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Welcome Back Dears
You should be able to know:

- What is The pituitary gland and its anatomy
- Pituitary gland hormones
- Anterior pituitary gland hormones
- Posterior pituitary gland hormones
The endocrine glands
Selected Hormones
II-The pituitary gland
An endocrine gland (pea size / 0.5 g), protruded from bottom of hypothalamus behind the nose bridge and rest in bony cavity of the sphenoid bone.

It is Known as the master endocrine gland although its lobes are under control of hypothalamus via pituitary stalk.

It secretes many important hormones that have different effect on other glands in the body.

When The pituitary gland is not working correctly, many things can go wrong in the body.

**Anatomy**

The pituitary is divided into two distinct lobes that arise from different embryological sources:

1. The anterior (front) lobe, or adenohypophysis.
2. The posterior (back) lobe, or neurohypophysis.

The two sections of the pituitary gland produce a number of Different hormones which act on different target glands or cells
II-The pituitary gland

1. The anterior pituitary hormones

The anterior pituitary synthesizes and secretes ACTH, TSH, PRL, GH, FSH, LH, and endorphins under influence of hypothalamic hormones secreted via a special capillary system (*hypothalamic-hypophyseal portal system*).

Anterior Pituitary gland secretes hormones that control secretion of other endocrine glands such as adrenal and thyroid glands and are called “glandotropic hormones or adeno-hypophyseal hormones”.

2. The posterior pituitary hormones

The posterior pituitary stores and releases: Oxytocin (OT) and Antidiuretic hormone (ADH or vasopressin), majorly released from the supraoptic nucleus in the hypothalamus
**II-The pituitary gland**

1. **The anterior pituitary hormones.**

The hypothalamus controls the anterior pituitary by producing releasing and release-inhibiting hormones.

*For example,* there is a gonadotropic-releasing hormone (GnRH) and a gonadotropic-release-inhibiting hormone (GnRIH).

The first hormone stimulates the anterior pituitary to *release its gonadotropic hormones,*

and the second inhibits the anterior pituitary from releasing the same hormones.

Releasing and release-inhibiting hormones are transported from the hypothalamus to the anterior pituitary by way of a *portal system that connects the anterior pituitary to the hypothalamus.*

Thyroid-Stimulating Hormone (TSH) or thyrotropin.

Adrenocorticotrophic Hormone (ACTH). Luteinising Hormone (LH).

II-The pituitary gland

1. The anterior pituitary hormones.

i) Thyroid-stimulating hormone (TSH) or thyrotropin

* TSH is a peptide hormone synthesized and secreted by thyrotrrope cells in the anterior pituitary gland, which regulates the endocrine function of the thyroid gland.
* TSH is a glycoprotein and consists of two subunits, the $\alpha$ and the $\beta$ subunit.
* The $\beta$ subunit (TSHB) is unique to TSH, and therefore determines its function.
  * It stimulates the growth of thyroid cells and leads to increased blood flow through the gland.
  * TSH stimulates the thyroid gland to secrete the hormones thyroxine (T4) and triiodothyronine (T3).

*Somatostatin* has an opposite effect on the pituitary production of TSH, decreasing or inhibiting its release.

*The level of T3 and T4 in the blood has an effect on the pituitary release of TSH; when the levels of T3 & T4 dec., the production of TSH is increased, and, vise versa
II-The pituitary gland

1. The anterior pituitary hormones.

i) **Thyroid-stimulating hormone (TSH)** or **thyrotropin**

**Diagnostic use:**
TSH levels are tested in the blood of patients suspected of suffering from excess (hyperthyroidism), or deficiency (hypothyroidism) of thyroid hormone.

In general, a **standard reference range** for TSH for adults is between **0.4** and **5.0** mIU/L.

The **therapeutic target range** TSH level for patients on treatment ranges between **0.3** to **3.0** mIU/L.

Both TSH and T3 and T4 should be measured to ascertain where a specific thyroid dysfunction is caused by primary pituitary or by a primary thyroid disease.

**Therapeutic use:**
A drug, recombinant human TSH (rhTSH), called **Thyrogen**.

The rhTSH is used in patients with thyroid cancer.
II-The pituitary gland

1. The anterior pituitary hormones.

ii) Adrenocorticotropic hormone Corticotropin or ACTH

Structure: ACTH consists of 39 amino acids, the first 13 of which may be cleaved to form α-melanocyte-stimulating hormone (α-MSH).

After a short period of time, ACTH is cleaved into α-melanocyte-stimulating hormone (α-MSH) and CLIP, a peptide with unknown activity in humans.

Function: ACTH acts through the stimulation of cell surface ACTH receptors, (located on adrenocortical cells of the adrenal cortex).

This results in the following:
Stimulate growth of the cells adrenal cortex and secretion of the gluco- and mineral-corticosteroids.
α- and β-melanotropin (melanocyte-stimulating hormone, MSH), which increases pigmentation of the skin.
β-lipotropin (LPH), which stimulates the release of fatty acids from adipose tissue. Small fragment of ACTH thought to improve memory; and β-endorphin

Control: Feed-back inhibition by corticosteroids.
Uses: Diagnosis of Adrenal insufficiency.
III) Luteinizing hormone (LH)

**Structure:** LH is a heterodimeric glycoprotein. Its structure is similar to the other glycoprotein hormones, (FSH), (TSH), and human (hCG).
* The protein contains 2 glycopeptidic subunits, α and the β subunit, that are non-covalently associated (i.e. without any disulfide bridge linking them).
* The α subunits of LH, FSH, TSH, and hCG are identical, and contain 92 amino acids.
* The β subunits vary (121 amino acids) (LHB) that confers its specific biologic action and is responsible for the specificity of the interaction with the LH receptor.

**Activity:** In both males and females, LH is essential for reproduction.

In the male: LH acts upon the Leydig cells of the testis and is responsible for the production of testosterone, that exerts both endocrine activity and intratesticular activity on spermatogenesis.

In Females: LH triggers ovulation thereby not only releasing the egg, but also initiating the conversion of the residual follicle into a corpus luteum that, in turn, produces progesterone to prepare the endometrium for a possible implantation. LH is necessary to maintain luteal function for the first two weeks.
II-The pituitary gland

1. The anterior pituitary hormones.

iv) Follicle-Stimulating Hormone (FSH).

FSH regulates the development, growth, pubertal maturation, and reproductive processes of the body. FSH and (LH) act synergistically in reproduction.

**Structure:** FSH is a glycoprotein. Each monomeric unit is a protein molecule with a sugar attached to it. The α subunits is identical with LH, FSH, TSH, and hCG. Are identical and contain 92 amino acids. The β subunits consists of 118 amino acids.

**Activity:** FSH regulates the development, growth, pubertal maturation, and reproductive processes of the human body. In both males and females, FSH stimulates the maturation of germ cells.

**High LH & FSH levels** may be a sign of: Premature menopause also known as Premature Ovarian Failure.

**Low LH and FSH levels** cause: Polycystic Ovarian Syndrome+ Obesity + Hirsutism + Infertility
II-The pituitary gland

1. The anterior pituitary hormones.

vi) Gonadotropins (GnHs).

Gonadotropins are protein hormones secreted by gonadotrope cells (7% of the pituitary gland). They include Luteinizing Hormone (LH), Follicle-Stimulating Hormone (FSH), Chionic Gonadotropin (CG).

Structures: They are glycoproteins heterodimers. They share identical α-polypeptide subunits (92 amino acids long), whereas β-polypeptide subunits (120 amino acids long), provide specificity for receptor interactions. These subunits are modified by one N-linked oligosaccharide chains (in case of LH) or two N-linked oligosaccharide chains (in case of FSH and hCG).

Regulation: Stimulation: GnRH from hypothalamus. Inhibition: Feedback mechanism by sex hormones and hCG produced by placenta after fertilization.

Physiological effects: In Males: LH: Stimulate production of androgens by Leydig cells. FSH: Enhance normal sperm production by Sertoli cells.

In Females: LH: Induce Ovulation and stimulate Progesterone production.

FSH: Enhance production of Estrogen and development of follicles.
II-The pituitary gland

1. The anterior pituitary hormones.

vii) Prolactin (PRL).

PRL is a single-chain polypeptide hormone, of 199-amino acid residues and 3 disulfide linkages, that is essential for milk production by mammary glands of human female

**Function:** The act of nipple suckling in breast-feeding, stimulates PRL release $\rightarrow$ lactogenesis $\rightarrow$ fills breast with milk for the next feed. Oxytocin (OT) is also released by suckling $\rightarrow$ triggers milk let-down.

**Regulation:** Prolactin secretion is regulated by neuroendocrine system in hypothalamus $\rightarrow$ secrete dopamine (DA) to act on lactotrops receptors in anterior pituitary $\rightarrow$ ↓PRL secretion. PRF &TRH has +ve effect on PRL release.

**Hyperprolactinemia:** HP is the presence of abnormally-high blood levels of PRL (normal is <580 mIU/L for women -< 450 mIU/L for men). **Symptoms:** In females: Galactorrhea(spontaneous flow of breast milk ), Amenorrhea(irregular menses), Infertility. In males: Erectile dysfunction and Infertility, rarely galactorrhea. **Causes:** Tumors in the lactotropes at AP (diagnosed by MRI or CAT Scan). Hypothalamus or Anterior Pituitary disorders. Dopamine antagonists. Hypothyroidism associated with high level of TRH. Disease of other organs such as the liver, kidneys, ovaries and thyroid. Treatment according to the cause.
1. The pituitary gland

viii) Growth Hormone (GH, somatotropin)

Growth hormone (GH) = Somatotropic hormone (STH) is a single-chain polypeptide hormone, of 191-amino acid residues and 2 disulfide linkages, that stimulates growth.

Functions of GH
* Main pathways in endocrine regulation of growth.
* Effects of growth hormone on the tissues of the body can generally be described as anabolic (building up).
* Increased height during childhood.
* It stimulates production of insulin-like growth factor 1 (IGF-1), a hormone homologous to proinsulin which has growth-stimulating effects on a wide variety of tissues.
* Growth hormone has many other effects on the body e.g.:
  * Increases; calcium retention, mineralization of bone, muscle mass. Promotes lipolysis and protein synthesis.
  * Stimulates the growth of all internal organs excluding the brain.
II-The pituitary gland

1. The anterior pituitary hormones.

viii) Growth Hormone (GH, somatotropin)

Regulation of GH

GHRH (somatocrinin) and GHIH (somatostatin) released by hypothalamus majorly control GH secretion by somato-tropes. However, the GHRH/GHIH balance is affected by many physio-hormonal stimulators and inhibitors.

Stimulators of GH secretion: Peptide hormones: GHRH from hypothalamus and Ghrelin from stomach and pancreas (stimulates hunger). Sex hormones: androgens during puberty (in males from testes and in females from adrenal cortex) and estrogen. Drugs stimulating GHRH release e.g. clonidine (α2 adrenergic agonist) and L-DOPA. Deep sleep Intensive exercise Inhibition of somastatin e.g. by hypoglycemia, arginine

Inhibitors of GH secretion: Somatostatin from the hypothalamus Dihydro testosterone and glucocorticoids. Negative feedback concentrations of GH and IGF-1Hyperglycemia.
II-The pituitary gland
1. The anterior pituitary hormones.

viii) Growth Hormone (GH, somatotropin)

**Physiological effect**

GH has two distinct effects: **Direct effects** (via GH binding to its receptor on target cells) e.g. adipose cells → stimulation → ↑ lipolysis and ↓ lipogenesis. **Indirect effects** (via IGF-I secreted from liver and other tissues in response to GH) → major growth promoting effects.

1. **Stimulation of Growth**
IGF-I → ↑ proliferation of chondrocytes → linear bone growth.
IGF-I → ↑ differentiation and proliferation of myoblasts and ↑ amino acid uptake and protein synthesis in muscle and other tissues.

2. Effects on protein, lipid and carbohydrate metabolism by direct and indirect effects:
  * Protein metabolism: GH stimulates protein anabolism through ↑ amino acid uptake, protein synthesis and ↓ proteins oxidation.
  * Fat metabolism: GH ↑ utilization of fat by stimulating triglyceride breakdown and oxidation in adipocytes.
  * Carbohydrate metabolism: GH has diabetogenic or anti-insulin activity (it ↓ abilities of insulin to stimulate glucose uptake in peripheral tissues and ↑ glucose synthesis in the liver).
Hypothalamus secretes growth hormone-releasing hormone (GHRH), and somatostatin (GHIH).

Anterior pituitary

Feedback mechanism

Inhibits GHRH release
Stimulates GHIH release

Inhibits GH synthesis and release

Growth hormone

Direct effects

Liver and other tissues

Insulin-like growth factors (IGFs)

Indirect growth-promoting actions

Skeletal effects
Increased cartilage formation and skeletal growth

Extraskeletal effects
Increased protein synthesis, and cell growth and proliferation

Fat
Increased lipolysis

Carbohydrate metabolism
Increased blood sugar and other anti-insulin effects

Key:

- Increases, stimulates
- Reduces, inhibits

Initial stimulus
Physiological response
Result
II-The pituitary gland
1. The anterior pituitary hormones.

viii) Growth Hormone (GH, somatotropin)

Diseases correlated to GH

**Deficiency:** (may be due to mutation of genes or congenital damage of pituitary) lead to Dwarfism (abnormal short height -normal body proportion -appear younger than age -delayed sexual development -dental problems due to underdeveloped jaws).

**Hypersecretion:** (may be due to pituitary adenoma or autoimmune hypophysitis)

1. **Gigantism:** (hypersecretion in young children or adolescents lead to increase long bone length – increase height – weakness

2. **Acromegaly:** (occurs after epiphyseal plate closure at puberty – rare disease :3/Million) lead to enlarged cranium and jaw - bulging forehead - thick lips - enlarged hands & feet - painful joints - muscle weakness - Risk of falls
1. The anterior pituitary hormones.

viii) Growth Hormone (GH, somatotropin)

**Uses:**

Replacement therapy for children with GH deficiency by daily IM or SC injection (cost $10,000-40,000 USD/year).

Controversial treatment (unrelated to GH deficiency)

* Anti-aging agent for older adults.
* Improvement of athletic performance of professional male athletes
* To enhance weight loss in some cases of obesity

**GH Source:** Until 1985, GH obtained by extraction of autopsied human PA. Since 1985, recombinant hGH is produced by genetically engineered bacteria, manufactured by recombinant DNA technology.

**Treatment of Acromegaly**

1. Surgery to remove AP tumor followed by radiation therapy
2. Drug Therapy: Synthetic Somatostatin analogs e.g. Octreotide (Sandostatin). Bromocriptine = semisynthetic ergot alkaloid (Parlodel®) which is dopamine D2 agonist, suppressing prolactin and high level of GH in acromegalic patients.
II-The pituitary gland
1. The anterior pituitary hormones.

iv) Melanocyte-Stimulating Hormone (MSH)

MSH causes the melanocytes, which are located in abundance at the border between the dermis and the epidermis of the skin, to form the pigment melanin and to disperse it in the cells of the epidermis. It is a class of peptide hormones that in nature are produced by cells in the intermediate lobe of the pituitary gland.

Structure: Melanocyte-stimulating hormone belongs to a group called the melanocortins. This group includes ACTH, α-MSH, β-MSH and γ-MSH; these peptides are all cleavage products of pro-opiomelanocortin (POMC). α-MSH is the most important melanocortin for pigmentation.

Function: They stimulate the production and release of melanin (melanogenesis) by melanocytes in skin and hair. MSH signals to the brain have effects on appetite and sexual arousal.
II-The pituitary gland

1. The Posterior Pituitary hormones.

It is largely a collection of axonal projections from the hypothalamus that terminate behind the anterior pituitary gland. Two major neurohypophyseal hormones are synthesis:

1- vasopressin (antidiuretic hormone ADH)  
2- oxytocin

i) vasopressin (antidiuretic hormone ADH)

Antidiuretic Hormone (ADH) or Arginine-Vasopressin (AVP)

Arginine vasopressin (AVP), also known as vasopressin, or antidiuretic hormone (ADH), is a hormone found in most mammals, including humans.

Vasopressin is a peptide hormone that inhibits or prevents the formation of urine.
II-The pituitary gland

1. The Posterior Pituitary hormones.

i) vasopressin (antidiuretic hormone ADH)

Structure: The vasopressins are peptides consisting of nine amino acids (nonapeptides). The amino acid sequence of arginine vasopressin is Cys-Tyr-Phe-Gln-Asn-Cys-Pro-Arg-Gly, with the cysteine residues forming a sulfur bridge. Lysine vasopressin has a lysine in place of the arginine.

Function: It plays a key role in homeostasis, and the regulation of water, glucose, and salts in the blood. AVP regulates the body's retention of water; it is released when the body is dehydrated and causes the kidneys to conserve water, thus concentrating the urine, and reducing urine volume.

Role in disease: Decreased vasopressin release leads to diabetes insipidus, a condition featuring hypernatremia (increased blood sodium concentration), polyuria (excess urine production), and polydipsia (thirst).

High levels of AVP secretion (syndrome of inappropriate antidiuretic hormone, SIADH) and resultant hypernatremia (low blood sodium levels) occurs in brain diseases and conditions of the lungs (Small cell lung carcinoma).
II-The pituitary gland

1. The Posterior Pituitary hormones.

i) vasopressin (antidiuretic hormone ADH)

ADH regulation:
Dehydration lead to increase plasma osmolality which lead to ADH secreted.
Over hydration lead to decrease plasma osmolarity which increase ADH inhibited

Uses of vasopressin and its analogs

*Treatment of diabetes insipidus (hypernatremia + poly-uria +polydipsia + dry skin).
*Control of bleeding (in some of von Wille brand disease).
*Vasopressin infusion can be used in management of hypotensive septic shock as a second line for patients not responding to high dose of inotropes (e.g.norepinephrine).

*Vasopressin analogues are used for esophageal varices since 1970.
*Control of extreme cases of bedwetting by children.
*Terlipressin and related analogs are used as vasoconstrictors in certain hypotensive conditions.
*It can be more effective than epinephrine in asystolic cardiac arrest.
II-The pituitary gland

1. The Posterior Pituitary hormones.

ii) oxytocin

OT is a nonapeptide chain with one disulfide bridge secreted from posterior pituitary (PP). The only hormone regulated by +ve feedback mechanism. It is best known for its roles in female biology:

1) Induction of labor by uterine contraction (stimulus: cervix dilatation).
2) Contraction of mammary glands lead to milk ejection in breast feeding (stimulus: suckling & baby’s cry).
3) Establish Maternal Behavior