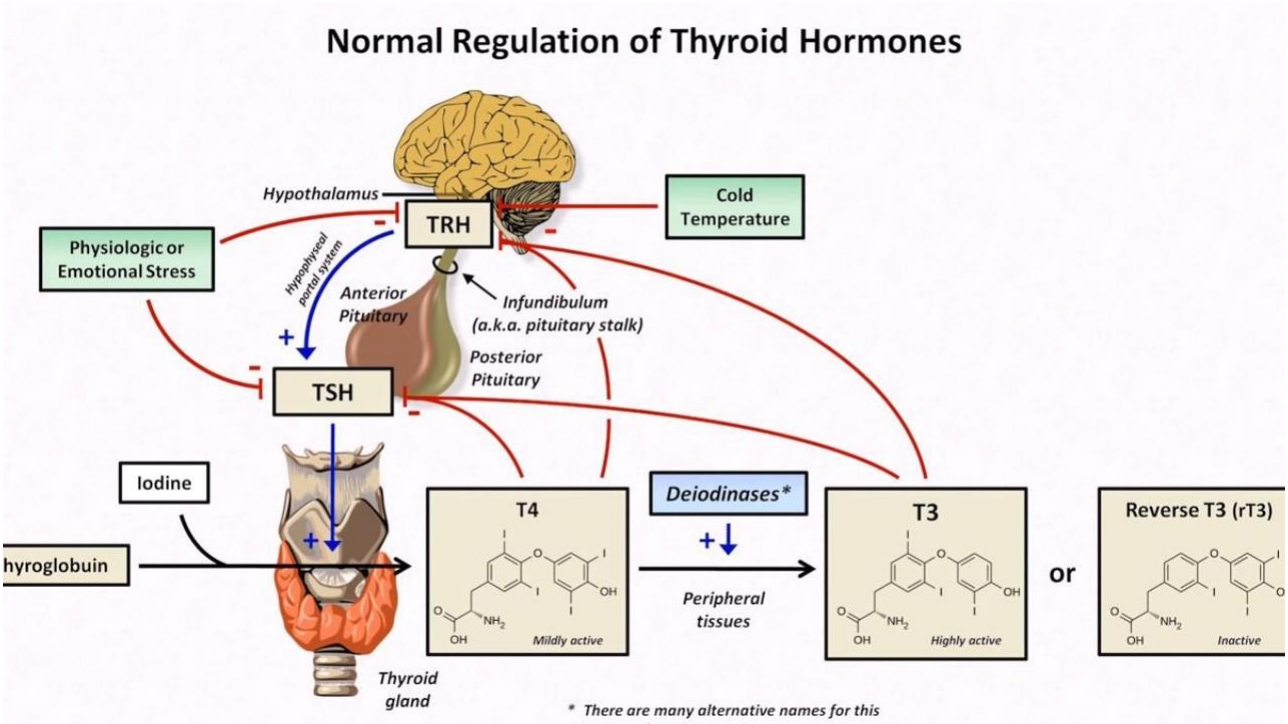
- Thyroid hormones are synthesized in the thyroid gland by the iodination and coupling of two molecules of the amino acid tyrosine a process that is dependent on an adequate supply of iodide.
- Iodide in the diet is absorbed rapidly from the small intestine
- Low iodide in diet can cause enlargement of the thyroid gland (Goiter).
- fish and iodized salt are the main dietary sources of the element.

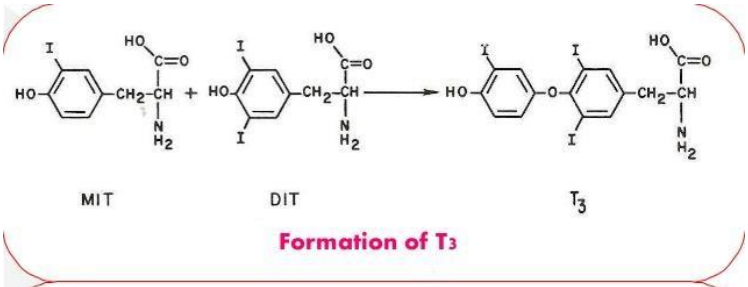
Synthesis of thyroid hormones

- Iodide is actively taken up by the thyroid gland under the control of thyroid-stimulating hormone (TSH) via a sodium/iodide symporter.
- The concentration of iodide in the gland is at least 20 times that in plasma and may exceed it by 100 times or more.
- Iodide is rapidly converted to iodine within the thyroid gland, catalysed by thyroid peroxidase (TPO).
- Iodination of tyrosine residues in a large 660-kDa glycoprotein, thyroglobulin, takes place to form mono-iodotyrosine (MIT) and di-iodotyrosine (DIT) mediated by the enzyme TPO.
- Iodotyrosines are coupled to form T4 (DIT and DIT) and T3 (DIT and MIT)

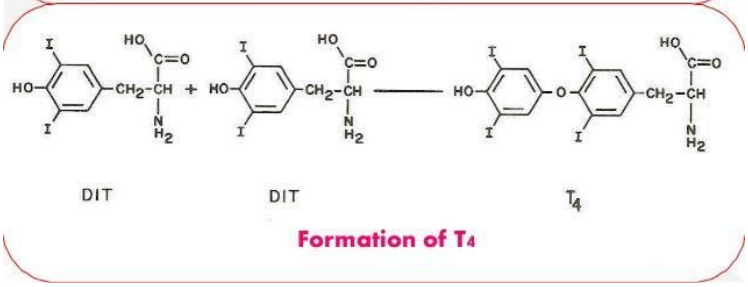
Chemical structure of the thyroid hormones: The uptake of iodide, as well as the synthesis and secretion of thyroid hormones, is regulated by TSH, secreted from the anterior pituitary gland.

By Dr. Safa Ammer

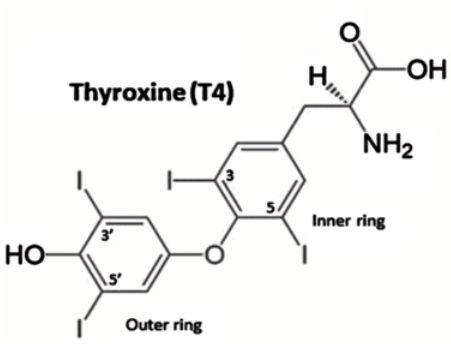


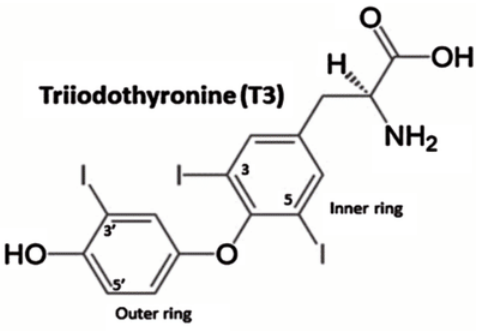


Formation of T3



Formation of T4



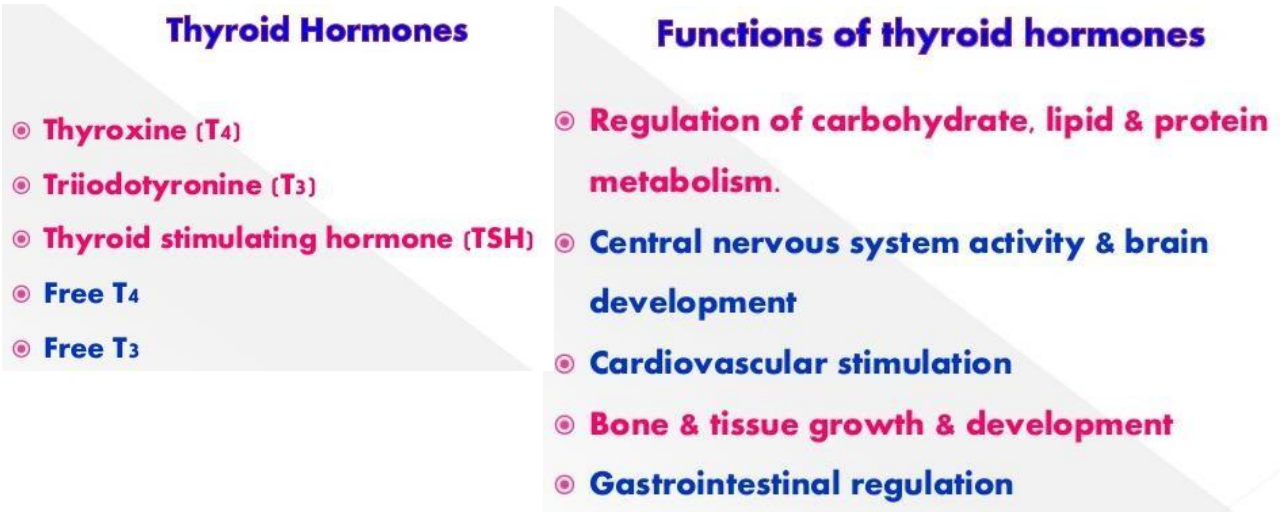


Effect of thyrotrophin-releasing hormone TRH

Pituitary TSH synthesis and release are stimulated by TRH, a tripeptide produced in the hypothalamus and released into the portal capillary plexus. The action of TRH can be over-ridden by high circulating free T4 (fT4) concentrations, and therefore exogenous TRH has little effect on TSH secretion in hyperthyroidism. Once TRH reaches the pituitary, it binds to TRH receptors, members of the seven-transmembrane-spanning receptor family, which are coupled to G proteins.

Effects of thyroid hormones in the control of thyroid stimulating hormone secretion

Thyroid hormones reduce TSH secretion by negative feedback. Triiodothyronine binds to anterior pituitary nuclear receptors. In the anterior pituitary gland, most of the intracellular T3 is derived from circulating fT4. Therefore this gland is more sensitive to changes in plasma T4 than to T3 concentrations.



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THYROID FUNCTION TESTS

Assessment of thyroid hormone secretion can be made by measuring plasma TSH as well as either fT4 or total T4 [sometimes also free T3 (fT3) or total T3]. Each test has its advantages and disadvantages, although probably most laboratories now offer fT4 and fT3 assays rather than total hormone concentrations.

Definitions

Hypothyroidism is a clinical state resulting from underproduction of the thyroid hormones thyroxine (T4) and triiodothyronine (T3). Most cases are due to primary hypothyroidism, a failureof the thyroid gland to produce thyroid hormones.

Primary hypothyroidism is defined as thyroid-stimulating hormone (TSH) concentrations above the reference range and free thyroxine concentrations below the reference range

Secondary hypothyroidism is due to underproduction of TSH by the pituitary gland.

Sub-clinical hypothyroidism is a state of usually asymptomatic, mild thyroid failure, with normal levels of T4 and T3, and minimal elevation of TSH.

Myxoedema coma is a rare severe form of hypothyroidism with multi-organ failure.

Thyroxine-binding globulin (TBG)

- **Thyroxine binding globulin (TBG)** is the high-affinity serum binding protein for thyroxine and triiodothyronine. Normally, the thyroid adjusts to changing concentrations of TBG by producing more, or less, thyroid hormone to maintain a constant level of metabolically important free hormone.
- Elevated TBG levels are associated with influences such as pregnancy, genetic predisposition, oral contraceptives, and estrogen therapy. TBG levels can decrease with androgenic or anabolic steroids, large doses of glucocorticoids, hypoproteinemic states, liver disease, nephrotic syndrome, and congenital TBG variants.

Plasma thyroid-stimulating hormone

- Concentrations of TSH are high in primary hypothyroidism and low in secondary or pituitary hypothyroidism.
- In hyperthyroidism, high plasma T4 and T3 concentrations suppress TSH release from the pituitary, resulting in very low or undetectable plasma TSH concentrations.
- Plasma TSH assays are used as first-line assays for thyroid function assessment.

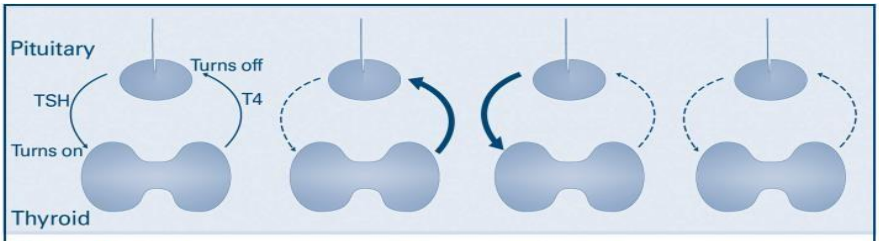
Plasma total or free tri-iodothyronine T3

- Total T3 or fT3 concentrations may help in the diagnosis of hyperthyroidism but are not usually used routinely to diagnose hypothyroidism because **normal plasma concentrations are very low.**
- In hyperthyroidism, the increase in plasma T3 or fT3 concentrations is greater, and usually occurs earlier than that of T4 or fT4.
- Occasionally in hyperthyroidism the plasma T3 or fT3 concentrations are elevated but not those of T4 or fT4 (T3 toxicosis).
- Like T4, T3 is bound to protein. It is usually preferable to measure the plasma concentration of fT3 rather than total T3, as the latter may be altered by changes in the plasma concentrations of TBG.

DISORDERS OF THE THYROID GLAND

The most common presenting clinical features of thyroid disease are the result of:

- hypothyroidism, due to deficient thyroid hormone secretion,
- hyperthyroidism, due to excessive thyroid hormone secretion,
- goitre, either diffuse or due to one or more nodules within the gland there may or may not be abnormal thyroid hormone secretion and thus the patient may be euthyroid.



CONDITION:	Normal	Hyperthyroidism	Hypothyroidism Primary	Hypothyroidism Secondary
TSH	Normal	Low	High	Low
T4	Normal	High	Low	Low

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