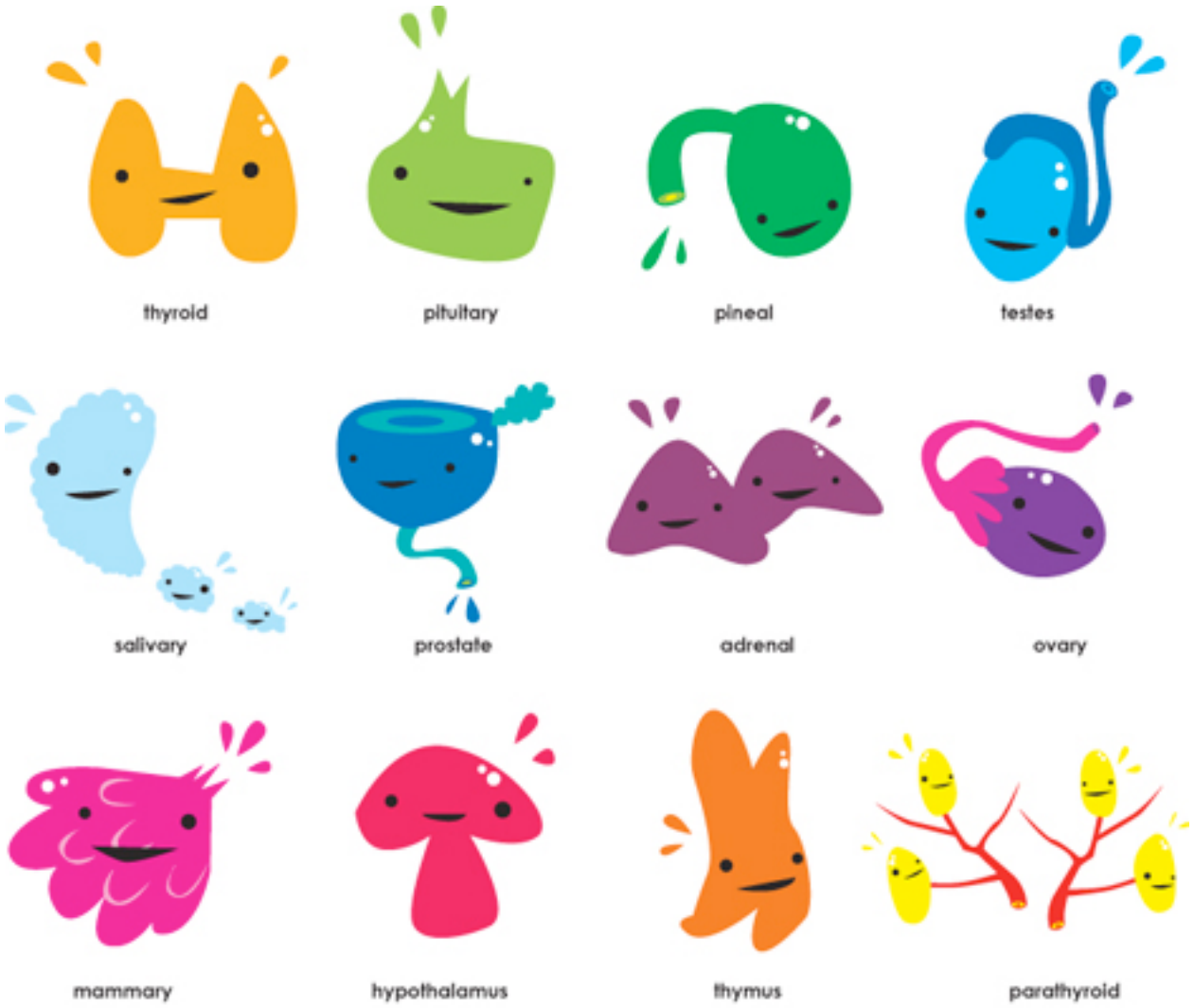
LECTURE 2 & 3: PHYSIOLOGY OF ANTERIOR PITUITARY GLAND



Note: 1) This is a rearrangement of the slides + Few notes

2) Focus on every figure and graph. Do not ignore them!

notes are in purple

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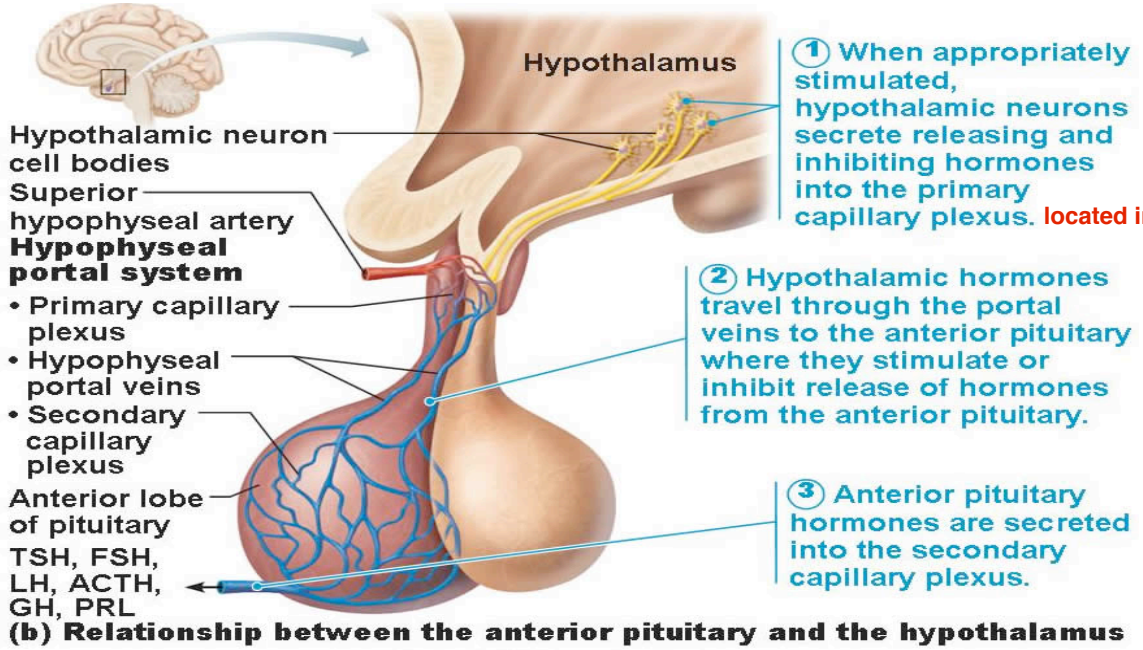
HYPOTHALAMIC-PITUITARY AXIS

- **Coordinate the functions of pituitary either hormonally through hypophyseal-portal system [Ant. pituitary] or neuronally [Post. pituitary]**
- Control **Thyroid gland, adrenal gland and reproductive glands function , control growth, milk production, and osmoregulation.**

HYPOTHALAMUS

- **Control pituitary gland secretion.**
- **Composed of number of nerve cells. Those neurons ① synthesize and secrete the hypothalamic releasing and inhibitory hormones that control secretion of anterior pituitary hormones, and ② synthesize hormones which are stored and then secreted from posterior pituitary.**

from now on we will talk about anterior pituitary:



located in the median eminance

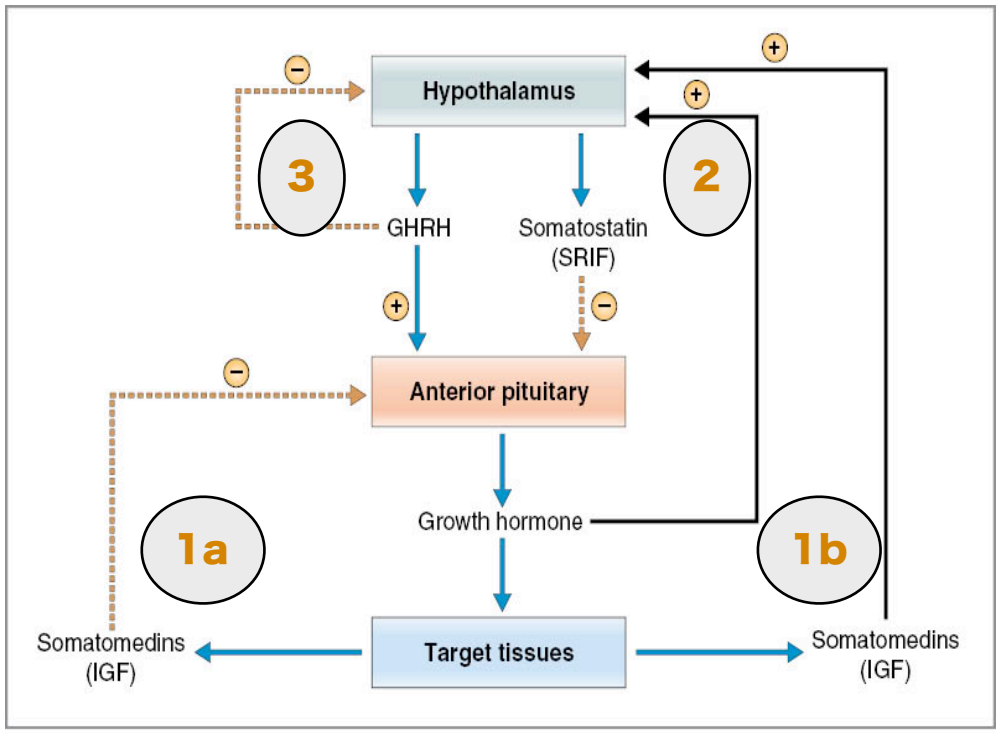
(b) Relationship between the anterior pituitary and the hypothalamus

Hypothalamic hormones:

- Growth hormone releasing hormone **GHRH**.
- Thyrotropin-releasing hormone **TRH**.
- Corticotropin-releasing hormone **CRH**.
- Gonadotropin releasing hormone **GnRH**.
- Prolactin inhibiting factor (or hormone) **PIF**.

GHRH/GHIH(SRIF)

- **Growth hormone releasing hormone (GHRH)**
  - Stimulates release of growth hormone
- **Growth hormone inhibiting hormone (GHIH) also called Somatostatin**
  - Inhibits release of growth hormone



1a **Growth hormone is metabolised in the liver to produce somatomedins which are more potent and have a negative feedback effect on growth hormone secretion from anterior pituitary [short loop]**

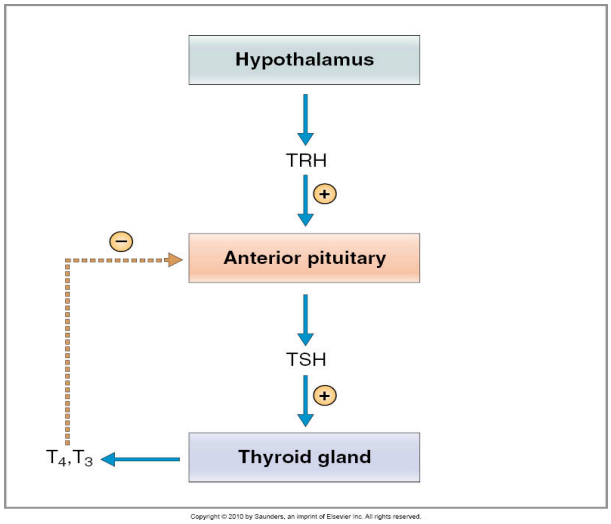
1b **On the same time, somatomedins have a positive feedback effect on somatostatin secretion from hypothalamus resulting in inhibition of GH secretion from anterior pituitary. [long loop]**

2 **Growth hormone itself has positive feedback effect on somatostatin secretion from hypothalamus resulting in inhibition of its [GH] secretion from anterior pituitary.** [long loop]

3 **GHRH has an autocrine negative feedback effect on its secretion from hypothalamus [ultrashort loop]**

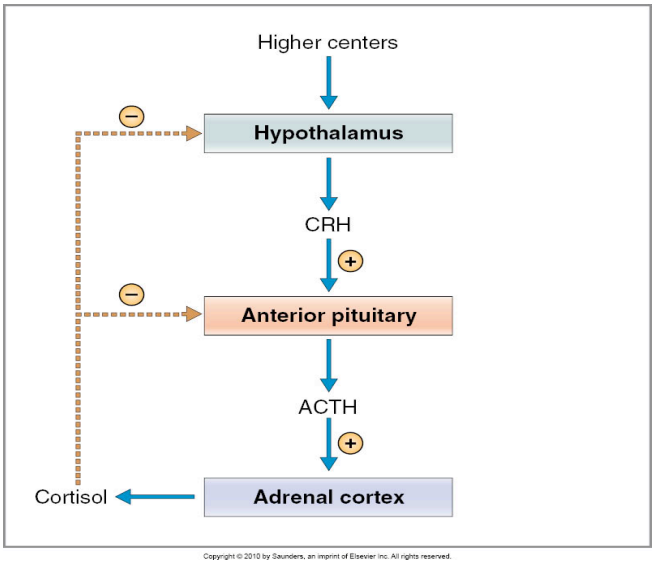
TRH

- **Thyrotropin-releasing hormone (TRH)**
  - Stimulates release of thyroid stimulating hormone (TSH)
  - Also, stimulate prolactin secretion.



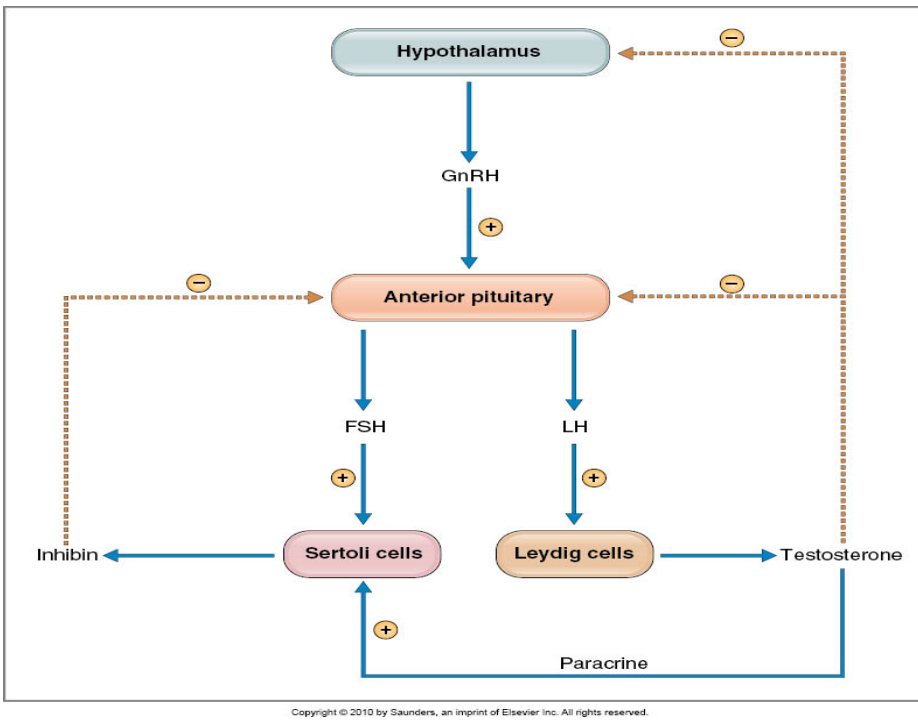
CRH

- **Corticotropin-releasing hormone (CRH)**
  - Stimulates release of adrenocorticotropin hormone (ACTH)



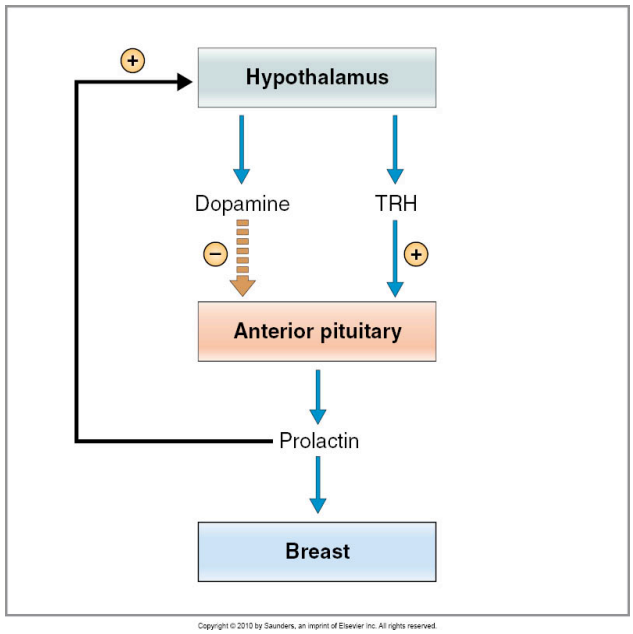
GnRH

- **Gonadotropin releasing hormone**
- causes release of :
  - Luteinizing (**LH)**
  - follicle-stimulating hormone **FSH**



PIH

- **Prolactin inhibitory hormone or factor(PIH)** [It is Dopamine]
  - Inhibits prolactin secretion



Anterior Pituitary

Origin of Pituitary [embryology]:

Anterior pituitary originates from **Rathke's pouch** (pharyngeal epithelium)

Posrterior pituitary originates from hypothalamus (glial-type cells) [remember it's neural tissue so it originates from neuroectoderm]

AP secretes 6 hormones:

1- TSH
2- FSH
3- LH
4- GH
5- PROLACTIN
6- ACTH.

1, 2 & 3 Same family [related to each other]

4 & 5 Same family [related to each other]

- there are 5 cell types in the anterior pituitary

1.**Somatotrophs** secrete **GH**
2.**Corticotrophs** secrete **ACTH**
3.**Gonadotrophs** secrete **FSH & LH**
4.**Thyrotrophs** secrete **TSH**
5.**Lactotrophs** secrete **prolactin**

Table 11.6 | Anterior Pituitary Hormones

Hormone	Target Tissue	Principal Actions	Regulation of Secretion
ACTH (adrenocorticotropic hormone)	Adrenal cortex	Stimulates secretion of glucocorticoids	Stimulated by CRH (corticotropin-releasing hormone); inhibited by glucocorticoids
TSH (thyroid-stimulating hormone)	Thyroid gland	Stimulates secretion of thyroid hormones	Stimulated by TRH (thyrotropin-releasing hormone); inhibited by thyroid hormones
GH (growth hormone)	Most tissue	Promotes protein synthesis and growth; lipolysis and increased blood glucose	Inhibited by somatostatin; stimulated by growth hormone-releasing hormone
FSH (follicle-stimulating hormone)	Gonads	Promotes gamete production and stimulates estrogen production in females	Stimulated by GnRH (gonadotropin-releasing hormone); inhibited by sex steroids and inhibin
PRL (prolactin)	Mammary glands and other sex accessory organs	Promotes milk production in lactating females; additional actions in other organs	Inhibited by PIH (prolactin-inhibiting hormone)
LH (luteinizing hormone)	Gonads	Stimulates sex hormone secretion; ovulation and corpus luteum formation in females; stimulates testosterone secretion in males	Stimulated by GnRH; inhibited by sex steroids

PROLACTIN

- **secreted from lactotrophs.(15%)**
- **198 Amino acids in single chain of polypeptide**
- **Related to GH**
- **Actions:**
  - **The major function of prolactin is ① milk production [lactose,casein & lipid synthesis]**
  - **Other functions are ② Breast development and ③ Inhibition of ovulation by inhibiting GnRH**
- **REGULATION OF SECRETION**
  - prolactin Stimulates the secretion of dopamine in median eminence (inhibits its own secretion)

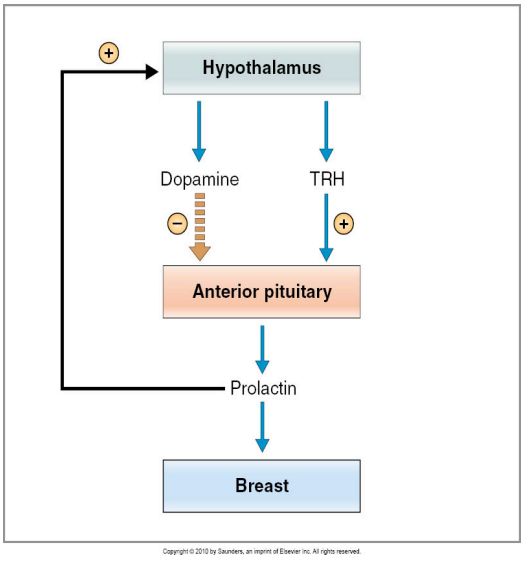
+ve feedback on dopamine >> inhibition of prolactin secretion from AP

- In males and non-pregnant females,

It regulated by 2 main mechanisms :

1- **Dopamine** (main mechanism) :
Has strong inhibitory effect on production of Prolactin

2- **TRH** (which is hormone produced from Hypothalamus)
It has stimulatory effect on production of prolactin



Estrogen stimulates prolactin secretion from AP but inhibit its effect in breast by down-regulating prolactin receptors. That's why pregnant women don't lactate until they deliver when estrogen levels fall.

Breast feeding : the main stimulus – mainly during suckling (secretion increase about 10 fold)

Stimulatory Factors	Inhibitory Factors
Pregnancy (estrogen)	Dopamine
Breast-feeding	Bromocriptine (dopamine agonist)
Sleep	Somatostatin
Stress	Prolactin (negative feedback)
TRH	
Dopamine antagonists	

- **Sources of dopamine:**

1- Dopaminergic neurones in the hypothalamus.
2- Dopaminergic neurones in the posterior pituitary.
3- Nonlactotrophs cells of the anterior pituitary.

- **Abnormalities:**

  - **Prolactin deficiency >> Failure to lactate.**
  - **Prolactin excess >> Galactorrhea &Infertility.**

Hyperprolactenemia is treated with Bromocriptine a dopamine agonist

Hypothyroidism can lead to hyperprolactinemia due to high TRH which lead to hypersecretion of prolactin

GROWTH HORMONE

- **also called Somatotropic hormone, somatotropin.**
- **secreted from Somatotrophs.(20%)**
- **191 amino acids in a straight-chain polypeptide**
- **GHRH (ventromedial nucleus).**
- **Cellular mechanism of GHRH & Somatostatin action on anterior pituitary**

◉**GHRH** binds to a membrane receptor -on the somatotrophs - , which is coupled through a G_s protein to *both* adenyl cyclase and phospholipase C. GHRH utilizes both cAMP and IP_3/Ca^{2+} as second messengers to stimulate growth hormone secretion.

◉**Somatostatin** binds to its own membrane receptor, which is coupled to adenyl cyclase by a G_i protein, inhibiting the generation of cAMP and decreasing growth hormone secretion.

Same mechanism one Stimulatory G protein [GHRH] and the other inhibitory G protein [somatostatin]

- **Actions:**

A) **Long term effect:**

- **Promotion of growth: ↑ cellular sizes & ↑ mitosis + ↑ tissue growth & organ size**

- Indirect effect

Depends on somatomedin 'insulin- like growth factor'

[IGF-I& II] secreted by the liver, which is responsible for effect of GH on ① bone & cartilage growth and ② increase the synthesis of protein in skeletal muscles.

Remember somatomedin acts through tyrosine-kinase mechanism thats why it's called insulin-like growth factor [IGF]

MECHANISMS OF BONE GROWTH

1. Linear growth of long bones:
   - causing deposition of **New Cartilage** (↑collagen synthesis) followed by its conversion into bone.
   - When bony fusion occurs between shaft & epiphysis at each end [closure of epiphyseal plates] , no further lengthening of long bone occur.

2. Deposition of **New Bone** (↑ cell proliferation) on surfaces of older bone & in some bone cavities, ↑ thickness of bone.
   - Occurs in membranous bones, e.g. jaw, & skull bones.

B) Short term

- **Metabolic effects:**

6.Protein metabolism (Anabolic)

↑ rate of protein synthesis in all cells through:

(a) ↑ amino acids transport into cells

(b) ↑ DNA transcription= RNA synthesis

(c) ↑ RNA translation= protein synthesis

(d) ↓ protein catabolism "protein sparer"

7.Fat metabolism (Catabolic)

↑ mobilization of FFAs from adipose tissue stores

Conversion of FFT to acetyl CoA to provide energy

GH could lead to ketoacidosis due to the increased levels of free fatty acids .

8.CHO metabolism (Hyperglycemic or diabetogenic effect)

(a) ↓ glucose uptake by tissues (skeletal muscles and fat).

(b) ↑ glucose production by the liver (↑ gluconeogenesis)

(c) ↓ rate of glucose utilization throughout the body

(d) ↑ insulin resistance (↑FFA)

Other effects:

1.Increases calcium absorption from GIT

2.Strengthens and increases the mineralization of bone

3.Retention of Na+ and K+

4.Increases muscle mass

5.Stimulates the growth of all internal organs excluding the brain

6.Contributes to the maintenance and function of pancreatic islets

7.Stimulates the immune system

- **Secretion is** Pulsatile every 2H.
- Secretion rate ↑ steadily from birth to childhood then remain stable. At puberty ↑ greatly induced by ↑ in sex hormones. After pubertal growth it slightly ↓ and remain stable until old age when it ↓ to its lowest level.

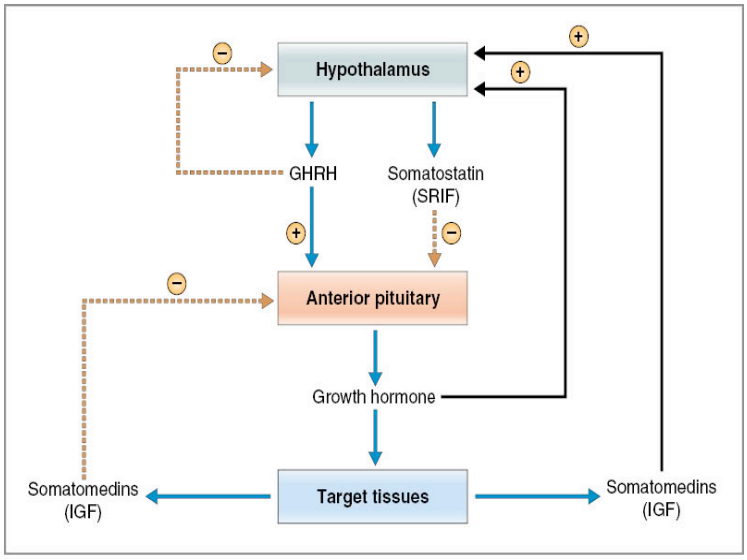
See figure explanation page 3

- **Regulation of GH secretion:**

The hypothalamus:

a. GHRH → ↑ GH secretion.

b. GHIH (somatostatin) → ↓ GH secretion



"ghrelin" which is a hormone secreted from the stomach has a positive feedback on GH

Children sleep more = more growth

Table 9-4 Factors Affecting Growth Hormone Secretion

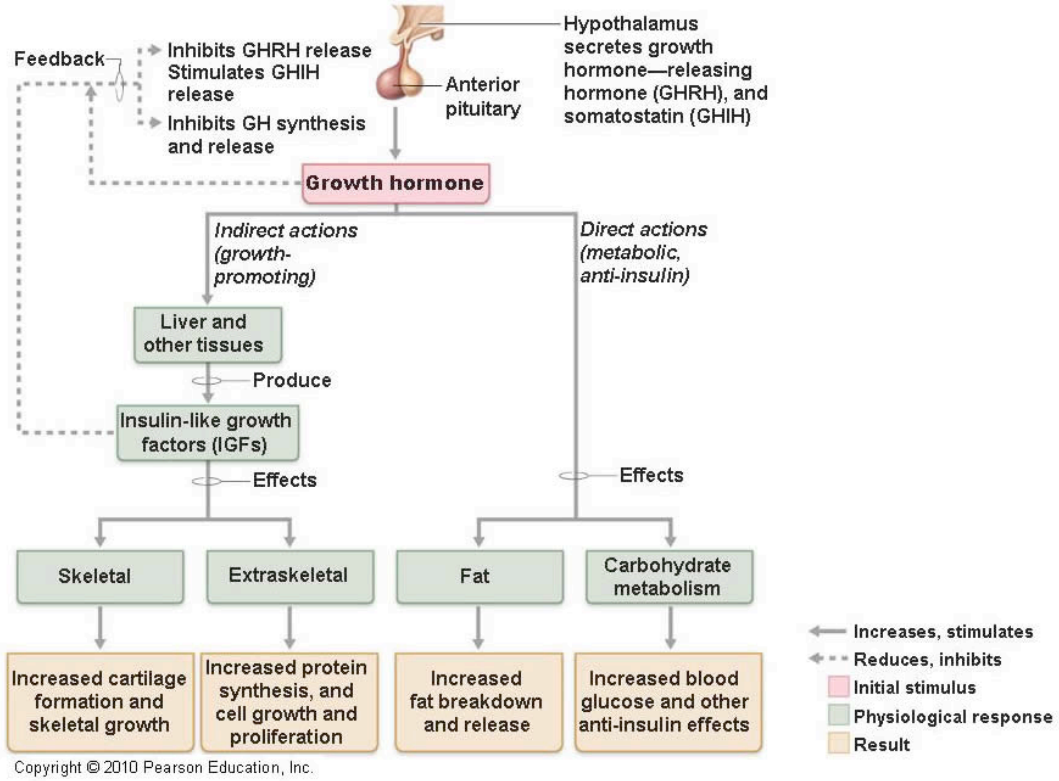
Stimulatory Factors	Inhibitory Factors
Decreased glucose concentration	Increased glucose concentration
Decreased free fatty acid concentration	Increased free fatty acid concentration
Arginine	Obesity
Fasting or starvation	Senescence
Hormones of puberty (estrogen, testosterone)	Somatostatin
Exercise	Somatomedins
Stress	Growth hormone
Stage III and IV sleep	β-Adrenergic agonists
α-Adrenergic agonists	Pregnancy

- **Summary:**

TABLE 16.1 Pituitary Hormones: Summary of Regulation and Effects

HORMONE (CHEMICAL STRUCTURE AND CELL TYPE)	REGULATION OF RELEASE	TARGET ORGAN AND EFFECTS	EFFECTS OF HYPOSECRETION ↓ AND HYPERSECRETION ↑
Anterior Pituitary Hormones			
Growth hormone (GH) (Protein, somatotroph)	**Stimulated** by GHRH* release, which is triggered by low blood levels of GH as well as by a number of secondary triggers including hypoglycemia, increases in blood levels of amino acids, low levels of fatty acids, exercise, other types of stressors, and estrogens **Inhibited** by feedback inhibition exerted by GH and IGFs, and by hyperglycemia, hyperlipidemia, obesity, and emotional deprivation via either increased GHIH* (somatostatin) or decreased GHRH* release	Liver, muscle, bone, cartilage, and other tissues: anabolic hormone; stimulates somatic growth; mobilizes fats; spares glucose Growth-promoting effects mediated indirectly by IGFs	↓ Pituitary dwarfism in children ↑ Gigantism in children; acromegaly in adults

*Indicates hypothalamic releasing and inhibiting hormones:
GHRH = growth hormone–releasing hormone; GHIH = growth hormone–inhibiting hormone



ABNORMALITIES

1- Hyposecretion of GH >> Dwarfism.

2- Hypersecretion.

- **Often associated with tumor.**

- **'in childhood':**

Gigantism,

as all body tissues grow rapidly, including bones.

Height ↑ as it occurs before epiphyseal closure

Hyperglycemia (diabetes).

- **'in adults':**

Acromegally,

person can't grow taller, BUT soft tissue continue to grow in thickness (skin, tongue, liver, kidney, ...)

- Enlargement of bones of hands & feet.

- Enlargement of membranous bones including cranium, nose, forehead bones, supraorbital ridges.

- Protrusion of lower jaw.

- Hunched back (kyphosis) (enlargement of vertebrae).

- **Treated with Octreotride, a somatostatin agonist.**

TSH

- **secreted from Thyrotrophs.(5%)**
- **Glycoproteins.**
- **α and β subunits;** the α subunit is identical with **α** subunit of FSH & LH while the **β** is what makes the different.
- **Related to FSH and LH.**

HCG is related to this family and has the same **α** subunit with different **β** subunit

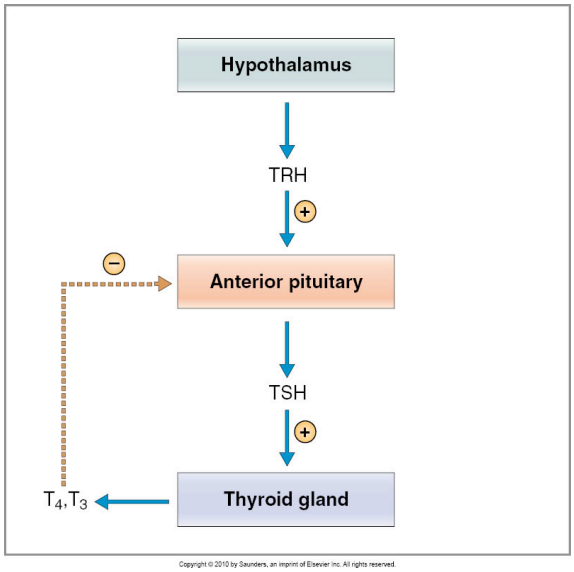
- **Actions: 1- Increase synthesis and secretion of thyroid hormones.**

2- Trophic effect increase the size of thyroid [goiter]

- **Regulation of TSH secretion:**

Pretty simple, TRH stimulate TSH secretion

Thyroid hormones -ve feedback and inhibit TSH

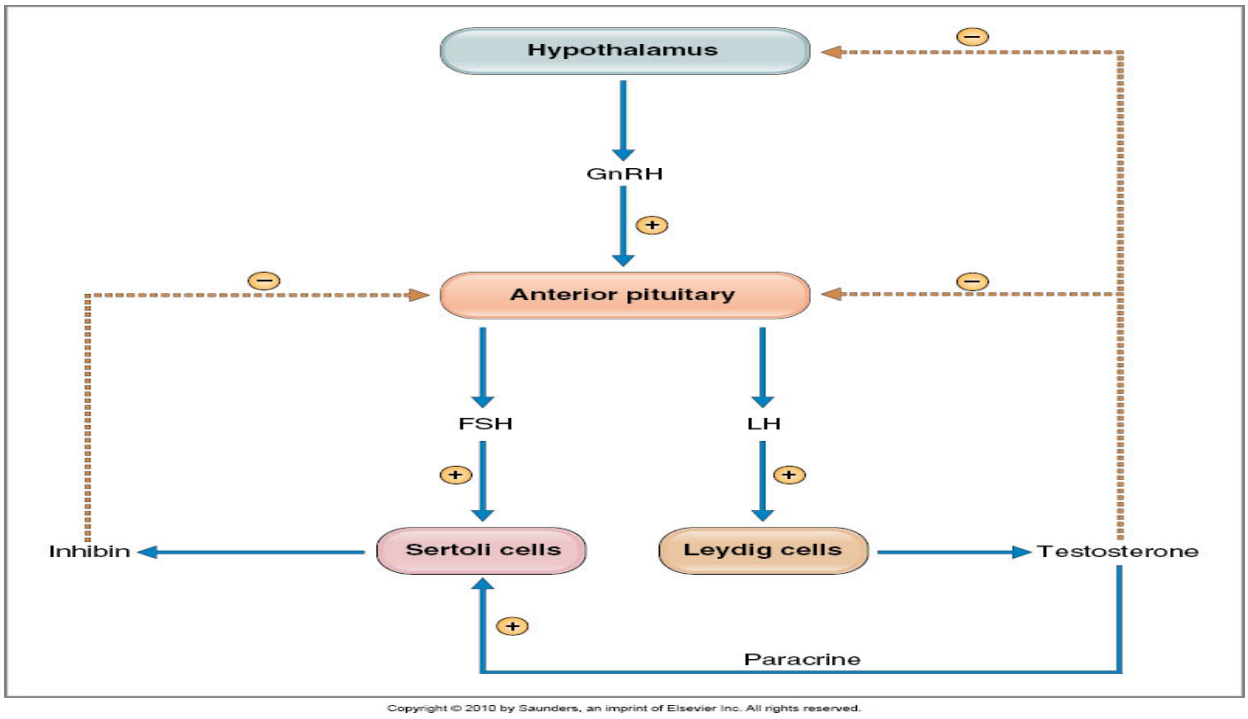


- **Abnormalities:** **Hyperthyroidism and hypothyroidism will be explained in thyroid lectures**

FSH AND LH

- **Glycoproteins.**
- **secreted from Gonadotrophs (15%)**
- **α and β subunits.**
- **Related to TSH.**

SECRETION



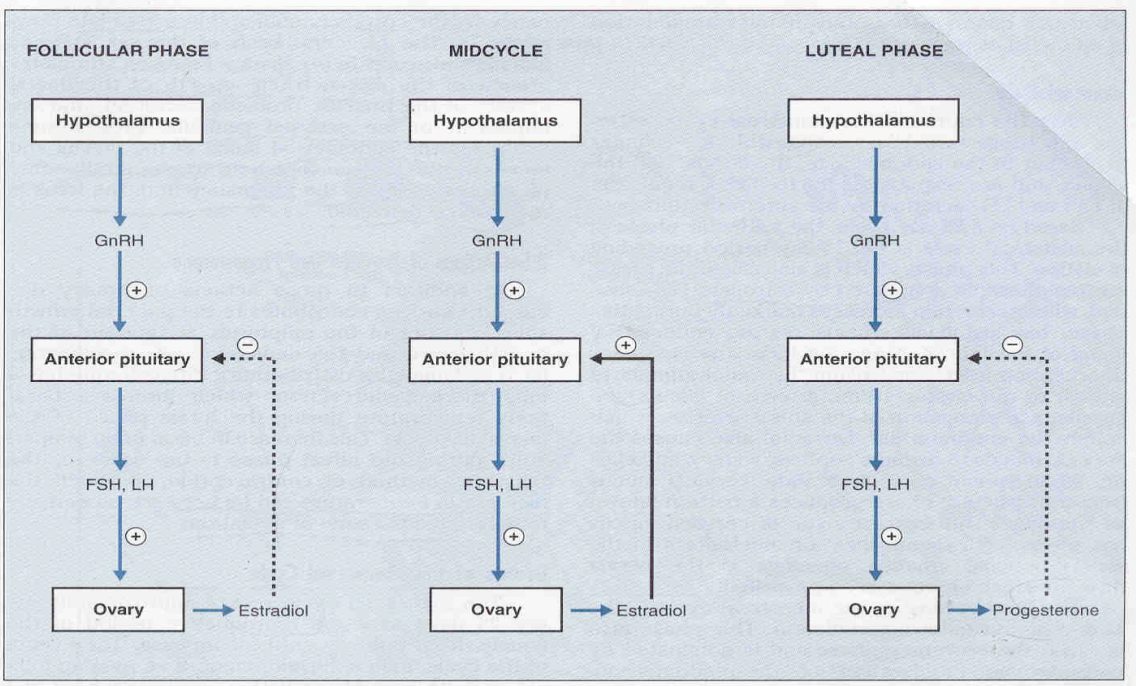
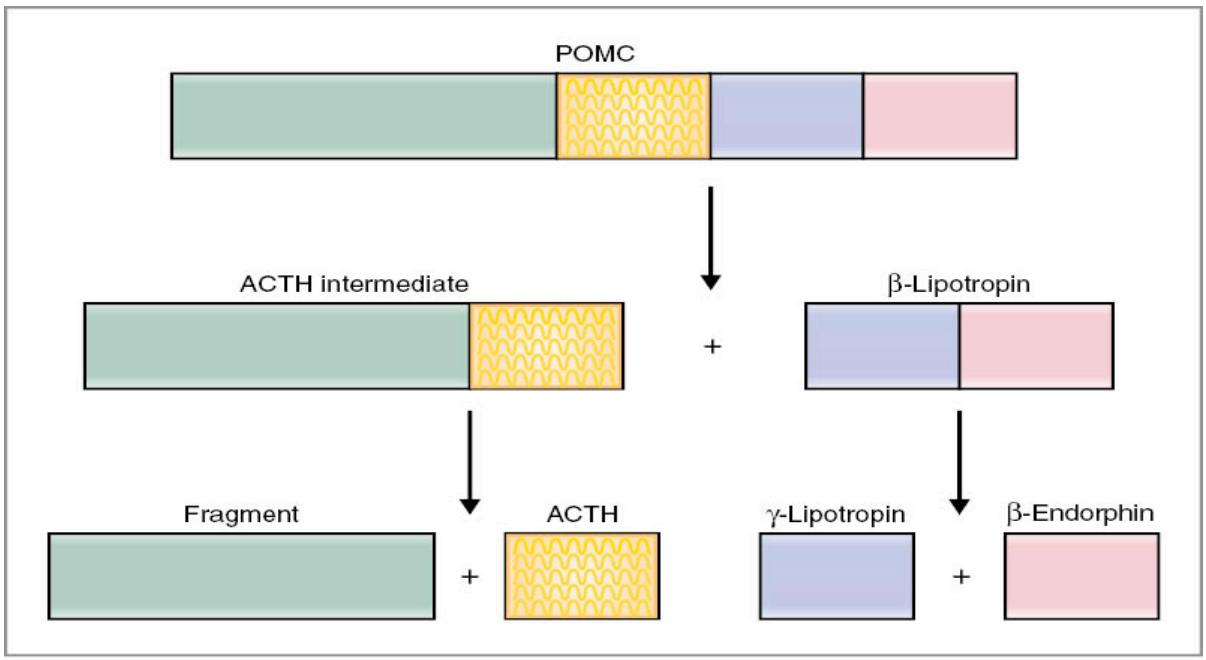


FIGURE 10–9. Control of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) secretion in females during the menstrual cycle. The follicular and luteal phases are characterized by negative feedback of estradiol and progesterone, respectively, on the anterior pituitary. Midcycle is characterized by positive feedback of estradiol on the anterior pituitary. GnRH, gonadotropin-releasing hormone.

ACTH

- **secreted from Cortictrophs.(15%)**
- **Melanocyte stimulating hormone [MSH] and β-endorphin are secreted with ACTH** *
- **ACTH is first synthesized as Preproopiomelanocortin (POMC)** then cleaved and secreted. see figure.

* In Addison's disease [adrenal insufficiency] there's hypersecretion of ACTH and MSH. Therefore, as a symptom, there's skin pigmentation.



- **Actions**

Stimulate synthesis and secretion of adrenal cortical hormones.

- **Regulation of ACTH secretion:**

Simple too, do it yourself!

Note that its feedback is

on both : hypothalamus & anterior pituitary

because it has receptors on both .

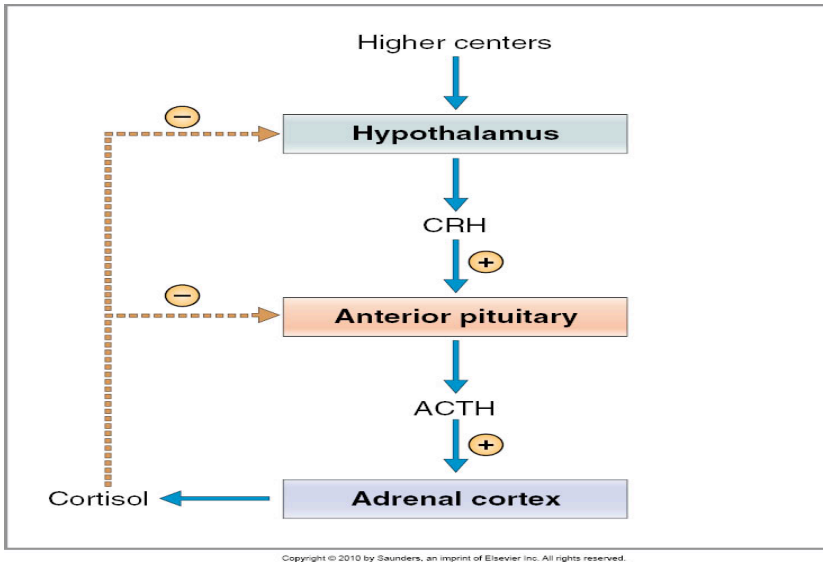


Table 9-10 Factors Affecting ACTH Secretion

Stimulatory Factors	Inhibitory Factors
Decreased blood cortisol levels	Increased blood cortisol levels
Sleep-wake transition	Opioids
Stress; hypoglycemia; surgery; trauma	Somatostatin
Psychiatric disturbances	
ADH ★	
α-Adrenergic agonists	
β-Adrenergic antagonists	
Serotonin	

★ ADH increase ACTH to compensate its anti diuretic effect and maintain osmolality through aldosterone action.

ADH keeps water # Aldosterone keeps Na

Source: Physiology by Linda Costanzo

Doctor's Handouts