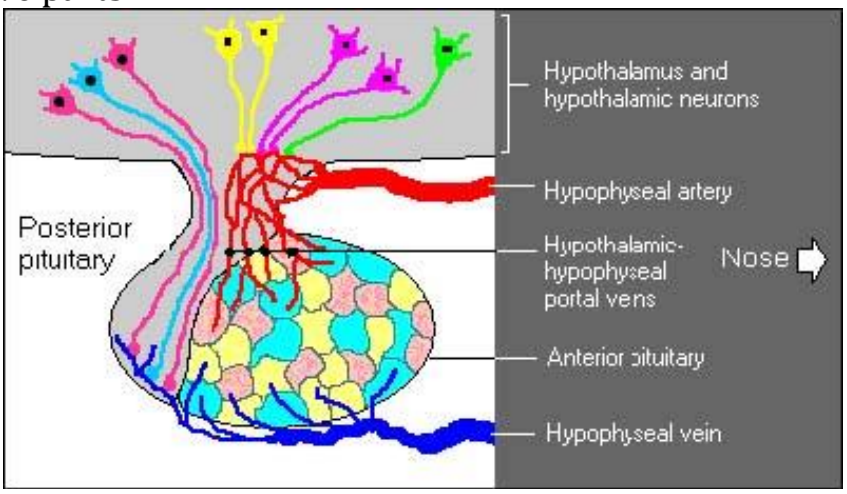
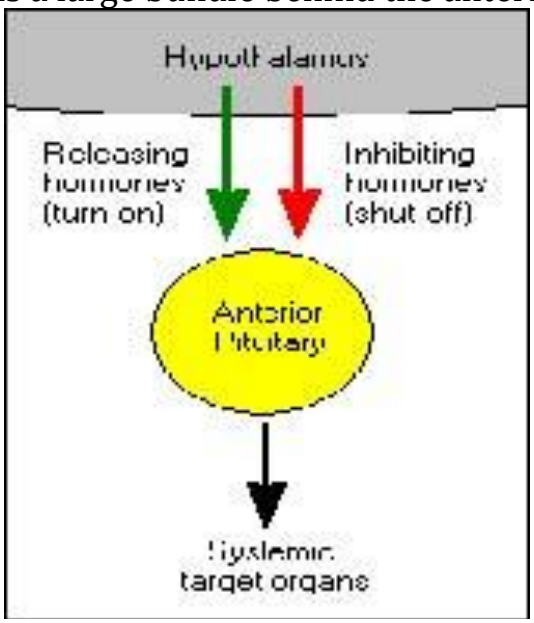
2. Hormones of the Pituitary gland

The pituitary gland, also known as the *hypophysis*, is a roundish organ that lies immediately beneath the hypothalamus. Careful examination of the pituitary gland reveals that it composed of two distinctive parts:



A. The **anterior pituitary** (adenohypophysis) is a classical gland composed predominantly of cells that secrete protein hormones.
B. The **posterior pituitary** (neurohypophysis) is not really an organ, but an extension of the hypothalamus. It is composed largely of the axons of hypothalamic neurons which extend downward as a large bundle behind the anterior pituitary.



The pituitary gland is often called the "master gland" of the body. The anterior and posterior pituitary secretes a number of hormones that collectively influence all cells and affect virtually all physiologic processes. The target cells for most of the hormones produced in these tissues are themselves endocrine cells.

Table: The major hormones synthesized and secreted by the pituitary gland, along with summary statements about their major target organs and physiologic effects.

	Hormone	Major target organ(s)	Major Physiologic Effects
AnteriorPituitary	**Growth hormone**	Liver, adipose tissue	Promotes growth (indirectly), control of protein, lipid and carbohydrate metabolism
	Thyroid-stimulating h.	Thyroid gland	Stimulates secretion of thyroid hormones
	Adrenocorticotropic h.	Adrenal gland (cortex)	Stimulates secretion of glucocorticoids
	Prolactin	Mammary gland	Milk production
	Luteinizing hormone	Ovary and testis	Control of reproductive function
	Follicle-stimulating h.	Ovary and testis	Control of reproductive function
Posterior Pituitary	**Antidiuretic hormone**	Kidney	Conservation of body water
	Oxytocin	Ovary and testis	Stimulates milk ejection and uterine contractions

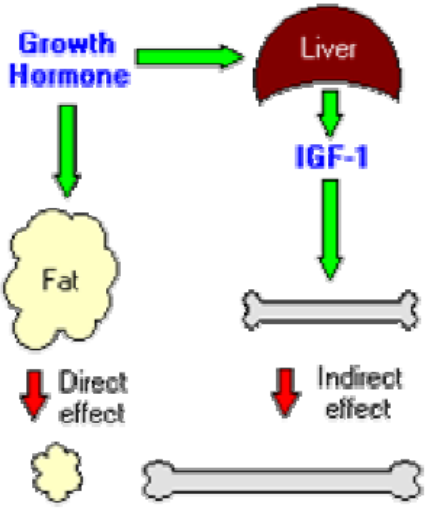
As seen in the table above, the anterior pituitary synthesizes and secreted six major hormones. **Individual cells within the anterior pituitary secrete a single hormone** (or possibly two in some cases). Thus, the anterior pituitary contains at least six distinctive endocrinocytes The cells that secrete thyroid-stimulating hormone do not also secrete growth hormone, and they have receptors for thyroid-releasing hormone, not growth hormone-releasing hormone.

Anterior Pituitary Hormones

1. Growth Hormone

Growth hormone, also known as *somatotropin*, is a protein hormone of about 190 amino acids that is synthesized and secreted by cells called *somatotrophs* in the anterior pituitary. It is a major participant in control of several complex physiologic processes,

including growth and metabolism. Growth hormone is also of considerable interest as a drug used in both humans and animals.



Physiologic Effects of Growth Hormone

A critical concept in understanding growth hormone activity is that it has two distinct types of effects:

Direct effects are the result of growth hormone binding its receptor on target cells. Fat cells (adipocytes), for example, have growth hormone receptors, and growth hormone stimulates them to break down triglyceride and suppresses their ability to take up and accumulate circulating lipids.

Indirect effects are mediated primarily by a **insulin-like growth factor-1 (IGF-1)**, a hormone that is secreted from the liver and other tissues in response to growth hormone. A majority of the growth promoting effects of growth hormone is actually due to IGF-1 acting on its target cells. IGF-1 also appears to be the key player in muscle growth. It stimulates amino acid uptake and protein synthesis in muscle and other tissues.

Metabolic Effects

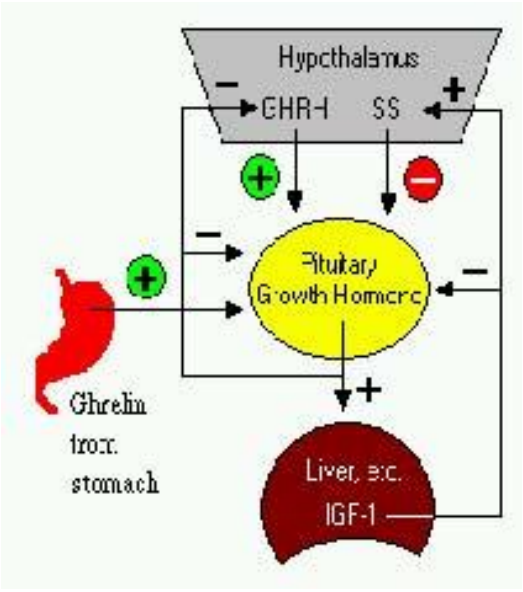
- Protein metabolism: In general, growth hormone stimulates protein anabolism in many tissues. This effect reflects increased amino acid uptake, increased protein synthesis and decreased oxidation of proteins.
- Fat metabolism: Growth hormone enhances the utilization of fat by stimulating triglyceride breakdown and oxidation in adipocytes.
- Carbohydrate metabolism: Growth hormone is one of a battery of hormones that serves to maintain blood glucose within a normal range. Growth hormone is often said to have anti-insulin activity, because it suppresses the abilities of insulin to

stimulate uptake of glucose in peripheral tissues and enhance glucose synthesis in the liver.

- Mineral metabolism: promotes a positive calcium, magnesium and phosphate balance and causes the retention of Na+, K+ and Cl-.

Control of Growth Hormone Secretion

Production of growth hormone is modulated by many factors, including stress, exercise, nutrition, sleep and growth hormone itself. However, its primary controllers are two hypothalamic hormones and one hormone from the stomach:



- **Growth hormone-releasing hormone** (GHRH) is a hypothalamic peptide that stimulates both the synthesis and secretion of growth hormone.
- **Somatostatin** (SS) is a peptide produced by several tissues in the body, including the hypothalamus. Somatostatin inhibits growth hormone release in response to GHRH and to other stimulatory factors such as low blood glucose concentration.
- **Ghrelin** is a peptide hormone secreted from the stomach. Ghrelin binds to receptors on somatotrophs and potently stimulates secretion of growth hormone.

Disease States:

Growth hormone secretion is also part of a negative feedback loop involving IGF-1. High blood levels of IGF-1 lead to decreased secretion of growth hormone not only by directly suppressing the somatotroph, but by stimulating release of somatostatin from the hypothalamus. Growth hormone also feeds back to inhibit GHRH secretion and probably has a direct (autocrine) inhibitory effect on secretion from the somatotroph. Integration of all the factors that

affect growth hormone synthesis and secretion lead to a pulsatile pattern of release. In children and young adults, the most intense period of growth hormone release is shortly after the onset of deep sleep.

A deficiency state can result not only from a deficiency in production of the hormone, but in the target cell's response to the hormone. Clinically, deficiency in growth hormone or receptor defects are **known as growth retardation or dwarfism**. The manifestation of growth hormone deficiency depends upon the age of onset of the disorder and can result from either heritable or acquired disease. The effect of excessive secretion of growth hormone is also very dependent on the age of onset and is seen as two distinctive disorders:

- **Gigantism:** is the result of excessive growth hormone secretion that begins in young children or adolescents. It is a very rare disorder, usually resulting from a tumor of somatotropes.
- **Acromegaly:** results from excessive secretion of growth hormone in adults. The excessive growth hormone and IGF-1 also lead to metabolic derangements, including glucose intolerance.

2. Thyroid Stimulating Hormone

Thyroid-stimulating hormone, also known as thyrotropin, is secreted from cells in the anterior pituitary called *thyrotrophs*, finds its receptors on epithelial cells in the thyroid gland, and stimulates that gland to synthesize and release thyroid hormones.

TSH is a glycoprotein hormone composed of two subunits, which are non-covalently bound to one another. The alpha subunit of TSH is also present in two other pituitary glycoprotein hormones, follicle-stimulating hormone and luteinizing hormone. In other words, TSH is composed of alpha subunit bound to the TSH beta subunit, and TSH associates only with its own receptor. Free alpha and beta subunits have essentially no biological activity. TSH has several acute effects on thyroid function. These occur in minutes and involve increases of all phases of T3 and T4 biosynthesis. TSH also has several chronic effects on the thyroid. These require several days and include increases in the synthesis of proteins, phospholipids, and nucleic acids and in the size of number of thyroid cells.

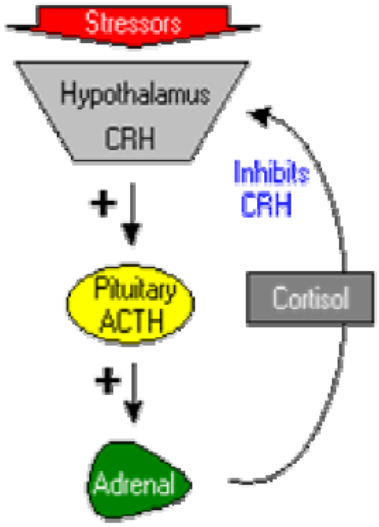
The most important controller of TSH secretion is thyroid-releasing hormone. Secretion of thyroid-releasing hormone, and hence, TSH, is inhibited by high blood levels of thyroid hormones in a classical ***negative feedback loop***.

3. Adrenocorticotropic Hormone

Adrenocorticotropic hormone, stimulates the adrenal cortex by enhancing the conversion of cholesterol to pregnenolone. More specifically, it stimulates secretion of glucocorticoids such as cortisol, and has little control over secretion of aldosterone, the other major steroid hormone from the adrenal cortex. Another name for ACTH is *corticotropin*.

ACTH is secreted from the anterior pituitary in response to corticotropin-releasing hormone from the hypothalamus. Corticotropin-releasing hormone is secreted in response to many types of stress, which makes sense in view of the "stress management" functions of glucocorticoids.

Corticotropin-releasing hormone itself is inhibited by glucocorticoids, making it part of a classical ***negative feedback loop.***



Within the pituitary gland, ACTH is produced in a process that also generates several other hormones. A large precursor protein named proopiomelanocortin (POMC) is synthesized and proteolytically chopped into several fragments as depicted below.
The major attributes of the hormones other than ACTH that are produced in this process are summarized as follows:

- **Lipotropin:** Originally described as having weak lipolytic effects, its major importance is as the precursor to beta-endorphin.
- **Beta-endorphin and Met-enkephalin:** Opioid peptides with pain-alleviation and euphoric effects.
- **Melanocyte-stimulating hormone (MSH):** Known to control melanin pigmentation in the skin of most vertebrates.