PITUITARY ANTERIOR GLAND

The hormones secreted by the anterior lobe of the pituitary gland are:
• ***Growth hormone***
• ***Pituitary tropic hormones*** such as **prolactin**, gonadotropins **FSH and LH**, Thyrotropic hormones **(TSH),** and Adrenocorticotropic Hormone **(ACTH).**

GROWTH HORMONE (SOMATOTROPIN)

The growth hormone (or somatotropin) is produced by somatotropin, a special group of acidophilic cells of the anterior pituitary.

Regulation of GH release: Two hypothalamic factors play a prominent role in the release of growth hormones. These are the growth hormone-releasing hormone (GRH) that stimulates and the growth hormone release-inhibiting hormone (GRIH, somatostatin) that inhibits. This, in turn, is regulated by a feedback mechanism. Growth hormone production is influenced by many factors, such as sleep, stress (pain, cold, surgery), exercise, food intake, etc. It is observed that the largest increase in the production of GH occurs after the onset of sleep. This supports the adage, "If you don't sleep, you won't grow."

Biochemical functions of GH: Growth hormone promotes growth and also influences the normal metabolisms (protein, carbohydrate, lipid, and mineral) in the body.

1. **Effects on growth:** As is obvious from the name, GH is essential for growth. Its growth-related effects are mediated through insulin-like growth factor I (IGF-I), which is also known as somatomedin C (formerly sulfation factor), produced by the liver.

2. **Effects on protein metabolism:** Growth hormone has an anabolic effect on protein metabolism. It promotes the uptake of amino acids into the tissues and increases protein synthesis. The overall effect of GH is a positive nitrogen balance that leads to an increase in body weight.

3. **Effects on carbohydrate metabolism:** Growth hormone is antagonistic to insulin and causes

Hyperglycemia. GH increases gluconeogenesis, decreases glucose utilization, impairs glycolysis, and reduces the tissue uptake of glucose.

4. **Effects on lipid metabolism:** Growth hormone promotes lipolysis in the adipose tissue and increases the circulatory levels of free fatty acids and their oxidation. It increases ketogenesis, particularly in diabetes.

5. **Effects on mineral metabolism:** Growth hormone promotes bone mineralization and its growth, as clearly observed in growing children.

Abnormalities of GH production

Deficiency of GH: Impairment in the secretion of growth hormones in growing age causes **dwarfism**.
The other deficiency metabolic effects are not that serious in nature.
Overproduction of GH: Excessive production of GH causes **gigantism in children** and **acromegaly in adults**. This usually occurs in the acidophil tumor of the pituitary gland. Gigantism is characterized by increased growth of long bones, which is observed before the epiphyseal plates close. Acromegaly occurs after epiphyseal closure and is characterized by an increase in the size of hands, facial changes (enlarged nose, protruding jaw), excessive hair, thickening of skin, etc.

PITUITARY TROPIC HORMONES

In addition to GH, the anterior pituitary gland secretes some tropic hormones, usually called pituitary tropins.

What are "tropins"?
A tropin or tropic hormone influences the activities of other endocrine glands,
Principally, those involved in stress and reproduction. The blood carries these to another target gland. The pituitary tropins are under the positive and negative control of peptide factors from the hypothalamus. Further, the tropic hormones are usually subject to feedback inhibition at the pituitary or
hypothalamic level by the hormone product of the final target gland. Prolactin (mammotropin), TSH (thyrotropin), FSH and LH (gonadotropins), and ACTH (corticotropin) are the tropic hormones secreted by the pituitary gland.

A. Prolactin: PRL or Leuteotropic Hormone (LTH)

Lactotroph α-cells of the anterior pituitary secrete it and, as already mentioned, has sequence homology with growth hormone.

Metabolic role

• The main function of PRL is ***to stimulate mammary growth and the secretion of milk.*** By acting through specific glycoprotein receptors on the plasma membrane of

mammary gland cells, it stimulates mRNA synthesis. This ultimately leads to the enlargement of breasts during pregnancy. This is called as ***mammotropic action.***

• After parturition, the synthesis of milk proteins such as lactalbumin and casein takes place; this effect is called ***lactogenic action.***

• Estrogens, thyroid hormones, and glucocorticoids increase the number of prolactin receptors on the mammary cell membrane.

• Progesterone has the opposite effect.

B. Thyrotropic Hormone or Thyroid Stimulating Hormone (TSH)

This is ***produced by basophil cells*** of the anterior pituitary and is a ***glycoprotein*** in nature. This ***consists of α and β subunits.***

Note: The *α-subunit of TSH, LH, HCG, and FSH are nearly identical.*

Metabolic role

There are receptors on the thyroid cell membrane that bind to the receptor binding site on the β-subunit of TSH. The complex then activates ***adenylate cyclase,*** which catalyzes the formation of c-AMP, which acts as the second messenger for most TSH actions as follows:

• The TSH stimulates the synthesis of thyroid hormones at all stages, such as Iodine uptake,
organification and coupling.

• It enhances the release of stored thyroid hormones.

• It increases DNA content, RNA, and translation of proteins, as well as cell size.

• It stimulates glycolysis, TCA cycle, HMP, and phospholipid synthesis. Stimulation of the last two does not involve c-AMP.

• It activates adipose tissue ***lipase*** to enhance the release of fatty acids (lipolysis).

C. Adrenocorticotropic Hormone (ACTH) or Corticotropin. Two forms have been isolated, *α-corticotropin* and *β-corticotropin.*

ACTH is ***synthesized as a part of a precursor peptide.*** The precursor molecule is synthesized as a glycoprotein called **Pro-opiomelanocortin peptide (POMC)**. Various proteolytic enzyme hydrolyses POMC to give different peptides. ***Thus, POMC is broken down into ACTH and β-lipotropin (LPH). β-LPH is further cleaved into γ-LPH and endorphins.***

Metabolic role

• The principal actions of corticotropin are exerted on the adrenal cortex and extra-adrenal tissue. ***ACTH increases the synthesis of corticosteroids by the adrenal cortex and also stimulates their release from the gland.*** Profound changes in the adrenal structure, chemical composition and enzymatic activity are observed as a response to ACTH. Total protein synthesis is found to be increased. Thus, ACTH produces both a tropic effect on steroid production and a tropic effect on adrenal tissue. It is observed that ACTH has specific receptors on cells of fasciculata, which increases c-AMP levels in the cell. This activation is calcium-dependent. This results in DNA content, and RNA is transcribed. This leads to the proliferation of fasciculate cells and the growth of the adrenal cortex.

• ACTH also stimulates the synthesis and secretion of glucocorticoids.

• ACTH is found to increase the transfer of cholesterol from plasma lipoproteins into the fasciculata cells.

• The ACTH induces a rise in c-AMP, bringing about phosphorylation and activation of cholesterol esterase. The enzyme action ultimately makes a large pool of free cholesterol.

• Corticotropin promotes the binding of cholesterol to mitochondrial cytochrome P450 required for hydroxylating cholesterol.

• It activates the rate-limiting enzyme for the conversion of cholesterol to pregnenolone.

• It activates dehydrogenases of HMP to increase the conc. Of NADPH required for hydroxylation.

• By activating *adenylate cyclase* of adipose tissue, it increases intracellular C-AMP, which in turn activates hormone-sensitive lipase. This enzyme is involved in lipolysis, which increases the level of free fatty acids.

• It leads to increased ketogenesis and decreased RQ.

• Direct effects on carbohydrate metabolism include:

• **Lowering of blood glucose ↓;**

• Increase in glucose tolerance;

• The increased deposition of glycogen in adipose tissue is regarded as being due to the stimulation of insulin secretion.

• ***It has MSH activity*** due to homology in amino acid sequence.

D. Pituitary Gonadotropins

These tropic hormones influence the function and maturation of the testes and ovary and are of **two types:**

- ***Follicle Stimulating Hormone (FSH)***
- ***Luteinizing Hormone (LH)***

Both of them are glycoproteins with sialic acid. As already mentioned, FSH and LH are dimers of α and β-chains linked noncovalent. ***The α-chain is identical for TSH, FSH, and LH of the same species.***

Metabolic Role of FSH

It brings about its action by specific receptor binding and c-AMP.

Role of FSH in Spermatogenesis

FSH stimulates the conversion of primary spermatocytes into secondary spermatocytes in the seminiferous tubules. ***In the absence of FSH, spermatogenesis cannot proceed. However, FSH by itself cannot cause complete formation of spermatozoa. Testosterone is also required for its completion.***

Thus, FSH seems to initiate the proliferation process of spermatogenesis, and testosterone is ***necessary for the final maturation of spermatozoa.*** Since testosterone is secreted under the influence of LH, ***both FSH and LH must be secreted for normal spermatogenesis.***

Metabolic Role of LH

This hormone is **also known as interstitial cells stimulating hormone (ICSH).**

The action of LH in Ovulation: Ovulatory surge for LH is necessary for final follicular growth and ovulation. Without this hormone, even though large quantities of FSH are available, the follicle will not progress to the stage of ovulation. ***LH acts synergistically with FSH to cause rapid swelling of the follicle shortly before ovulation.*** It is worth noting that an especially large amount of LH called ***ovulatory surge*** is secreted by the pituitary during the day immediately preceding ovulation.

Regulation of Testosterone Secretion by LH Testosterone is produced by the interstitial cells of Leydig only when LH stimulates the testes from the pituitary gland, and the quantity of testosterone secreted varies approximately in proportion to the amount of LH available. Thus, ***in males, LH stimulates the development and functional activity of Leydig cells (interstitial) and, consequently, testicular androgen.***