Endocrine System

Pituitary Gland

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The neuroendocrine system, which coordinate body functions by transmitting messages between individual cells and tissues is controlled by the **pituitary and hypothalamus**

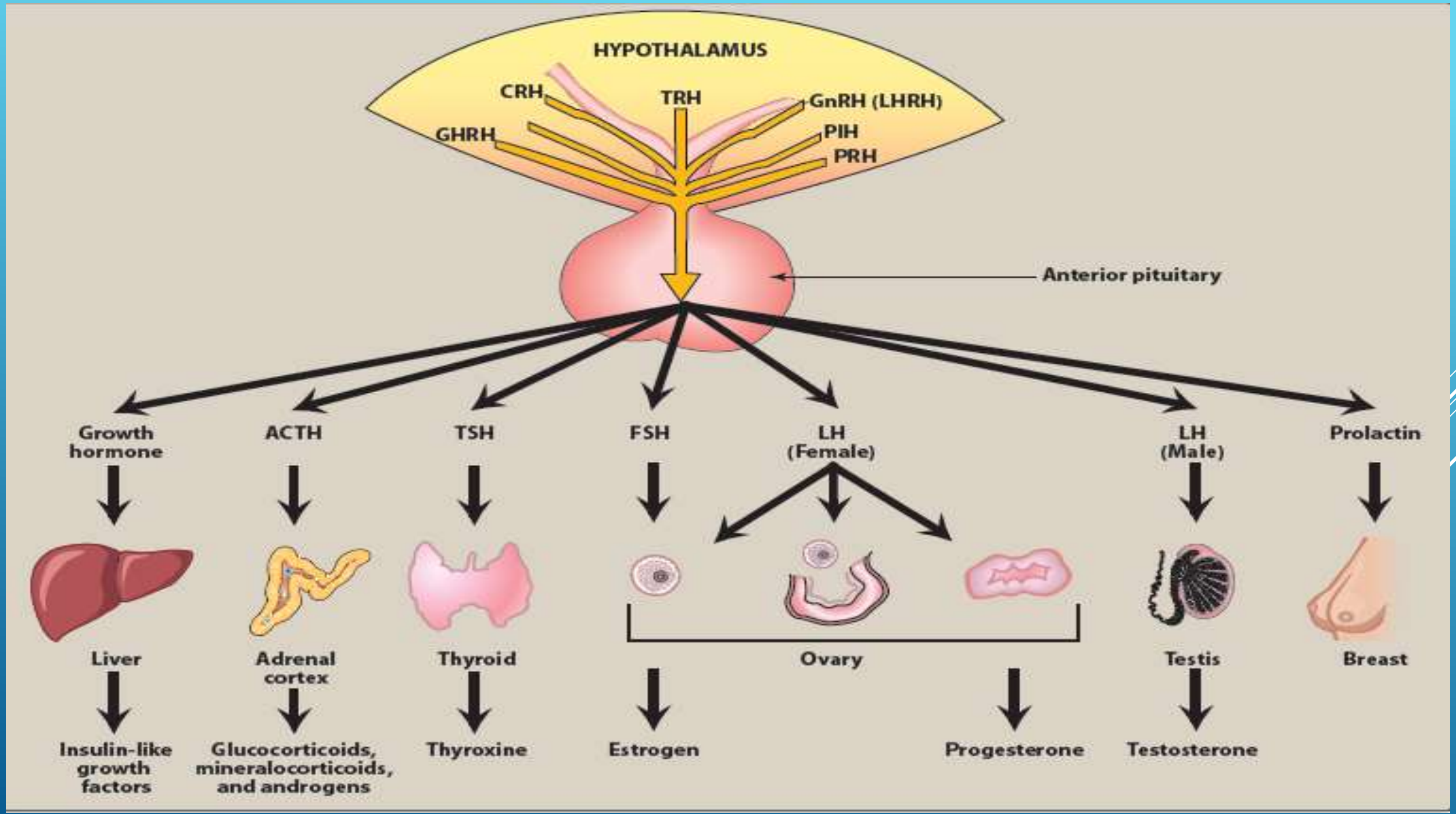
The hormones secreted by the hypothalamus and the pituitary are peptides or low-molecular-weight proteins that act by binding to specific receptor sites on their target tissues.

The hormones of the anterior pituitary are regulated by neuropeptides that are called either **“releasing” or “inhibiting”** factors or hormones.

Each **hypothalamic** regulatory hormone controls the release of a specific hormone from the **anterior pituitary**.

The hypothalamic-releasing hormones are primarily used for diagnostic purposes (that is, to determine pituitary insufficiency).

Hormones of the anterior and posterior pituitary are administered either intramuscularly (IM), subcutaneously, or intranasally, but not orally, because their peptidyl nature makes them susceptible to destruction by the proteolytic enzymes of the digestive tract.


HYPOTHALAMUS
CRH
TRH
GnRH (LHRH)
GHRH
PIH
PRH
Anterior pituitary
Growth hormone
ACTH
TSH
FSH
LH (Female)
LH (Male)
Prolactin
Liver
Adrenal cortex
Thyroid
Ovary
Testis
Breast
Insulin-like growth factors
Glucocorticoids, mineralocorticoids, and androgens
Thyroxine
Estrogen
Progesterone
Testosterone

A. ADRENOCORTICOTROPIC HORMONE (CORTICOTROPIN)

Corticotropin-releasing hormone (**CRH**) is responsible for the synthesis and release of the *Adrenocorticotropic hormone* (**ACTH**) (*corticotropin)*.

ACTH is released from the pituitary in pulses with an principal diurnal rhythm, with the highest concentration occurring at approximately 6 AM and the lowest in the late evening.

Stress stimulates its secretion, whereas **cortisol** acting via negative feedback suppresses its release.

1. Mechanism of action: The target organ of ACTH is the **adrenal cortex**, where it binds to specific receptors on the cell surfaces.

The occupied receptors activate G protein-coupled processes to increase CAMP, which in turn stimulates the rate-limiting step in the adrenocorticosteroid synthetic pathway (cholesterol to pregnenolone).

A. ADRENOCORTICOTROPIC HORMONE (CORTICOTROPIN)

2. Therapeutic uses:

diagnostic tool for differentiating between primary adrenal insufficiency (Addison disease, associated with adrenal atrophy) and secondary adrenal insufficiency (caused by the inadequate secretion of ACTH by the pituitary).

ACTH is used in the treatment of multiple sclerosis and infantile spasm (West syndrome).

3. Adverse effects: osteoporosis, hypertension, peripheral edema, hypokalemia emotional disturbances, and increased risk of infection.

B. GROWTH HORMONE (SOMATOTROPIN)

Somatotropin is a large polypeptide that is released by the anterior pituitary in response to **growth hormone (GH)-releasing hormone** produced by hypothalamus .

Secretion of GH is inhibited by another pituitary hormone, **somatostatin**.

GH is released in a pulsatile manner, with the highest levels occurring during sleep.

With increasing age, GH secretion decreases, being accompanied by a decrease in lean muscle mass.

1. Mechanism of action: Although many physiologic effects of GH are exerted directly at its targets, others are mediated through the somatomedins—insulin-like growth factors I and II (IGF-I and IGF-II).

2. Therapeutic uses: *Somatotropin* is used in the treatment of GH deficiency or growth failure in children., management of AIDS wasting syndrome, short bowel syndrome, and GH replacement in adults with confirmed GH deficiency.

C. SOMATOSTATIN (GROWTH HORMONE–INHIBITING HORMONE)

In the pituitary, somatostatin binds to distinct receptors, SSTR2 and SSTR5, which inhibits the release of GH but, also, that of insulin, glucagon, and gastrin.

Octreotide is a synthetic analoge of somatostatin. Its half-life is longer than that of the natural compound, and a depot form is also available.

They have found use in the treatment of acromegaly caused by hormone-secreting tumors .

Adverse effects: diarrhea, abdominal pain, flatulence, nausea, and steatorrhea. Gallbladder emptying is delayed, and asymptomatic cholesterol gallstones can occur

D. GONADOTROPIN-RELEASING HORMONE (LUTEINIZING HORMONE–RELEASING HORMONE)

Gonadotropin-releasing hormone (GnRH), also called ***gonadorelin***, is a decapeptide obtained from the hypothalamus.

Pulsatile secretion of GnRH is essential for the release of **follicle-stimulating hormone** (FSH) and **luteinizing hormone** (LH) from the pituitary.

A number of synthetic analogs, such as ***leuprolide , goserelin, nafarelin,* and *histrelin***, act as agonists at GnRH receptors .

These are effective in the treatment of prostatic cancer, endometriosis, and precocious puberty.

Adverse effects: In women, may cause hot flushes and sweating as well as diminished libido, depression, and ovarian cysts. They are contraindicated in pregnancy and breast-feeding.

In men, they initially cause a rise in testosterone that can result in bone pain; hot flushes, edema, gynecomastia, and diminished libido.

D. GONADOTROPIN-RELEASING HORMONE

The gonadotropins are glycoproteins that are produced in the anterior pituitary.

The regulation of gonadal steroid hormones depends on these agents. They find use in the treatment of infertility in men and women.

Menotropins (*human menopausal gonadotropins*) are obtained from the urine of postmenopausal women and contain *FSH* and *luteinizing hormone (LH)*.

Chorionic gonadotropin (hCG) is a placental hormone structurally related to LH which is an LH receptor agonist. It is also excreted in the urine.

Urofollitropin is FSH obtained from postmenopausal women

Follitropin alpha **and** ***follitropin beta*** are human *FSH* products manufactured using recombinant DNA technology.

All of these hormones are injected via the IM or subcutaneous route.

Adverse effects:

In men who are lacking gonadotropins, treatment with *hCG* causes external sexual maturation, and with the subsequent injection of *hMG or follitropin*, spermatogenesis occurs.

In females adverse effects include ovarian enlargement and possible hypovolemia. Multiple births are not uncommon. Men may develop gynecomastia.

F. PROLACTIN

Prolactin is a peptide hormone similar in structure to GH, and is also secreted by the anterior pituitary.

Its secretion is inhibited by dopamine acting at D2 receptors.

Its primary function is to stimulate and maintain lactation.

In addition, it decreases sexual drive and reproductive function.

The hormone binds to a transmembrane receptor which activates a tyrosine kinase to promote tyrosine phosphorylation and gene activation.

There is no preparation available for hypoprolactinemic conditions.

For hyperprolactinemia, which is associated with galactorrhea and hypogonadism, is usually treated with D2-receptor agonists, such as ***bromocriptine* and *cabergoline*.**

HORMONES OF THE POSTERIOR PITUITARY

A. Oxytocin

Oxytocin , originally extracted from animal posterior pituitaries, is now chemically synthesized.

It only used to stimulate uterine contraction to induce labor.

Oxytocin causes milk ejection by contracting the myoepithelial cells around the mammary alveoli.

S.E hypertension, uterine rupture, water retention, and fetal death have been reported.

B. Vasopressin (antidiuretic hormone)

It is structurally related to *oxytocin*. *It* has both antidiuretic and vasopressor effect.

In the kidney, it binds to the V2 receptor to increase water permeability and reabsorption in the collecting tubules. Thus, the major use of *vasopressin* is to treat **diabetes insipidus.** It also finds use in the management of cardiac arrest and in controlling bleeding due to esophageal varices or colonic diverticula.

Adverse effects:

water intoxication and hyponatremia. Headache, bronchoconstriction, and tremor can also occur.

Caution must be used when treating patients with coronary artery disease, epilepsy, and asthma.

To avoid its pressor properties, *vasopressin* has been modified to *desmopressin* which has minimal activity at the V1 receptor, making it largely free of pressor effects.

This analog is now preferred for diabetes insipidus and nocturnal enuresis and is longer-acting than *vasopressin*.

Desmopressin is administered intranasally or orally. However, the nasal formulation is no longer indicated for enuresis due to reports of seizures in children using the nasal spray. Local irritation may occur with the nasal spray.

Thank You