M.Sc. 4th Semester

Subject: Human Physiology

Paper: PHY-401

Unit:33

Module: 03 (Part-I)

Topics: Thyroid gland and pituitary thyroid axis

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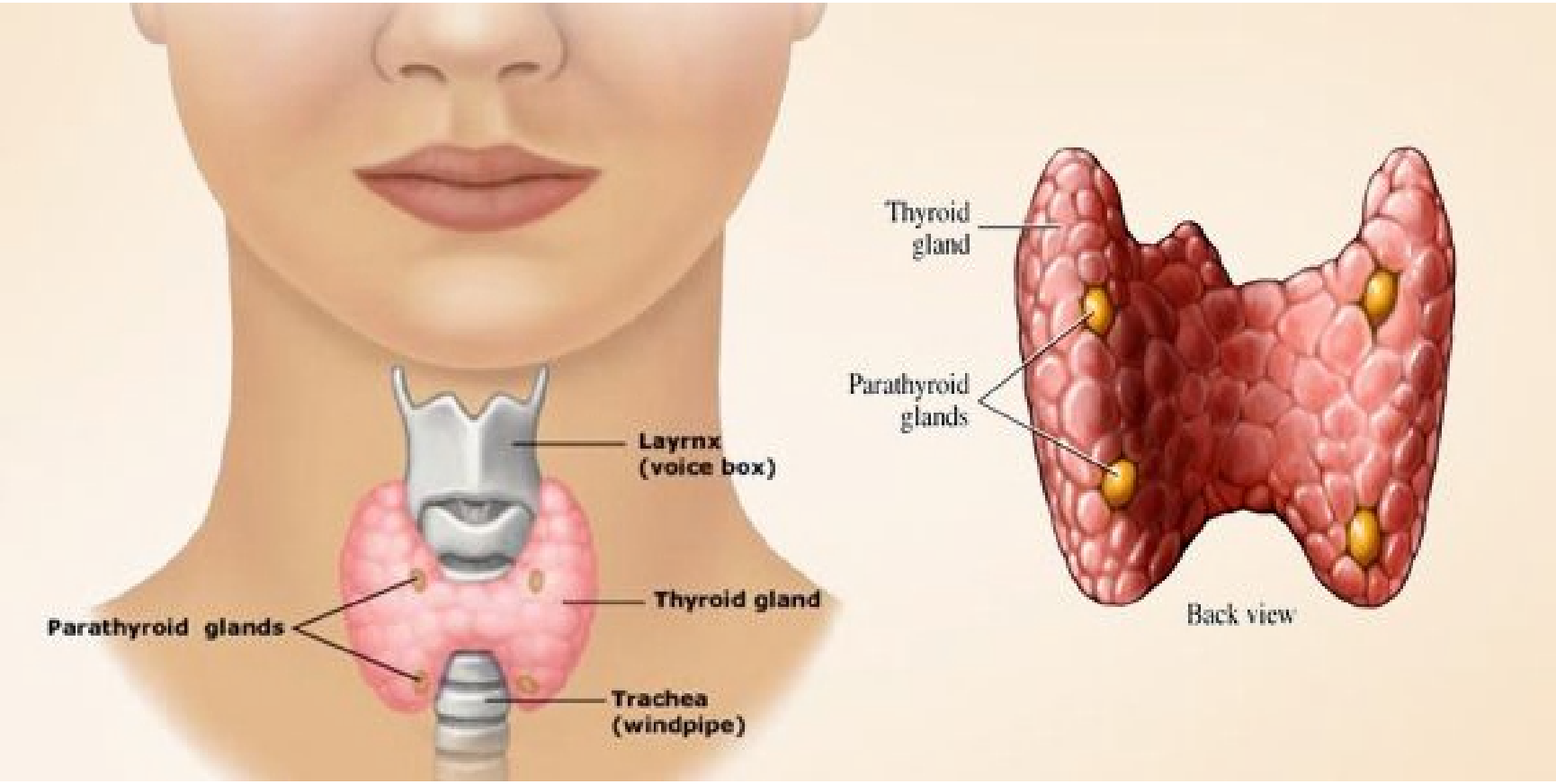
THYROID PHYSIOLOGY

Dr. Ankita Das

- The thyroid is a small gland, measuring about 2 inches (5 centimeters) across, that lies just under the skin below the Adam's apple in the neck. The two halves (lobes) of the gland are connected in the middle (called the isthmus), giving the thyroid gland the shape of a bow tie.

- Normally, the thyroid gland cannot be seen and can barely be felt. If it becomes enlarged, doctors can feel it easily, and a prominent bulge (goiter) may appear below or to the sides of the Adam's apple.

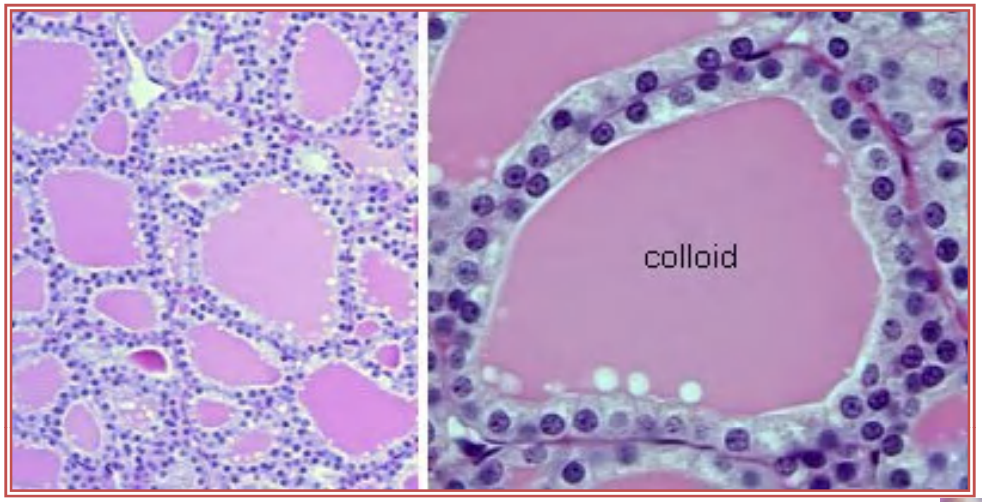

Layrnx
(voice box)
Thyroid gland
Parathyroid glands
Trachea
(windpipe)
Thyroid
gland
Parathyroid
glands
Back view

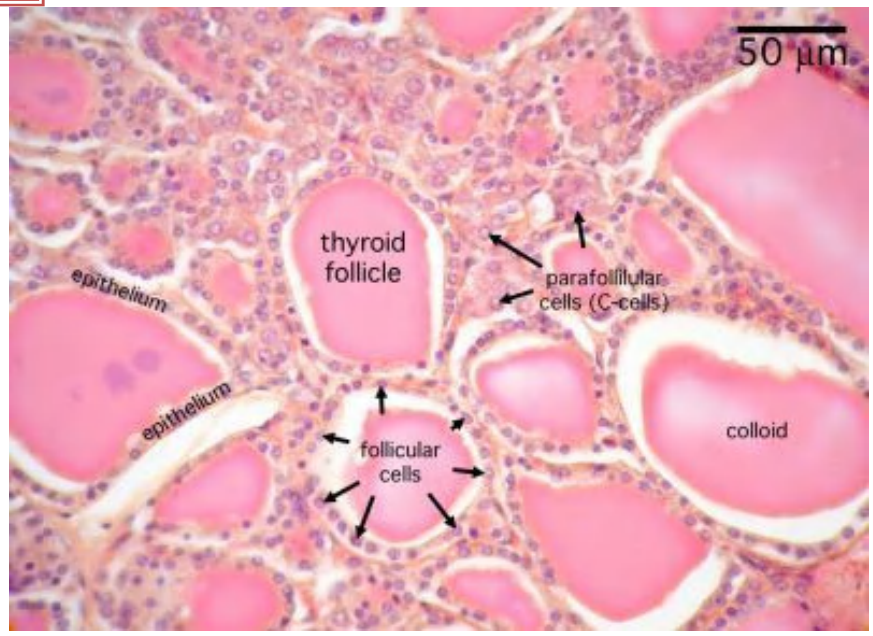
The thyroid gland secretes thyroid hormones, which control the speed at which the body's chemical functions proceed (metabolic rate).

Thyroid hormones influence the metabolic rate in two ways:

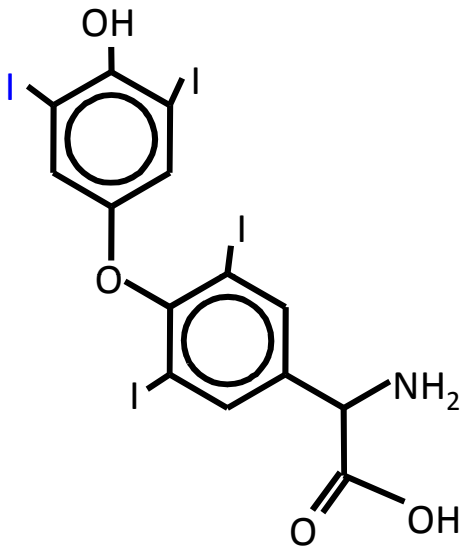
- By stimulating almost every tissue in the body to produce proteins
- By increasing the amount of oxygen that cells use
- Thyroid hormones affect many vital body functions, such as the heart rate, the rate at which calories are burned, skin maintenance, growth, heat production, fertility, and digestion.

THYROID GLAND HISTOLOGY

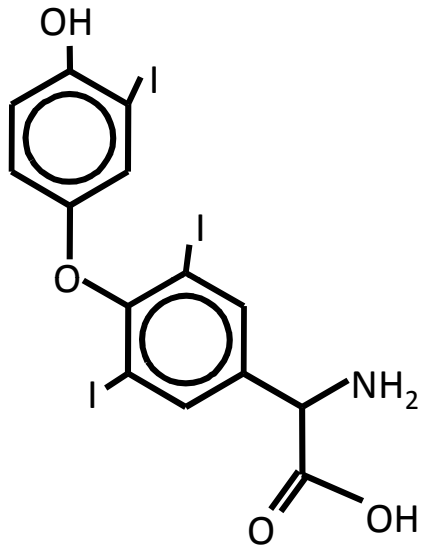




THYROID HORMONES



Thyroxine (T_4)



3,5,3'-Triiodothyronine (T_3)

FEEDBACK REGULATION
THE HYPOTHALAMIC-PITUITARY-THYROID AXIS

Hormones derived from the pituitary that regulate the synthesis and/or secretion of other hormones are known as trophic hormones.

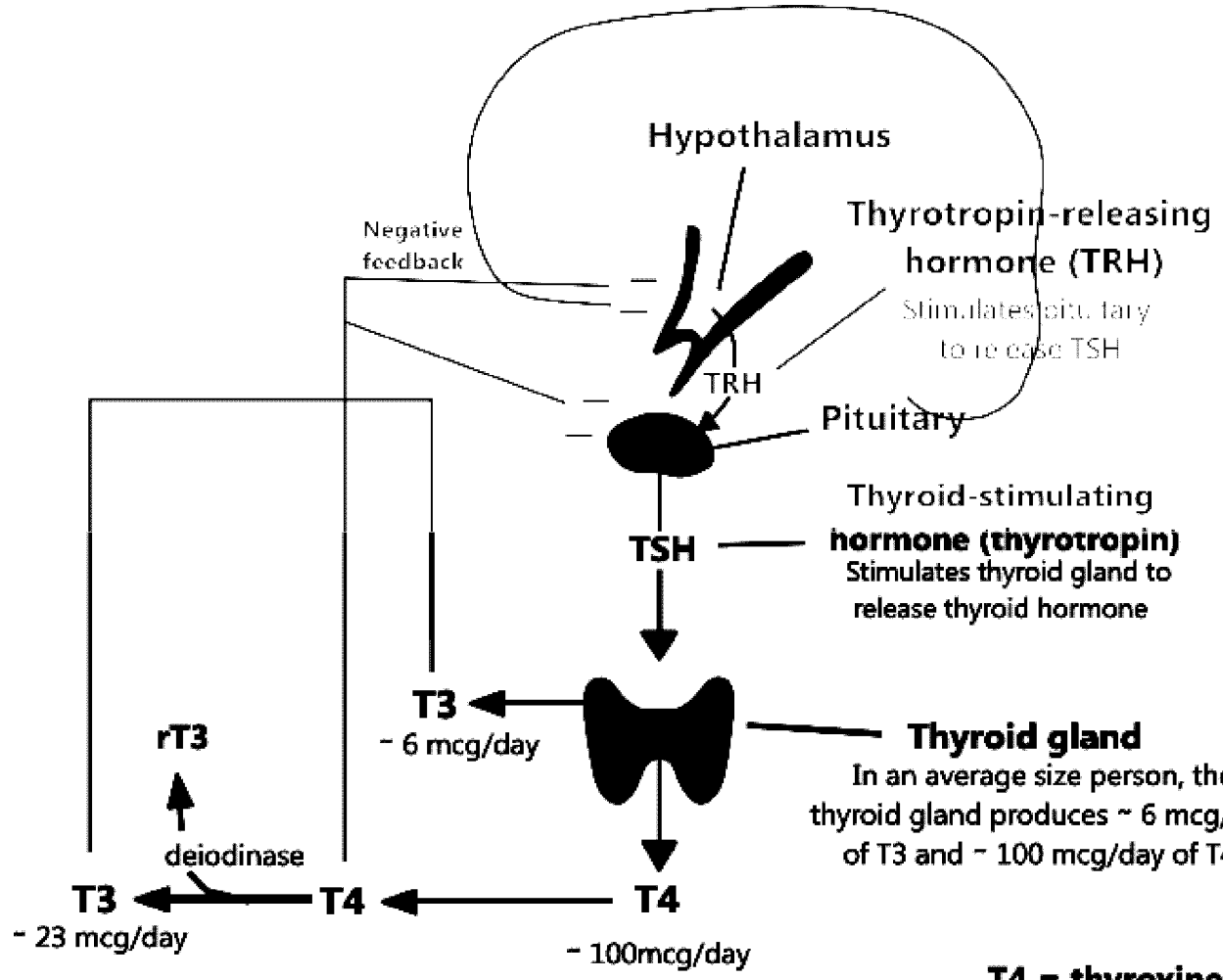
Key players for the thyroid include:

TRH - Thyrotropin Releasing Hormone

TSH - Thyroid Stimulating Hormone

T_4/T_3 - Thyroid hormones

Hypothalamic-pituitary-thyroid axis



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TSH REGULATION OF THYROID FUNCTION

- TSH binds to specific cell surface receptors that stimulate adenylate cyclase to produce cAMP.
- TSH increases metabolic activity that is required to synthesize Thyroglobulin (Tg) and generate peroxide.
- TSH stimulates both I^- uptake and iodination of tyrosine residues on Tg.

THYROID HORMONES IN THE BLOOD

- Approximately 99.98% of T_4 is bound to 3 serum proteins: **T**hyroid **b**inding **g**lobulin (TBG) ~75%; **T**hyroid **b**inding **p**re**a**lbumin (TBPA or transthyretin) 15-20%; albumin ~5-10%

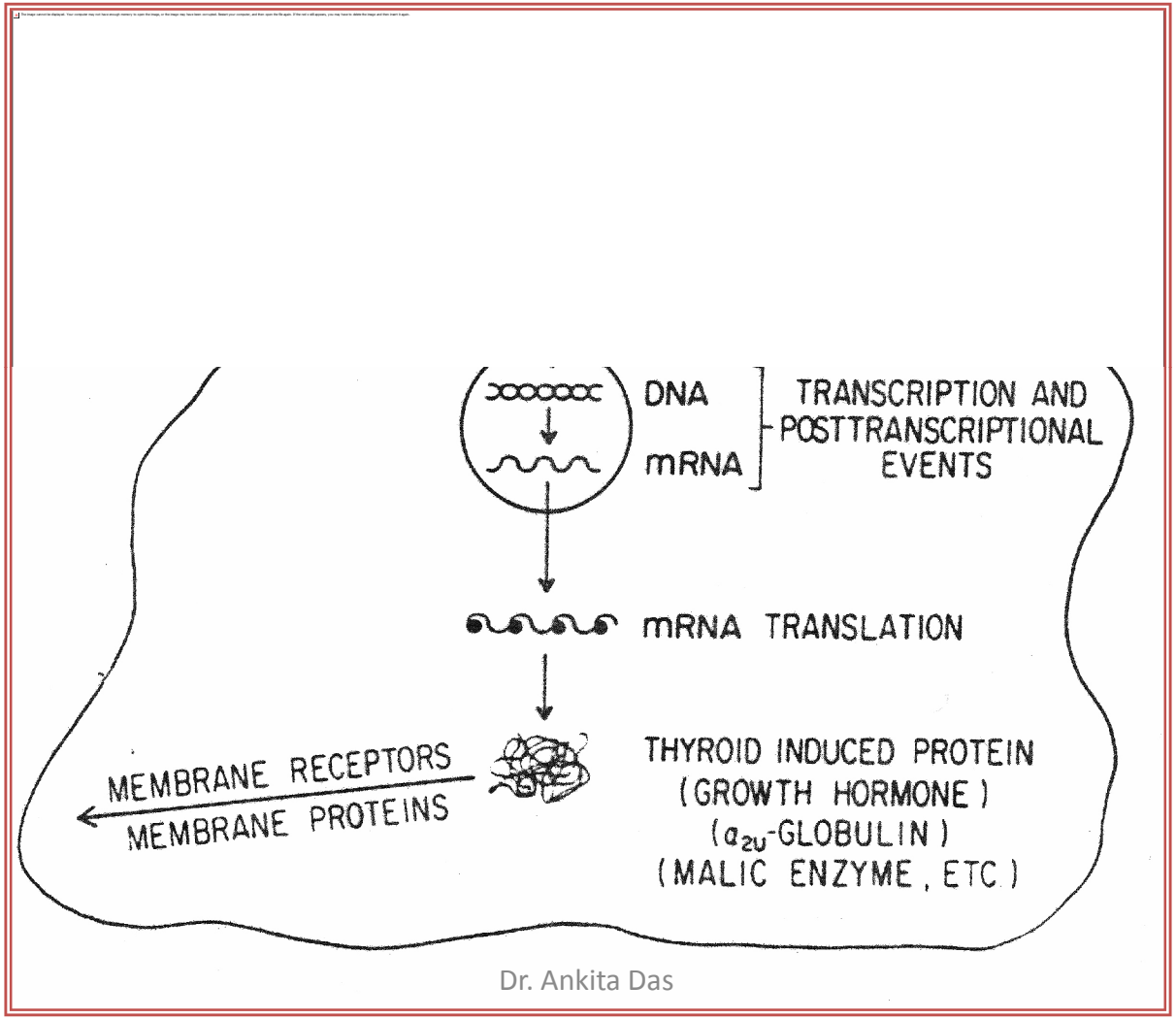
- Only ~0.02% of the total T_4 in blood is unbound or *free*.

- Only ~0.4% of total T_3 in blood is *free*.

THYROID HORMONE DEIODINASES

- Three deiodinases (D1, D2 & D3) catalyze the generation and/disposal of bioactive thyroid hormone.
- D1 & D2 “bioactivate” thyroid hormone by removing a single “outer-ring” iodine atom.
- D3 “inactivates” thyroid hormone by removing a single “inner-ring”iodine atom.
- All family members contain the novel amino acid selenocysteine (SeC) in their catalytic center.

BASICS OF THYROID HORMONE ACTION IN THE CELL



SPECIFIC ACTIONS OF THYROID HORMONE: METABOLIC

- Regulates of Basal Metabolic Rate (BMR).
- Increases oxygen consumption in most target tissues.
- *Permissive actions:* TH increases sensitivity of target tissues to catecholamines, thereby elevating lipolysis, glycogenolysis, and gluconeogenesis.

SPECIFIC ACTIONS OF THYROID HORMONE: DEVELOPMENT

- TH is critical for normal development of the skeletal system and musculature.
- TH is also essential for normal brain development and regulates synaptogenesis, neuronal integration, myelination and cell migration.
- **Cretinism** is the term for the constellation of defects resulting from untreated neonatal hypothyroidism.

EXAMPLES OF THYROID DISEASES

Hypothyroidism

Hyperthyroidism

EXAMPLES OF THYROID DISEASES

Juvenile Hypothyroidism

Congenital Hypothyroidism

THE PITUITARY-THYROID AXIS

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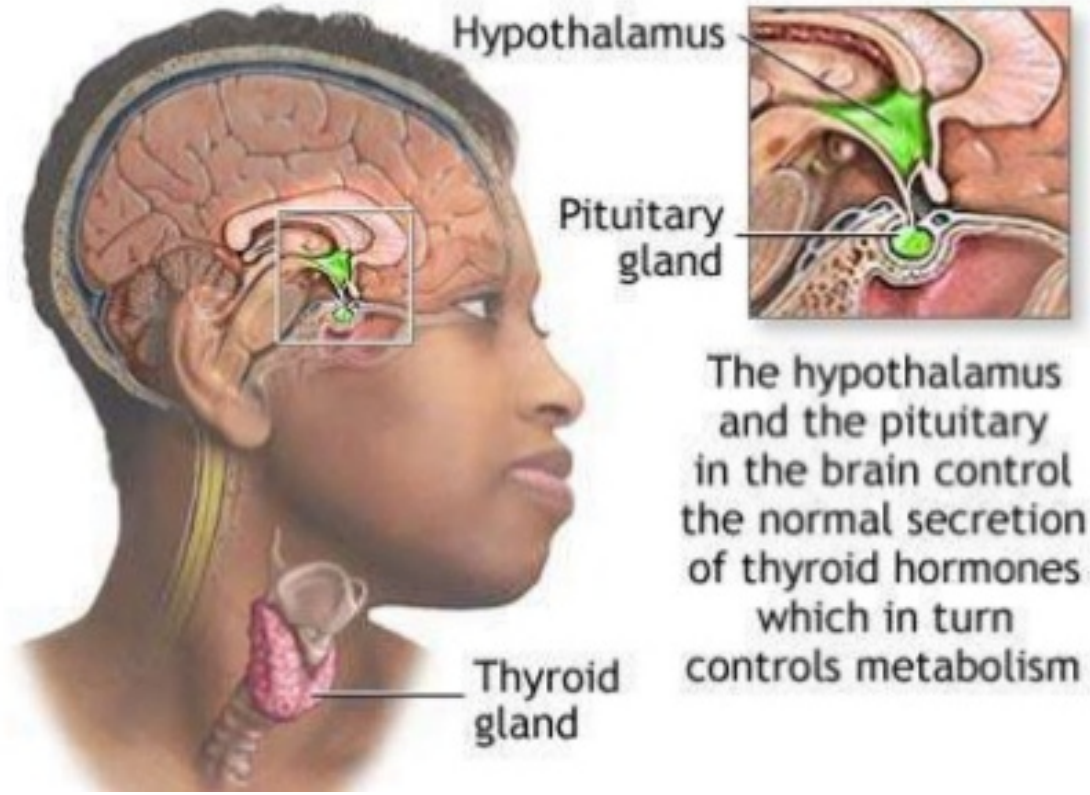
Thyroid Physiology



The hypothalamus and the pituitary in the brain control the normal secretion of thyroid hormones which in turn controls metabolism

•The **hypothalamic–pituitary–thyroid axis** (**HPT axis** for short, a.k.a. thyroid homeostasis or thyrotropic feedback control) is part of the neuroendocrine system responsible for the regulation of metabolism.

•As its name suggests, it depends upon the hypothalamus, the pituitary gland, and the thyroid gland.

•The hypothalamus senses low circulating levels of thyroid hormone (Triiodothyronine (T3) and Thyroxine (T4)) and responds by releasing thyrotropin-releasing hormone (TRH).

•The TRH stimulates the anterior pituitary to produce thyroid-stimulating hormone (TSH). The TSH, in turn, stimulates the thyroid to produce thyroid hormone until levels in the blood return to normal.

•Thyroid hormone exerts negative feedback control over the hypothalamus as well as anterior pituitary, thus controlling the release of both TRH from hypothalamus and TSH from anterior pituitary gland.

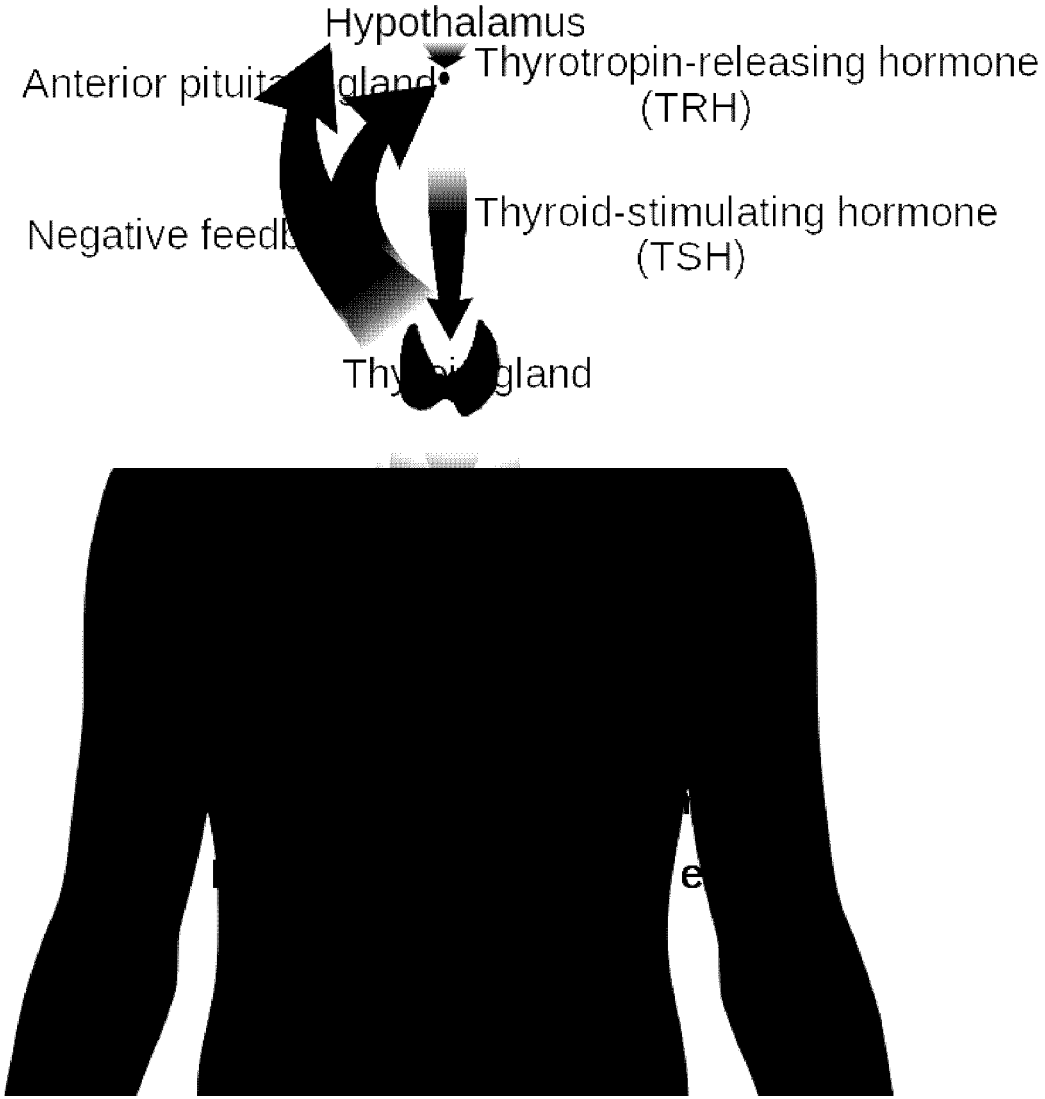
- The pituitary gland secretes thyrotropin (TSH; Thyroid Stimulating Hormone) that stimulates the thyroid to secrete thyroxine (T4) and, to a lesser degree, triiodothyronine (T3).

- The major portion of T3, however, is produced in peripheral organs, e.g. liver, adipose tissue, glia and skeletal muscle by deiodination from circulating T4.

- Deiodination is controlled by numerous hormones and nervous signals including TSH, vasopressin and catecholamines.

- Both peripheral thyroid hormones (iodothyronines) inhibit thyrotropin secretion from the pituitary (negative feedback). Consequently, equilibrium concentrations for all hormones are attained.

Thyroid system



- Hypothalamic-Pituitary-Thyroid Axis
- This is a negative feedback system.
- TRH produced in the paraventricular nuclei of the hypothalamus stimulates release of TSH from the pituitary.

- TSH stimulates thyrocytes to pump in iodine.
- Then there is “organification” of iodine by thyroid peroxidase.
- This forms T3 and T4, which is stored as colloid.
- T4 secretion >> T3 secretion.

- Most T3 is formed peripherally, by deiodination of T4.
- T3 is far more active, T4 is a prohormone.
- Conversion of T4 to T3 is inhibited by starvation, illness, drugs (amiodarone, contrast dyes).
- More than 99% of T3 and T4 in blood is bound to Thyroid Binding Globulin (TBG) and albumin.

- Only free hormone is active.
- Changes in the level of binding proteins such as TBG alters total T3 and T4 but not free hormone!

- T3 acts at nuclear receptors to stimulate CHO/fat metabolism, glycogenolysis, thermogenesis, protein synthesis, myocardial contractility, oxygen delivery, digestion, and sympathetic activity.
- It is critical for normal growth and metabolism.

- Assessing Thyroid Function
- The most common hormone measurements are free T4 and TSH.
- These have an inverse log-linear relationship, in which TSH varies logarithmically with T4.

- Therefore, the TSH level is the most sensitive index of thyroid function.
- Low TSH suggests hyperthyroidism.
- High TSH suggests primary hypothyroidism.
- Always rely on the TSH levels above other lab results.
- Also, do not evaluate thyroid function during acute illnesses, which may artifactually suppress TSH.

Thyroid hormone synthesis, metabolism and action

- Iodine enters thyroid gland and is used for T3 and T4 production
- Hormones are released from the thyroid and vast majority are protein bound (TBG) and deposited in peripheral cells
- T4 has 4 iodine atoms, removal of one produces T3

Total= Bound to TBG

Free= Unbound

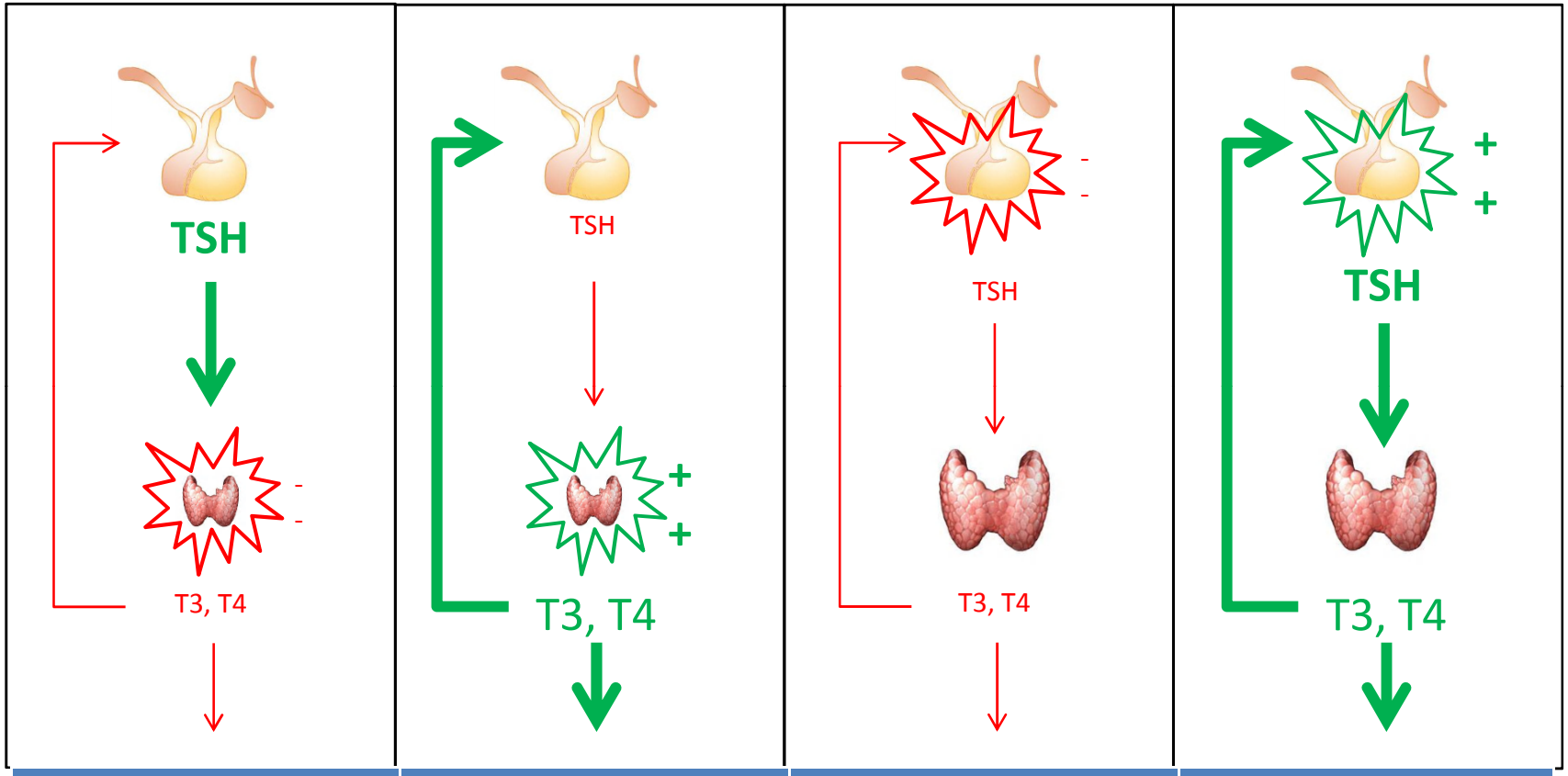
T3 & T4

- Facilitate normal growth and development
- Increase metabolism
- Increase catecholamine effects

TSH

- Most useful marker of thyroid hormone function
- Released in a pulsatile diurnal rhythm- highest at night

Investigations – Thyroid Function Tests



Hypothyroidism	Hyperthyroidism	Hypopituitarism	TSH secreting tumour
↑TSH; ↓T4,T3	↓TSH; ↑T4,T3	↓TSH; ↓T4,T3	↑TSH; ↑T4,T3

Books to refer:

1.Medical Physiology, Guyton and Hall
2.Medical Physiology, Ganong
3.General Physiology, A.K. Jain
4. Human Physiology, Dr. C. C. Chatterjee

Practice Questions:

1. How thyroid hormone is transported in the blood?
2. Discuss the negative feedback regulation of thyroid hormone secretion.
3. Briefly describe the pituitary thyroid axis.
4. Why T3 is far more active than T4?
5. Discuss the clinical manifestations of various thyroid function tests.
6. Describe the action of thyroid hormone on body metabolism.
7. How the symptoms of hypothyroidism differ from hyperthyroidism?
8. What do you mean by organification of iodine?