

THE ANTERIOR PITUITARY

BY
MISPA ZUH
HS09A179

Embryology of the pituitary

- ❖ The pituitary is formed early in embryonic life from the fusion of the Rathke's pouch (anterior) and the diencephalon (posterior)
- ❖ Rathke's pouch is an invagination of the oral ectoderm
- ❖ The posterior pituitary originates from the neuroectoderm.

Embryology cont.

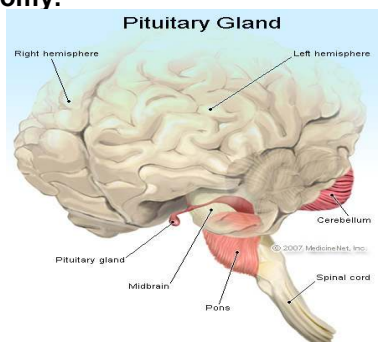
1. TSH producing cells appear first, fades away and later reappear as distinct populations of TSH cells in different locations of the pituitary.
2. Gonadotrophs appear next
3. Somatotrophs and lactotrophs appear last and later differentiate to distinct populations.

Embryology cont.

- ❖ By the 9th week of gestation, anterior hormone production is largely established.
- ❖ By the 12-17th weeks, the anatomic and biosynthetic mechanisms that comprise an active hypothalamic- pituitary system is functional.

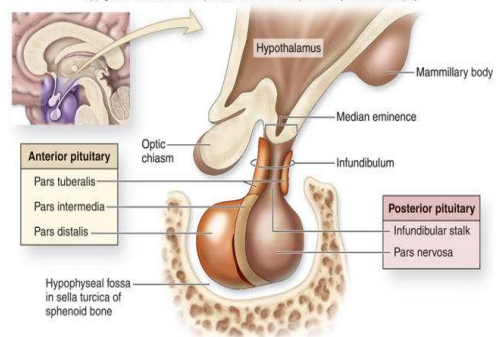
THE PITUIYARY GLAND

Anatomy:



ANTERIOR PITUITARY

Copyright © The McGraw-Hill Companies, Inc. Permission required for reproduction or display.



❖ The pituitary is lies in the hypophyseal fossa of the **sella turcica** at the base of the brain.

❖ It is covered by the **diaphragma sella**

❖ Weighs about 0.6g(range 0.4-0.9g)

❖ Joined to the hypothalamus by the pituitary stalk- **infundibulum**

ANATOMY CONT.

❖ The anterior pituitary is divided into two parts **pars intermedia** and **pars anterior** separated by a narrow cleft and connective tissues

❖ Anterior pituitary consists about 80% of the pituitary.

❖ It has six major cell types(hormone producing criterion)

ANATOMY CONT.

Somatotrophs(40-50%)	Growth hormone (GH) producing
Lactotrophs(15-25%)	Prolactin (PRL) producing
Corticotrophs(10-20%)	Adrenocorticotrophic hormone (ACTH) producing
Gonadotrophs(10%)	Luteinizing and Follicle stimulating hormone
Thyrotrophs(5%)	Thyroid stimulating hormone producing
Folliculostellate cells	No classical pituitary hormone

Anatomy cont.

According to **staining reactions**, these cells can be grouped into **three cell types**.

Acidophils: Prolactin and growth hormone producing cells

Basophils: LH, TSH.FSH, and ACTH producing cells

Chromophobes: thought to be involved with non secretory stages of development

Major hormones of the anterior pituitary

Hormone	Nature	Target gland
ACTH	Polypeptide	adrenal
GH	Polypeptide	multiple
PRL	Polypeptide	breast
LH	Glycopeptide	gonads
FSH	Glycopeptide	gonads
TSH	Glycopeptide	thyroid

Growth Hormone

❖ Polypeptide(191 amino acids), two intramolecular disulfide bridges.

Physiological action

Overall

❖ Promotes growth (linear growth) in all tissues capable of growth (soft tissues, cartilage) indirectly by stimulating the liver to produce growth factors which accelerates amino acid transport into cells.

❖ Increase amino acids in the cell accelerates protein anabolism

Specifically

- ❖ Stimulates fat metabolism
- ❖ Accelerates mobilization of lipids from adipose tissue and speed up their catabolism as they enter other cells.
- ❖ Shifts cells' nutrients away from carbohydrates (glucose) catabolism toward lipid catabolism as energy source.

- ❖ GH therefore has a **hyperglycemic effect** as oppose to insulin which promotes glucose uptake by cells - **hypoglycemic effect**

On electrolytes

- ❖ Increases plasma phosphorus
- ❖ Increases intestinal absorption of calcium
- ❖ Decrease urinary excretion of sodium and potassium

Relationship between GH and insulin-like growth factor (IGF)

Most metabolic effects of GH are transmitted indirectly via the action of IGF.

- ❖ IGF is produced in many tissues following stimulation by GH , where it exerts autocrine or paracrine effects.
- ❖ IGF-1 is the most important and function by:
- ❖ Enhancing addition of sulfate to cartilage
- ❖ Stimulating transport of amino acids into cells
- ❖ Increasing Ca, K, and Mg metabolism.

Clinical significance of GH

- ❖ GH vary widely under normal circumstances, making its measurement of little or no clinical significance.
- ❖ Serum levels of IGF-1(ref. range 135-449ng/ml) are fairly constant and a single dose can be considered an accurate reflection GH status
- ❖ IGF-1 levels are elevated in conditions of GH excess and vice versa

Regulation of GH secretion

GH secretion is regulated mainly growth hormone releasing hormone (GHRH) and growth hormone inhibiting hormone (GHIH) from the hypothalamus and by the IGF produced by target cells.

Other stimuli include:

- ❖ **Exercise:** 20mins after exercise begun
- ❖ **Sleep:** 1hr from sleep onset and peaks at deepest sleep
- ❖ **Insulin:** 45-75 mins after administration
- ❖ **Glucagon:** 120-180mins
- ❖ **Pentagastrin**(IV infusion):75mins

Growth Hormone excess

- ❖ Mostly caused by tumours which involve neoplastic proliferation of somatotrophs.
- ❖ Manifest as acromegaly (adults) or gigantism (in children) depending on the age of onset.
- ❖ Headaches, visual defects, and other neurological symptoms depend on the location and extent of tumour growth.

Growth hormone deficiency

- ❖ Causes include hypothalamic disorders, GHRH receptor mutations, GH gene mutation, GH receptor mutation, IGF-1 receptor mutation, etc.
- ❖ Clinical manifestations depends on time of onset and the severity of the hormone deficiency.
- ❖ Children have slow linear growth rates, they have normal skeleton proportions.
- ❖ GH replacement effective only before puberty.

Prolactin (PRL)

- ❖ Polypeptide of 198 amino acids with three intramolecular disulfide bridges.
 - ❖ Main function is to initiate and sustain lactation.
- Regulation of secretion**
- ❖ Secretion is under hypothalamic control and this control is very unique in that it is always inhibitory rather than stimulatory.
 - ❖ Dopamine is one of the dominant influence for PRL secretion so it is one pituitary hormone that increases after pituitary stalk section

- ❖ Main physiological stimulus for PRL release is suckling.
- ❖ PRL release increases with sleep, stress, chest wall stimulation and pregnancy.
- ❖ High levels of oestrogen and progesterone inhibit lactation during pregnancy

PRL deficiency:

- ❖ Rare and occur primarily in the setting of combine hormone deficiency. It is not much of a problem and only recognized in the absence of post partum lactation

Hyperporlactinemia

- ❖ Causes involve compression of the pituitary stalk, neoplastic conditions, alterations in the pathways that control the secretion of PRL, etc.
- ❖ Causes amenorrhea and infertility in premenopausal women and impotency and hypogonadism in males with suppressed LH,FSH and low testosterone levels.

Adrenocorticotrop hormone(ACTH)

- ❖ Peptide of 39 amino acids derived from a polypeptide precursor POMC
 - ❖ Primary effect is to stimulate the adrenals to produce cortisol.
 - ❖ Also stimulate secretion of adrogens and mineralocorticoids
- ❖ Regulation**
- ❖ Secretion is regulated by the hypothalamic-pituitary- adrenal axis.

- ❖ CRH is the most important stimulator of ACTH secretion.
- ❖ Arginine vasopressin(AVP) weakly stimulates ACTH secretion when given alone , but acts synergistically when administered with CRH .
- ❖ Several other hypothalamic factors (angiotensin II, catecholamines, gastrin releasing peptide,) also enhance ACTH secretion by either stimulating CRH or by acting at the level of the pituitary gland.

ACTH deficiency

- ❖ Most common cause is treatment with exogenous glucocorticoids which causes suppression of hypothalamic-pituitary-adrenal axis.
- ❖ Congenital causes are rare and occurs in combination with loss of other pituitary hormones.
- ❖ Manifestations are vomiting, fatigue, fever, weakness and hypotension.

Excess ACTH

- ❖ **Cushing disease** results from a pituitary adenoma that causes excess ACTH secretion.
- ❖ **Cushing syndrome:** excess glucocorticoids, which include adrenal causes of cortisol excess, ectopic production of ACTH and CRH and any physiologic cause of overproduction of cortisol.

Gonadotropins (FSH and LH)

- ❖ Glycoprotein hormones together with TSH.
- ❖ Composed of alpha and beta sub units.

- ❖ Alpha subunit-no biological activity
- ❖ Beta subunit- confer hormonal activity

- ❖ Must come together for full activity
- ❖ Both sub units have carbohydrates groups attached (mannose, galactose, sialic acid , etc)

Physiologic action

- ❖ Involve in sexual differentiation, sex steroid production, and gametogenesis.
- ❖ In males, receptors for FSH are located in the sertoli cells and seminiferous tubules, whereas receptors of LH are located on the Leydig cells in the testis. FSH is involve primarily in sperm maturation.
- ❖ In females, FSH receptors are located on the granulosa cells- biosynthesis of oestrogen. LH receptors are found predominantly on the thecal cells of the ovary .

Regulation of Gonadotropins

- ❖ It is regulated by the hypothalamic – testicular/ovarian axis .

- ❖ Gonadotropin releasing hormone (GnRH), from the hypothalamus causes the release of LH and FSH from the pituitary and hormones produced by their action on the testis or ovary provide a negative or positive feed back which in turn control the secretion of GnRH, and FSH and LH

- ❖ The hypothalamic gonadal axis is activated during foetal development .
- ❖ However, LH and FSH levels fall and remain suppressed during the first two years of life(mechanisms still not well understood)

Hypogonadotropic hypogonadism

- ❖ Clinical features in women are primarily due to oestrogen deficiency and include breast atrophy, vaginal dryness, and diminished libido.
- ❖ In men we have decrease libido and sexual function.
- ❖ Secondary hypogonadism is caused by GnRH deficiency
- ❖ Hyperprolactinemia can suppress GnRH and lead to hypogonadism.

Excess FSH and LH production

- More often than not produced by macroadenomas, most symptoms and signs are related to mass effects.
- Cause hypertrophy of the testes and increase levels of testosterone.
- Premenopausal women may experience irregularities in their menstrual periods.

Thyroid stimulating hormone(TSH)

- ❖ Heterodimer like other glycopeptide hormones.
- ❖ TSH controls thyroid hormone (T_4 and T_3) synthesis and release.
- ❖ Thyroid hormone have an inhibitory effect on the production of TRH and TSH and comprise a powerful negative feedback loop.
- ❖ Hyperthyroidism occurs when TSH response to TRH are blunted while hypothyroidism occurs when TSH response to exogenous TRH is exaggerated.

Conclusion

- ❖ Anterior pituitary hormones are tropic hormones whose production is under the influence of the hypothalamus and hormones produced from their target cells through negative and positive feed back mechanisms.
- ❖ The proximity with the hypothalamus and the nature of the hypophyseal portal system allows hormones from the hypothalamus to reach the anterior pituitary without much dilution. Hence increase sensitivity.

THANK YOU