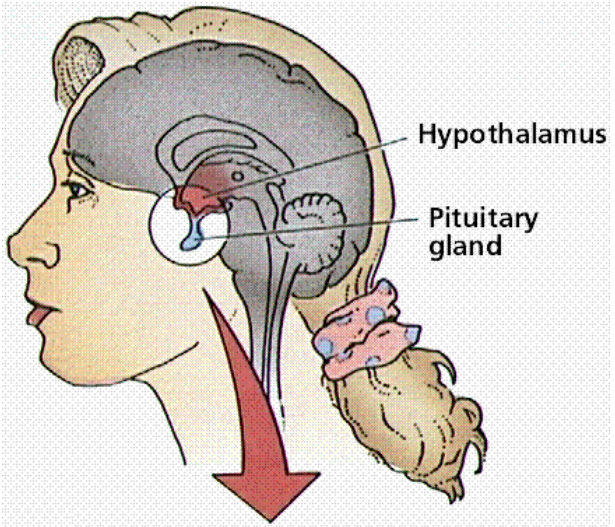
Hypothalamic and pituitary hormones

Introduction

- The endocrine system is regulatory system.
- The Neuroendorine system is controlled by the pituitary and hypothalamus.
- The endocrine system releases hormones into the bloodstream >>>> throughout the body.
- Hormones have a much broader range of response than the nerve do.



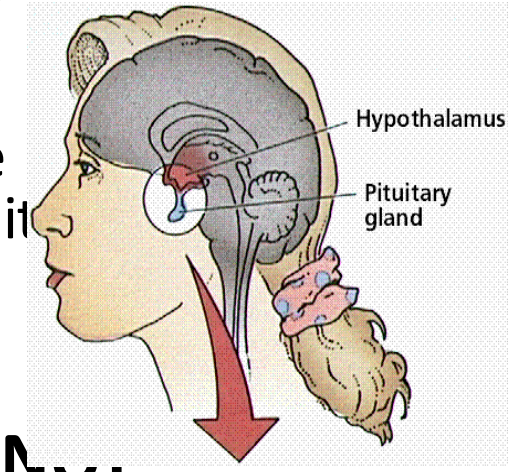
Hypothalamic and pituitary hormones

- The hormones secreted by the hypothalamus and the pituitary are all peptide 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 produced in hypothalamus.

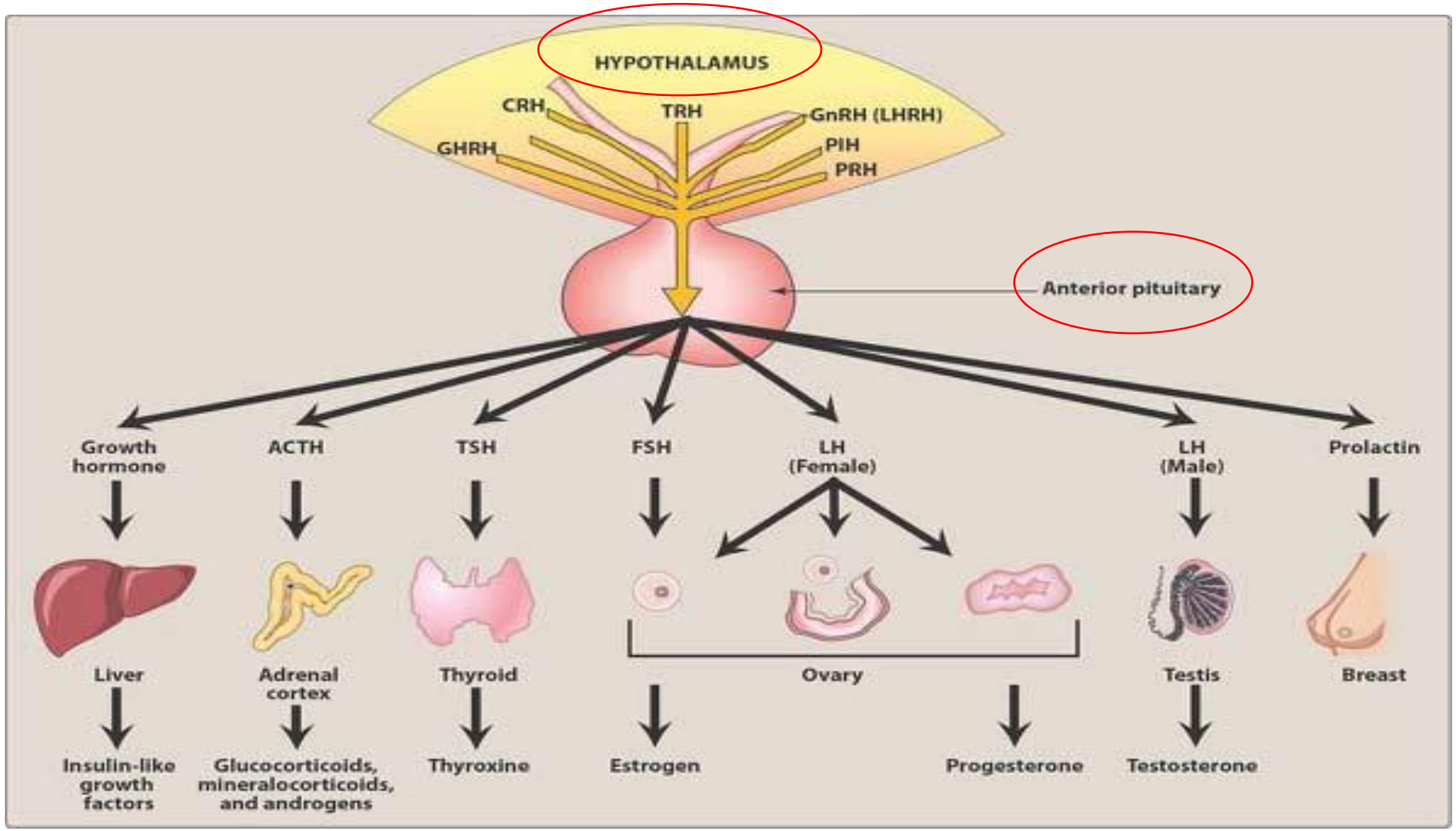
- Each hypothalamic regulatory hormone controls the release of a specific hormone from the anterior pituit

- Hormones of the pituitary are administered either intramuscularly, subcutaneously,or intranasally, but NOT orally (WHY?) >>> They are Proteins!!!



- Why are most hypothalamic and pituitary hormones **not administered orally**?

Hypothalamic and pituitary hormones



Anterior pituitary hormones

Hypothalamic and pituitary hormones

Growth hormone (somatotropin)

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

Hypothalamic and pituitary hormones

Growth hormone (somatotropin)

- Somatotropin influences a wide variety of biochemical processes:

1. Stimulation of protein synthetic processes
2. Cell proliferation
3. Bone growth are promoted.
4. Increased formation of hydroxyproline from proline boosts cartilage synthesis.

Hypothalamic and pituitary hormones

Growth hormone (somatotropin)

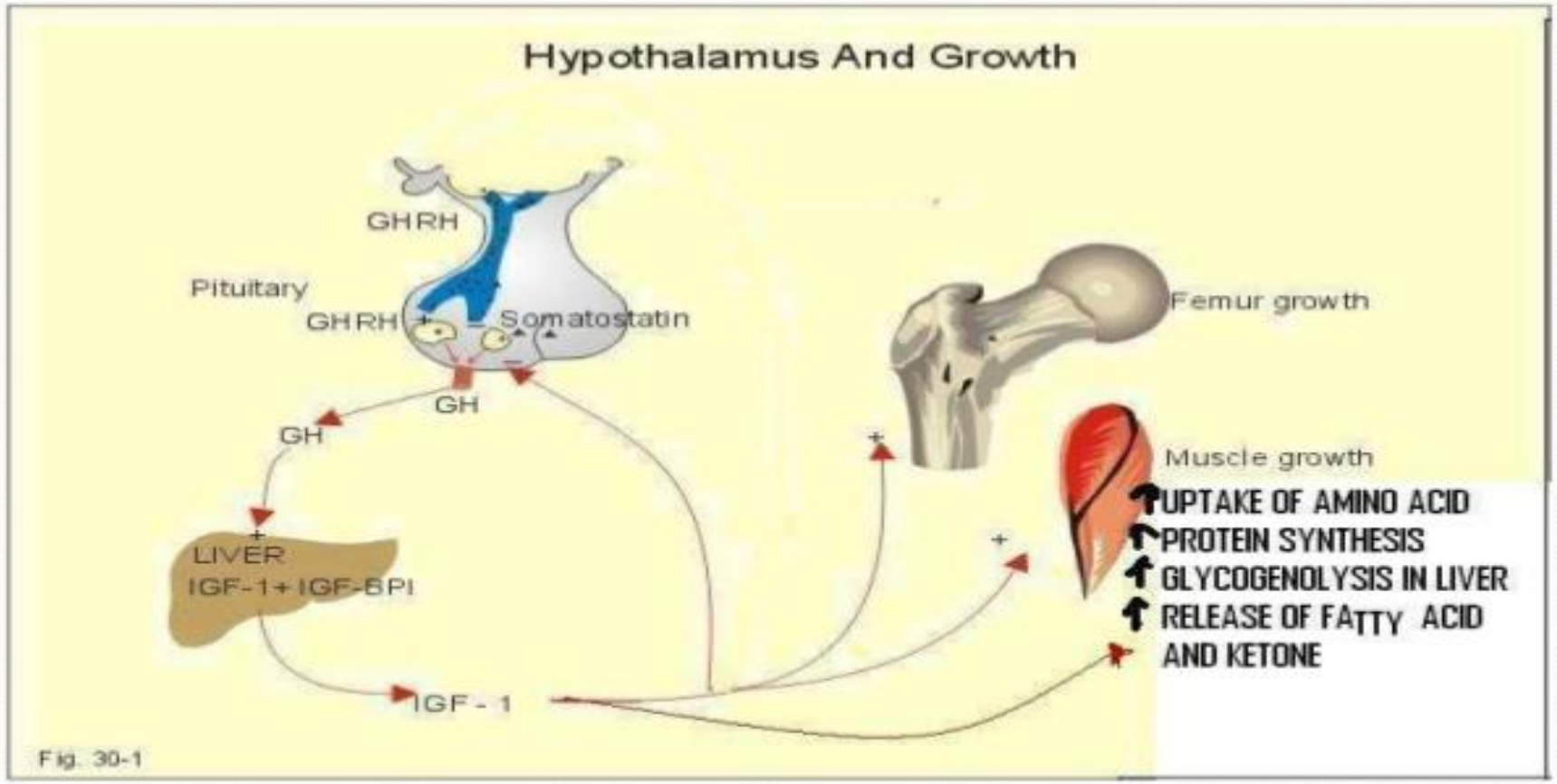
Mechanism of action:

A. Direct at its targets

B. Indirect: mediated through the somatomedins-insulin-like growth factors I and II (IGF-I and IGF-II).

Therapeutic uses:

1. In the treatment of GH deficiency in children.
2. GH is antiaging hormones!!!! Is misused with Athletes >>> Diabetes
3. Human synthetic GH, **somatrem**, induces the release from the liver of IGF-I (formerly somatomedin C), which is responsible for subsequent GH-like actions.
4. Somatotropin and somatrem should not be used in individuals with closed **epiphyses** (stoppage of bone growth) or an **enlarging intracranial** mass.


Hypothalamus And Growth
GHRH
Pituitary
GHRH
Somatostatin
GH
GH
LIVER
IGF-1+IGF-BPI
IGF - 1
Femur growth
Muscle growth
UPTAKE OF AMINO ACID
PROTEIN SYNTHESIS
GLYCOGENOLYSIS IN LIVER
RELEASE OF FATTY ACID
AND KETONE
Fig. 30-1

Hypothalamic and pituitary hormones

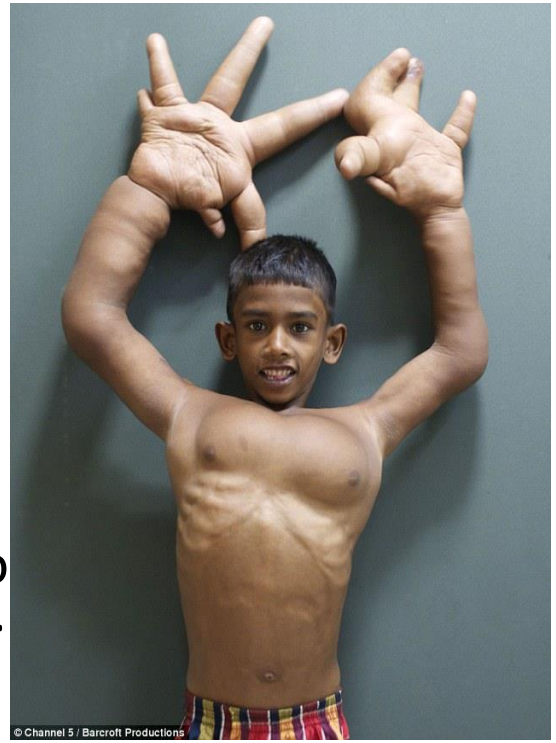
Growth hormone-inhibiting hormone (somatostatin)

- Is found mainly in the hypothalamus.
- Is also found in neurons throughout the body and in the intestine and pancreas.
- In the pituitary, somatostatin binds to distinct receptors, somatostatin receptor (SSTR2) and (SSTR5), which suppress GH and TSH release.

- It inhibits GH, insulin, glucagon, and gastrin release.

Hypothalamic and pituitary hormones

Octreotide



- is a synthetic analog of somatostatin.
- Its t1/2 is longer than that of somatostatin.
- Suppress GH and IGF-I.

Used in:

1. The treatment of <u>acromegaly</u>.
2. Secretory diarrhea associated with tumors producing vasoactive VIP (VIPomas). VIPoma causes cells in the pancreas to produce a high level o a hormone called vasoactive intestinal peptide (VIP).

Adverse effects:

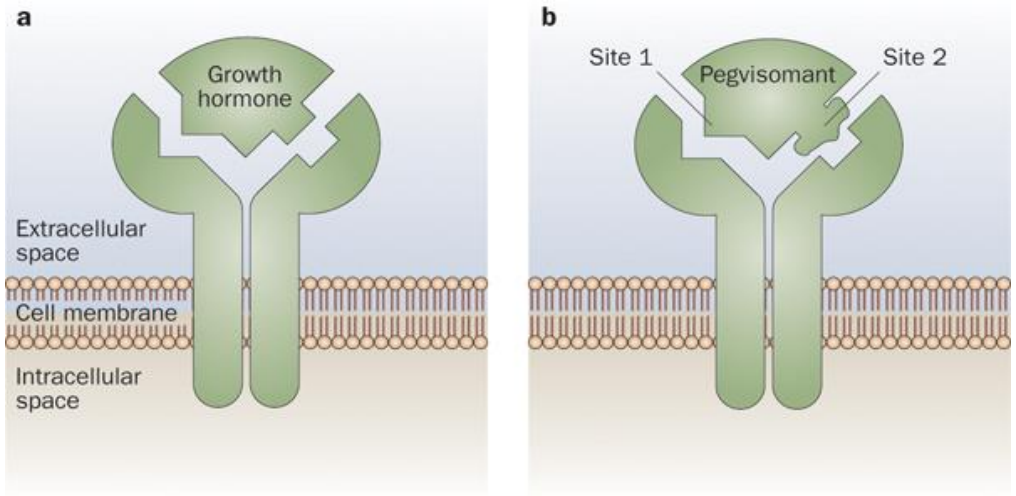
1. Flatulence, nausea, and steatorrhea. the excretion of abnormal quantities of fat with the faeces owing to reduced absorption of fat by the intestine. >>> GH plays a major role in fat absorption
2. Gallbladder emptying is delayed, and asymptomatic cholesterol gallstones can occur with long-term treatment.

Hypothalamic and pituitary hormones

Pegvisomant

- It acts as an antagonist at one of the GH receptors and results in the normalization of IGF-I levels.

- Is employed in the treatment of refractory acromegaly.

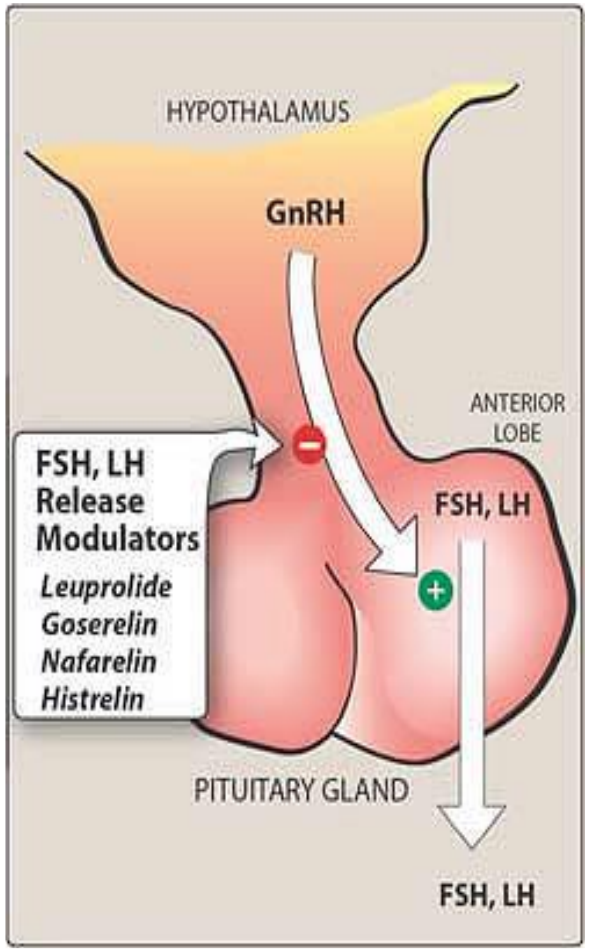


- Growth hormone promotes body growth. Why, then, is GH **misused by athletes**, and what is one important adverse effect?

Hypothalamic and pituitary hormones

Gonadotropin-releasing hormone/luteinizing hormone-releasing hormone

- Gonadotropin-releasing hormone (GnRH), also called **gonadorelin.**
- GnRH is released from the **hypothalamus**.
- GnRH is essential for the release of Follicle-stimulating hormone (FSH) and luteinizing hormone (LH) in the **pituitary**.
- GnRH stimulates gonadal hormone production in **hypogonadism**.(diminished functional activity of the gonads – the testes and ovaries in males and females)

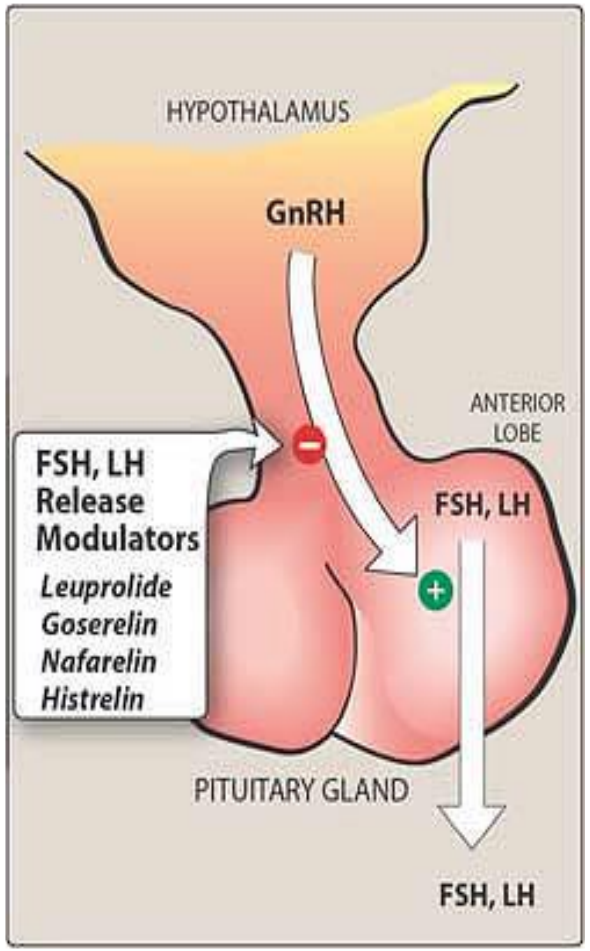


Hypothalamic and pituitary hormones

- *Gonadotropin-releasing hormone/luteinizing hormone-releasing hormone*

- Leuprolide and nafarelin are:

1. Synthetic analogs to GnRH.
2. Act as <u>agonists</u> at GnRH receptors. This causes marked increases in LH, FSH and testosterone.
3. Are effective in suppressing production of the gonadal hormones Sustained pituitary overstimulation will eventually down-regulate/desensitize GnRH receptors with a consequent decrease in hormone levels).
4. Therefore, are effective in the treatment of prostatic cancer, endometriosis, and precocious puberty.



Hypothalamic and pituitary hormones

Gonadotropin-releasing hormone/luteinizing hormone-releasing hormone

- Adverse effects of gonadorelin include:

1. Hypersensitivity
2. Dermatitis

- **In women**, the **analogs** may cause hot flushes and sweating as well as diminished libido, depression, osteoporosis and ovarian cysts (is a fluid-filled sac within the **ovary)**.

- They are **contraindicated** in pregnancy (may cause miscarriage) and breast-feeding (small amounts are found in breast milk).

- **In men**, they initially cause a rise in testosterone result in bone pain; hot flushes, edema, gynecomastia, and diminished libido also occur.

Hypothalamic and pituitary hormones

Gonadotropins: Human menopausal gonadotropin (hMG), follicle-stimulating hormone, and human chorionic gonadotropin (hCG)

- They are used in the treatment of infertility in men and women.
- **Menotropins (hMG)** are obtained from the urine of menopausal women and contain FSH and LH.
- hCG is a placental hormone and an LH agonist, to which it is structurally related. It is also excreted in the urine.
- Urofollitropin is FSH obtained from menopausal women.
- Follitropin beta is human FSH manufactured by recombinant DNA technology.

Hypothalamic and pituitary hormones

- *Gonadotropins: Human menopausal gonadotropin (hMG), follicle-stimulating hormone, and human chorionic gonadotropin (hCG)*

- *Injection of hMG or FSH over a period of 5 to 12 days causes ovarian follicular growth and maturation, and with subsequent injection of hCG, ovulation occurs.*

- **In men** lacking gonadotropins, **hCG** causes external sexual maturation, and with the subsequent injection of **hMG**, spermatogenesis occurs.

Adverse effects:

1. ovarian enlargement and possible hypovolemia.
2. Multiple births.
3. Men may develop gynecomastia (is a non-cancerous increase in the size of male breast tissue).

- Leuprolide is a GnRH agonist.

If it is an agonist, why does it decrease testosterone after long-term administration?

Posterior pituitary hormones

Hypothalamic and pituitary hormones

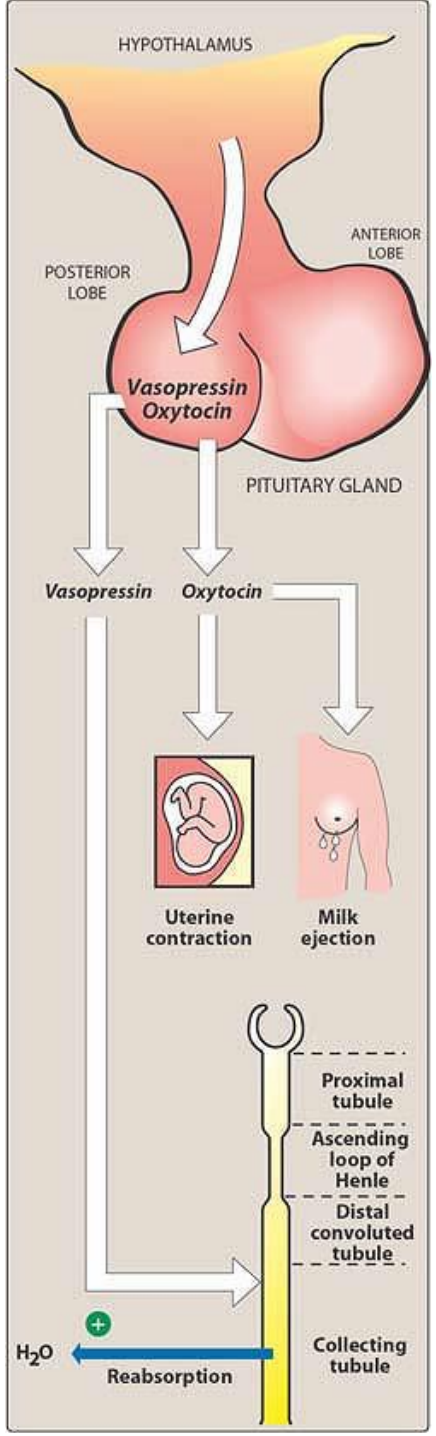
Oxytocin

- Its only use is in obstetrics to:

1. Stimulate uterine contraction to induce or reinforce labor
2. To promote ejection of breast milk.

- The sensitivity of the uterus to oxytocin increases with the duration of pregnancy when it is under estrogenic dominance.

- Oxytocin causes milk ejection by contracting the myoepithelial cells around the mammary alveoli حويصلات الثدية. given as a nasal spray.



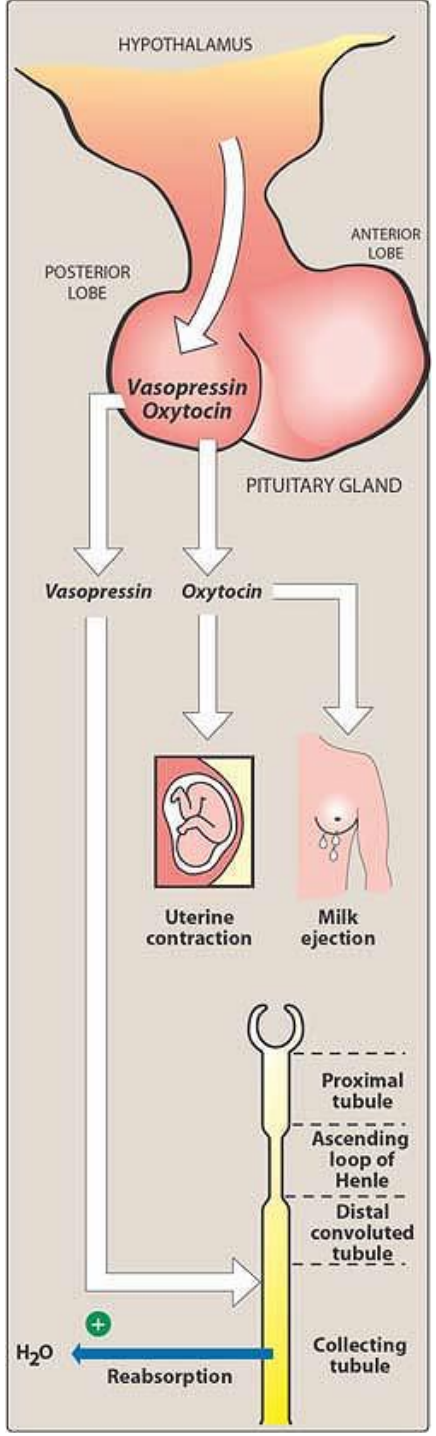
Hypothalamic and pituitary hormones

Oxytocin

Side effects:

1. Toxicities are uncommon when the drug is used properly.
2. Hypertensive crises
3. Uterine rupture
4. Water retention
5. Fetal death have been reported

- Its antidiuretic and pressor activities are very much lower than those of vasopressin.



Hypothalamic and pituitary hormones

Vasopressin

- Vasopressin (ADH), is structurally related to oxytocin.

Vasopressin has both:

1. Antidiuretic (V2 receptorin the kidney) and
2. Vasopressor (V1 receptor in BV) effects.

Major uses are:

- To treat diabetes insipidus
- Control bleeding of esophageal varices or colonic diverticula (saclike protrusion in the colonic wall).

Side effects:

1) Water intoxication 2) hyponatremia 3) bronchoconstriction 4) tremor

- Caution must be used in patients with CAD, epilepsy, and asthma.

Hypothalamic and pituitary hormones

Desmopressin

- 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.

- Which receptor is responsible for the antidiuretic effect?

Which hormone from this lecture would you prescribe for each patient?

1. Child with growth hormone deficiency
2. Acromegaly
3. Diabetes insipidus
4. Induction of labor
5. Prostate cancer