The pituitary gland, also known as the hypophysis, is a small pea-sized gland about 1 cm in diameter and 0.5 to 1 gram in weight. The pituitary gland resides in a small bony cavity situated at the base of the brain, known as sella turcica, and a pituitary stalk (infundibulum) maintains a connection between the pituitary gland and hypothalamus. The secretion of hormones by the pituitary gland is under the influence of the hypothalamus through its various hormonal and neuronal signals. There are two distinct divisions of the pituitary gland: the posterior pituitary and the anterior pituitary. Between these two, there is a small zone, which is relatively avascular and less well-developed in humans, known as pars intermedia.
Corticotropes (C) is at the posterior tip.
- Thyrocytes (Tr) is at the opposite corner.
- The most ventral cells are the gonadotropes (G), followed by the main thyrotropes (T), the somatotropes and lactotrophs (S/L), and the melanotropes (M).
- After compartmentalized cell-type specification, the cells become mixed.

Pituitary Hormones Secreted by the Posterior Pituitary

The posterior pituitary (or neurohypophysis) is made up of modified glial cells (termed pituicytes) and axonal processes of neurons which extend from nerve cell bodies located in the supraoptic and paraventricular nuclei of the hypothalamus. The posterior pituitary secretes two peptide hormones:

1. Arginine vasopressin (AVP) formerly called ADH (antidiuretic hormone)
2. Oxytocin

Both hormones are synthesized by the cell bodies of supraoptic and paraventricular nuclei in the hypothalamus. They are released in response to the action potential that travels from axon bodies in the hypothalamus, to their nerve terminals in the posterior.
pituitary where they are stored as well. Both the hormones of posterior pituitary are made as pre-pro-hormones, processed as nonpeptides and they are released directly into the systemic circulation.

Image: “Hypothalamus–Pituitary Complex” by Phil Schatz. License: CC BY 4.0

**ADH or Vasopressin**

ADH is predominantly formed in the **supraoptic nucleus** and it controls the rate of excretion of water into the urine, thus controlling the water concentration of body fluids. ADH effectively controls osmolarity, ECF volume and water excretion.

**Functions of ADH**

**Antidiuretic hormone (ADH)** plays an important role in volume regulation, sodium homeostasis, regulation of serum osmolality, and possibly also learning and memory modulation. Three receptor subtypes that mediate the actions of ADH have been identified: V1A, V1B, and V2.

One main action of ADH is to increase the water re-absorption (causing water retention) through the distal tubules and collecting ducts of the **kidneys**. This effect is mediated through the V2 receptors via the actions of cAMP leading to the increased number of aquaporins on the distal tubules and collecting ducts.

The other important function of ADH is to cause constriction of the vascular smooth muscles, causing generalized vasoconstriction, being mediated through V1 receptors.

**Regulation of ADH Release**

There are various factors that influence the release of ADH. The factors which increase the release of ADH include: **increased osmotic pressure** in the ECF/increased plasma osmolality (sensed by hypothalamic osmoreceptors), **decreased blood volume** (sensed by cardiac baroreceptors), **decreased blood pressure**, stress, hypoglycemia, nausea, emotional stress, pain, and physical trauma, etc. However, alcohol, decreased plasma osmolality, the release of atrial natriuretic peptide (ANP) and alpha-agonists are among
Disorders of ADH Secretion

- Syndrome of inappropriate ADH release (SIADH)

It is an overproduction of ADH, characterized by abnormally high levels of circulating vasopressin which may arise as a result of certain drug treatments, after surgery, brain traumas, or from vasopressin-secreting tumors such as bronchial carcinoma. Patients with SIADH usually produce highly concentrated urine and water retention decreased plasma osmolality and hyponatremia (sodium depletion).

- Diabetes insipidus

Lack of ADH produces diabetes insipidus, characterized by an inability to produce concentrated urine with polyuria, polydipsia and increased plasma osmolality.

It is of two types: central diabetes insipidus arising as a result of head injuries or tumors that damage the hypothalamus or posterior pituitary gland and is effectively treated with ADH (desmopressin), and nephrogenic diabetes insipidus caused by the loss or increased resistance of V2 receptors (vasopressin receptors) in collecting ducts of the kidneys.

Oxytocin

Oxytocin is formed predominantly in the hypothalamic paraventricular nuclei and it helps in breastfeeding and the delivery of the baby.

Functions of Oxytocin

Oxytocin is responsible for the ejection of milk from the lactating female breasts in response to suckling via contraction of myoepithelial cells of the alveoli and alveolar ducts. Oxytocin also helps in the delivery of the baby at the end of gestation, by promoting the contractions of the uterus and increasing the sensitivity of the myometrium (uterine smooth muscles) to other spasmogenic agents. Effective smooth muscle contractions, caused by oxytocin, help expel the baby and placenta during labor.
The anterior pituitary (or adenohypophysis) secretes six peptide hormones which are crucial to the control of metabolic functions throughout the human body:

1. **Growth hormone (GH)**
2. **Thyroid-stimulating hormone (TSH)**
3. **Adrenocorticotropic hormone (ACTH)**
4. **Prolactin (PRL)**
5. **Follicle-stimulating hormone (FSH)**
6. **Luteinizing hormone (LH)**

The anterior pituitary has several cell types responsible for the synthesis and secretion of anterior pituitary hormones. With the help of histology, five basic cell types can be identified:

1. **Somatotropes** – which secrete growth hormone (GH)
2. **Thyrotropes** – thyroid-stimulating hormone (TSH)
3. **Corticotropes** – adrenocorticotropic hormone (ACTH)
4. **Lactotropes** – prolactin (PRL)
5. **Gonadotropes** – which secrete gonadotropic hormones including follicle-stimulating hormone (FSH) and luteinizing hormone (LH)
Hypothalamic Control of Pituitary Secretion

There is a system of blood vessels, known as the hypothalamohypophysial portal system, present between the hypothalamus and the anterior pituitary. The hypothalamus regulates the pituitary secretion by the release of hypothalamic hormones into the hypophyseal portal blood. A negative feedback mechanism operates within the hypothalamic-pituitary axis and the target tissues to regulate endocrine and metabolic functions. The hypothalamic “releasing hormones” are thought to enhance the secretion of all anterior pituitary hormones, with the exception of prolactin, whose secretion is mainly regulated by the inhibitory effect of dopamine.

Hypothalamic factors or releasing hormones, that control the secretion of anterior pituitary hormones includes:

- Thyrotropin-releasing hormone (TRH)
- Gonadotrophin-releasing hormone (GnRH)
- Growth hormone-releasing hormone (GHRH)
- Corticotrophin-releasing hormone (CRH)
- Dopamine (DA) or prolactin inhibitory factor (PIF)
- Somatostatin (SS)

Growth Hormone (GH)

The secretion of growth hormone is regulated primarily via hypothalamic GHRH stimulation and somatostatin inhibition. Growth hormone targets almost all of the body tissues. GH exerts negative feedback on its release from the anterior pituitary via the hypothalamic-pituitary axis.

**Actions of Growth Hormone**

Growth hormone plays an important role in:

- Stimulation of growth and metabolism of almost all body tissues
Production of Insulin-like Growth Factor (IGF) in the liver
- Maintenance of tissues and promoting linear growth during childhood and adolescence (acting indirectly via IGF)
- Increased protein synthesis and Lipolysis (lipid breakdown)
- Decreases glucose uptake in cells, thus resulting in increased blood glucose level (diabetogenic action)

Disorders of GH Production

Hypersecretion of GH during early life leads to the development of Gigantism which is characterized by the symmetrical enlargement of body tissues leading to having an overgrowth of long bones, connective tissue, and visceral organs.

Image: “As compared with the hand of an unaffected person (left), the hand of a patient with acromegaly (right) is enlarged, the fingers widened, thickened and stubby, and the soft tissue thickened.” by Philippe Chanson and Sylvie Salenave. License: CC-BY 2.0

However, if hypersecretion of GH occurs after the body growth has stopped or complete, it results in Acromegaly, characterized by asymmetrical growth with overgrown cancellous bones, leading to a protruding jaw, thickening of phalanges and abnormally enlarged soft tissues and visceral organs.

Thyroid Stimulating Hormone (TSH)

TSH stimulates the secretion of thyroid hormones from the thyroid gland. TSH secretion is stimulated by TRH from the hypothalamus and is inhibited by the negative feedback of circulating T3 (triiodothyronine).

In Grave’s disease, thyroid auto-antibodies bind to TSH receptor and mimic the action of TSH itself, which leads to the persistent stimulation of thyroid and increased levels of thyroid hormones in the body.

Adrenocorticotropic Hormone (ACTH)

ACTH is produced in the anterior pituitary by the proteolytic processing of Pre-pro-opiomelanocortin (also known as POMC) and the other related neuropeptide products include β and γ-lipotropin, β-endorphin, and α-melanocyte-stimulating hormone (α-MSH). CRH, ADH; stress and hypoglycemia stimulate the release of ACTH from the anterior pituitary. ACTH acts on the adrenal cortex to stimulate the growth of the adrenal cortex, which causes the release of glucocorticoid (and steroid hormone synthesis) and is a key regulator of the stress response.
Overproduction of ACTH from the anterior pituitary is known as Addison's disease which is characterized by the lack of cortisol production by the zona fasciculata of adrenal glands and thus the loss of negative feedback suppressing ACTH release, resulting in large amounts of ACTH in the body exerting various effects, such as the darkening of skin etc.

Prolactin (PRL)

Prolactin is the only hormone of the anterior pituitary, which is primarily negatively controlled by the hypothalamus with dopamine (or PIF) suppressing its release. TRH and oxytocin stimulate the release of prolactin. Prolactin stimulates the development of mammary glands and lactogenesis. It is known to inhibit ovulation by blocking the gonadotrophin-releasing hormone (GnRH). Its function in males is not well defined; however, it is suggested to be involved in the development of Leydig cells in pre-pubertal males.

Deficiency of PRL is not a usual clinical concern; however, its over-production may lead to the amenorrhea-galactorrhea syndrome.

Follicle-stimulating hormone (FSH) and Luteinizing hormone (LH):

FSH and LH are produced by the gonadotropes in the anterior pituitary. GnRH from the hypothalamus stimulates the synthesis and secretion of these gonadotropic hormones with a major control on LH. FSH secretion is mainly controlled by inhibin (produced by testes and ovaries).

FSH is known to stimulate the growth and maturation of ovarian follicles (Oocytes) in females while, in men, it stimulates the production and maturation of sperm. LH, on the other hand, triggers ovulation and enhances the secretion of estrogen and progesterone in females, while, in males, it stimulates the production of testosterone.

Review Questions

The correct answers are below the references.

1. Which of the following is known to stimulate the release of prolactin (PRL) from the anterior pituitary?
   - A. Dopamine
   - B. Prolactin inhibitory factor (PIF)
   - C. Thyroid releasing hormone (TRH)
   - D. Estrogen

2. Central diabetes insipidus (CDI) is characterized by the production of large amounts of diluted urine. ADH administered, while managing CDI, exerts its action through receptors known as:
   - A. Aquaporins
   - B. V1A
   - C. V1B
   - D. V2

3. A 42-year-old patient comes to you with diffuse goiter and exophthalmos.
Lab results show the presence of TSH antibodies, greatly suppressed TSH level and elevated T3 and T4. What is the most likely diagnosis?

A. Hypothyroidism
B. Thyrotoxicosis
C. Grave's disease

- Euthyroid

References


Textbook of Biochemistry, with clinical correlations, Ed. By T. M. Devlin, 4th Ed.

Correct answers: 1C, 2D, 3C

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