Al-Mustaqbal University

College of Medical and Health Techniques

Medical Laboratories Techniques Departments

Biochemistry Lectures for 2nd Year Students

(2 Credit Hrs. Theory + 2 Credit Hrs. Practice / Week = 3 Credit Unit

Academic Year: 2024 - 2025

Course Organizers:

1. **Prof. Dr. Fadhil Jawad Al-Tu'ma, Ph.D., Professor of Clinical Biochemistry.**
2. **Assistant Prof. Dr. Ali M. A. Al-Kufaishi**
3. **Dr. Dalya Shakir Obaida, Ph.D. Lecturer of Clinical Biochemistry.**

Lecture No. 2

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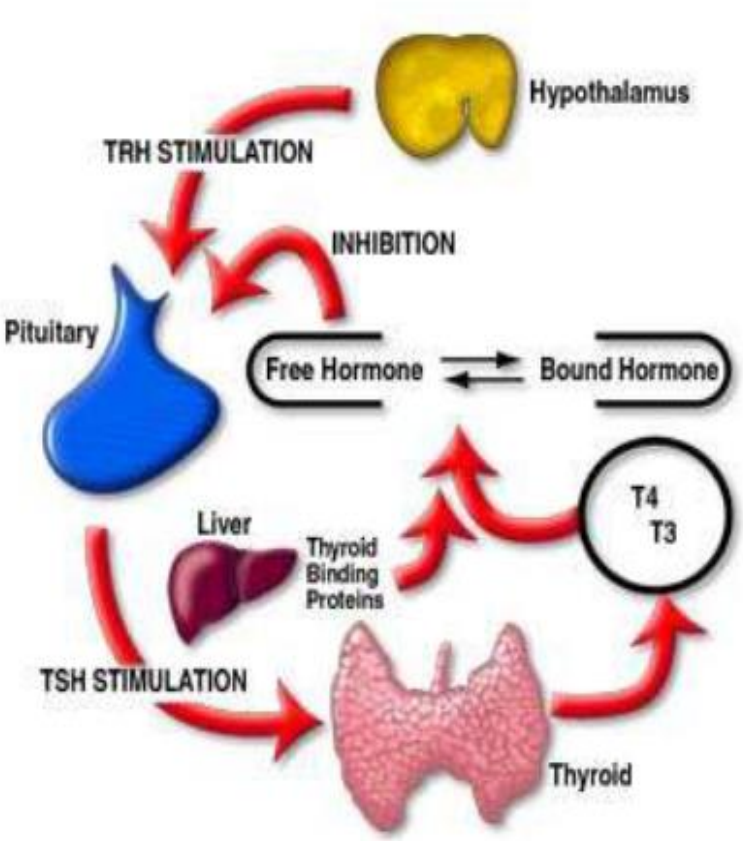
Feedback Control of Hormone Production

Feedback circuits are at the root of most control mechanisms in physiology, and are particularly prominent(obvious) in the endocrine system. Instances of positive feedback certainly occur, but negative feedback is much more common.

Feedback loops are used extensively to regulate secretion of hormones in the hypothalamic-pituitary axis. An important example of a negative feedback loop is seen in control of thyroid hormone secretion. The thyroid hormones thyroxine and triiodothyronine("T4 and T3") are synthesized and secreted by thyroid glands and affect metabolism throughout the body. The basic mechanisms for control in this system are:

1. Neurons in the hypothalamus secrete thyroid releasing hormone (TRH), which stimulates cells in the anterior pituitary to secrete thyroid-stimulating hormone(TSH).
2. TSH binds to receptors on epithelial cells in the thyroid gland, stimulating synthesis and secretion of thyroid hormones, which affect probably all cells in the body.
3. When blood concentrations of thyroid hormones increase above a certain threshold, TRH-secreting neurons in the hypothalamus are inhibited and stop secreting TRH.

   This is an example of "negative feedback".



Inhibition of TRH secretion leads to shut-off of TSH secretion, which leads to shut-off of thyroid hormone secretion. As thyroid hormone levels decay below the threshold, TRH secretion starts again, leading to TSH secretion.

Hypothalamus – pituitary hormones

Hypothalamus – pituitary hormones Two lobes of pituitary gland. Anterior lobe is adenohyophysis. Posterior lobe is neurohypophysis which is an outgrowth of the hypothalamus. There is only vascular connection via hypophyseal portal veins which carry releasing and inhibiting hormones secreted by hypothalamus to anterior pituitary gland in order to regulate the activity of secretory cells in anterior pituitary. Anterior pituitary is referred to as the Master gland. It secretes six hormones as well as a number of other active molecules. Four of these hormones are the tropic hormones which regulate secretory activity of other endocrine glands:

a. TSH—thyroid-stimulating hormone

b. ACTH—adrenocorticotropic hormone

c. FSH—follicle-stimulating hormone

d. LH—lutenizing hormone

The other two hormones have neuroendocrine targets which are:

a. PRL—Prolactin

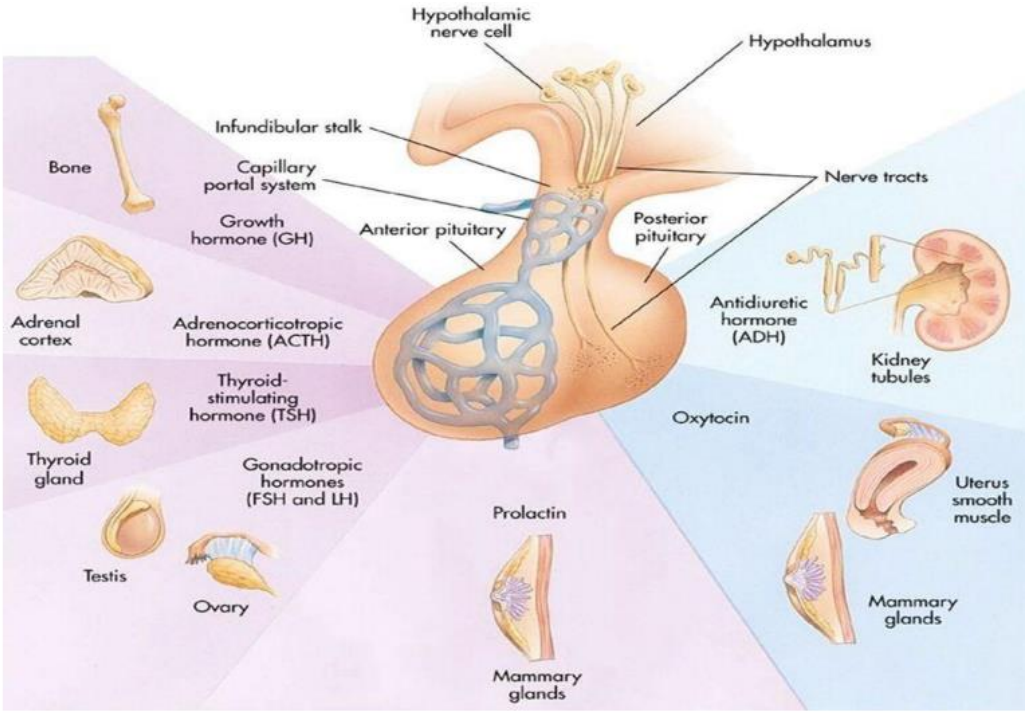
b. GH—growth hormone

Growth hormone (GH): GH stimulates most cells in the body to grow and divide but the major targets are bones and muscles. GH is anabolic hormone which promotes metabolism. Regulation of GH secretion is by hypothalamic hormones (negative feedback) where it is stimulated by somatotropin (GHRH growth hormone releasing hormone) and inhibited by somatostatin (GHIH growth hormone inhibiting hormone). Abnormalities of GH secretion

Adolescent hypersecretion: gigantism (excessive proportional growth)

Adult hypersecretion: acromegaly (tissues grow disproportionately) Adult hyposecretion: little effect but Adolescent hyposecretion results in pituitary dwarfism

Prolactin: It stimulates milk production. Its secretion is controlled by PRH and PIH (serotonin and dopamine). The levels of prolactin parallel those of estrogen.



Thyroid-stimulating hormone (TSH)

TSH stimulates normal growth and activity of the thyroid gland. It is controlled by hypothalamic TRH (thyrotropin releasing hormone). Thyroid hormones signal hypothalamus and anterior pituitary to stop TRH and TSH respectively. GHIH also inhibits TRH. Thyroid hormones (TH): T3 and T4 Follicle cells produce thyroglobin and lumen stores colloid (thyroglobin in association with iodine). T2, T3 and T4 are iodinated thyroglobins. The metabolically active hormones are thyroxine (T4) and triiodothyronine (T3). Thyroxine (T4) is produced by thyroid gland while triiodothyronine (T3) is formed at target tissue when T4 is converted into T3. They increase metabolism in most tissues by stimulating glucose oxidation. They increase adrenergic receptors in blood vessels and regulates tissue growth and development. Thyroid disorders: -

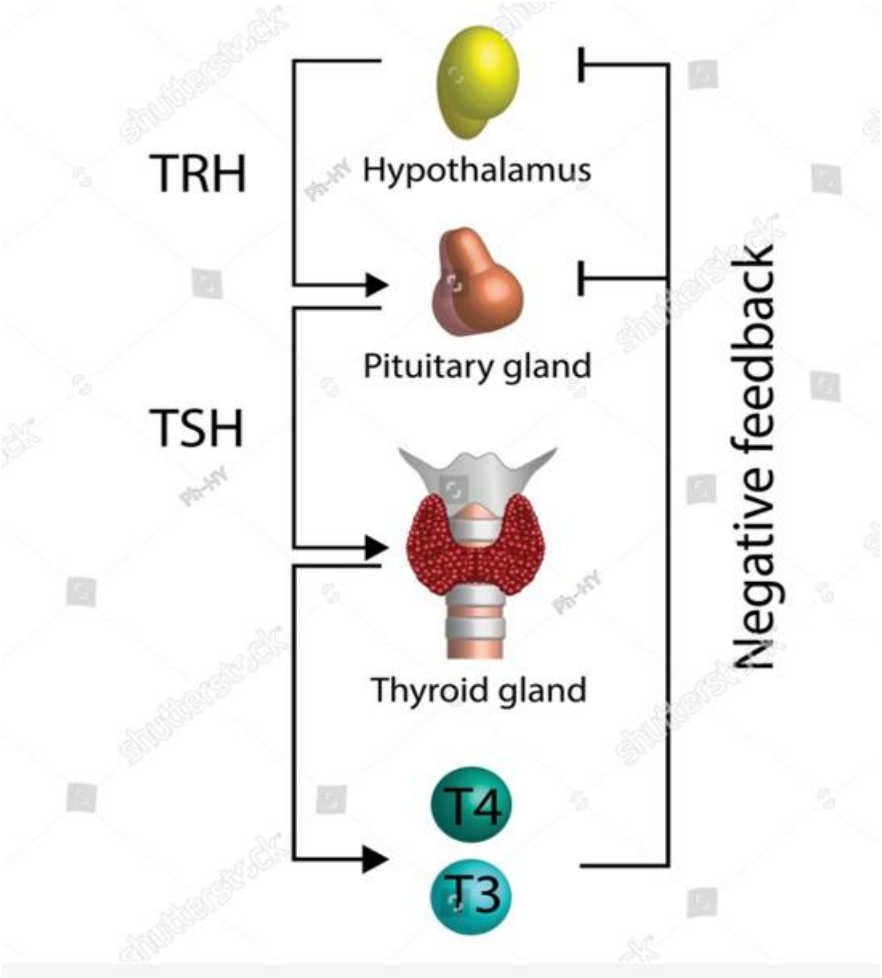
Hyposecretion of TSH:

Hypothyroidism - Hypothyroidism in infants (Cretinism)

-In adulthood: Myxedema

Hypersecretion of TSH: Grave's disease

Hyperthyroidism: (thyrotoxicosis)



Gonadotropins

FSH and LH They regulate gonads. FSH stimulates gamete production. LH promotes production of gonadal hormones. FSH and LH work in concert to cause follicle to mature. In females; LH causes egg to be extruded from follicle. In males; LH stimulates interstitial cells of the testes to produce testosterone. LH and FSH release is controlled by the hypothalamic GnRH (gonadotropin releasing hormone). Negative feedback inhibition regulates FSH and LH release (testosterone, estrogen, inhibin)

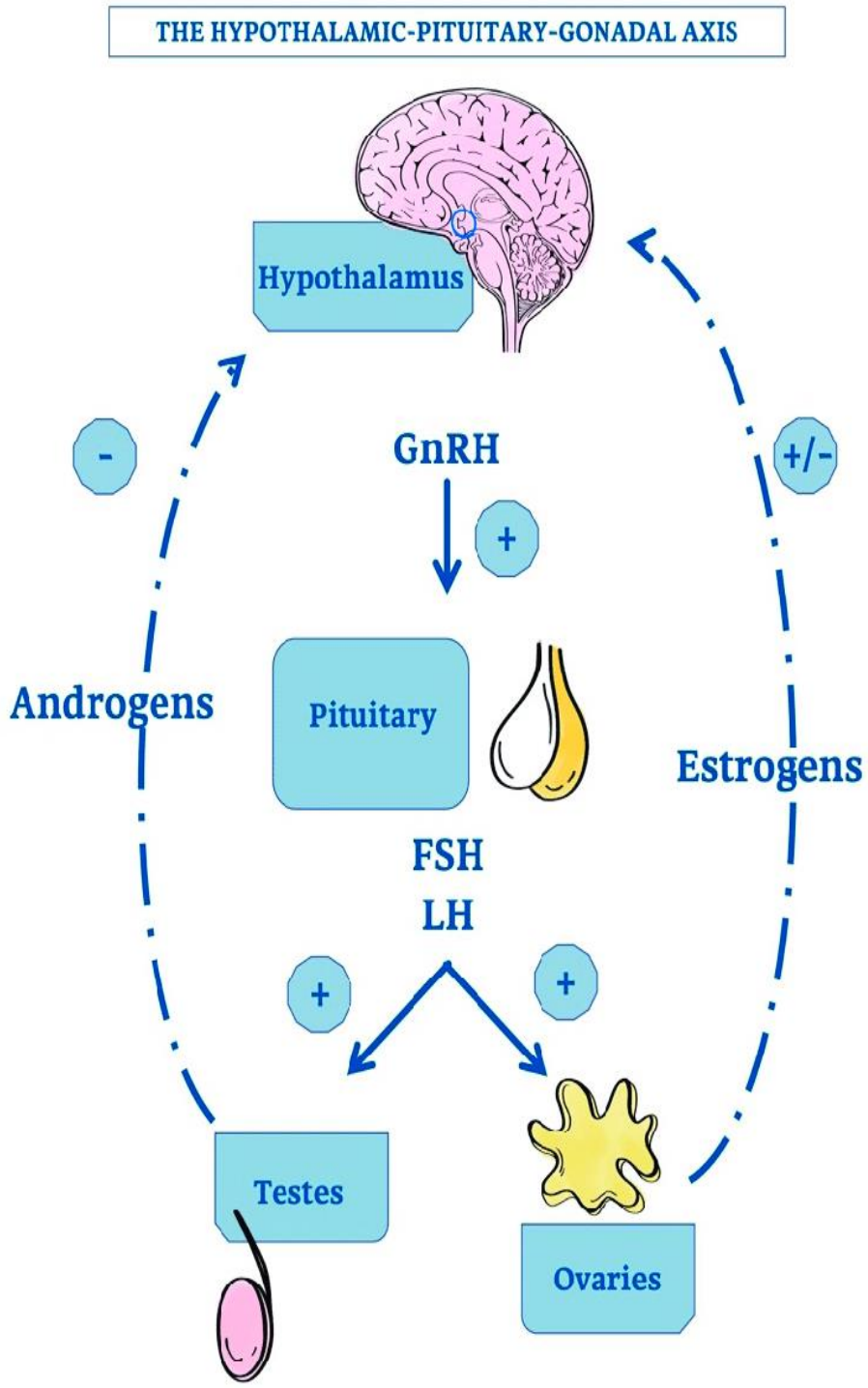
Hypersecretion of gonadotropins:

1- Hypersecretion of FSH: Kleinfelter's syndrome
2- Hypersecretion of LH: Turner syndrome Posterior pituitary hormones

Gonads Hormones:

Testosterone: It is formed by the interstitial cells of Leydig which lie in adult testes. In general, testosterone is responsible for the distinguishing characteristics of the masculine body. It affects the distribution of body hair. It also decreases the growth of hair on the top of the head. It causes typical adult masculine voice. It increases the thickness of the skin over the entire body. It increases the ruggedness of the subcutaneous tissues (acne). It increases musculature. Testosterone also increases the total quantity of bone matrix and causes calcium retention.

Estrogen & progesterone They are secreted by ovaries in response to FSH and LH. Estrogen regulates the menstrual cycle. Progesterone functions mainly to prepare the uterus for pregnancy and the breasts for lactation. Disturbances in testosterone, estrogen or progesterone results in disturbance in sexual function and mood.



Adrenocortical hormones Adrenal glands

represent two endocrine glands; adrenal medulla and cortex. They are involved in response to stressful conditions. Adrenal cortex secretes corticosteroids which are synthesized from cholesterol. Corticosteroids are: mineralocorticoids, glucocorticoids and gonadocorticoids.

A. Mineralocorticoids: They regulate electrolyte concentrations in extracellular fluid. Aldosterone is the most abundant mineralocorticoid. It reduces excretion of sodium from the body and stimulates reabsorption of sodium in the distal tubule of kidney.

Hypersecretion of aldosterone: - Primary aldosteronism (due to adrenal tumors).

Hyposecretion of aldosterone: - Addison's disease

B. **Glucocorticoids:** They influence metabolism and mediate response to stress. They are: cortisol (hydrocortisone), cortisone and corticosterone. Only cortisol is secreted in significant amounts. If there is no stress: cortisol inhibit CRH and ACTH. In stress: Sympathetic nervous system triggers CRH release.

Hypersecretion of cortisol: - Cushing syndrome

Hyposecretion of cortisol: - Addison's disease

C. Gonadocorticoids (Sex hormones): Primarily androgens: androstenedione converted to testosterone and dihydrotestosterone with small amounts of estrogens. Adrenal cortex secretes very small amounts of sex hormones with possible role in onset of puberty.

Adrenal medulla It is composed of chromaffin cells which secrete epinephrine and norepinephrine. This is the initial response to stress mediated by sympathetic NS. Activation of adrenal medulla and associated release of catecholamines (EPI and NE) prolongs sympathetic response resulting in elevated BP and HR, mobilization of glucose and shunt blood from GIT.

Hyposecretion of adrenal medulla: No significant effect

Hypersecretion of adrenal medulla: - Tumor of chromaffin cells called pheochromocytoma (uncontrolled sympathetic system activity)

ADH (antidiuretic hormone)

It prevents urine production. Hypothalamus has osmoreceptors and ADH is released from hypothalamus in response to increased solute concentration. ADH causes kidney tubules to reabsorb more water. At high doses, causes vasoconstriction (increases systolic blood pressure).

Hypersecretion of ADH: - Syndrome of inappropriate antidiuretic hormone (SIADH)

Hyposecretion of ADH: - Diabetes insipidus

Oxytocin (OXT): It stimulates smooth muscle contraction. The number of its receptors increases during pregnancy. During pregnancy signals release of oxytocin during late stages of pregnancy resulting in hormonal trigger for milk ejection (positive feedback mechanism)

Hypersecretion of Oxytocin (OXT): - Prostatic hyperplasia

Hyposecretion of Oxytocin (OXT): - Depression.

Pancreatic hormones Pancreas: **is** both endocrine and exocrine organ. Exocrine secretions are the pancreatic juice enzymes to the pancreatic duct. Endocrine secretions are insulin, glucagon, somatostatin and pancretic peptide (PP). Beta cells of pancreas produce insulin which is hypoglycemic hormone. Alpha cells produce glucagon.

Hypersecretion of insulin: - Hyperinsulinism: (hypoglycemia)

Hyposecretion of insulin: - Diabetes mellitus (DM) is hyposecretion or hypoactivity of insulin: (hyperglycemia)

Hypersecretion of glucagon: - Hyperglucagonemia: Glucagonoma syndrome (hypoglycemia)

Hyposecretion of glucagon: - glucagon deficiency (hyperglycemia)