Udai Pratap (Autonomous) College, Varanasi

E-learning Material

Module/Lecture	01
Subject	Zoology
Year/Semester	M.Sc. II Semester BRZ VII
Unit	I
Topic	Endocrinology
Sub-topic	Hypothalmo-Hypophysial System
Key-Words	
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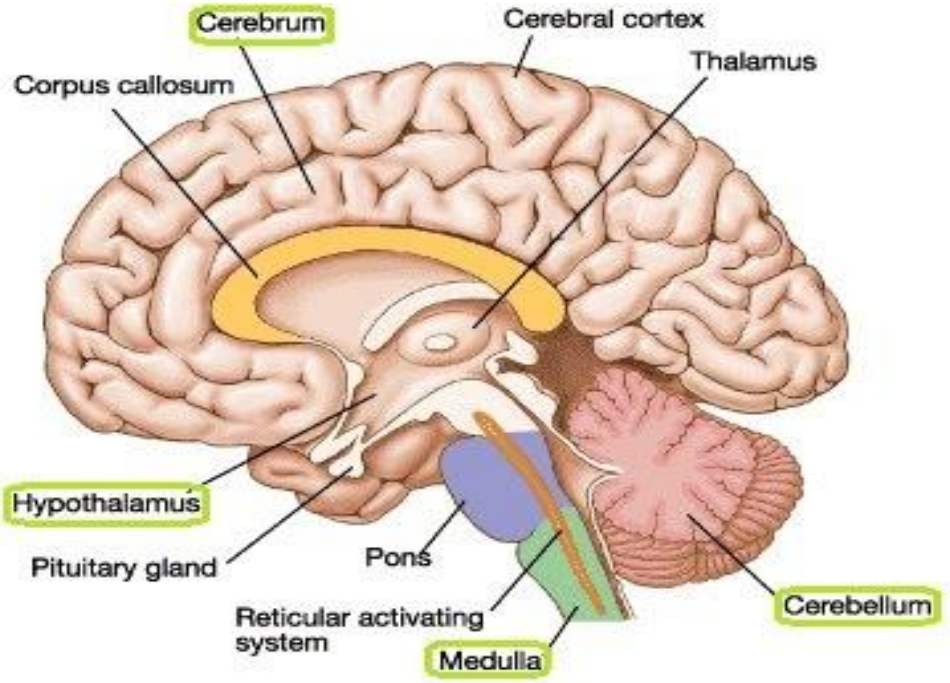
Hypothalmo- Hypophyseal System :

Master gland is a misleading term often used to refer to hypophysis (Pituitary) and to some of the later is subservient to nervous system (and to some of the other endocrine glands also). The pituitary is closely applied to the floor of the brain and remain attached to it by means of delicate stalk. The functional capacity of the anterior pituitary depends upon its neural and vascular connection with the hypothalamus. In this way the pituitary present itself as an essential link between the two vital system of the vertebrate physiology viz nervous system and endocrine system. Thus making possible establishment of a neuroendocrine system.

In other words, hypothalamus and Hypophysis are entirely studying a joint hypothalmo-hypophysial system. Hypothalamo-hypophyseal system or Hypophyseal portal system is also known as the system of blood vessels which conduit and connects the hypothalamus (Brain) to the anterior pituitary (adenohypophysis).



Brain and its Parts

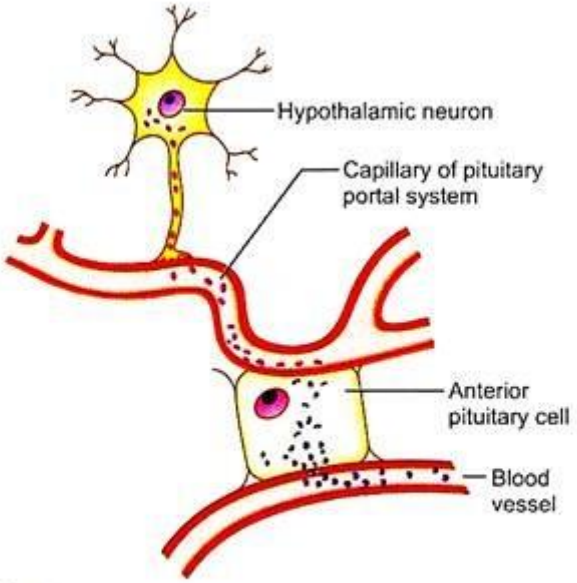


Fig. 6.8: Connection between hypothalamus and anterior pituitary gland (vascular connection—hypothalamohypophyseal portal system)

HYPOTHALAMUS :

The diencephalon is a smaller and posterior part of the forebrain. The wall of diencephalon thickened to form the thalamus above and hypothalamus below.

Hypothalamus is mainly concerned with the regulation of visceral function for many internal sensory fibres end here it regulates temperature, Sleep, Water Balance, Feeding, Drinking, Emotions and Reproductive behaviour.

A part from these functions it is also the seat of neuro-secretion by virtue of which it exert considerable influence called pituitary gland and other endocrine of the body. Hypothalamus also influence the various body activities (i.e. **Heart rate, Respiration, Gastro-intestinal mortality, their autonomic nervous system and the endocrine system**).

Origin of Hypothalamus:

Hypothalamus develops from the ectoderm of the embryo.

Location and Structure of Hypothalamus:

It lies below or inferior to the thalamus. It provides the anatomical connection between the nervous and endocrine systems. This connection is through the hypophysis (pituitary gland).

The hypothalamus is connected to the anterior lobe of pituitary gland by hypophysial portal veins, however, it is connected to the posterior lobe of pituitary gland mainly by axons of neurosecretory cells. The hormones of the hypothalamus influence the functioning of the pituitary gland. The hypothalamus is often called the control centre or **'supreme commander'** of endocrine regulation.

Hormones of Hypothalamus:

Cells in the hypothalamus synthesize at least (09) nine different hormones. The neurosecretory cells (neurons) of hypothalamus secrete hormones called neurohormones (= releasing factors) which are summarised below.

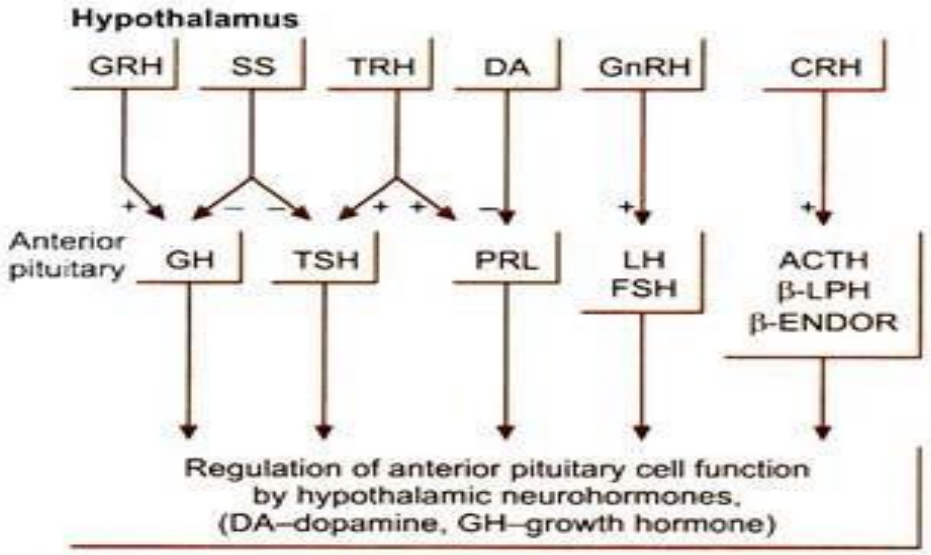


Fig. 6.7: Regulation of secretion of anterior pituitary hormones by the releasing and release-inhibiting hormones secreted by hypothalamus. GRH—Growth hormone releasing hormone, SS—Somatostatin, TRH—Thyrotropin-releasing hormone, DA—Dopamine, GnRH—Gonadotropic-releasing hormone, CRH—Corticotropin-releasing hormone, GH—Growth hormone, TSH—Thyroid-stimulating hormone, PRL—Prolactin, LH—Luteinizing hormone, FSH—Follicular-stimulating hormone, ACTH—Adrenocorticotropic hormone, βLPH—βLipotropin, βENDOR—βEndorphin

(i) Adrenocorticotropic Releasing hormone (ARH) or Corticotropin Releasing Hormone (CRH) :

It stimulates the anterior lobe of the pituitary gland to secrete its adrenocorticotropic hormone (ACTH).

(ii) Thyrotropin Releasing Hormone (TRH):

It stimulates the anterior lobe of the pituitary gland to secrete its thyroid stimulating hormone (TSH) or thyrotropin.

(iii) Growth Hormone-Releasing Hormone (GHRH):

It stimulates the anterior lobe of the pituitary gland to release its growth hormone (GH) or somatotrophin.

(iv) Growth Hormone-Inhibitory Hormone (GHIH):

This hormone is also called somatostatin (SS). It inhibits the secretion of growth hormone from the anterior lobe of the pituitary gland.

(v) Gonadotropin Releasing Hormone (GnRH):

It stimulates the anterior lobe of the pituitary gland to secrete two gonadotropic hormones: (follicle stimulating hormone (FSH) and luteinizing hormone (LH)).

(vi) Prolactin Releasing hormone (PRH):

It stimulates the anterior lobe of the pituitary gland to secrete its prolactin.

(vii) Prolactin Inhibitory Hormone (PIH):

It inhibits the secretion of prolactin from the anterior lobe of pituitary gland.

(viii) MSH Releasing Hormone (MSHRH):

It stimulates the intermediate lobe of the pituitary gland to secrete its melanocyte stimulating hormone (MSH).

(ix) MSH Inhibitory Hormone (MSHIH):

It inhibits the secretion of melanocyte stimulating hormone from the intermediate lobe of the pituitary gland.

Target Cells: Neurohormones act on the cells of the pituitary gland.

Control ,secretion, regulation of anterior pituitary by the hypothalamus occurs as follows:

- The optic chiasma are clusters of neurons called neurosecretory cells. They synthesize the hypothalamic releasing and inhibiting

hormones in their cell bodies and package the hormones inside vesicles, which reach the axon terminals by fast axonal transport, where they are stored.

- ❖ When the neurosecretory cells of the hypothalamus are excited, nerve impulses trigger exocytosis of the vesicles. The hypothalamic hormones then diffuse into the blood of the primary plexus of the hypophyseal portal system.
- ❖ Quickly, the hypothalamic hormones are transported by the blood through the hypophyseal portal veins and into the secondary plexus. This direct route permits hypothalamic hormones to act immediately on anterior pituitary cells, before the hormones are diluted or destroyed in the general circulation.
- ❖ Within the secondary plexus the hypothalamic hormones diffuse out of the bloodstream and interact with anterior pituitary cells. When stimulated by the appropriate hypothalamic-releasing hormones, the anterior pituitary cells secrete hormones into the secondary plexus capillaries.
- ❖ From the secondary plexus capillaries, the anterior pituitary hormones drain into the hypophyseal veins and out into the general circulation. Anterior pituitary hormones then travel to target tissues throughout the body. Those anterior pituitary hormones that act on other endocrine glands are called tropic hormones or tropins.
- ❖ Release of anterior pituitary hormones is regulated not only by the hypothalamus but also by negative feedback. The secretory activity of three types of anterior pituitary cells (thyrotrophs, corticotrophs, and gonadotrophs) decreases when blood levels of their target gland hormones rise.

For example,

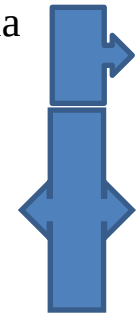
Adrenocorticotropic hormone (ACTH) stimulates the cortex of the adrenal gland to secrete glucocorticoids, mainly cortisol. In turn, an elevated blood level of cortisol decreases secretion of both ACTH (corticotropin) and corticotropin-releasing hormone (CRH) by suppressing the activity of the anterior pituitary corticotrophs and hypothalamic neurosecretory cells.

HYPOPHYSIS :

Pituitary gland is located in the Sell turcica, a concavity in the sphenoid bone. The gland is encapsulated by the dura matter and a shelf like fold of the later forms the diaphrogena sellae and extend around the infundibular stalk. Pituitary is derived from the epithelial and neural components. It is divisible into **two parts i.e. Adenohypophysis and Neurohypophysis**

Adenohypophysis :-

1. Pars Intermedia
2. Pars tuberalis
3. Pars Distalis



Anterior Lobe

Posterior Lobe

Neurohypophysis : -

1. Pars nervosa
2. Infundibulam

Infundibular stem median eminence

Parsintermedia :

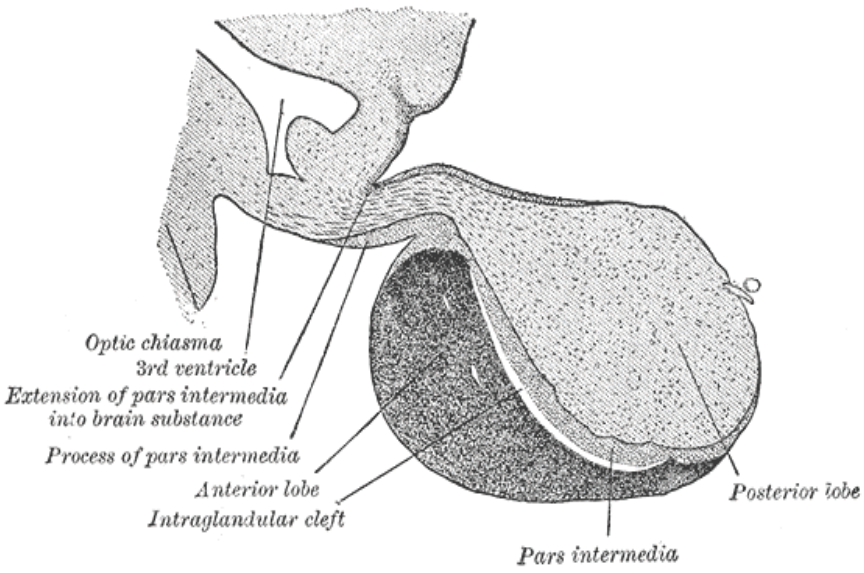
The pars intermedia is a zone of cells that is separated from the pars distalis by the hypophyseal cleft, which is the remnant of the embryonic Rathke's pouch that extended up from the roof of the oral cavity

Pars intermedia is **the boundary between the anterior and posterior lobes of the pituitary**. It contains colloid-filled cysts and

two types of cells - basophils and chromophobes. The cysts are the remainder of Rathke's pouch.

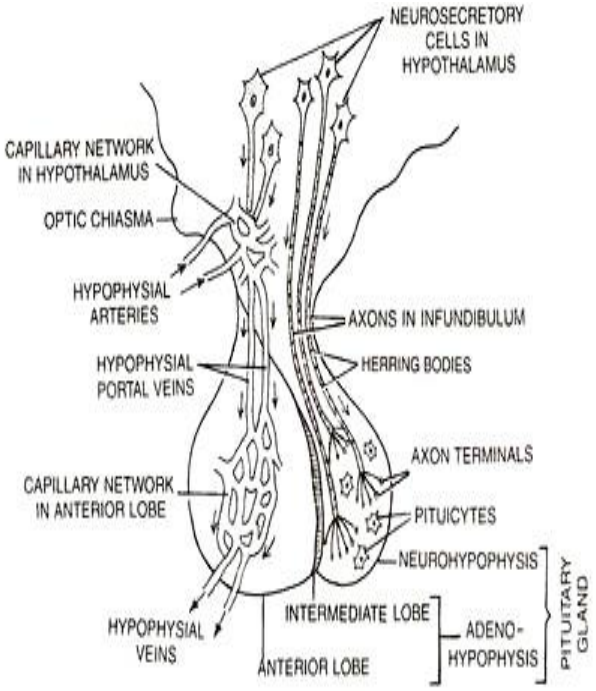
The pars intermedia is closely associated with pars nervosa and separated from the pars distalis by the hypophyseal cleft. This lobe of the pituitary shows considerable variation in size among species.

It is small in man, but much larger in species such as amphibians. The pars intermedia contains large pale cells that often surround follicles filled with ill-defined "colloid". Melanocyte-stimulating hormone is the predominant hormone secreted by the pars intermedia. The images below show pars intermedia from a cat at low and higher magnification.



The hypophyseal cleft is seen in the middle of the left image. In the right image, the three round, clear areas are follicles characteristic of this tissue.

Pars intermedia is present in young human being only merges into the neural lobe in adults. This lobe is absent in the birds and in certain mammals such as whales, Indian elephants.



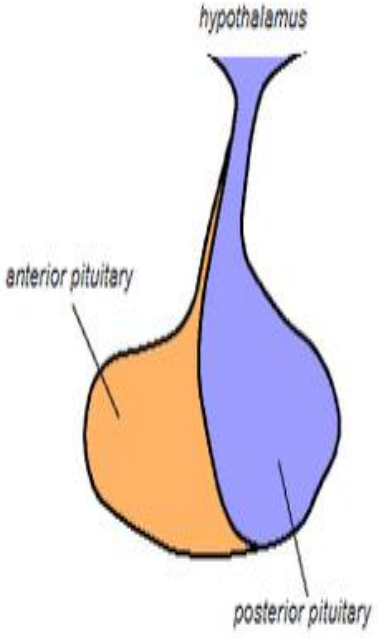
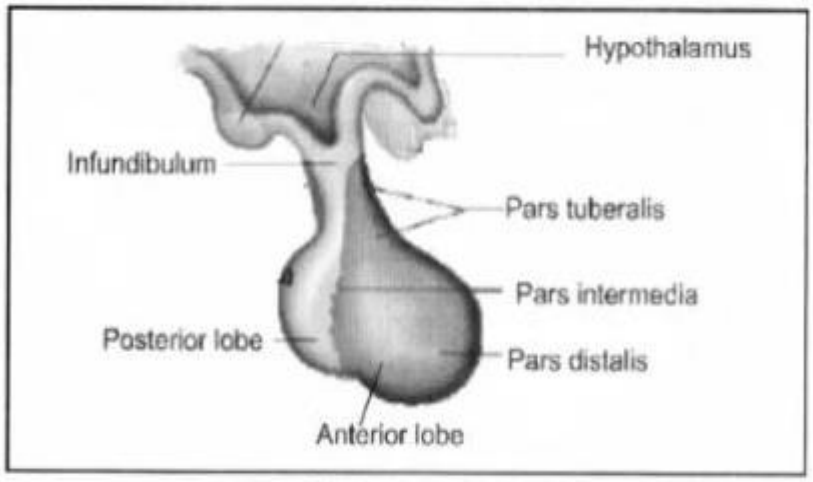


Fig. 22.14. Neurosecretory cells (neurons) of hypothalamus discharging their neurohormones into hypophysial portal veins and into neurohypophysis (posterior lobe) of pituitary gland.



Pituitary gland

Hormones are produced in the pars intermedia?

- Dopamine.
- Adrenocorticotropic Hormone.
- Proopiomelanocortin.
- Thyrotropin-Releasing Hormone.
- Cortisol.

- Dopaminergic.

Pars tuberalis : -

The pars tuberalis is **part of the anterior lobe of the pituitary gland** which wraps the pituitary stalk in a highly vascularized sheath. The pars tuberalis is constituted of the adenohypophysis which is a thin epithelial plate of cells that is formed by the fusion of two outgrowth from the embryonic pars distalis. Pars tuberalis is constituted of the adenohypophysis which is a thin epithelial plate of cells that is formed by the fusion of two outgrowth from the embryonic pars distalis.

Pars Distalis :

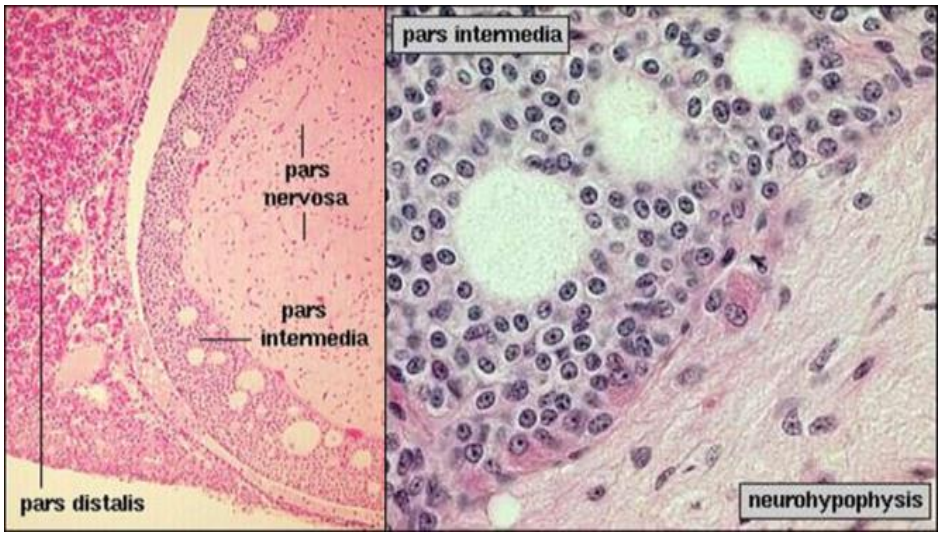
This is the portion in which the majority of the hormone production occurs. It is the distal part of the pituitary and forms the majority of adenohypophysis.The pars distalis have two general cell types chromophils (50%) and chromophobes (50%). The chromophils can be further subdivided into acidophils (40%) and basophils (10%).The acidophils secrete GH (somatotropes) and prolactin (mammotropes).

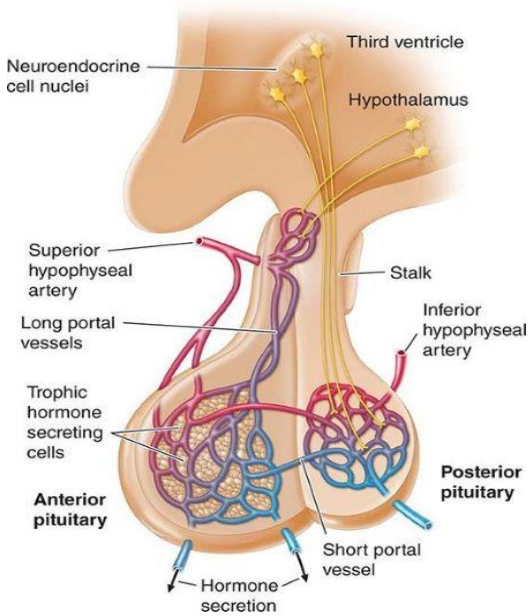
These cells all together produce hormones of the anterior pituitary and release them into the blood stream. The pars distalis produces **GH, PRL, GTHs, (FSH, LH), ACTH, TSH and endorphins (EOPs)**.

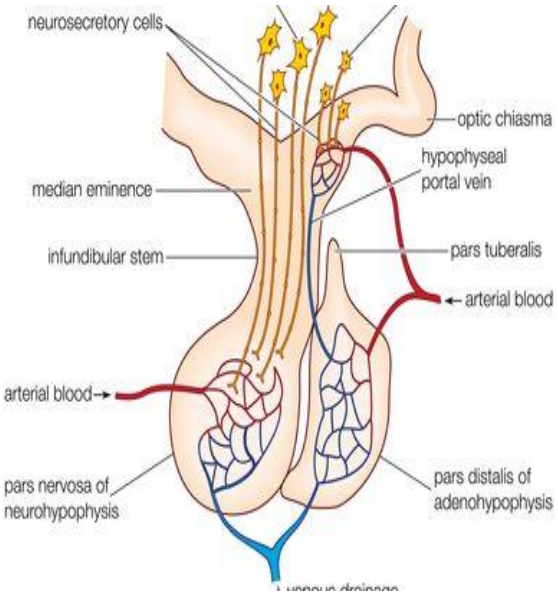
The posterior portion of the adenohypophysis is the pars intermedia, which is responsible for synthesis of a-MSH and endorphins. The pars tuberalis contains some stainable cell types and secretes tuberalin that stimulates PRL release.

Hypophyseal portal system allows endocrine communication between the hypothalamus and the anterior pituitary gland. The

anterior pituitary receives releasing and inhibitory hormones in the blood. Using these the anterior pituitary is able to fulfill its function of regulating the other endocrine glands.







The anterior pituitary (**adenohypophysis**) is derived from embryonic ectoderm. The anterior pituitary (adenohypophysis) secretes **five endocrine hormones** from five different types of epithelial endocrine cells. The release of anterior pituitary hormones is regulated by hypothalamic hormones (**releasing or inhibitory**), which are synthesized in the cell bodies of neurons located in several

nuclei that surround the third ventricle. These include the arcuate, the para ventricular and ventromedial nuclei and the medial preoptic and para ventricular regions. In response to neural activity, the hypothalamic hormones are released from the nerve endings into the hypophyseal portal blood and are then carried down to the anterior pituitary.

Hypothalamic hormones that releases or inhibit anterior pituitary hormones reach the anterior pituitary through a hypothalamic hypophyseal portal system. Usually, blood passes from the heart through an artery to a capillary to a vein and back to the heart.

In a portal system, blood flows from one capillary network into a portal vein and then into a second capillary network before returning to the heart. The name of the portal system indicates the location of the second capillary network. In the hypophyseal portal system, blood flows from capillaries in the hypothalamus into portal veins that carry blood to capillaries of the anterior pituitary (see Figure 1).

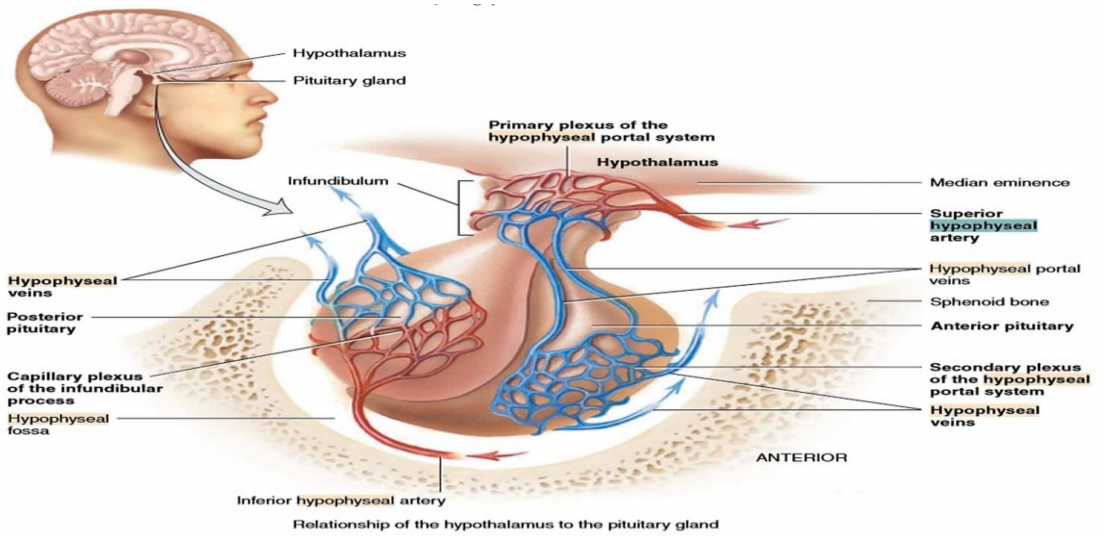
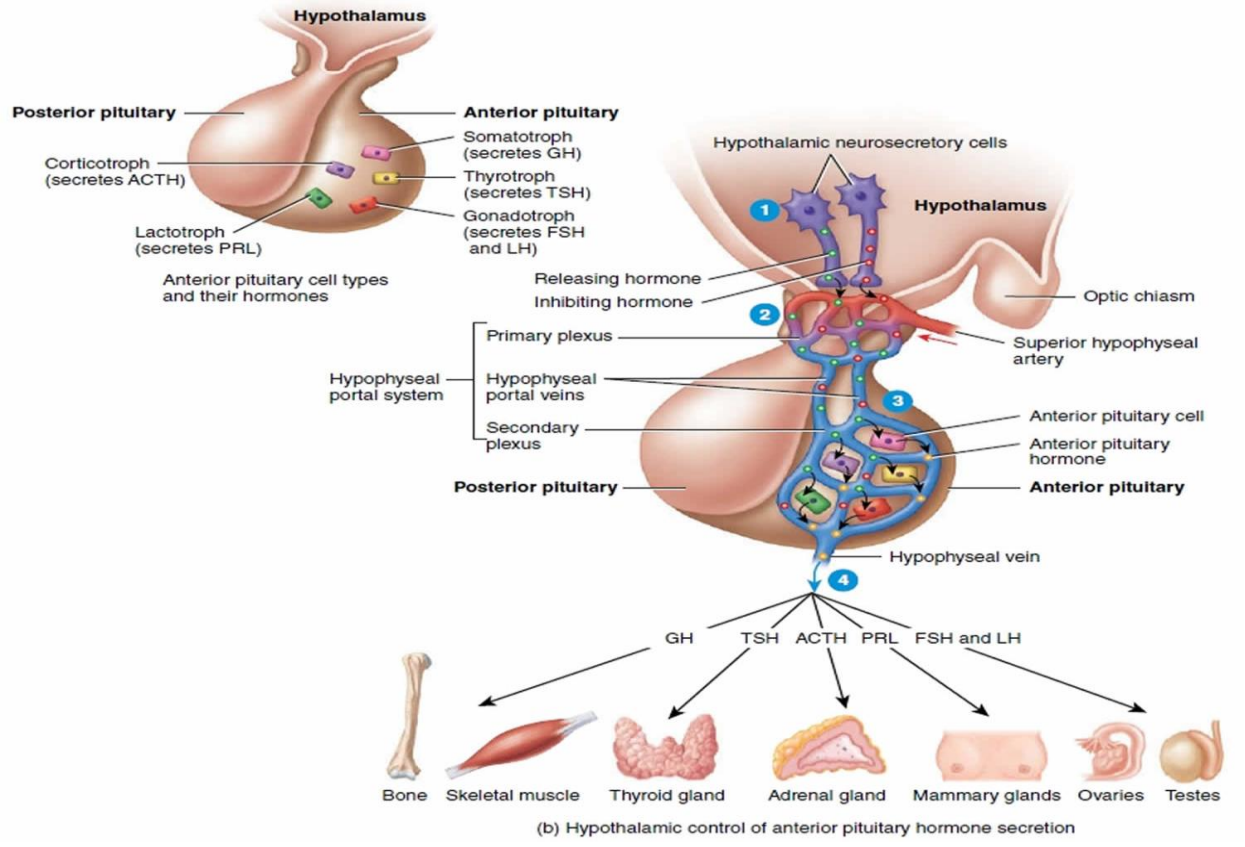


Figure 1. Hypophyseal portal system

In other words, the hormones carried by the hypothalamo-hypophyseal portal system allow communication between the

hypothalamus and anterior pituitary and establish an important link between the nervous system and the endocrine system. The superior hypophyseal arteries, branches from the medial aspect of the internal carotid artery just after leaving the cavernous sinus, bring blood into the hypothalamus.

The superior hypophyseal arteries emerge 5-mm distal to the origin of the ophthalmic artery and then will go on to form the primary capillary network found in the median eminence. At the junction of the median eminence of the hypothalamus and the infundibulum, these arteries divide into a capillary network called the primary plexus of the hypophyseal portal system. This capillary plexus supplies blood to the pars distalis.



From the primary plexus, blood drains into the anterior and posterior hypophyseal portal veins that pass down the outside of the infundibulum. It is via this system that peptides that are released at the

median eminence enter the primary plexus. From that point, the peptides would be transmitted to the adenohypophysis via the hypophyseal portal veins to the secondary plexus.

The portal system has fenestrated capillaries which would allow for exchange between the hypothalamus and the pituitary. The cells of the adenohypophysis express **G-protein coupled receptors** that bind to the peptides allowing the release of hormones from the anterior pituitary.

In the anterior pituitary, the hypophyseal portal veins divide again and form another capillary network called the secondary plexus of the hypophyseal portal system. Hypophyseal veins drain blood from the anterior pituitary.

The primary and secondary capillary plexuses in the pituitary gland, plus the intervening hypophyseal portal veins, constitute **the hypophyseal portal system**. Short veins from the pituitary gland drain into the neighboring dural venous sinuses.

The release of hormones from the anterior pituitary gland is generally controlled by hormones from the hypothalamus. The hypothalamus exerts its control by secreting peptide **hormones called releasing hormones (releasing factors)**, which then prompt the cells in the anterior lobe to release their hormones.

The hypothalamus also secretes inhibiting hormones, which turn off the secretion of hormones by the anterior lobe when necessary. There are distinct releasing and inhibiting hormones for almost every anterior lobe hormone.

Releasing hormones made in hypothalamic neurons are secreted like neurotransmitters from the axon terminals of these neurons. In this case, neurons are serving as endocrine cells. The secreted

releasing hormones enter a primary capillary plexus in the median eminence of the hypothalamus and then travel inferiorly in hypophyseal portal veins to a secondary capillary plexus in the anterior lobe. The releasing hormones leave the bloodstream and attach to the anterior lobe cells and stimulate these cells to secrete hormones (GH, LH, TSH, PRL, and ACTH). The hormones secreted from the anterior lobe cells enter the secondary plexus. From there the newly secreted anterior lobe hormones proceed into the general circulation and travel to their target organs throughout the body.

Hypophyseal portal circulation:

The hypophyseal portal circulation connects the anterior pituitary gland with the hypothalamus. Also known as the hypothalamic-hypophyseal portal system, it helps control the endocrine regulatory mechanisms in the adenohypophysis region of the pituitary gland.

The hypothalamic nuclei produce multiple releasing or inhibiting hormones (TSH, FSH, GnRH). These either stimulate or inhibit the secretion of the responsible hormones from the adenohypophysis through a feedback mechanism.

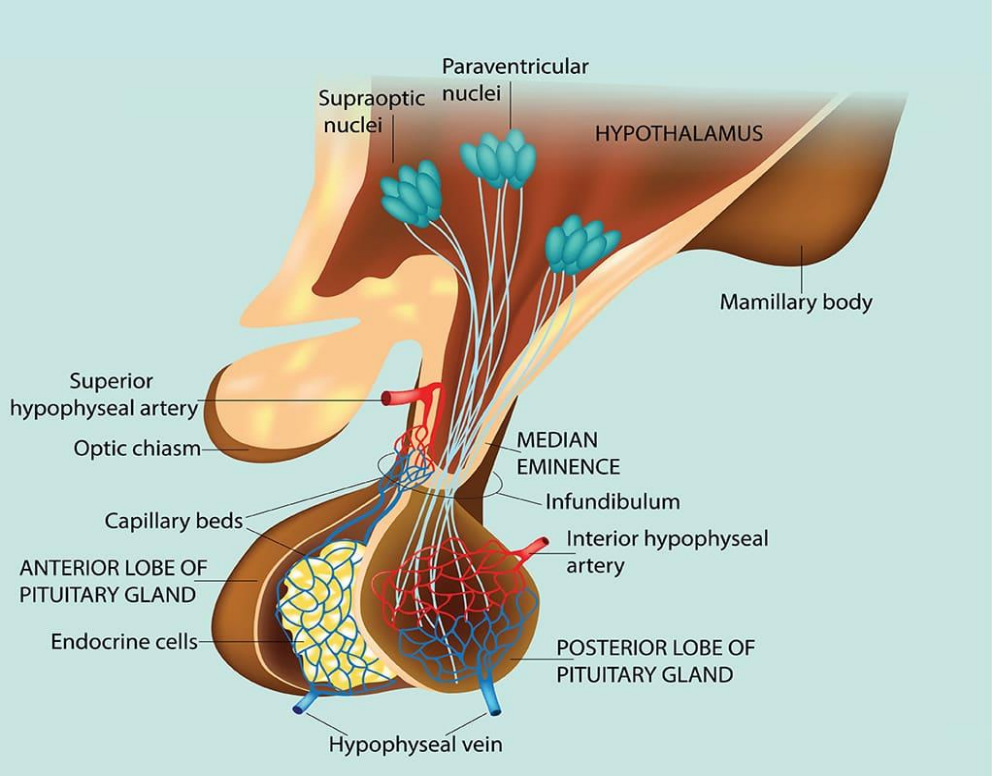
The hypophyseal portal circulation receives these signals from the hypothalamus. Then, it carries the stimulating/inhibitory message to the anterior pituitary system, which releases the hormone for the target organ.

The role of hypothalamic nuclei in the body :

The hypothalamus is called the master of the master gland. Its ability to coordinate all neural signals using autonomic, somatic and endocrine mechanisms makes it a seamless control centre. The

hypothalamic nuclei functions as a moderator in the human body. This includes:

- **Internal homeostasis (maintaining body temperature)**
- **Balancing blood pressure**
- **Managing hunger and thirst (satiety)**
- **Emotional mood and psychological well-being**



- **Inducing or suppressing the sex drive**
- **Monitoring the sleep cycle**

The hypothalamic nuclei and their functions coordinate the following functions of the **autonomic nervous system (ANS):**

- **Breathing rate**
- **Heartbeat**

The hypothalamus produces many hormones. Some of them get stored in the posterior pituitary for further release, while the rest hit the anterior pituitary through the hypophyseal circulation, further secreting hormones.

The role of the hypophyseal portal system :

- ❖ It transmits endocrine messages to the adenohypophysis for stimulation or inhibition of any hormone complexes (through fenestral capillaries)
- ❖ The fenestral capillaries play a crucial role in maintaining the connectivity (an artery cannot supply blood/a vein cannot receive blood directly in a portal circulation)
- ❖ Hypothalamic nuclei secrets neurotransmitters which travel as endocrine signals through the hypophyseal portal system towards the adenohypophysis

Hypothalamic nuclei:

The hypothalamus is a collection of multiple nuclei that performs the following roles:

- ❖ **Regulation of the endocrine system (periventricular zone nuclei)**
- ❖ **Regulates autonomic functions (medial nuclei)**
- ❖ **Regulates somatic functions (lateral nuclei)**
- ❖ **Lying centrally in the brain cavity, it maintains connectivity with the following organelles:**
- ❖ **Amygdala (via the stria terminalis)**
- ❖ **The brain stem (via the dorsal longitudinal fasciculus)**
- ❖ **The cerebral cortex (via the median forebrain bundle)**
- ❖ **Hippocampus (via the formix)**
- ❖ **Pituitary gland (via the median eminence)**

- **Retina (via the retinohypothalamic tract)**
- **Thalamus (via the mammillothalamic tract)**

Hypothalamic nuclei : Hormones secreted from the hypothalamus

The hypothalamic nuclei produce various releasing hormones. The hypophyseal portal circulation channels them to the adenohypophysis for producing hormones. Here we discuss the former's hormones:

- Growth hormone-releasing hormone (GHRH)
- Gonadotropin-releasing hormone (GnRH)
- Corticotrophin-releasing hormone (CRH)
- Thyrotrophin-releasing hormone (TRH)
- Dopamine

Functions of hypothalamic nuclei hormones

- These releasing hormones have a crucial role in maintaining homeostasis. Here's a brief description of their functions:
- GHRH stimulates the secretion of GH (Growth hormone), which enhances the growth and the extension of long bones and muscles.
- GnRH helps secrete LH (Luteinizing hormone) and FSH (Follicle-stimulating hormone), which sets in the menstrual cycle in females while males experience spermatogenesis (sperm production)

- ❖ CRH triggers the production of ACTH (Adreno Cortico trophic hormone), which releases cortisol from the adrenal gland and plays a crucial role in immunity and metabolism.
- ❖ TRH leads to the secretion of the TSH (Thyroid-stimulating hormone) responsible for secreting T4 (tetra-iodothyronine) and T3 (tri-iodothyronine)
- ❖ The hypothalamic nuclei also secrete dopamine. It's antagonistic to prolactin secretion necessary for milk formation.
- ❖ Besides, the hypothalamus also secretes vasopressin (ADH) and oxytocin. These hormones get stored in the posterior pituitary gland.

Clinical significance of the hypothalamic nuclei and hypophyseal portal system

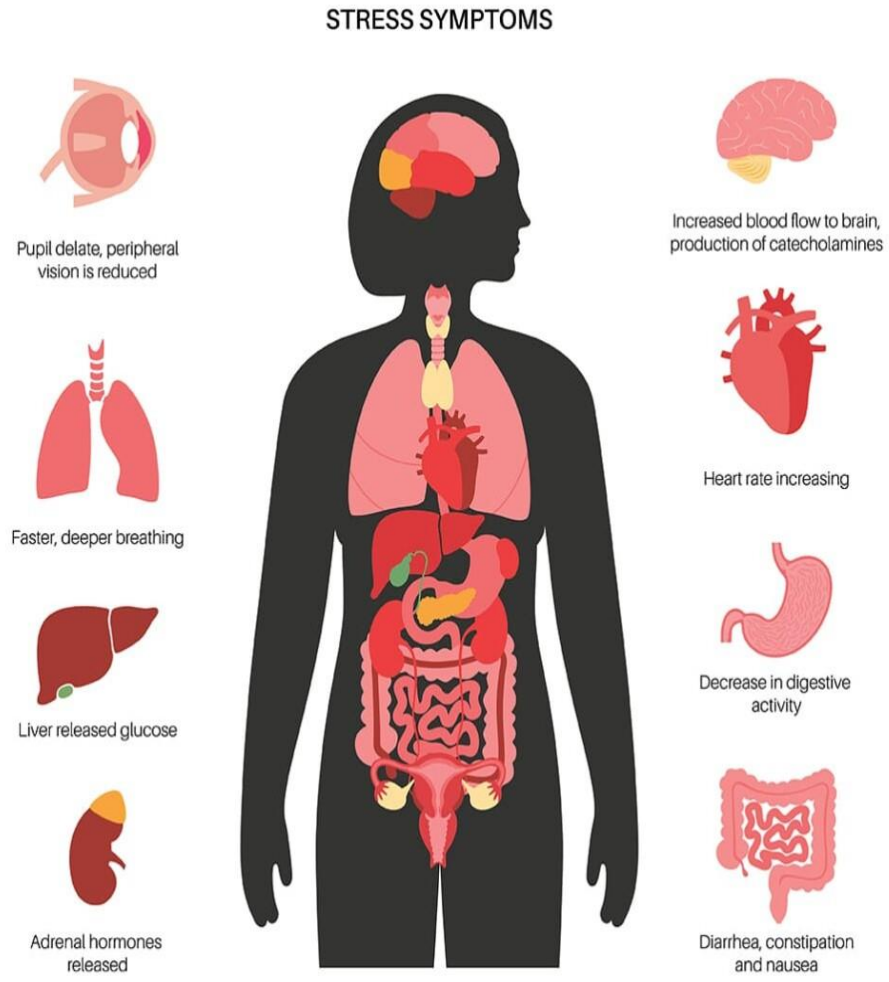
- ❖ **The hypothalamus moderates food intake using the satiety centre as a mechanism to counter obesity.**
- ❖ **It induces an acute-phase immune response to destroy pathogens incubating in the body (fever).**
- ❖ **It controls dopamine-prolactin balance in lactating women.**
- ❖ **It induces natural growth, development and maturity through the proper functioning of the hypothalamic nuclei.**
- ❖ **It balances blood sugar levels and ADH secretion to prevent diabetes development.**

Hypothalamic nuclei : Disorders and Illnesses

The hypothalamic nuclei can get damaged from the following possibilities:

- ❖ **Blunt trauma**
- ❖ **Pathogenic infection**
- ❖ **Brain aneurysm**

- **Side effects of anorexia and bulimia**
- **Inherited defects**
- **Brain damage from multiple sclerosis**
- **Side effects of medicinal therapy**
- **It can lead to various hypothalamic dysfunctions, like:**
- **Hormonal disorders (acromegaly, diabetes insipidus, hyperprolactinemia, hypopituitarism)**
- **Genetic disorders (Kallman syndrome, Prader-Willi syndrome)**
- **Central hypothyroidism (pituitary adenoma & hypophysitis)**
- **Functional hypothalamic amenorrhoea**



Hypothalamic disease symptoms:

Any potential hypothalamic dysfunction will show the following symptoms in advance:

- **Abnormal blood pressure**
- **Irregular breathing rate/heartbeat**
- **An abrupt change in body weight**
- **Loss of bone weight (frequent bone injury from a minor blow)**
- **Irregular menstrual cycle**

- **Sleeplessness (insomnia)**
- **Frequent tendency to pee (polyuria)**
- **Unable to concentrate or feelings of anxiety**

Anterior Pituitary Hormones

Growth Hormone (GH) Or Somatotropic hormone (SP) or somatotropin :

This hormone stimulates growth. Growth hormone promotes protein anabolism, the absorption of calcium from the bowel and the conversion of glycogen to glucose.

Precursor cells: Somatotrophs in the anterior pituitary

Target cells: Almost all tissues of the body

Transport : 60% circulates free and 40% bound to specific growth hormone-binding proteins (GHBPs)

Mechanism of action:

Growth hormone binds to growth hormone receptors (GHRs) causing dimerization of growth hormone receptor, activation of the growth hormone receptor-associated JAK2 tyrosine kinase, and tyrosyl phosphorylation of both JAK2 and growth hormone receptor. This causes recruitment and/or activation of a variety of signaling molecules, including Manterior pituitary kinases, insulin receptor substrates, phosphatidylinositol 3′ phosphate kinase, diacylglycerol, protein kinase C, intracellular calcium, and Stat transcription factors. These signaling molecules contribute to growth hormone-induced changes in enzymatic activity, transport function, and gene expression that ultimately culminate in changes to growth and metabolism.

Regulation of growth hormone secretion:

The release of growth hormone is under dual control by the hypothalamus. Growth hormone secretion is stimulated by growth hormone-releasing hormone (GHRH) but suppressed by another hormone peptide, somatostatin (also known as growth hormone-inhibiting hormone (GHIH)). Insulin-like growth factor-1 (IGF-1) provides negative feedback for inhibiting growth hormone release from somatotrophs. Thyroid hormones (T3 and T4) up-regulate growth hormone gene expression in somatotrophs.

Physiological Functions:

Growth hormone acts almost on every type of cell. Its principal targets are bones and skeletal muscles. It has direct metabolic effects on fats, proteins and carbohydrates and indirect actions that result in skeletal growth.

Direct Metabolic Functions:

Growth hormone is anabolic. It stimulates the growth of almost all tissues of the body that are capable of growing (increase in the number of cells). growth hormone also increases the rate of protein synthesis in most cells of the body and decreases the rate of glucose utilization throughout the body (diabetogenic action). Also, it increases mobilization of fatty acids from adipose tissue and increases levels of free fatty acids in the blood.

Indirect Actions on Skeletal Growth:

Growth hormone stimulates the production of insulin-like growth factor-1 (IGF-1) from hepatocytes. IGF-1 mediates the growth-promoting effects of growth hormone on the skeleton. IGF-1 exerts direct actions on both cartilage and bone to stimulate growth and differentiation. These effects are crucial for growth during childhood to the end of adolescence.

Thyroid stimulating hormone (TSH) or Thyrotropin:

This hormone controls the growth and activity of the thyroid gland. It influences the uptake of iodine, the synthesis of the hormones, thyroxine and tri-iodothyronine by the thyroid gland and the release of stored hormones into the blood stream.

Target Cells: Cells of thyroid.

Mechanism of Action :

Thyroid hormone is produced by the thyroid gland, which consists of follicles in which thyroid hormone is synthesized through iodination of tyrosine residues in the glycoprotein thyroglobulin. Thyroid stimulating hormone (TSH), secreted by the anterior pituitary in response to feedback from circulating thyroid hormone, acts directly on the TSH receptor (TSH-R) expressed on the thyroid follicular cell basolateral membrane.

TSH regulates iodide uptake mediated by the sodium/iodide symporter, followed by a series of steps necessary for normal thyroid hormone synthesis and secretion. Thyroid hormone is essential for normal development, growth, neural differentiation, and metabolic regulation in mammals and is required for amphibian metamorphosis. These actions are most apparent in conditions of thyroid hormone deficiency during development, such as maternal iodine deficiency or untreated congenital hypothyroidism, manifesting as profound neurologic deficits and growth retardation.

Physiological Functions:

Metabolism: thyroid hormone increases the basal metabolic rate. It increases the gene expression of Na+/K+ ATPase in different tissues leading to increased oxygen consumption, respiration rate, and

body temperature. Depending on the metabolic status, it can induce lipolysis or lipid synthesis.

Prolactin hormone (PRL) or Mammotropin hormone (MTH) or Luteotropic hormone (LTH):

Prolactin is also called the **"hormone of maternity"** because its main physiological effect is to activate growth of breasts during pregnancy and secretion of mammary glands after child birth. The name luteotrophic hormone (LTH) refers to because it also stimulates the corpus luteum of the ovary to secrete progesterone hormone.

Precursor cells:

Mainly from lactotrophs in the anterior pituitary

Target cells:

Main target cells are mammary glands and gonads

Mechanism of action:

Binds to peptide hormone receptor (single transmembrane domain) to activate the JAK2-STAT intracellular signaling pathway similar to that of growth hormone

Regulation

Like growth hormone, dual hypothalamic inhibitory (from dopamine) and stimulatory hormones (prolactin-releasing hormone [PRH]) regulate prolactin secretion. The predominant hypothalamic influence is inhibitory.

Physiological functions:

The main functions of prolactin are stimulating mammary gland growth and development (mammographic effect) and milk production (lactogenic effect). It also has effects on the hypothalamic-pituitary-

gonadal axis and can inhibit pulsatile gonadotropin-releasing hormone (GnRH) secretion from the hypothalamus.

Follicle Stimulating Hormone (FSH) And Luteinizing Hormone (LH) :

Precursor cells: Gonadotrophs in the anterior pituitary

Target cells: Gonads (**ovaries and testes**)

Mechanism of action

Follicle stimulating hormone (FSH) and luteinizing hormone (LH) bind to G protein-coupled receptors to activate adenylyl cyclase enzyme, which in turn increases intracellular cAMP. cAMP activates protein kinase A (PKA) that phosphorylates intracellular proteins. These phosphorylated proteins then accomplish the final physiologic actions.

Regulation

Follicle stimulating hormone (FSH) and luteinizing hormone (LH) secretion are under the control of hypothalamic gonadotropin-releasing hormone (GnRH).

Physiological Functions:

Follicle stimulating hormone (FSH) and luteinizing hormone (LH) regulate the functions of the ovaries and the testes. In females, follicle stimulating hormone (FSH) stimulates growth and development of follicles in preparation for ovulation and secretion of estrogens by the mature Graafian follicle. luteinizing hormone (LH) triggers ovulation and stimulates the secretion of progesterone by the corpus luteum. In males, follicle stimulating hormone (FSH) is required for spermatogenesis, and luteinizing hormone (LH) stimulates testosterone secretion by Leydig cells.

Thyroid Stimulating Hormone (TSH) :

Precursor cells: Thyrotropes in the anterior pituitary

Target cells: thyroid follicular cells

Mechanism of action

TSH binds to the G-protein-coupled receptors on the basolateral membrane of the thyroid follicular cells. Similar to follicle stimulating hormone (FSH) and luteinizing hormone (LH), it activates the adenylyl cyclase-PKA-cAMP system to phosphorylate several proteins, which in turn achieve the final physiologic actions

Regulation

TSH secretion is under control of hypothalamic thyrotropin-releasing hormone (TRH). Also, T4 feeds back to the anterior pituitary to inhibit TSH secretion.

Physiological functions:

The main function of TSH is to stimulate synthesis and secretion of thyroid hormones (tri-iodothyronine [T3] and thyroxine [T4]) from thyroid follicles. It also maintains the structural integrity of the thyroid glands.

Adrenocorticotrophic Hormone (ACTH) :

This hormone stimulates the cortex of the adrenal gland to produce its hormones

Precursor cells: Corticotrophs in the anterior pituitary

Target cells: Cells in the cortex of the adrenal glands (adrenocortical cells)

Mechanism of action

ACTH binds to its G-protein coupled receptors on the adrenocortical cells. Similar to TSH, follicle stimulating hormone (FSH), and luteinizing hormone (LH), it activates adenylyl cyclase-PKA-cAMP system to phosphorylate several proteins, which in turn achieve the final physiologic functions.

Regulation

ACTH secretion is under control of hypothalamic corticotropin-releasing hormone (CRH). It is subject to negative feedback regulation.

Hormones of the Posterior lobe:

The secretion of the posterior lobe is known as pituitrin and it contains two hormones:

(i) Oxytocin or pitocin.

(ii) Antidiuretic hormone (ADH) or vasopressin.

(i) Oxytocin (OT):

Oxytocin promotes contraction of the uterine muscle and contraction of the myoepithelial cells of the lactating breast, squeezing milk into the large ducts behind the nipple. In late pregnancy the uterus becomes very sensitive to oxytocin.

The amount secreted is increased just before and during labour and by sucking of the baby. Because of its role, oxytocin is called "birth hormone" and "milk ejecting hormone". Milkmen inject synthetic oxytocin, called pitocin, into their cows and the buffaloes to get more milk.

Target Cells: Cells of mammary glands.

(ii) Antidiuretic hormone (ADH) or Vasopressin or Pitressin:

This hormone has two main functions:

(a) Antidiuretic effect:

It increases the reabsorption of water in the distal convoluted tubule and collecting ducts of the nephrons of the kidneys. As a result, the reabsorption of water from the glomerular filtrate is increased,

(b) Pressor effect:

Involuntary muscles in the walls of the intestine, gall bladder, urinary bladder and blood vessels are stimulated to contract by ADH. Contraction of the walls of the blood vessels raises the blood pressure and this may be its most important pressor effect.

Target Cells: Cells of kidneys.

The pituitary gland is also called "Master Endocrine Gland" of body or the **"Chief Executive of Endocrine System"** or **"The Leader of Endocrine Orchestra"** as it secretes the number of hormones (e.g., TSH, ACTH etc.) which regulate the working of other endocrine glands.

But it is not proper to call it as master endocrine gland because it is itself under the control of the releasing hormones secreted by the hypothalamus of the brain. Thus the hypothalamus is, in fact, the supreme commander of endocrine regulation.

Physiological functions:

The main function of ACTH is to stimulate secretion of adrenal cortex hormones (mainly glucocorticoids) during stress.

Comparative account of Hypothalmo- Hypophysial System of other vertebrates :-

The anatomic constituents of the vertebrates pituitary gland are remarkably constant. The most conspicuous phylogenic changes have been the appearance of a system of portal vessels passing from the median eminence to the adenohypophysis and the lack of the pars intermedia in birds and few mammals.

1. Cyclostomes :

The adenohypophysis of the cyclestomes is an elongated structure divided by connective tissues septa into the three regions. The most posterior component is the pars itermedia and the two anterior components are rostral pars distalis and the proximal pars distalis. The neurohypophysis is a slight thicken of the floor of the 3rd ventricle, separated from adenohypophysis by a thin layer of vascular tissues. Some of the hypothalamic neurosecretary axons terminates into neurohypophysis.

2. Elasmobranches and Teleost's :

The elasmobranches and teleostels are specialized groups in that their nerohypophysis is diffuse and intergumented with the pars intermedia. The two parts often being collectively referred to as the neurointermediates lobe. Neurosecretary axons from the lateral hypothalamus terminates in the neuro hypophysis. There is another

folded and highly vascularized structure lying posterior to the neurohypophysis known as saccus vasculosus. The later too receives some neurosecretary fibres from the hypothalamus. Its function in not yet known. The pasrs distalis lies below the infundibulam and is divisible into proximal and rostral zone.

The adenohypophysis of elasmobranches is peculiar in having a ventral lobe which varies gretatly in size and shape among different species and its function observe. A primitive system of hypophysial portal veins supply both the distal and neuro intermedia has been described. It is not clear wether an anatomically diffentiated median eminence is present or not.

In teleost's, the adenohypophysis consist of pars intermedia and an another lobe which is sometimes divisible topographically into rostral and proximal regions. These regions of pars distalis contains all of the cell types characteristics of mammalian anterior lobe. Neurohypophysis are too is diffuse and interdigitate with cells of the pars intermedia and to a lesser extent with pars distalis. Neurosecretary fibres from hypohthalamus terminates in the neurohypophysis but their secretions have also been found in pars distalis. The saccus vesculosus are well developed in many teleosts but it does not appears to be supplied by neurosecretary tract, the presence of a median eminence and a partial system is not clear.

3. Lung Fishes (Dipnoi) :

Among lung fishes the neurohypophysis is separable from pars intermedia and pars tuberalis is absent. A cleft is typically present between the pars distalis and Pars intermedia and the saccus vasculosus does not developed. A primitive system of portal veins conveyed blood from the median eminence to the pars distalis. There is still slight interwingling of hormones and pars intermedia tissues. Except for this and absence of pars tuberalis, the dipnoan pituitary is comparable to the pituitary of tetrapod's vertebrates.

4. Amphibians :

The Hypophysis of primitive urodels is very similar to that of living fishes. The median eminence is more advanced and the portal system is conspicuous. In some amphibians, a second distant portal system supplies the pores intermedia and pars nervosa.

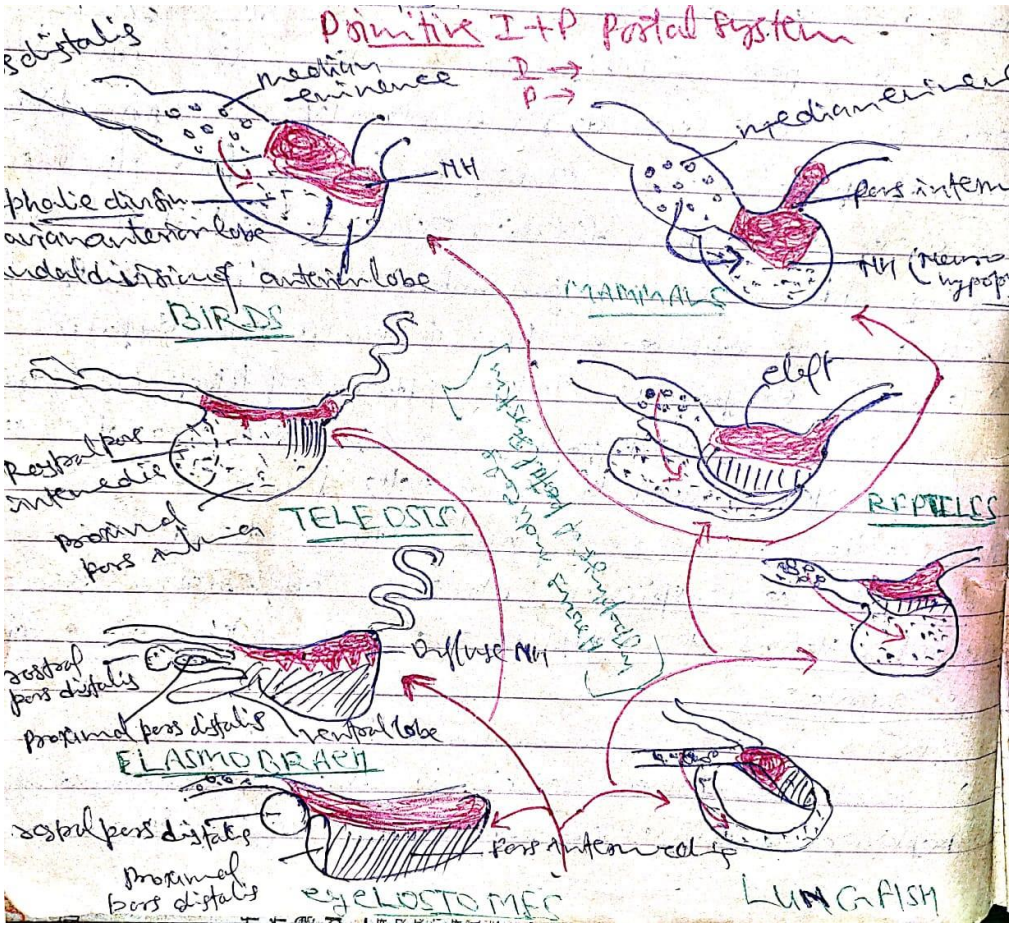
5. Higher Vertebrates : (Reptiles, Birds and Mammals) :

In these higher vertebrates the hypothalamo hypophysial system is very similar except some mior difference. Pars tuberalis is often laking in reptiles and clft is typically present between the pars intermedia and pars distalis. A pars intermedia is absent in birds the neural and anterior lobes being separated by a connective tissues septum.

The avian neurohypophysis is highly specialized and in certain cases the zona externa of median eminence as well as the pars

nervosa, serves as a storage site (Neurohaemal organ) for neurosecretary materials from hypothamic neurons.

The portal blood vessels of the avian pituitary runs to the anterior lobe via the pars tuberalis not in direct opposition to the infundibulam stalk as in mammals.



What causes hypothalamic dysfunction?

Hypothalamic dysfunction could be a potential side effect of a blunt head injury. It could also be from underlying complications (disorders) affecting the hypothalamus.

What is the location of the hypothalamus?

The name of the hypothalamus indicates its position (lying below the thalamus). The hypothalamic nuclei lie above the pituitary gland, sitting at the base of the brain on the brain stem.

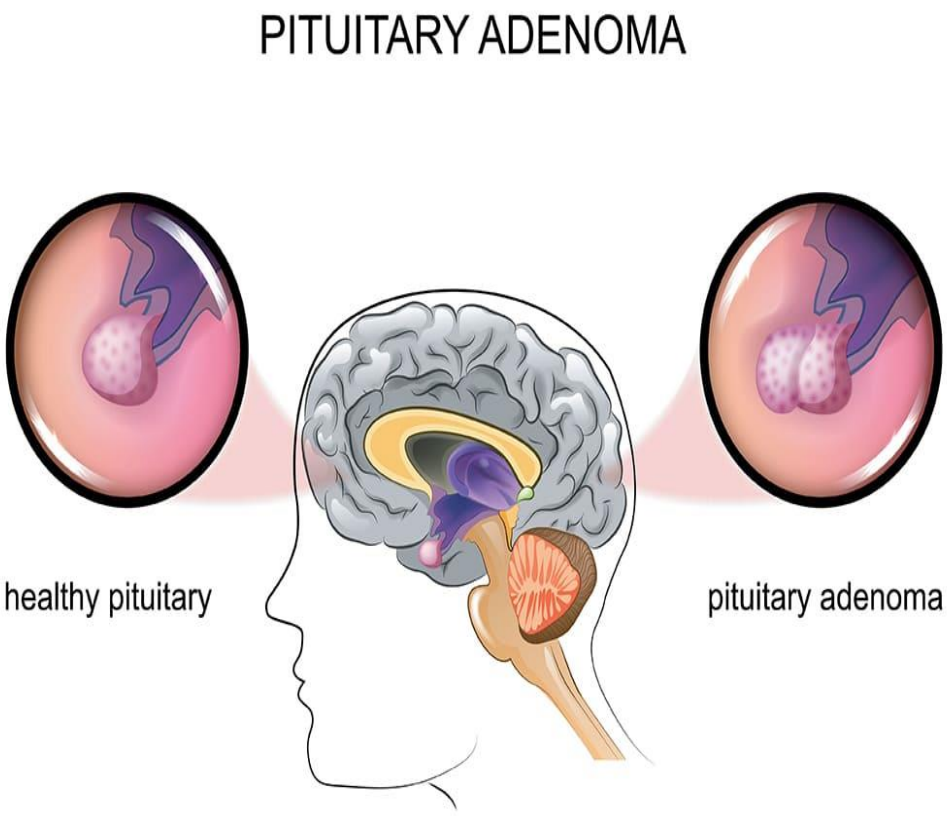
What happens if the hypothalamus gets damaged?

Even the slightest damage to your hypothalamus can lead to potential hypothalamic dysfunction. This can lead to various hormonal disorders (acromegaly), causing irreparable damage.

What symptoms show hypothalamus dysfunction?

Hypothalamic disease symptoms can range from abnormal blood pressure to insomnia. While these are common symptoms of other characteristic disorders, it's best to undergo a health check-up to diagnose the underlying reason.

Pituitary Disorders:

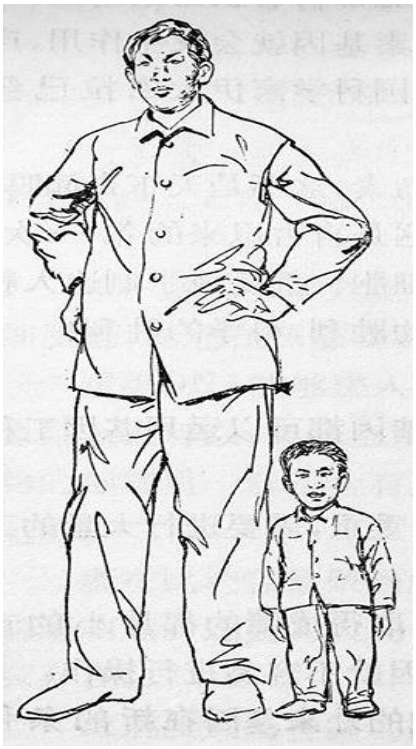


(a) Pituitary Dwarfism:

It is caused by the deficiency of growth hormones (GH) from childhood. It is characterised by small but well proportioned body and sexual immaturity. The dwarfs produced by the deficiency of growth hormone are different from those which are formed from the deficiency of thyroid hormone in having normal intelligence.

(b) Gigantism:

It is caused by excess of growth hormone from early age. It is characterised by large and well proportioned body. If size of pituitary gland increases, it affects (suppresses) optic chiasma and ultimately affects vision.



(c) Acromegaly (Aero- extremity, megaly- large):

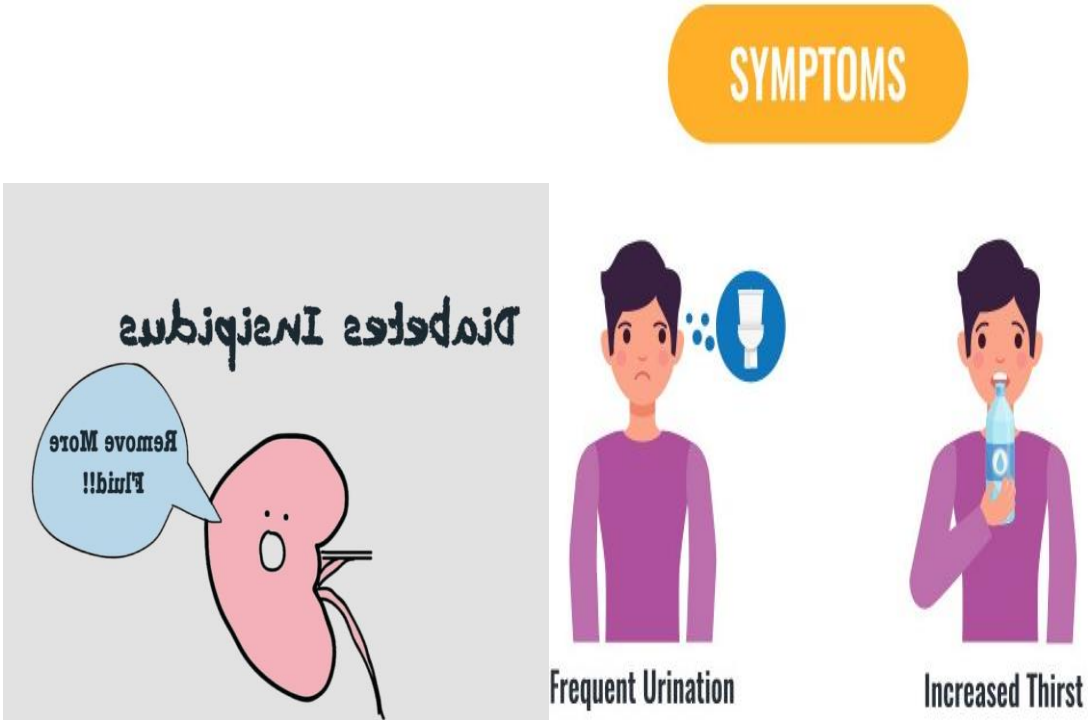
It is caused by excess of growth hormone after adult size is reached. It is characterised by disproportionate increase in size of bones of face, hands and feet.

Fig. 22.16. Acromegaly.

Khali

(d) Diabetes Insipidus:

It is caused by the deficiency of ADH. It is characterised by excessive dilute urine.



(e) Simmonds' Disease:

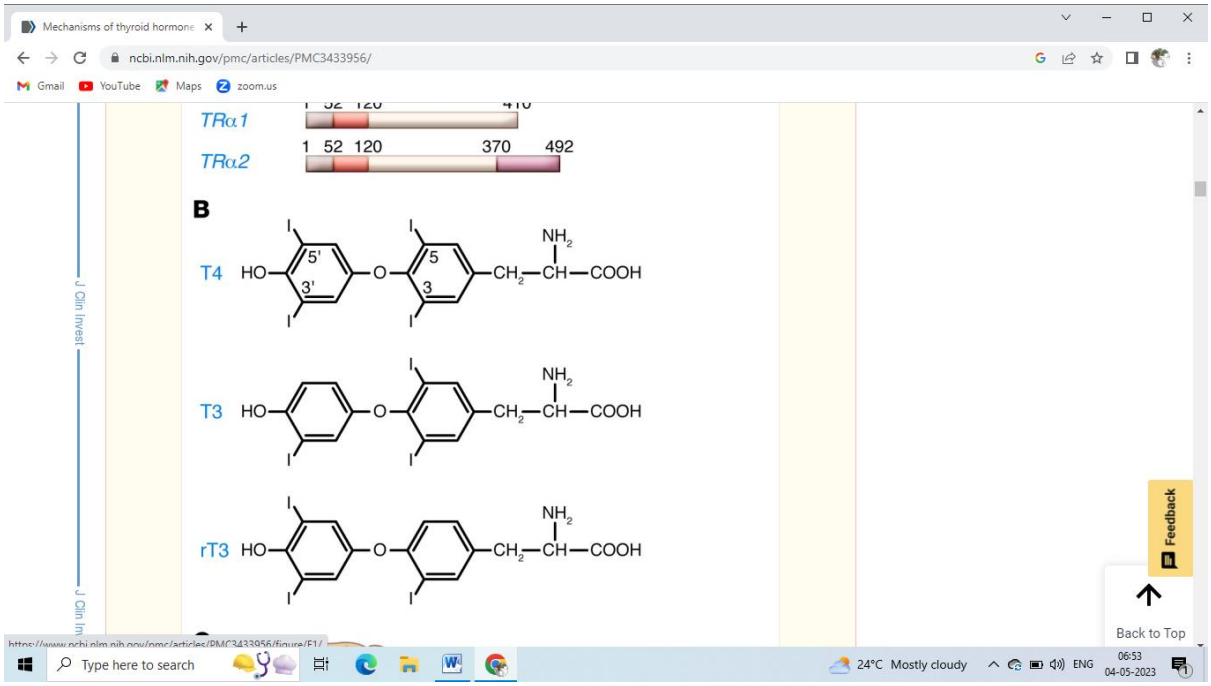
Cause atrophy or degeneration of anterior lobe of pituitary gland. Symptoms the skin of face becomes dry and wrinkled, premature ageing.

(f) High Blood Level of ADH:

It is caused by excessive secretion of ADH. It is characterised by excessively dilute blood and low plasma sodium.

Declaration

The content is exclusively meant for academic purpose and for enhancing teaching and learning. Any other use for



Mechanism of Action and Physiologic Effects of Thyroid Hormones

Thyroid Hormone Receptors and Mechanism of Action

Receptors for thyroid hormones are intracellular DNA-binding proteins that function as hormone-responsive transcription factors, very similar conceptually to the receptors for steroid hormones.

Thyroid hormones enter cells through membrane transporter proteins. A number of plasma membrane transporters have been identified, some of which require ATP hydrolysis; the relative importance of different carrier systems is not yet clear and may differ among tissues. Once inside the nucleus, the hormone binds its receptor, and the hormone-receptor complex interacts with specific sequences of DNA in the promoters of

responsive genes. **The effect of the hormone-receptor complex binding to DNA is to modulate gene expression**, either by stimulating or inhibiting transcription of specific genes.

For the purpose of illustration, consider one mechanism by which thyroid hormones increase the strength of contraction of the heart. Cardiac contractility depends, in part, on the relative ratio of different types of myosin proteins in cardiac muscle. Transcription of some myosin genes is stimulated by thyroid hormones, while transcription of others in inhibited. The net effect is to alter the ratio toward increased contractility.

For additional details on mechanism of action and how these receptors interact with other transcription factors, examine the section Thyroid Hormone Receptors.