PHARMACOLOGY OF THYROID DISORDERS

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Pharmacology II

Spring Semester

Third week

19/02/2025

Outline

- Thyroid hormones
- Thyroid disorders

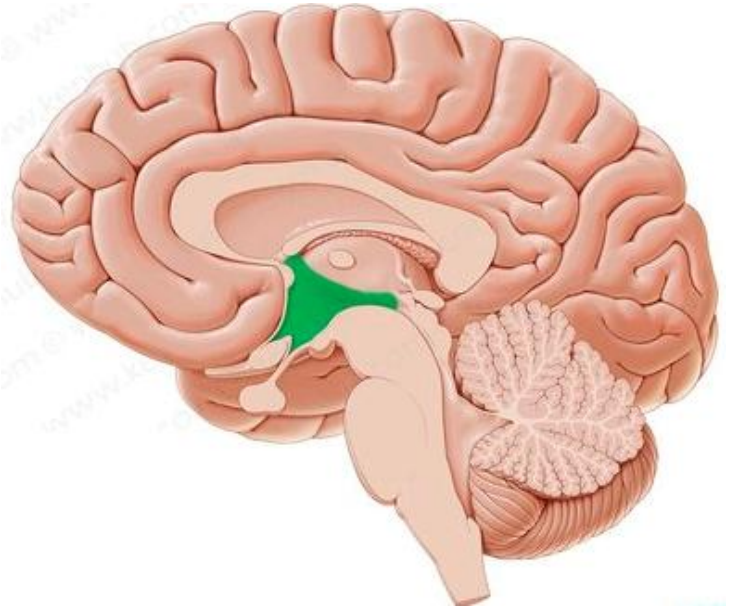
Objectives

By the end of this lecture, students should be able to:

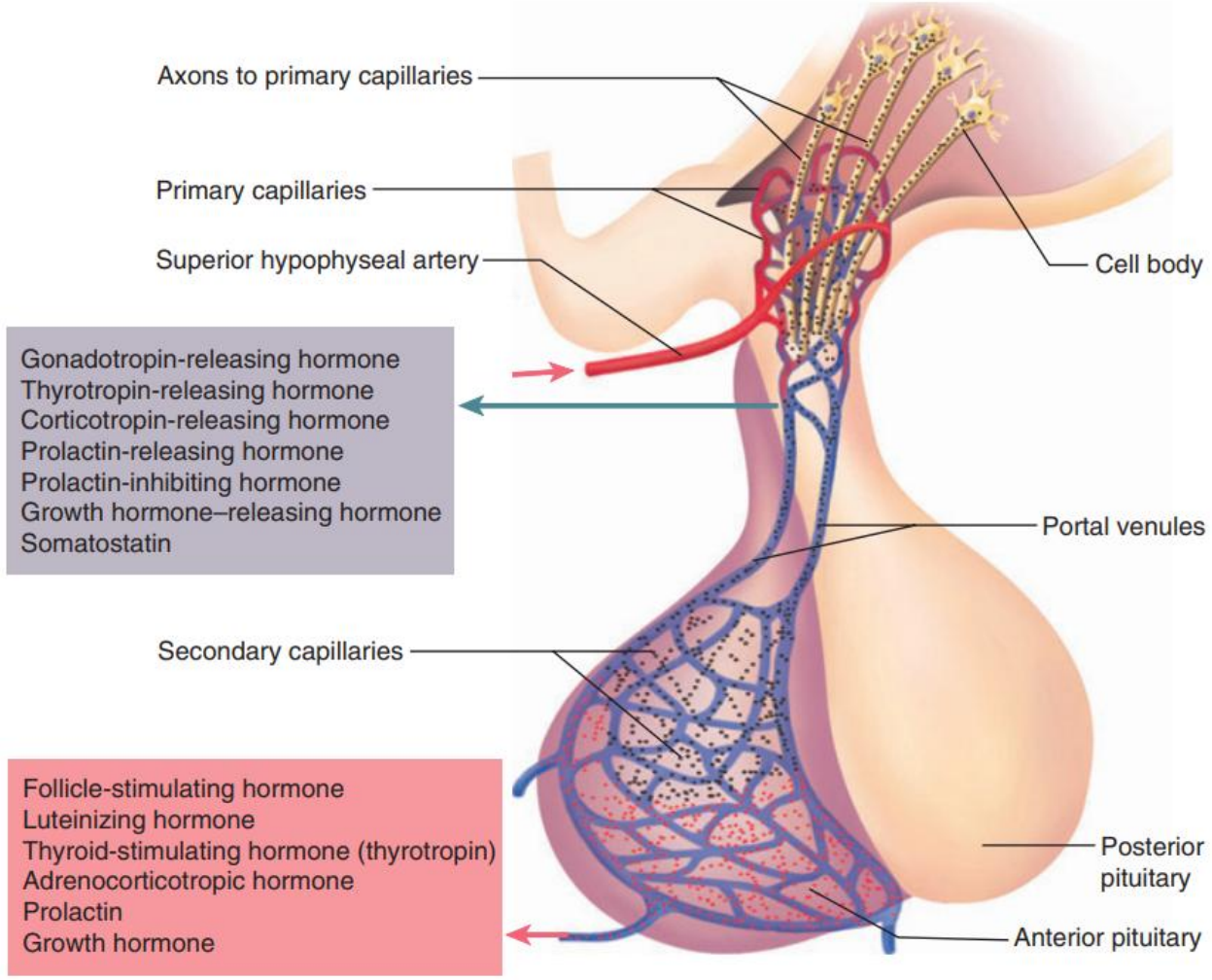
1. Understand the hypothalamic-pituitary-thyroid axis.
2. Being familiar with thyroid gland and thyroid hormones.
3. Describe effect of iodine deficiency on thyroid gland and thyroid hormones .
4. Learn about pharmacological management of hypothyroidism and hyperthyroidism.
5. Learn about physiotherapy considerations of hypothyroidism and hyperthyroidism.

Hypothalamus

- The hypothalamus is a gland in human brain that controls human hormone system.
- The hypothalamus connects the nervous system to the endocrine system. It receives and processes signals from other brain regions and pathways and translates them into hormones, the chemical messengers of the endocrine system.
- Hypothalamus releases hormones to another part of human brain called the pituitary gland, which sends hormones out to different organs.

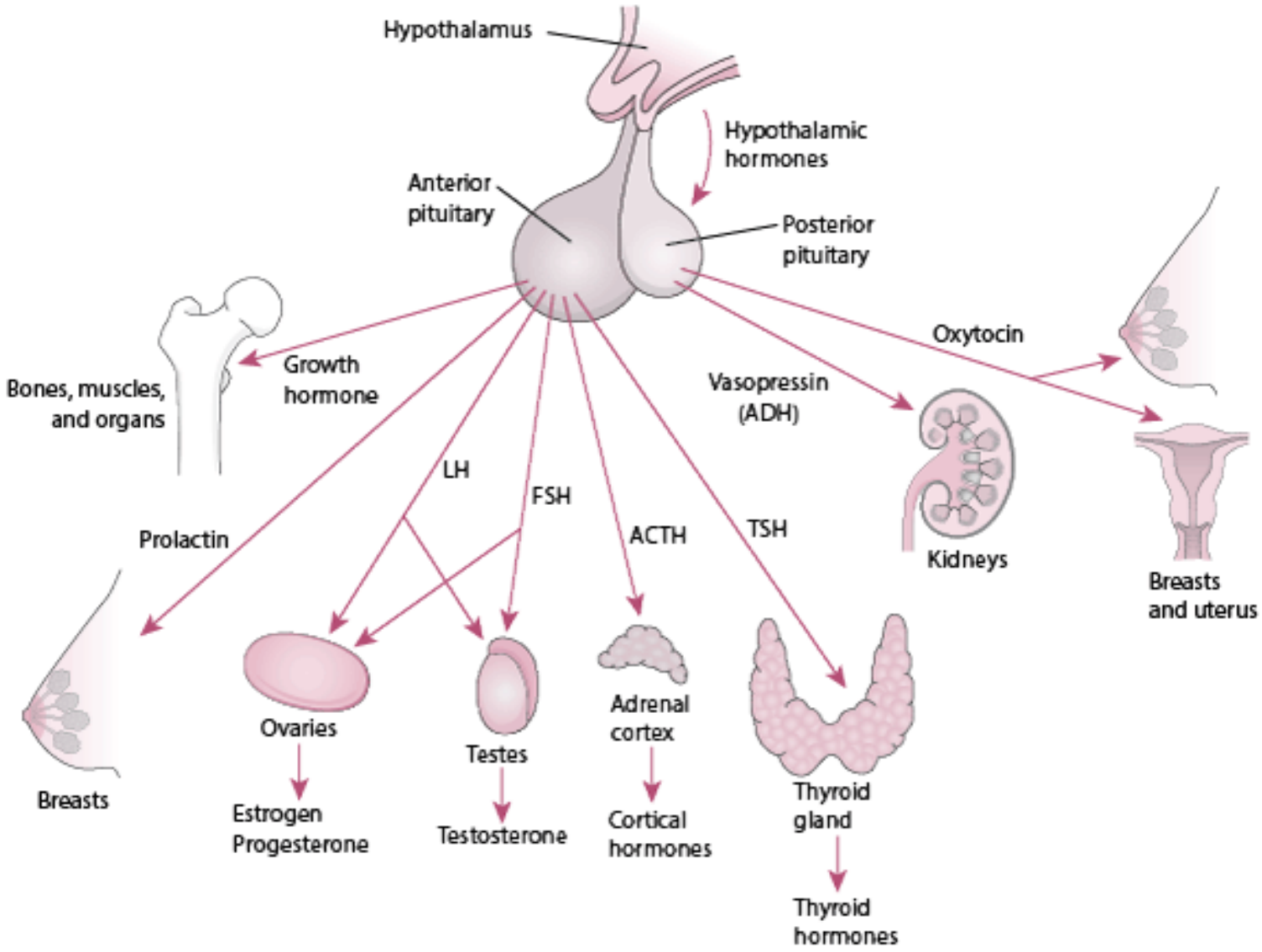


Hypothalamic hormones



- **Somatostatin** is also called growth hormone–inhibiting hormone. Its name derives from **somatotropin**, a synonym for **growth hormone (GH)**.

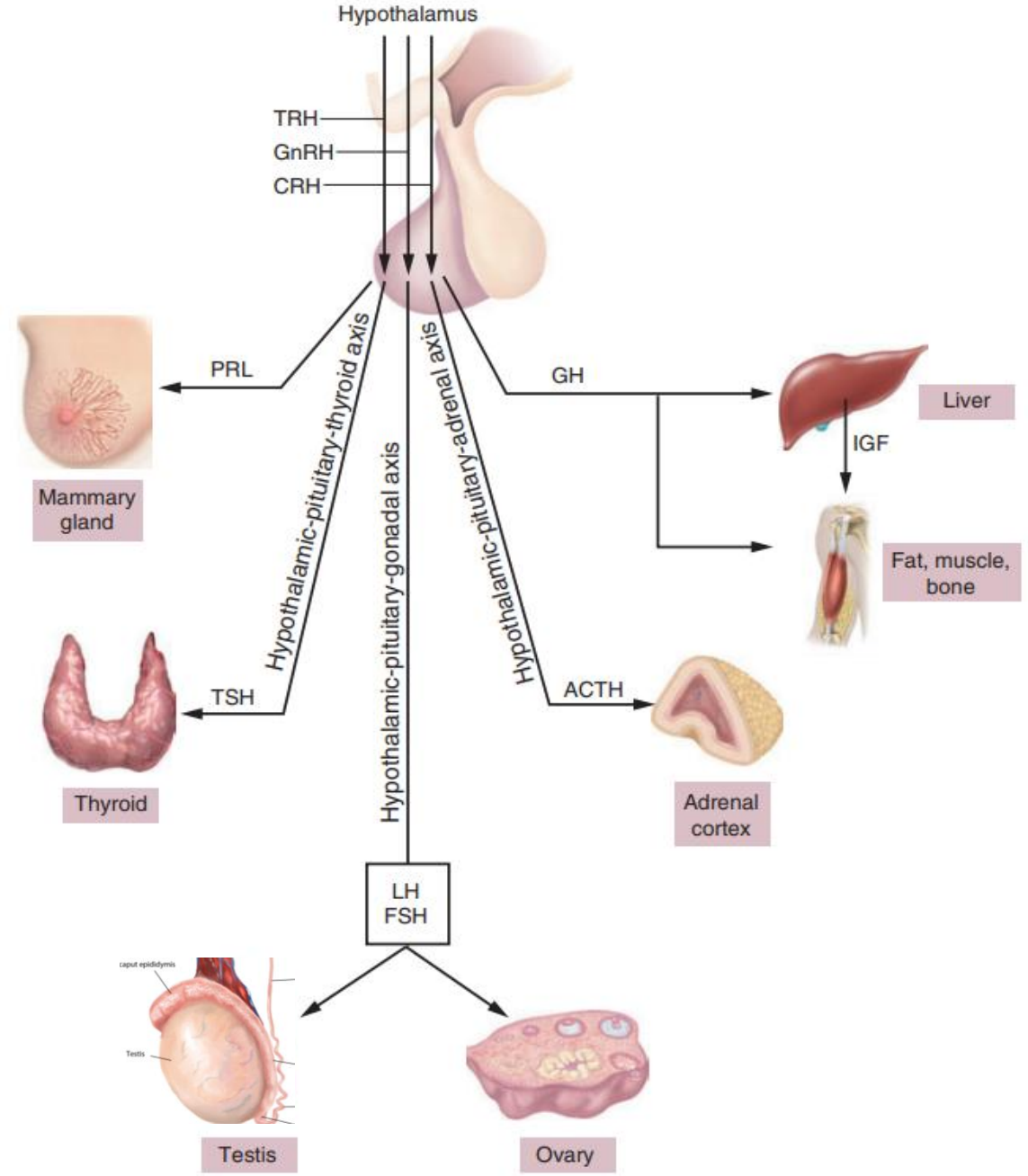
TSH and its target gland



Axes physiologically link pituitary function to the function of other endocrine glands

- The hormonal relationship between the hypothalamus, pituitary, and a more remote endocrine gland is called an axis.
- There are three such axes:

1. The hypothalamic-pituitary-gonadal axis involving GnRH, FSH, and LH
2. **The hypothalamic-pituitary-thyroid axis involving TRH and TSH**
3. The hypothalamic-pituitary-adrenal axis involving CRH and ACTH.


Hypothalamus
TRH
GnRH
CRH
PRL
Mammary gland
Hypothalamic-pituitary-thyroid axis
TSH
Thyroid
Hypothalamic-pituitary-gonadal axis
LH
FSH
Testis
Ovary
Hypothalamic-pituitary-adrenal axis
ACTH
Adrenal cortex
GH
Liver
IGF
Fat, muscle, bone

Negative feedback inhibition in the pituitary-thyroid axis

Negative feedback to control hormone secretion is explained in following points

1. The hypothalamus secretes thyrotropin-releasing hormone (TRH).
2. TRH stimulates the anterior pituitary to secrete thyroid-stimulating hormone (TSH).
3. TSH stimulates the thyroid gland to secrete the two thyroid hormones, T3 and T4.
4. T3 and T4 stimulate the metabolism of most cells throughout the body.
5. T3 and T4 also inhibit the release of TSH by the pituitary.
6. To a lesser extent, T3 and T4 also inhibit the release of TRH by the hypothalamus

Negative feedback inhibition in the pituitary-thyroid axis

Steps 5 and 6 are negative feedback inhibition of the pituitary and hypothalamus respectively. These steps ensure that when thyroid hormone levels are high, TSH secretion remains low. If thyroid hormone secretion drops, TSH secretion rises and stimulates the thyroid to secrete more hormone. This negative feedback keeps thyroid hormone levels fluctuating around a set point in typical homeostatic fashion.

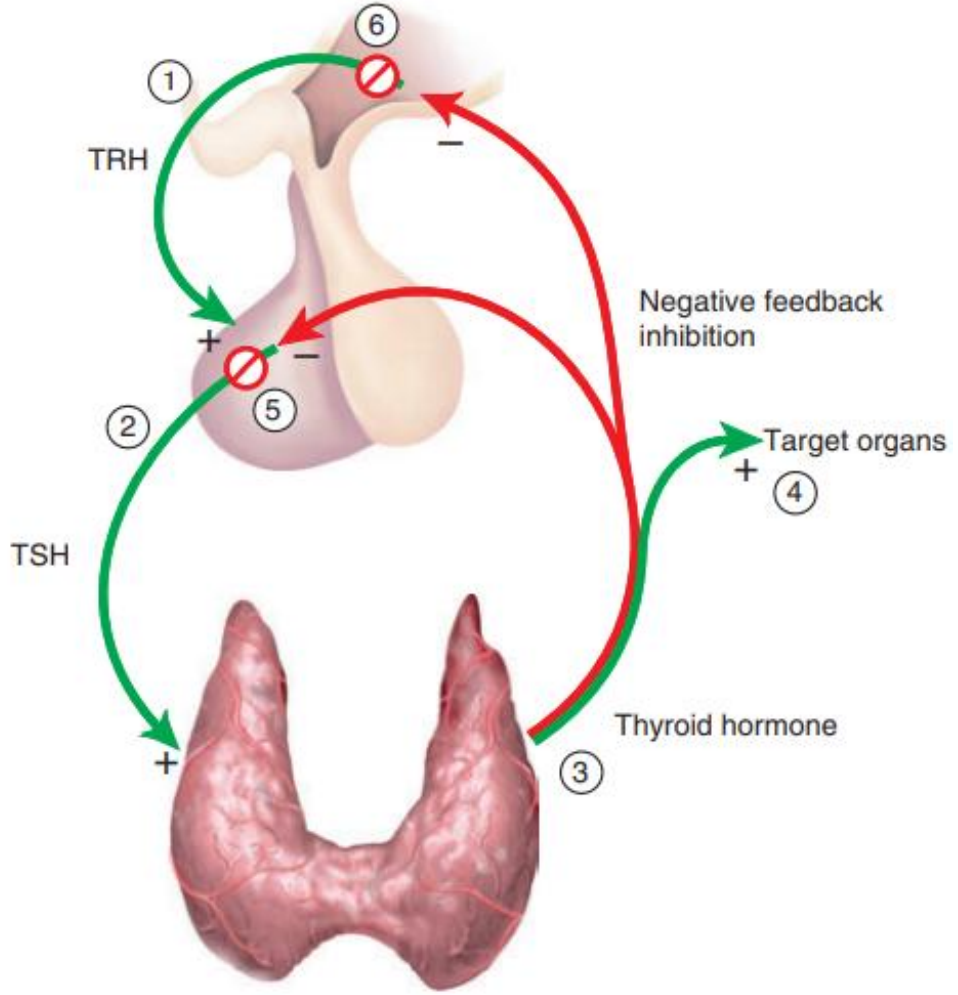
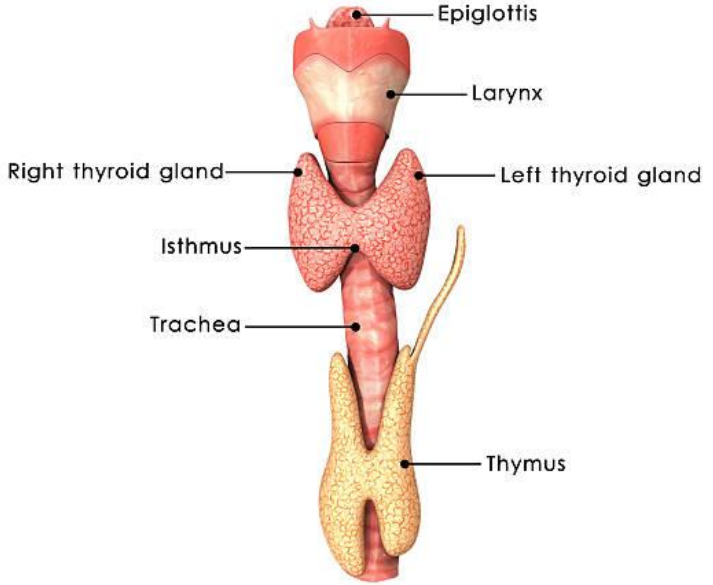
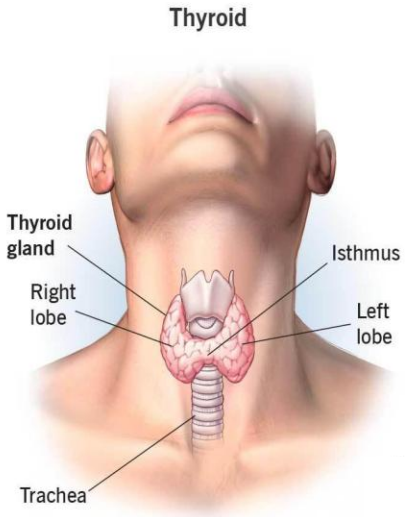


Figure. Negative feedback inhibition in the pituitary-thyroid axis.

The thyroid gland

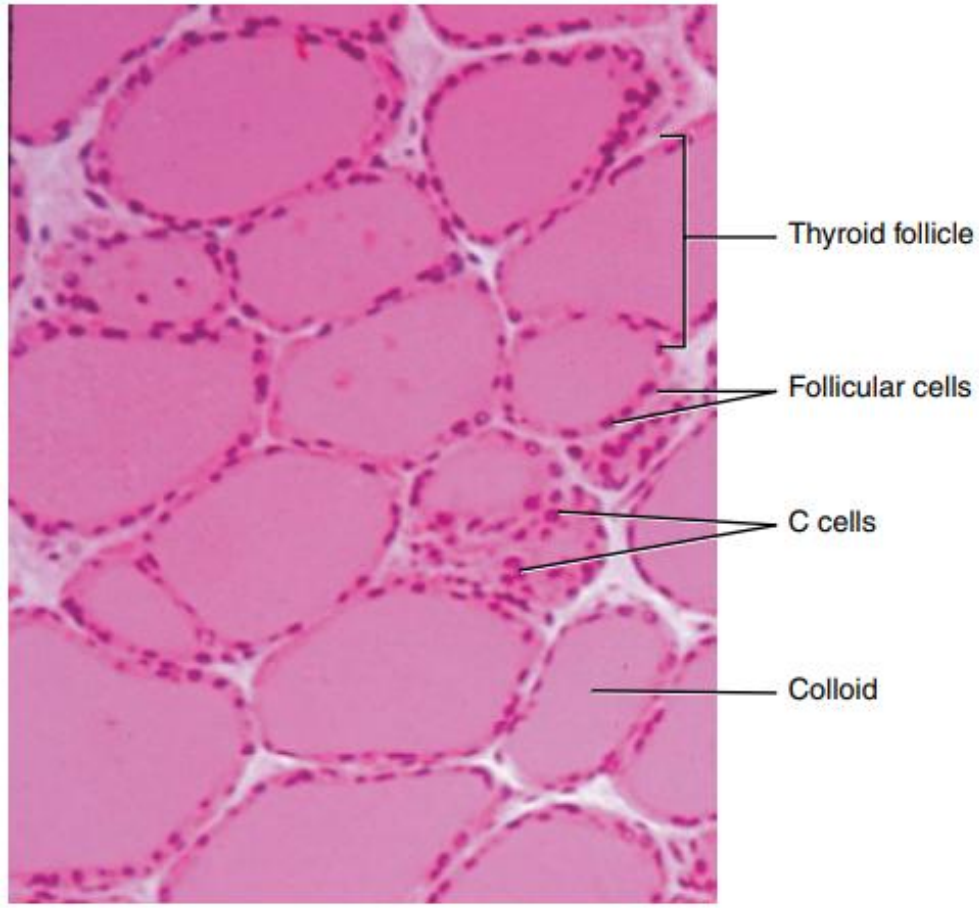
- The thyroid gland is the large endocrine gland; it weighs 20 to 25 g.
- The thyroid gland is located on the front and sides of the trachea just below the larynx.
- Thyroid gland consists of two lobes (right and left) that are connected by a middle piece called the isthmus.



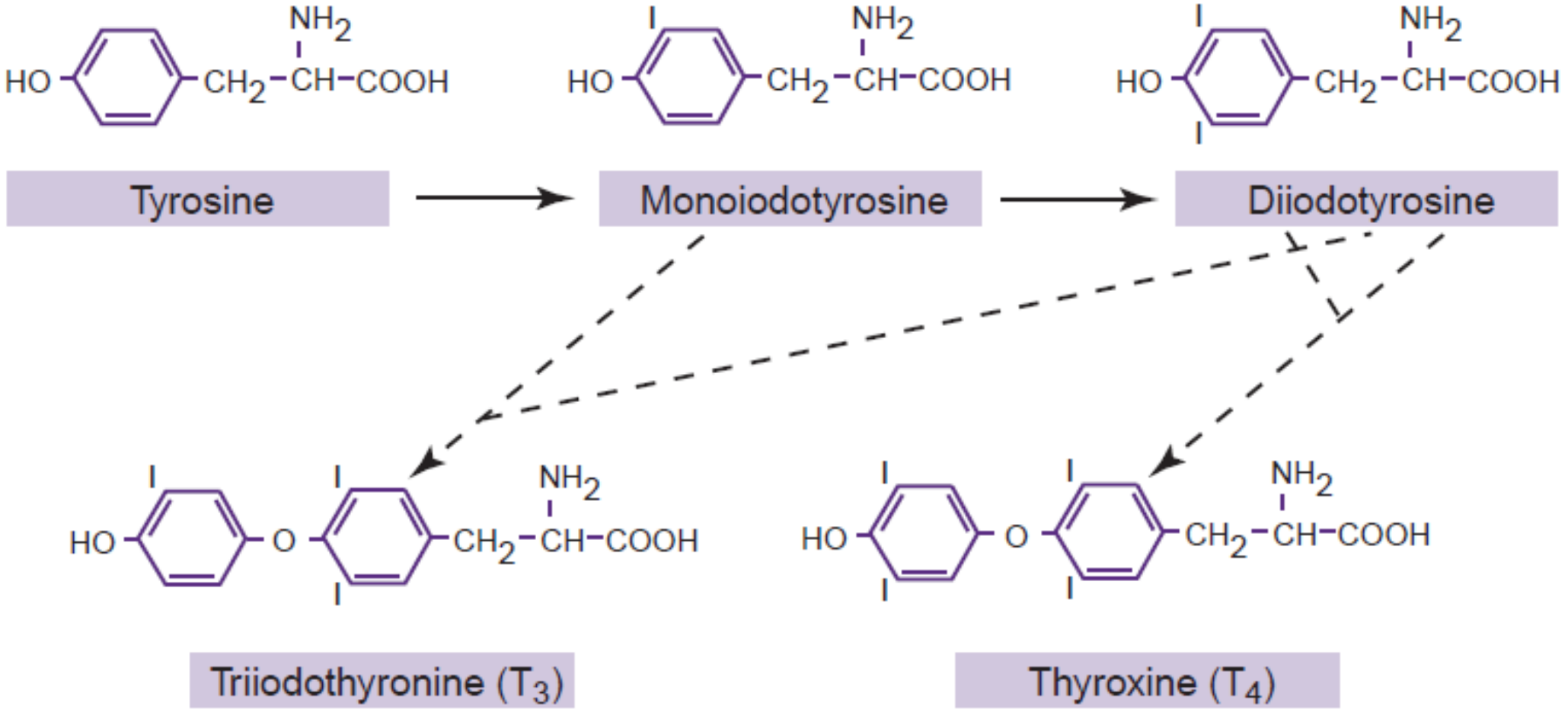


The thyroid gland

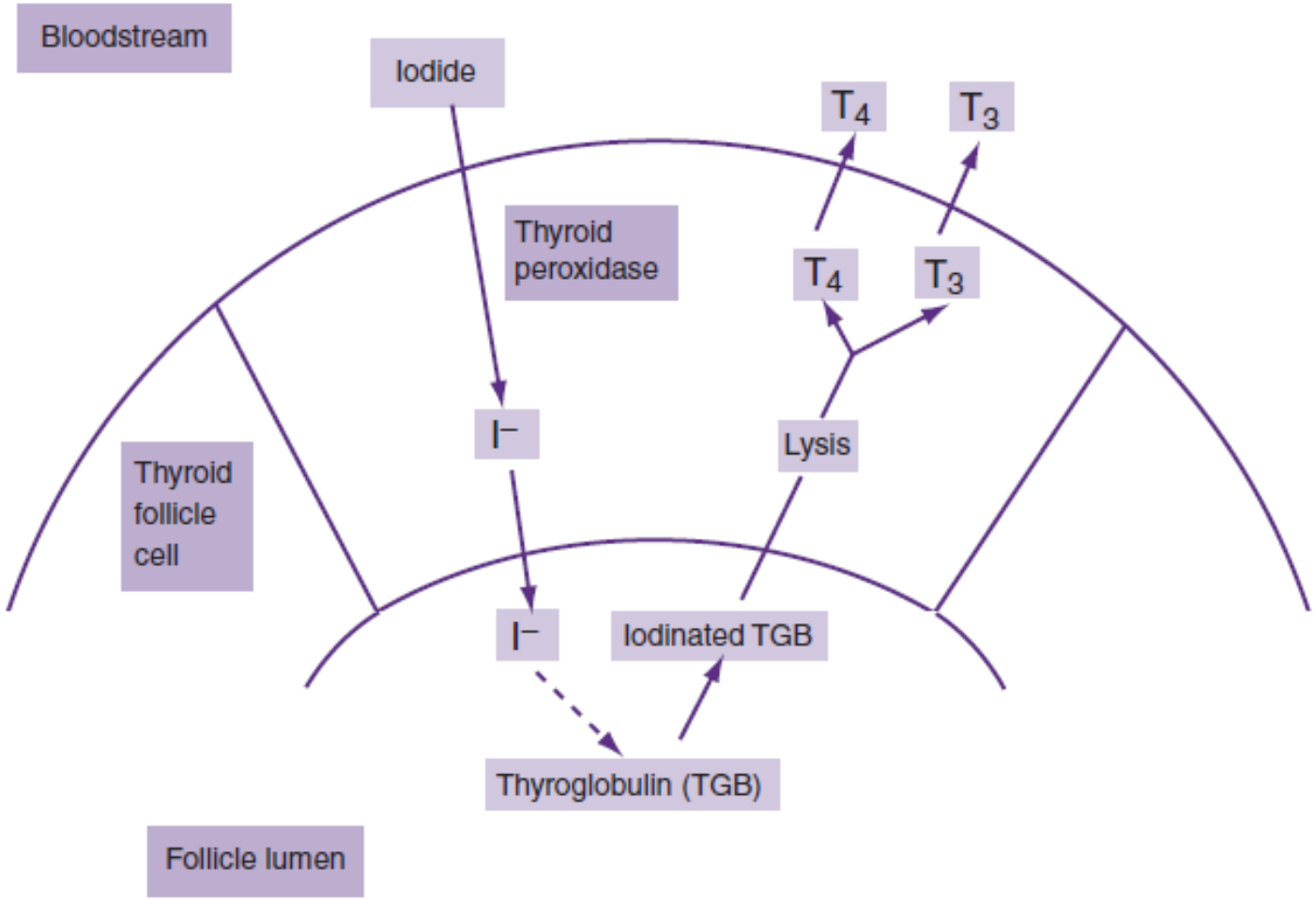
- Histologically, the thyroid gland is composed mostly of sacs called thyroid follicles.
- Each thyroid follicles is filled with a protein-rich colloid and lined by a simple cuboidal epithelium of follicular cells.
- Follicular cells secrete two main thyroid hormones T3, or triiodothyronine, and thyroxine, also known as T4 or tetraiodothyronine.
- These names refer to the fact that the two hormones contain three (T3) and four (T4) iodine atoms. Therefore, iodine is necessary for the synthesis of these hormones.



The thyroid hormones

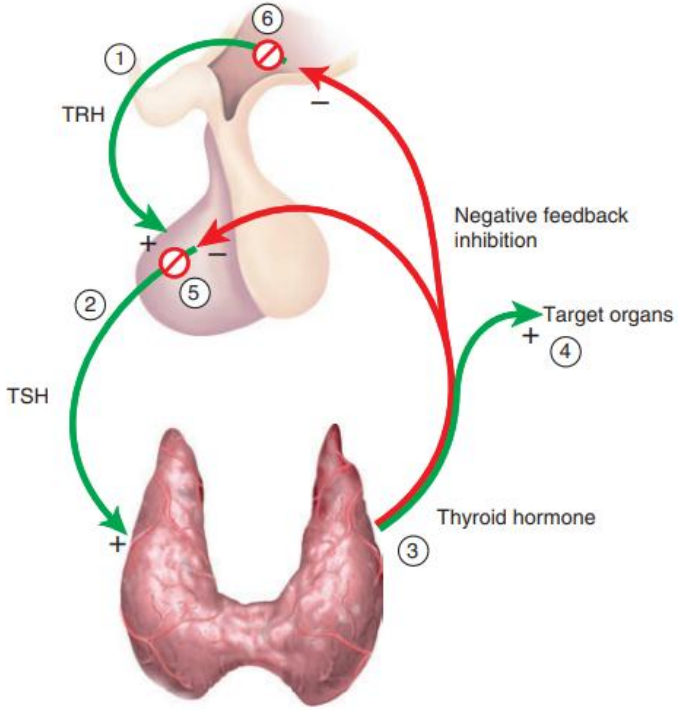


Thyroid hormone synthesis



Effects of iodine deficiency

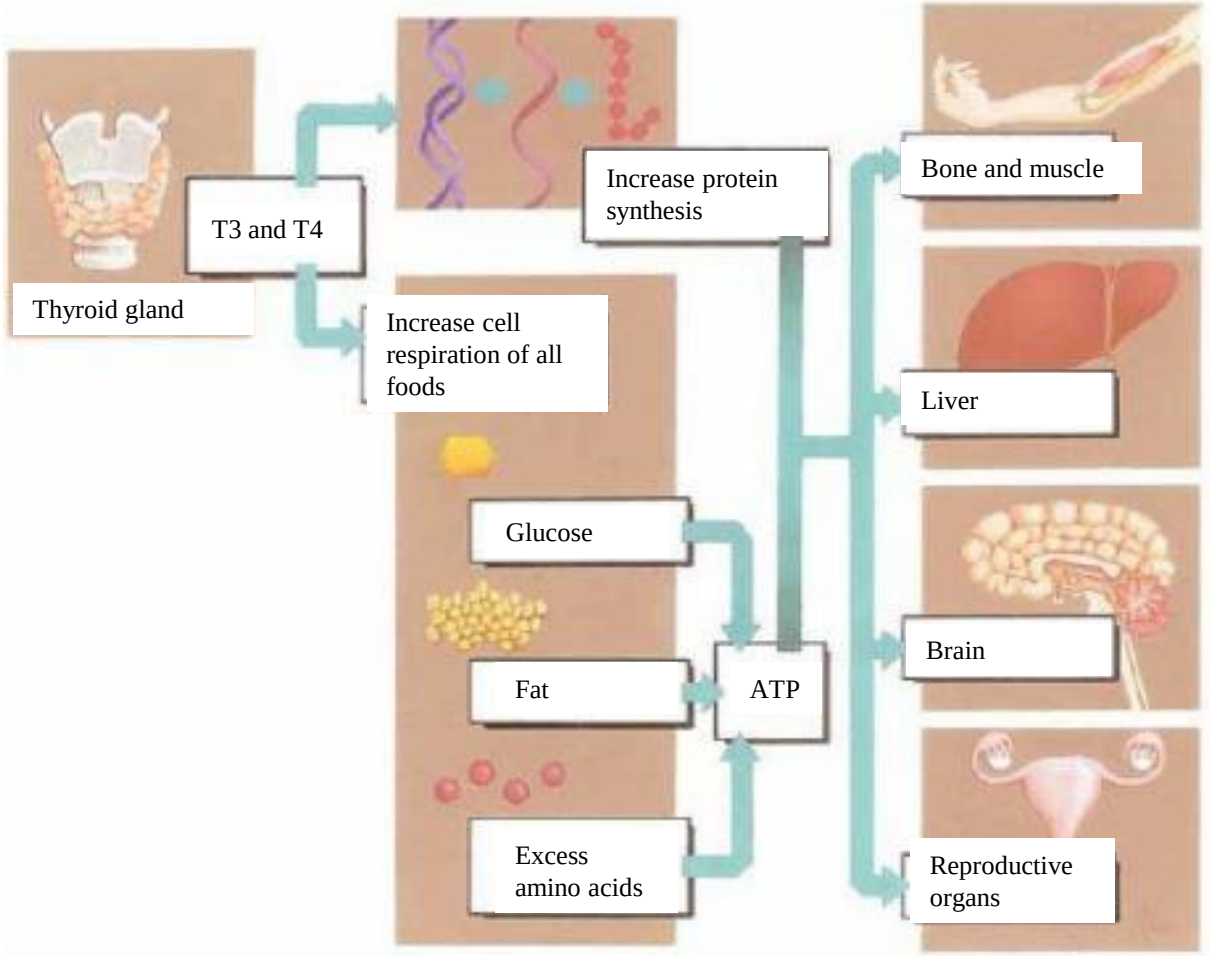
- If dietary iodine is deficient, the thyroid will not be able to make thyroid hormones. A lack of thyroid hormone will lead to decreased negative feedback on the pituitary, which in turn, will lead to increased production of thyroid-stimulating hormone, which causes the thyroid to enlarge (goiter).



Thyroid hormone functions

Thyroxine (T4) and T3 have the same functions:

1. Thyroxine and T3 increase cell respiration of all food types (carbohydrates, fats, and excess amino acids) and thereby increase energy and heat production.
2. Normal production of thyroxine and T3 is essential for physical growth, normal mental development, and maturation of the reproductive system.
3. They also increase the rate of protein synthesis within cells.



Thyroid function tests (TFT)

Thyroid function tests (TFT) include

1. **TSH (stimulate the growth of thyroid gland and production of T3 and T4)**
2. **T3**
3. **T4**
4. **FT3**
5. **FT4**

Abnormal of thyroid hormones secretions

Abnormal of thyroid hormones secretions includes

A. **Hypothyroidism** : happens when the thyroid gland doesn't make enough thyroid hormones

In case of hypothyroidism

1. T3 and T4 production will be low
2. TSH production will be more
3. TRH production will be more

Causes of hypothyroidism

1. Autoimmune diseases
2. Thyroid surgery
3. Radiation therapy
4. Thyroiditis
5. Medicine

Abnormal of thyroid hormones secretions

Symptoms of hypothyroidism

1. Fatigue
2. Weight gain
3. Cold intolerance
4. Dry skin, brittle hair
5. Depression
6. Bradycardia (slow heart rate)
7. Constipation

Abnormal of thyroid hormones secretions

Pharmacological management of hypothyroidism

1. 💊 Levothyroxine (T4) – First-line therapy

- ➢ Synthetic thyroid hormone replacement
- ➢ Dosage titrated based on TSH levels
- ➢ Taken on an empty stomach for better absorption

2. 💊 Liothyronine (T3) – Occasionally used

- ➢ Shorter half-life
- ➢ used in severe cases or combination therapy

Abnormal of thyroid hormones secretions

Physiotherapy Considerations

1. Monitor for fatigue and reduced exercise tolerance
2. Address muscle stiffness and weakness
3. Be cautious with cold exposure
4. Monitor cardiovascular responses due to bradycardia

Abnormal of thyroid hormones secretions

B. Hyperthyroidism: happens when the thyroid gland makes more thyroid hormones

In case of hyperthyroidism

1. T3 and T4 production will be mor
2. TSH production will be low
3. TRH production will be low

Causes of hyperthyroidism

1. Graves disease (most common cause of hyperthyroidism)
2. Taking too much thyroid hormone (common)
3. Noncancerous growths of the thyroid gland or pituitary gland (rare)

Abnormal of thyroid hormones secretions

Symptoms of hyperthyroidism

1. Weight loss despite increased appetite
2. Heat intolerance, sweating
3. Nervousness
4. Palpitations, tachycardia (fast heart rate)
5. Muscle weakness

Abnormal of thyroid hormones secretions

Pharmacological management of hyperthyroidism

1. 💊 Carbimazol

Carbimazole inhibits thyroid hormone synthesis by:

- Blocking thyroid peroxidase (TPO), preventing the oxidation of iodide to iodine
- Stopping iodine from binding to tyrosine residues, preventing the formation of T3 (triiodothyronine) and T4 (thyroxine

2. Surgery (Thyroidectomy): Used in severe cases or large goiters

Abnormal of thyroid hormones secretions

Physiotherapy Considerations

1. Monitor for tachycardia
2. Prevent heat intolerance & dehydration
3. Manage muscle weakness & fatigue