Anatomy of the Thyroid Gland and The Role of Thyroid Hormones

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The thyroid gland is an endocrine organ that regulates important processes in the metabolism, growth and cardiac function. However, the function of the thyroid gland itself must also be controlled. In order to understand the causes and symptoms of over- and under-functions of the thyroid, you should understand the regulatory mechanisms and effects of thyroid hormones.

Anatomy of the Thyroid

The thyroid gland is a butterfly-shaped organ located in the anterior neck, between the larynx and the trachea. The **isthmus** connects the right and the left lobes of the thyroid. The thyroid is attached to the trachea via the lateral suspensory ligament or Berry's ligament, which connects each of the thyroid lobes to the trachea. The isthmus continues cranially as lobus pyramidalis, which is a relic of the migrated tongue base. The thyroid gland is brownish-red and is richly vascularized with the immediate branches of large cardiac arteries. Nerves important for voice quality also innervate the thyroid.

Histologically, the thyroid gland is made up of follicles. The thyroid follicles are round structures enclosed by thyrocytes, which synthesize the thyroid hormones. This synthesis can be detected in the **colloid** that fills the follicles. Slumped follicles or cell clusters lacking the lumen represent the **secretory state.** The epithelial cells are isoprismatic in the secretory phase, while they appear flattened in the **stored form.**

The thyroid is vascularized cranially via a superior thyroid artery arising from the external carotid artery. In addition, the thyroid is vascularized caudally by the **inferior thyroid artery** arising from the thyrocervical trunk (also called trunk of the thyrocervical artery). A **plexus thyroideus impar** is involved in venous drainage and mostly drains the blood into the **left brachiocephalic vein (also known as a left innominate vein)**.

The proximity to the **recurrent laryngeal nerve**, which runs dorsally along both thyroid lobes, requires extreme prudence during thyroid surgery. An injury to the nerve can result in hoarseness (unilateral lesion), and in breathlessness under a worst-case scenario (bilateral lesion).

Regulation Axis—Control from Above

The hypothalamus produces **TRH**, the thyrotropin-releasing hormone. TRH is a tripeptide derived from its precursor via limited proteolysis. In addition to the concentration of thyroid hormones in the blood, even **cold** can trigger the secretion of TRH. Since TRH is a

hydrophilic hormone, it binds to membrane receptors in the pituitary glands and stimulates the formation and secretion of thyroidin stimulating hormone (**TSH**).

TSH is also **hydrophilic** and binds to receptors in the thyroid gland, which then receive **additional iodine** and synthesize **triiodothyronine** (T3) and **thyroxine** (T4). TSH also induces the **growth** of the thyroid gland. T3 and T4 inhibit the secretion of TRH as well as TSH. TSH also inhibits TRH secretion.

Thyroid Function: T3 and T4 Synthesis

In the thyroid gland, **iodine is actively added** (via sodium iodide symporters) and elemental iodine is released via **peroxidase.** In the colloid of the thyroid, iodine is linked to **thyroglobulin** at numerous **thyroxin residues** in the globulin. A residue may be iodinated once or twice and accordingly known as **mono- or diiodotyrosine,** respectively**.** They represent the storage form of thyroid hormones.

Secretion of iodinated tyrosines is followed by **intramolecular coupling** of the iodothyroxine residue, which is also referred to as **iodine oxidation.** The iodinated thyroxine residues are linked via an oxygen bridge, and **not a peptide bond.** The following intermediate products are formed during iodine oxidation:

- Diiodthyrosine + Diiodthyrosine = **T4**
- Diiodthyrosine + Monoiodthyrosine = **T3**
- Monoiodthyrosine + Diiodthyrosine = **rT3** = reverse T3

The rT3 is an **inactive** molecule, and is absorbed and dismantled in the thyrocytes.

T3 and T4 are released into the blood and transported bound to thyroxine-binding globulin (**TBG**), **prealbumin or albumin**, because they are **lipophilic** hormones.

The concentration of T4 in the blood is **20-fold higher** than that of T3, although T3 is **3 times more effective**. Approx. 30% of the T4 is therefore **converted** into T3 via **deiodase,** constituting about 80% of the total T3 in the blood, with only about 20% secreted directly. T3 has a **half-life** of **one day;** T4, however, has a half-life of **1 week!** Therefore, higher levels of T4 persist longer in the blood. In order to utilize the higher efficacy of T3, T4 is converted into T3.

Effects of Thyroid Hormones

Thyroxin binds to **intracellular, nuclear** receptors, which are concomitant **transcription factors.** Together with other activators, the hormone-receptor complex binds to thyroid hormone-responsive elements (**TREs**) in the DNA, which activates the synthesis of specific proteins.

T3 and T4 affect metabolism, growth and cardiac function. They increase the activity of **sodium-potassium ATPase**, resulting in an increased **basal metabolic rate** accompanied by increased **oxygen consumption.** Uncoupling of the respiratory chain leads to **increased heat production**. In addition, the levels of **gluconeogenesis, glycogen, lipolysis,** and **glycolysis** are increased.

The induction of HMG-CoA reductase increases **cholesterol formation** and **connective tissue metabolism**. T3 and T4 stimulate the synthesis of **growth hormone** in the pituitary gland and thus promote embryonic brain development. Therefore, pregnant and lactating women may have an increased need for iodine.

The thyroid hormones induce **contractility and frequency** of cardiac function via induction of β-receptors, which enhances **catecholamine sensitivity**. Similarly, the myocyte generates increased myosin levels after stimulation along with increased contractile force.

Functional Disorders of Thyroid

Based on the effects of thyroid hormones, the consequences that follow a functional disorder of the endocrine organ can be easily deduced.

Hyperthyroidism is a condition in which excessive T3 and T4 are produced, leading to:

- Weight loss (slender figure)
- Increased appetite
- Anxiety, sleep disorder
- Heat intolerance (warm hands)
- Increased perspiration
- Increased bowel movements leading to diarrhea
- Tremors
- Tachycardia
- Hypertension
- Greasy hair, hair loss
- Cycle or fertility disorder

In **hypothyroidism**, inadequate levels of T3 and T4 are produced due to iodine deficiency or dysfunction. The symptoms of hypothyroidism include:

- Mental and physical degradation, concentration disturbances
- Disinterest, lack of motivation, depression
- Increased need for sleep
- Cretinism (innate): mental retardation, dwarfism, speech disorders
- Constipation
- Cold intolerance
- Bradycardia
- Myxedema
- Thyroid cancer: curable with surgery, radiation, and hormone treatments
- Goiter (enlarged thyroid): harmless or represents iodine deficiency or a condition associated with thyroid inflammation called Hashimoto’s thyroiditis
- Dry skin, brittle hair
- Hyperthyroidism: excessive thyroid hormone production most often caused by Graves’ disease or an overactive thyroid nodule
- Thyroid storm: a rare form of hyperthyroidism characterized by extremely high levels of thyroid hormone causing severe illness
- Thyroid nodule: a small abnormal mass or lump in the thyroid gland, which may or may not be cancerous; may secrete excess hormones, causing hyperthyroidism

Treatment of hyperthyroidism

- Thyroid surgery (thyroidectomy): Partial or total resection is indicated for thyroid cancers or toxic goiters.
    - Preoperative radioactive iodine may reduce the blood supply and the size of the gland.
    - Preoperative propranolol is used to control symptoms of the disease

and for safer surgery.

- Antithyroid medications: Drugs can slow down the overproduction of thyroid hormone in hyperthyroidism. Two common antithyroid medicines are methimazole and propylthiouracil.
- Radioactive iodine: Radioactive iodine can be used in low doses to test the thyroid gland or destroy an overactive gland. Large doses can be used to destroy cancerous tissue.
- External radiation: A beam of radiation is directed at the thyroid in multiple sessions. The high-energy rays can be used to kill thyroid cancer cells.

Treatment for hypothyroidism

- Thyroid hormone pills: Daily treatment with thyroid hormone pills can be used to supplement the low levels seen in hypothyroidism, and to prevent thyroid cancer recurrence.
- Recombinant human TSH: Injection of recombinant human TSH enhances thyroid cancer detection in imaging tests.

References

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Notes