

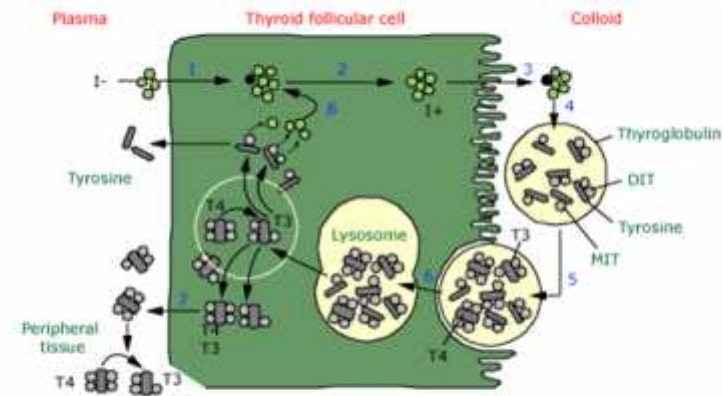
Thyroid Replacement

Robert Cordero DO PGY-2
Internal Medicine
Graduate Medical Education
Trios Health

Thyroid Synthesis

- Iodide is transported to thyroid follicles
- Iodide is ionized and organified with thyroglobulin at the apical cells
- T4 is formed by two units of diiodotyrosine
- T3 is formed by 1 unit diiodotyrosine and 1 unit of monoiodotyrosine intrathyroidal
- Extrathyroidal T3 formed by deiodination of T4

Thyroid hormone biosynthesis



Thyroid hormone synthesis includes the following steps: (1) iodide (I⁻) trapped by the thyroid follicular cells; (2) diffusion of iodide to the apex of the cells; (3) transport of iodide into the colloid; (4) oxidation of inorganic iodide to iodine and incorporation of iodine into tyrosine residues within thyroglobulin molecules in the colloid; (5) combination of two DIT molecules to form tetraiodothyronine (T4) or of MIT with DIT to form T3; (6) uptake of thyroglobulin from the colloid into the follicular cell by endocytosis, fusion of the thyroglobulin with a lysosome, and proteolysis and release of T4, T3, DIT, and MIT; (7) release of T4 and T3 into the circulation; and (8) deiodination of DIT and MIT to yield tyrosine. T3 is also formed from monoiodination of T4 in the thyroid and in peripheral tissues.

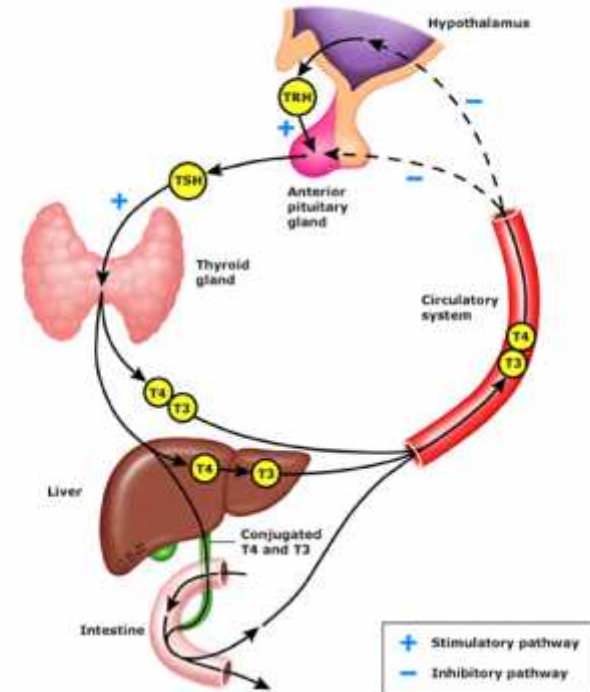
DIT: diiodotyrosine; MIT: monoiodotyrosine; T3: triiodothyronine; T4: thyroxine.

Modified from: *Scientific American Medicine*, Scientific American, New York, 1995.

Regulation of Thyroid Hormone

- TSH (Thyrotropin) regulates the synthesis and secretion of T4 and T3
- Thyrotropin releasing hormone (TRH) regulates TSH secretion
- Elevation of serum T4 and T3 decreases TSH and TRH

Regulation of thyroid hormone production



TRH increases the secretion of TSH, which stimulates the synthesis and secretion of T3 and T4 by the thyroid gland. T3 and T4 inhibit the secretion of TSH, both directly and indirectly by suppressing the release of TRH. T4 is converted to T3 in the liver and many other tissues by the action of T4 monodeiodinases. Some T4 and T3 is conjugated with glucuronide and sulfate in the liver, excreted in the bile, and partially hydrolyzed in the intestine. Some T4 and T3 formed in the intestine may be reabsorbed. Drug interactions may occur at any of these sites.

T3: triiodothyronine; T4: thyroxine; TRH: thyrotropin-releasing hormone; TSH: thyroid-stimulating hormone.

Function of Thyroid Hormone

- Mechanism of action through binding of DNA transcription
- Thyroid hormone essential for bone development and growth
- Regulation of heart rate and rhythm
- Influences activity of other hormones (catecholamine and insulin for example)

Causes of Hypothyroidism

- Primary Hypothyroidism
 - Hashimoto thyroiditis
 - Thyroidectomy/ Radioiodine therapy
 - Iodine deficiency/excess
 - Drugs: lithium, amiodarone
- Secondary/Tertiary Hypothyroidism
 - TSH deficiency
 - TRH deficiency

Clinical Manifestations

- Skin/Hair
 - Dry, coarse
- Eyes
 - Periorbital edema
- Heart
 - Heart failure, rate and rhythm abnormalities
- Neurologic
 - Congenital: mental retardation, impaired motor control
 - Peripheral neuropathy, movement disorders, Alzheimer's disease
 - Hashimoto's Encephalopathy

Thyroid Replacement

- First line: Levothyroxine which is a synthetic T4
- 80% absorption ideally. Should be taken 1 hour before breakfast
- Recommend to repeat TSH levels every 6 weeks to adjust dose
- Other formulations are not recommended since most doses are not regulated

Over Replacement

- Subclinical (Normal T4/T3 but low TSH) and overt hyperthyroidism
- Accelerated bone loss, bone remodeling, and bone density
- Elevated risk of arrhythmias with overcorrection of thyroid hormone
- Additional hyperthyroidism symptoms

Adjustment of Maintenance dose

- Routine TSH yearly after establishment of maintenance dose
- During pregnancy dose may need to increase and return post-partum
- Significant weight gain or conditions that impair thyroid hormone absorption
- Significant weight loss, aging or androgen therapy

References

- Ross, Douglas S. "Thyroid Hormone Synthesis and Physiology." *UpToDate*, edited by Ted W. Post.
- Ross, Douglas S. "Treatment of Hypothyroidism." *UpToDate*, edited by Ted W. Post.