

Physiology for Medical Students

Endocrine 5

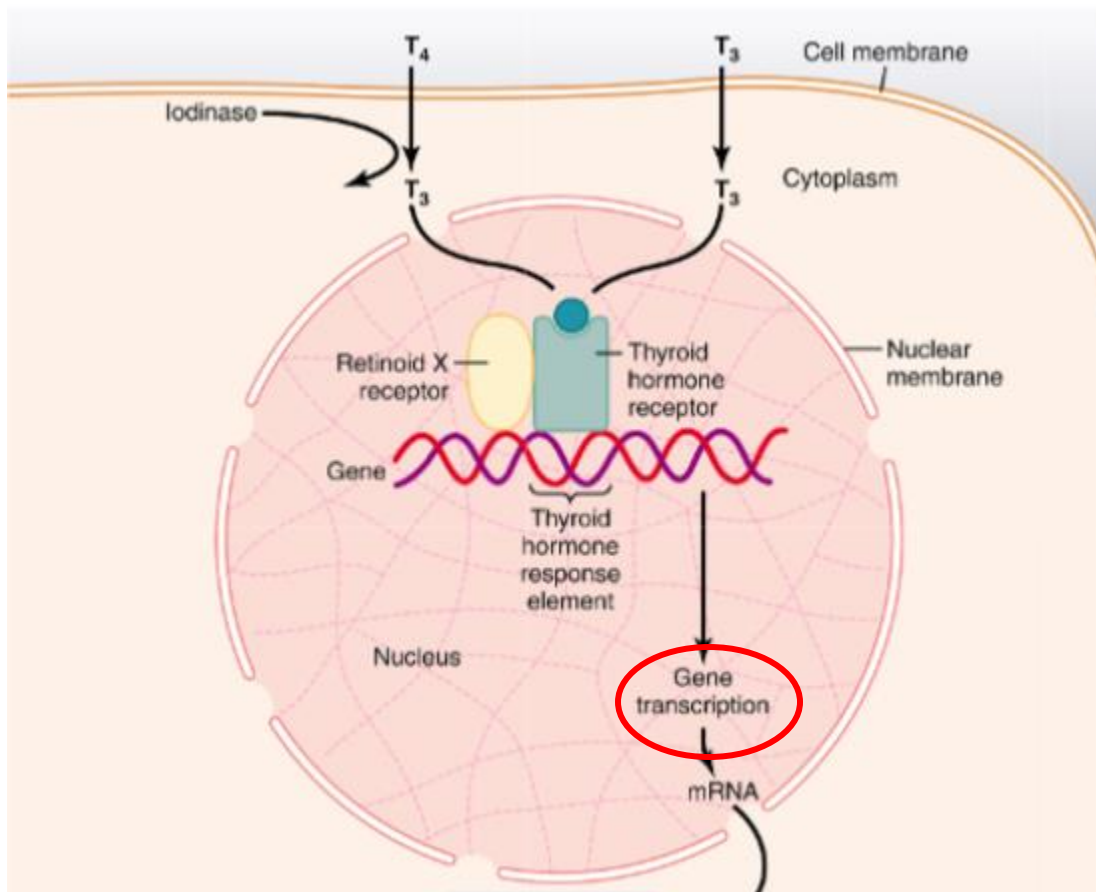
Fatima Daoud. MD. PhD.



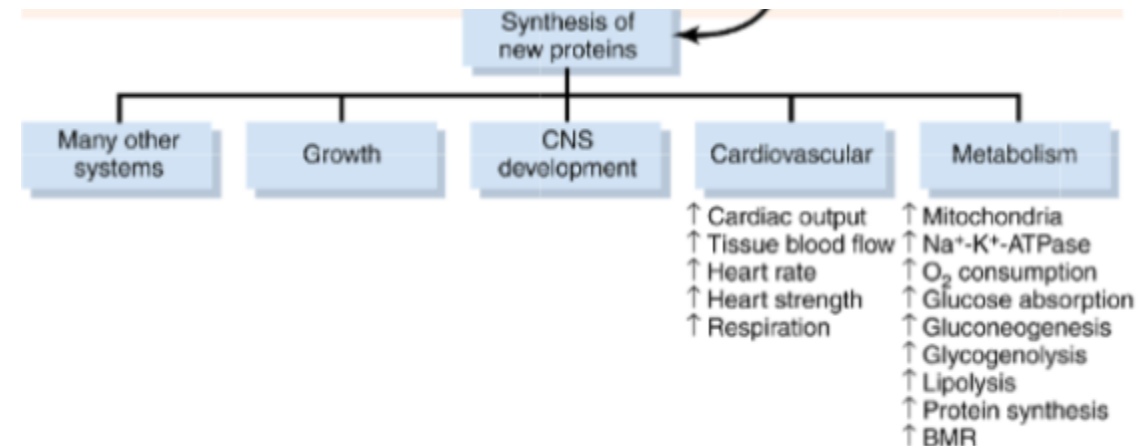
Physiological Functions of the Thyroid Hormones

CHAPTER 76

Hormones Increase the Transcription of Large Numbers of Genes



- **Thyroid hormone does not have any discrete target organs. It affects virtually every tissue in the body.**



The general effect of thyroid hormone is to **activate nuclear transcription of many genes. Therefore, in virtually all cells of the body, great numbers of **protein enzymes, structural proteins, transport proteins**, and other substances are synthesized. The net result is a generalized **increase in functional activity throughout the body**.

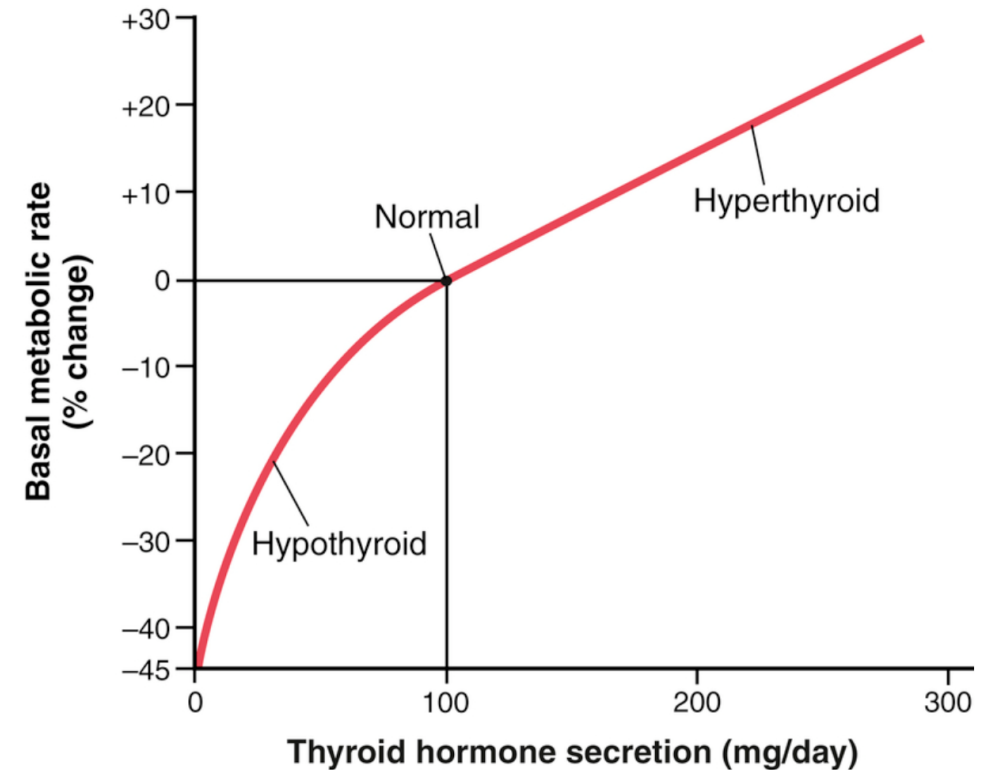
** Most of the thyroxine secreted by the thyroid is converted to triiodothyronine.

** more than 90% of the thyroid hormone that binds with the receptors is triiodothyronine.

** Thyroid hormones also appear to have nongenomic cellular effects that are independent of their effects on gene transcription.

Thyroid Hormones Increase Cellular Metabolic Activity

- ❖ Increase the number and activity of mitochondria (increased ATP production).
- ❖ Increase active transport of ions through cell membranes Na-K-ATPase.
- ❖ Increase the amount of heat.



** **The basal metabolic rate** can **increase** to 60% to 100% above normal when large quantities of thyroid hormones are secreted.

** basal metabolic rate (BMR), the rate of energy expenditure under standard or basal conditions (awake, at rest, and fasting). When BMR increases, cellular metabolism of carbohydrates, lipids, and proteins increases.

** The rate of **utilization of foods** for energy is greatly **accelerated**.

** Although the rate of protein synthesis is increased, at the same time the rate of protein catabolism is also increased.

** ** The **mental processes** are excited, and the activities of most of the other **endocrine glands** are increased.

Metabolic Effect of Thyroid Hormones

❖ Stimulation of carbohydrate metabolism

Thyroid hormone stimulates almost all aspects of carbohydrate metabolism.

❖ Stimulation of fat metabolism

- Essentially all aspects of fat metabolism are also enhanced.
- Decreases fat stores of the body.
- Increases free fatty acid concentration in the plasma.
- Accelerates oxidation of free fatty acids by the cells.
- Decreases the concentrations of cholesterol, phospholipids, and triglycerides in the plasma.

** Thyroid hormone stimulates almost all aspects of carbohydrate metabolism, including rapid glucose uptake by cells, enhanced glycolysis, enhanced gluconeogenesis, increased rate of absorption from the gastrointestinal tract, and even increased insulin secretion with its resultant secondary effects on carbohydrate metabolism. All these effects probably result from the overall increase in cellular metabolic enzymes caused by thyroid hormone.

** One of the mechanisms by which thyroid hormone decreases plasma cholesterol concentration is to **increase significantly cholesterol secretion in the bile** and consequent loss in the feces. A possible mechanism for the increased cholesterol secretion is that thyroid hormone induces **increased numbers of low-density lipoprotein** receptors on the liver cells, leading to rapid removal of low-density lipoproteins from the plasma by the liver and subsequent secretion of cholesterol in these lipoproteins by the liver cells.

Thyroid Hormones Effect on Growth and the Nervous System

- Thyroid hormone not only stimulates GH secretion and increases production of IGF-I by the liver
- Promotes the effects of GH and IGF-I on the synthesis of new structural proteins and on bone growth.
- Thyroid hormone plays a crucial role in development of the nervous system in children.
- Thyroid hormone is also essential for normal CNS activity in adults.

**nervous system: They promote synapse formation, myelin production, and growth of dendrites.

**Thyroid-deficient children have stunted growth that can be reversed by thyroid replacement therapy, but excess thyroid hormone does not produce excessive growth.

** In children with hyperthyroidism, excessive skeletal growth often occurs, causing the child to become considerably taller at an earlier age. However, the bones also mature more rapidly and the epiphyses close at an early age, so the duration of growth and the eventual height of the adult actually may be shortened.

**An important effect of thyroid hormone is to promote growth and development of the brain during fetal life and for the first few years of postnatal life. If the fetus does not secrete sufficient quantities of thyroid hormone, growth and maturation of the brain both before birth and afterward are greatly retarded and the brain remains smaller than normal. Without specific thyroid therapy within days or weeks after birth, the child without a thyroid gland will remain mentally deficient throughout life

Sympathomimetic Effect

- Thyroid hormone increases target-cell responsiveness to catecholamines.
- Thyroid hormone accomplishes this permissive action by causing a proliferation of catecholamine target-cell receptors.

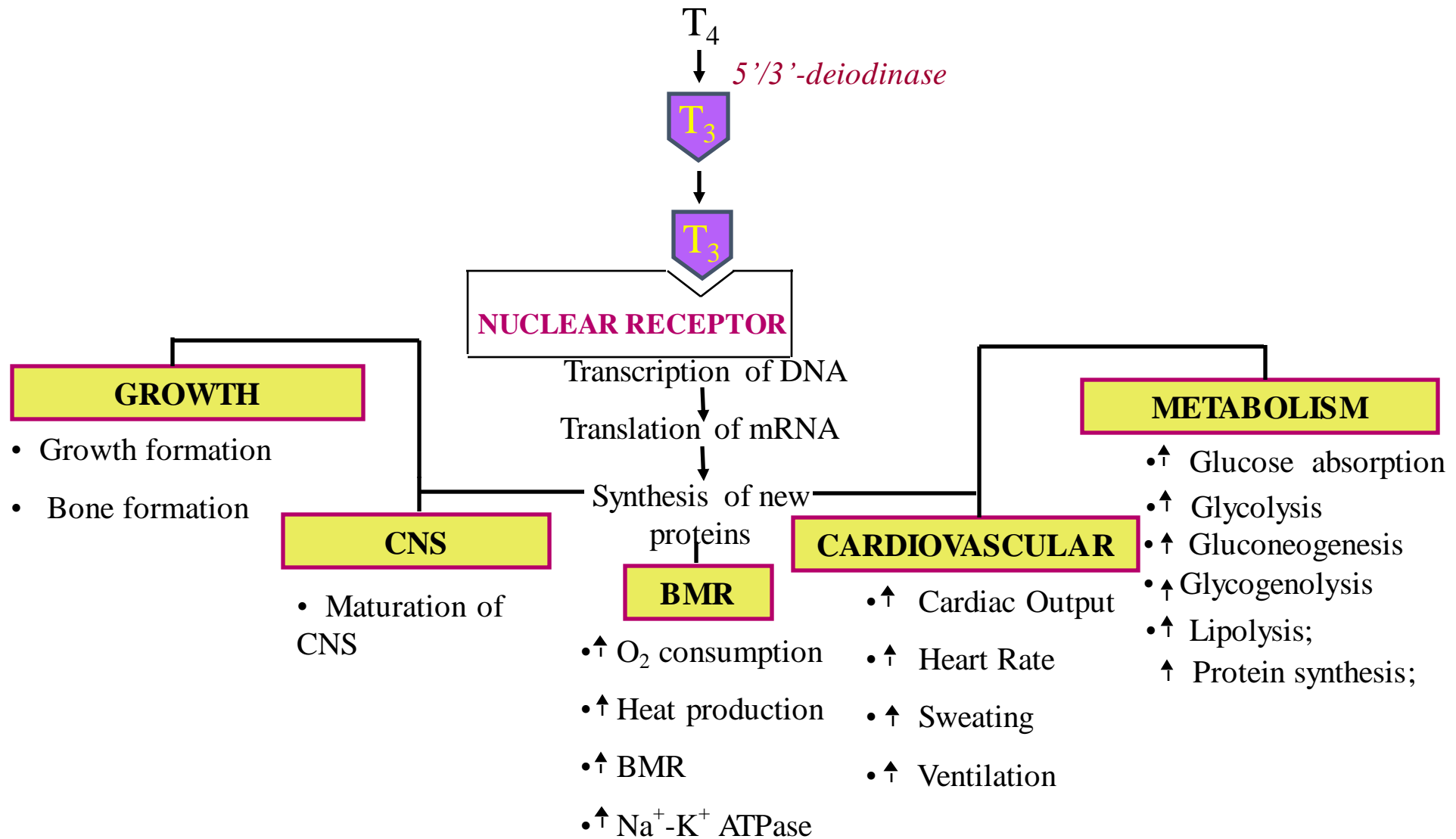
Effect of Thyroid Hormones

- ❖ Thyroid hormone increases heart rate and force of contraction, thus increasing cardiac output.
- ❖ Increased respiration.
- ❖ Increased gastrointestinal motility.
- ❖ Effect on the function of the muscles (vigorous, tremor).
- ❖ Increases the rates of secretion of several other endocrine glands, but it also increases the need of the tissues for the hormones.
(pancreases, ant. pituitry, parathyroid)

** CVS via both its direct effect on the heart, and through its effect of increasing the heart's responsiveness to catecholamines.

** slight increase in thyroid hormone usually makes the **muscles react with vigor** but, with **excessive** thyroid hormone, the muscles become **weakened because of excess protein catabolism**. Conversely, lack of thyroid hormone causes the muscles to become sluggish, and they relax slowly after a contraction.

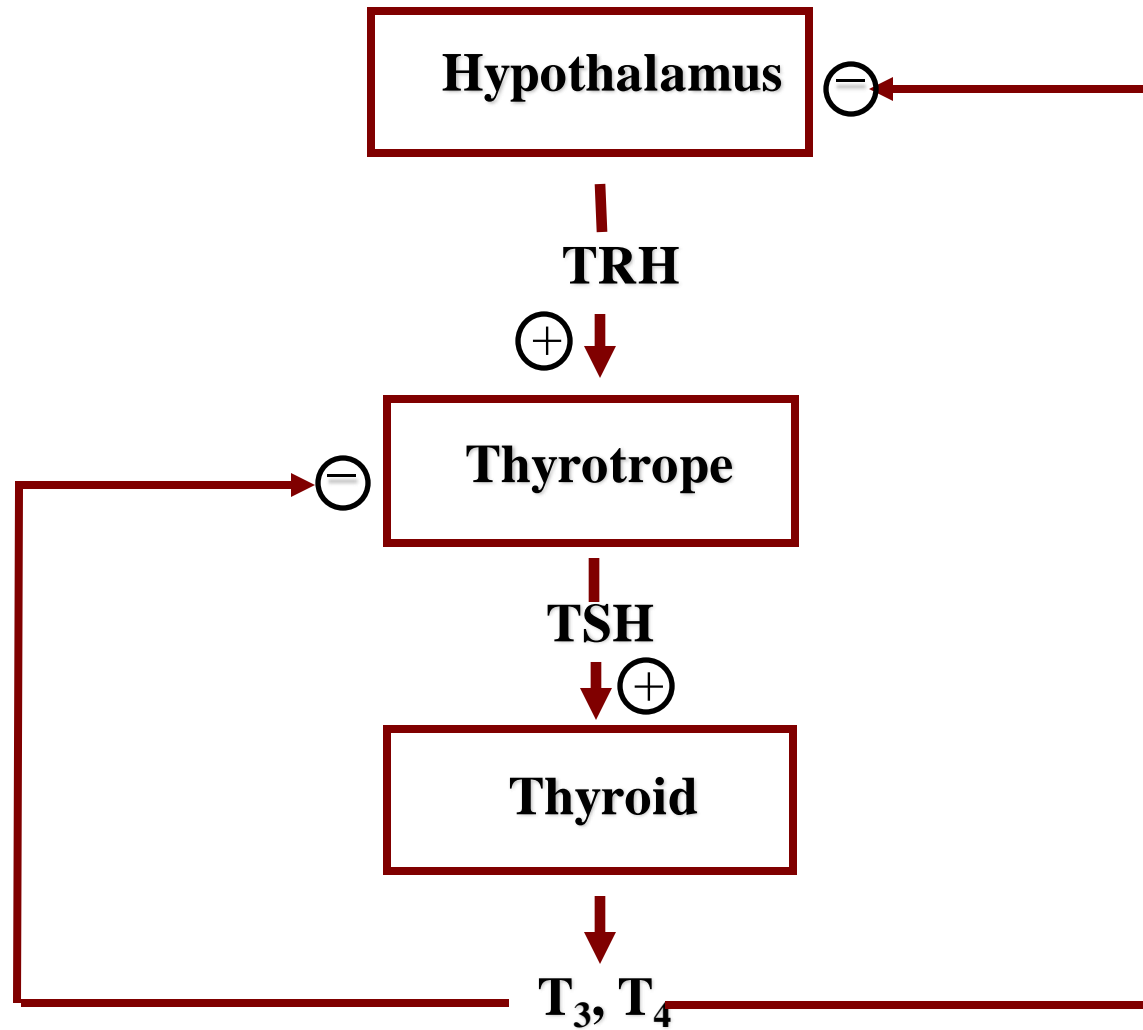
Actions of Thyroid Hormones



Regulation of Thyroid Hormone Secretion

CHAPTER 76

Hypothalamic hypophyseal thyroid axis



TSH Increases Thyroid Secretion

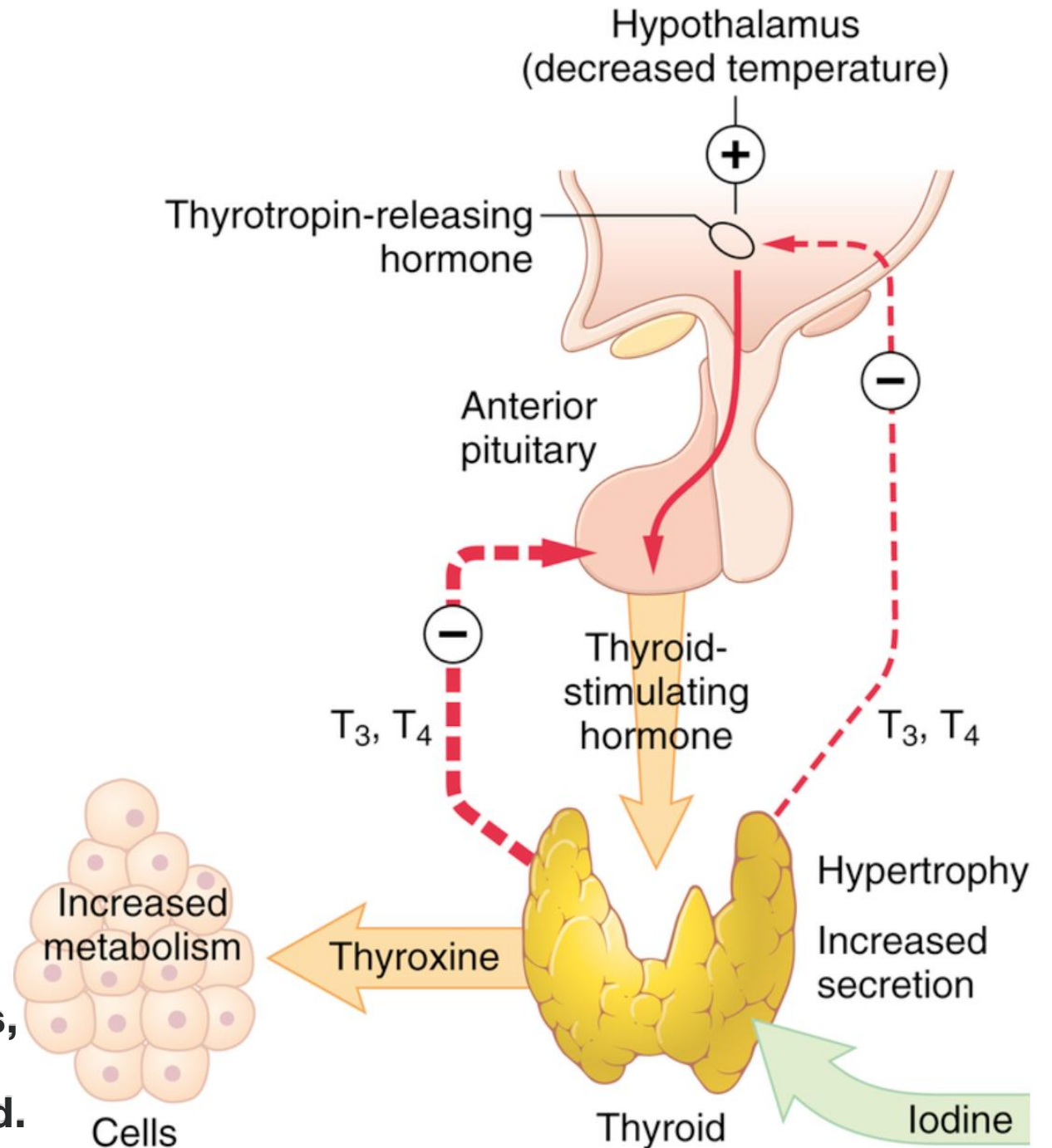
- ❖ Increased proteolysis of the thyroglobulin
- ❖ Increased activity of the iodide pump, which increases the rate of “iodide trapping”
- ❖ Increased iodination of tyrosine to form the thyroid hormones
- ❖ Increased size and increased secretory activity of the thyroid cells
- ❖ Increased number of thyroid cells.
- ❖ In summary, TSH increases all the known secretory activities of the thyroid glandular cells.

***The most important early effect after administration of **TSH is to initiate proteolysis of the thyroglobulin**, which causes release of thyroxine and triiodothyronine into the blood within 30 minutes. The other effects require hours or even days and weeks to develop fully.

TSH secretion Is Regulated by TRH

- ❖ Exposure to cold – Increase TRH.
- ❖ Prolonged fasting reduces plasma leptin levels which, in turn, inhibit TRH.
- ❖ Excitement and anxiety – conditions that greatly stimulate the sympathetic nervous system – cause an acute decrease in secretion of TSH, perhaps because these states increase the metabolic rate and body heat and therefore exert an inverse effect on the heat control center.

****One of the best-known stimuli for increasing the rate of TRH secretion by the hypothalamus, and therefore TSH secretion by the anterior pituitary gland, is exposure of an animal to cold.**



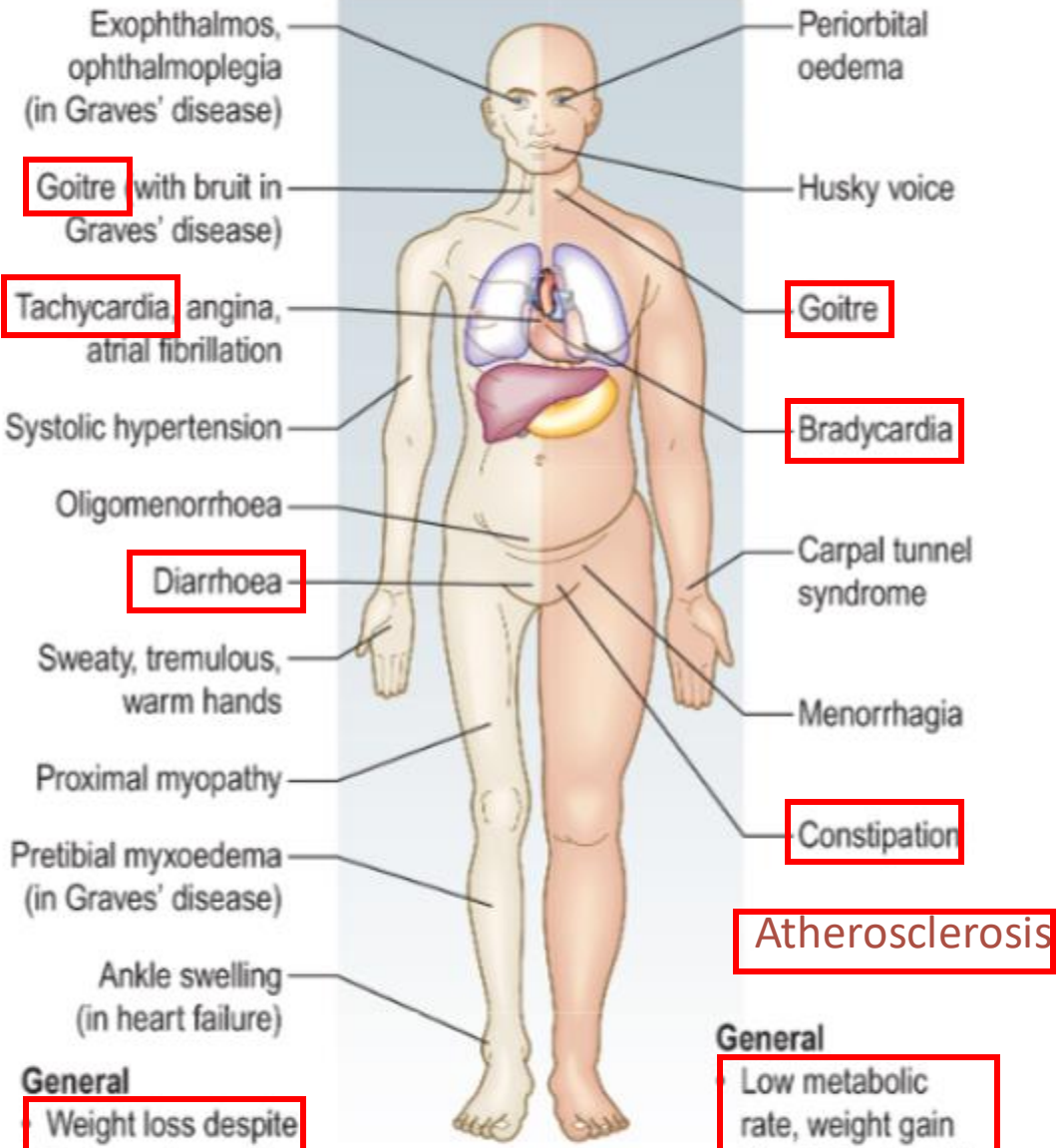


Thyroid Gland Disorder

CHAPTER 76

Hyperthyroidism

Hypothyroidism



General

Weight loss despite increased appetite
Heat intolerance
Anxiety, irritability
Fast, fine tremor

General

Low metabolic rate, weight gain
Sensitivity to cold
Lethargy, mental impairment, depression

The symptoms of hyperthyroidism are obvious from the preceding discussion of the physiology of the thyroid hormones: **(1) a high state of excitability, (2) intolerance to heat, (3) increased sweating, (4) mild to extreme weight loss (sometimes as much as 100 pounds), (5) varying degrees of diarrhea, (6) muscle weakness, (7) nervousness or other psychic disorders, (8) extreme fatigue but inability to sleep, and (9) tremor of the hands.**

Hypothyroidism: They include fatigue and extreme somnolence, with persons sleeping up to 12 to 14 hours a day, extreme muscular sluggishness, a slowed heart rate, decreased cardiac output, decreased blood volume, sometimes increased body weight, constipation, mental sluggishness, failure of many trophic functions in the body as evidenced by depressed growth of hair and scaliness of the skin, development of a froglike, husky voice, and, in severe cases, development of an edematous appearance throughout the body called myxedema.

Conversely, decreased thyroid secretion greatly increases the plasma concentrations of cholesterol, phospholipids, and triglycerides and almost always causes excessive deposition of fat in the liver as well. The large increase in circulating plasma cholesterol in prolonged hypothyroidism is often associated with severe atherosclerosis.

Hyperthyroidism

❖ Graves' disease, the most common form of hyperthyroidism, is an autoimmune disease in which antibodies called thyroid-stimulating immunoglobulins (TSIs) form against the TSH receptor in the thyroid gland.

❖ T3 and T4 (High)

❖ TSH (Low)

**** These antibodies bind with the same membrane receptors that bind TSH and induce continual activation**



Hypothyroidism

- ❖ Autoimmunity against the thyroid gland (Hashimoto disease).
- ❖ T3 and T4 (low)
- ❖ TSH (High)
- ❖ Thyroid peroxidase antibody test and the anti-thyroglobulin antibody test, are commonly used to detect the presence of Hashimoto's thyroiditis.

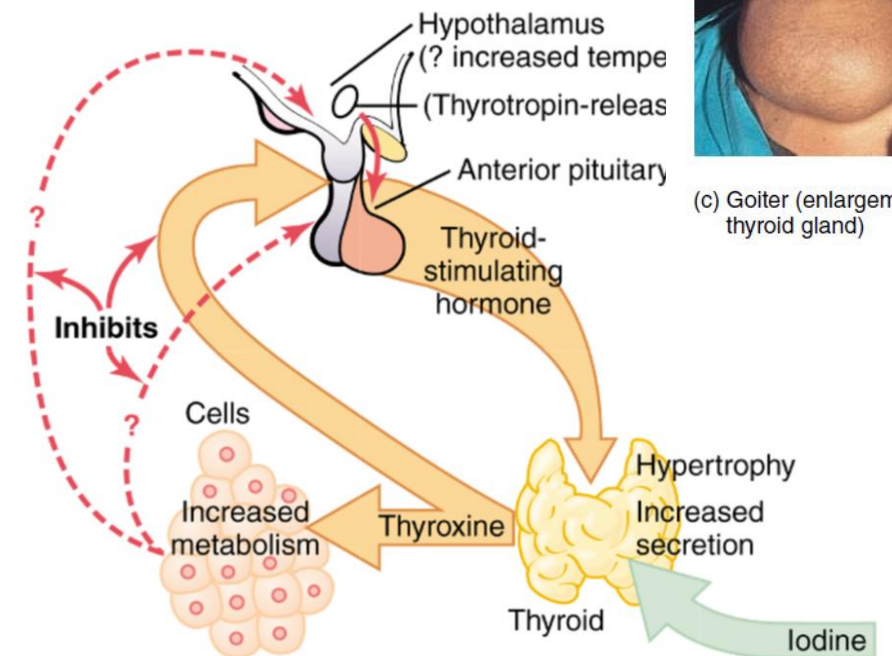
Treatment: Thyroxine



Endemic Colloid Goiter Caused by Dietary Iodide Deficiency

- ❖ Lack of iodine prevents production of both thyroxine and triiodothyronine.
- ❖ As a result, no hormone is available to inhibit production of TSH by the anterior pituitary.
- ❖ This causes the pituitary to secrete excessively large quantities of TSH.
- ❖ The TSH then stimulates the thyroid cells to secrete tremendous amounts of thyroglobulin colloid into the follicles, and the gland grows larger and larger.
- ❖ But because of lack of iodine, thyroxine and triiodothyronine production does not occur in the thyroglobulin molecule and therefore does not cause the normal suppression of TSH production by the anterior pituitary.

- ❖ The follicles become tremendous in size, and the thyroid gland may increase to 10 to 20 times' normal size



(c) Goiter (enlargement of thyroid gland)

Cretinism

- Extreme hypothyroidism during fetal life, infancy, or childhood.
- Characterized by failure of body growth and by mental retardation.
- Obese, stocky, and short appearance. Occasionally the tongue becomes so large in relation to the skeletal growth that it obstructs swallowing and breathing, inducing a characteristic guttural breathing that sometimes chokes the child.
- Treatment of the neonate with cretinism at any time with adequate iodine or thyroxine usually causes normal return of physical growth, but unless the cretinism is treated within a few weeks after birth, mental growth remains permanently retarded.

**Thyroid hormone is essential for growth but is not itself directly responsible for promoting growth. It plays a permissive role in skeletal growth; the actions of GH fully manifest only when enough thyroid hormone is present. As a result, growth is severely stunted in hypothyroid children, but hypersecretion of thyroid hormone does not cause excessive growth.

** A neonate without a thyroid gland may have a normal appearance and function because she or he was supplied with some (but usually not enough) thyroid hormone by the mother while in utero. A few weeks after birth, however, the neonate's movements become sluggish and both physical and mental growth begin to be greatly retarded. Treatment of the neonate with cretinism at any time with adequate iodine or thyroxine usually causes normal return of physical growth, but unless the cretinism is treated within a few weeks after birth, mental growth remains permanently retarded. This state results from retardation of the growth, branching, and myelination of the neuronal cells of the central nervous system at this critical time in the normal development of the mental powers.

Skeletal growth in a child with cretinism is characteristically more inhibited than is soft tissue growth. As a result of this disproportionate rate of growth, the soft tissues are likely to enlarge excessively, giving the child with cretinism an obese, stocky, and short appearance. Occasionally the tongue becomes so large in relation to the skeletal growth that it obstructs swallowing and breathing, inducing a characteristic guttural breathing that sometimes chokes the child.