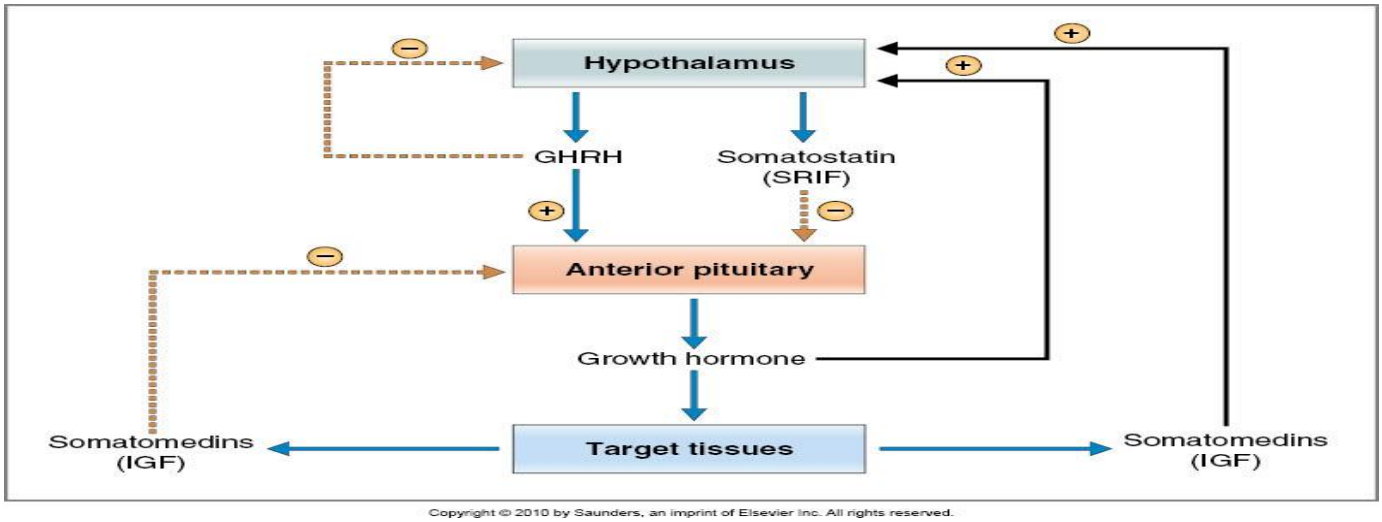
Cont . the last Lec.

Third : GROWTH HORMONE

- **Also called : Somatotropic hormone, somatotropin.**
- **It produced from the cell : Somatotrophs.(20%)**
- **The chemical structure : 191 AA.** (has height molecular weight)
- **It regulated (stimulated) by " GHRH (ventromedial nucleus).**:
- **Steps of production and regulation of Growth Hormon – GH -- :**
- 1- the **(GHRH)** from the hypothalamus stimulate the (somatotrophs cells) in the Anterioir pituitary gland to secrete the **(GH)**
- 2- after it secreted it head to the **liver** where it converted **to (somatomedins)** which has the same function of **GH** and has better effect
- **Regulation of the synthysis is by negative feedback :**

1) GHRH inhibits its own secretion from the hypothalamus via ultrashort-loop feedback .
2) Somatomedins inhibit secretion of GH by anterior pituitary .
3) Both GH & somatomedins stimulate the secretion of somatostatin by the hypothalamus which inhibit the GH secretion from anterior pituitary .



The mechanism of acting of the GHRH and SRIF on its receptors on anterioir pituitary Gland :

GHRH ⟶ receptor ⟶ Gs protein

Adenylyl cyclase and phospholipase C ⟶

cAMP and IP3/Ca ⟶ secretion + synthesis.

It use 2 second messangers **stimulatory** mechanisms :

1- Adenylyl cyclase
2- Phospholipase C

By acting on Gs receptor

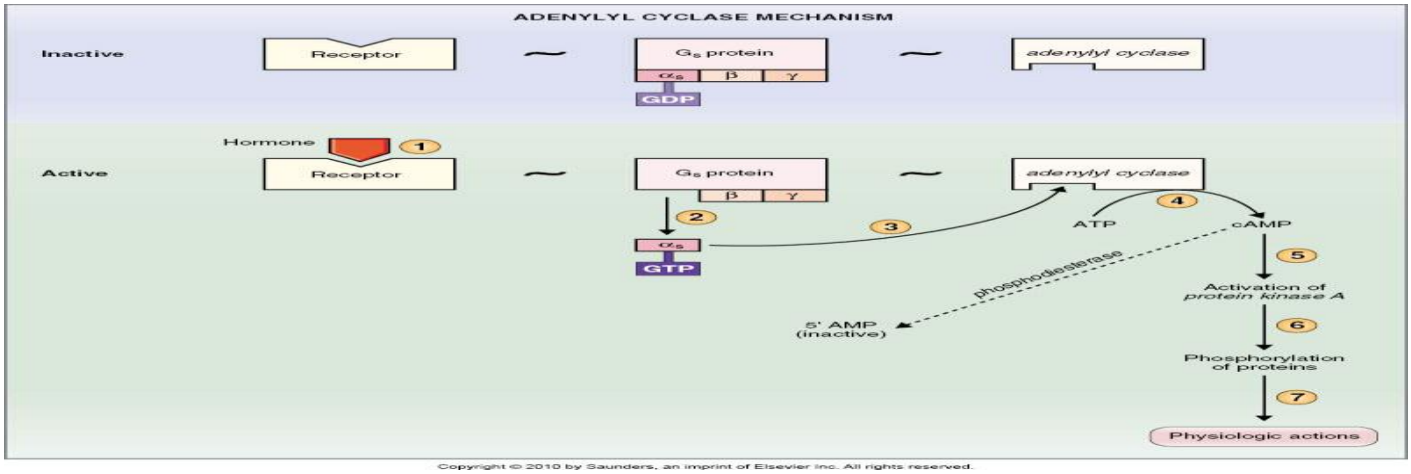
- **Somatostatin (SRIF) ⟶ receptor**

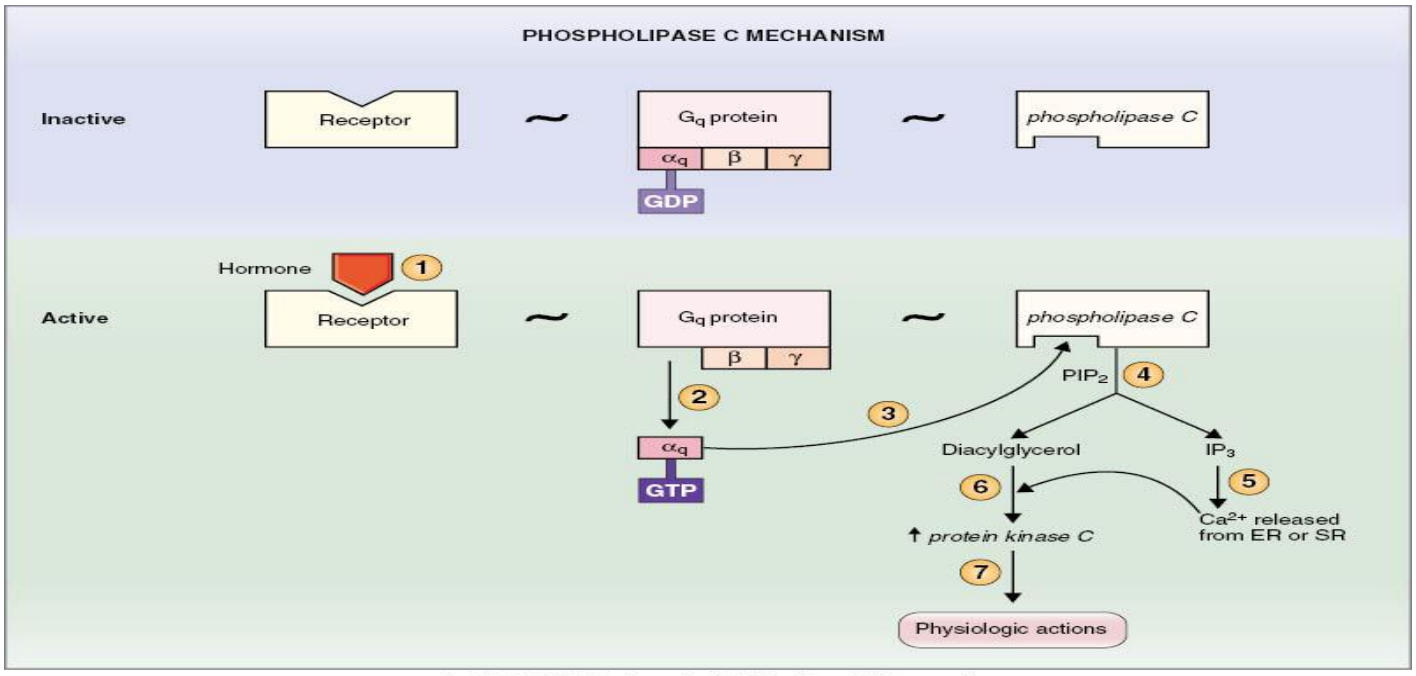
Gi ⟶ inhibit generation of cAMP ⟶

Decrease secretion.

It use **inhibitory** mechanisms by acting on :

Gi receptor





SECRETION OF GH

The GH has special mechanism in secretion that affected by many factors :

- **The pattern of secretion :** Pulsatile every 2H.
- **The frequency (How often) of secretion is constant but the Amount of secretion at each pulse is variable (According to the stimulus which acting)**

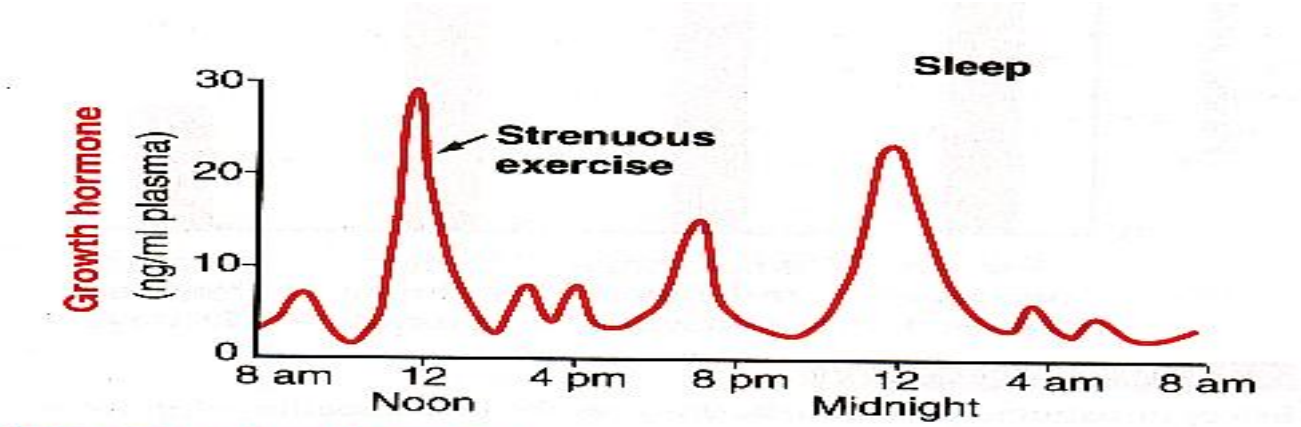


FIGURE 75 – 6

Typical variations in growth hormone secretion throughout the day, demonstrating the especially powerful effect of strenuous exercise and also the high rate of growth hormone secretion that occurs during the first few hours of deep sleep.

The Factors Affecting GH secretion :

1- **Stimulus Factors :** (before we get in this subject put on your mind that GH increase the Glucocse and fatty acid Level in the blood) so any factor lead to decrease Glucose or fatty acids level will lead to stimulation of GH secretion and vars versa والعكس صحيح

   a- Decrease Glucose level (وستفصل لاحقا ولكن اعرف هنا انها عامل يعمل على زياده افراز هرمون النمو)

   b- Decrease FA level (---)

   c- Arginine – it is amino acid has stimulatory effect on GH with no Kown reason

d- Fasting and starvation – because they lead to decrease glucose blood level

e- Hormons of puberty / these hormons work on stimulation of GH and Its receptors (females : estrogen , males : testosterone)

f- Exercise - stress : because it lead to decrease Glucose level

g- Deep steges of sleep (3 and 4) – most of the hormons increase during this period

2- **Inhibitory factors :** look the Table below

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
	Somatomedins
Exercise	Growth hormone
Stress	β-Adrenergic agonists
Stage III and IV sleep	Pregnancy
α-Adrenergic agonists	

note : the highest rates of GH secretion occur during puberty , and the lowest rates occur in senescence .

ملخص لبعض ما سبق

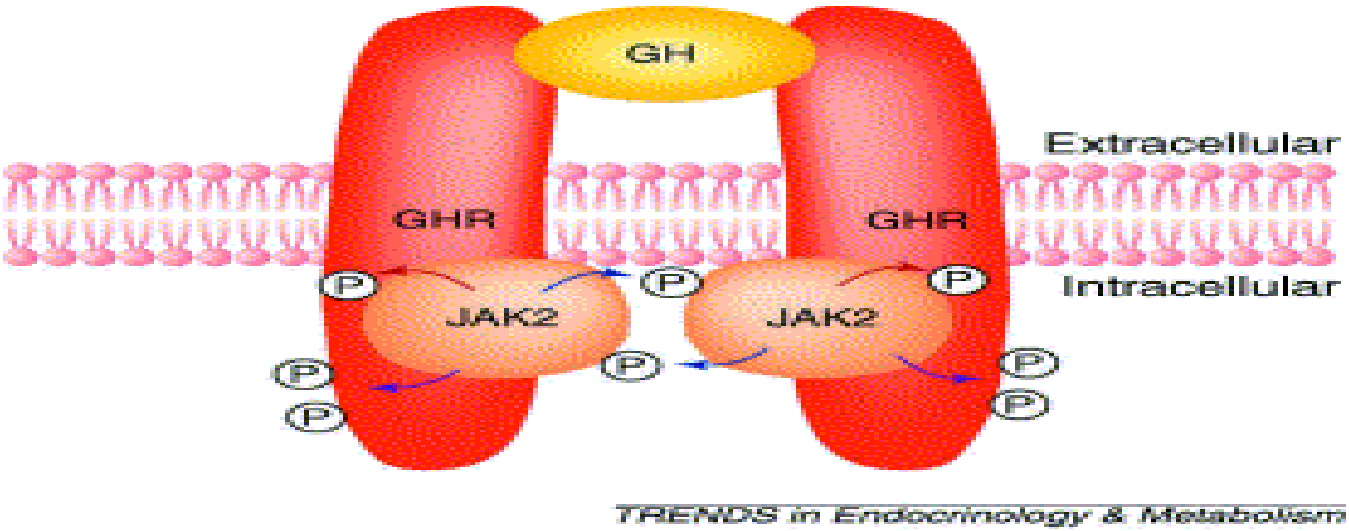
TABLE 16.1 Pituitary Hormones: Summary of Regulation and Effects

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

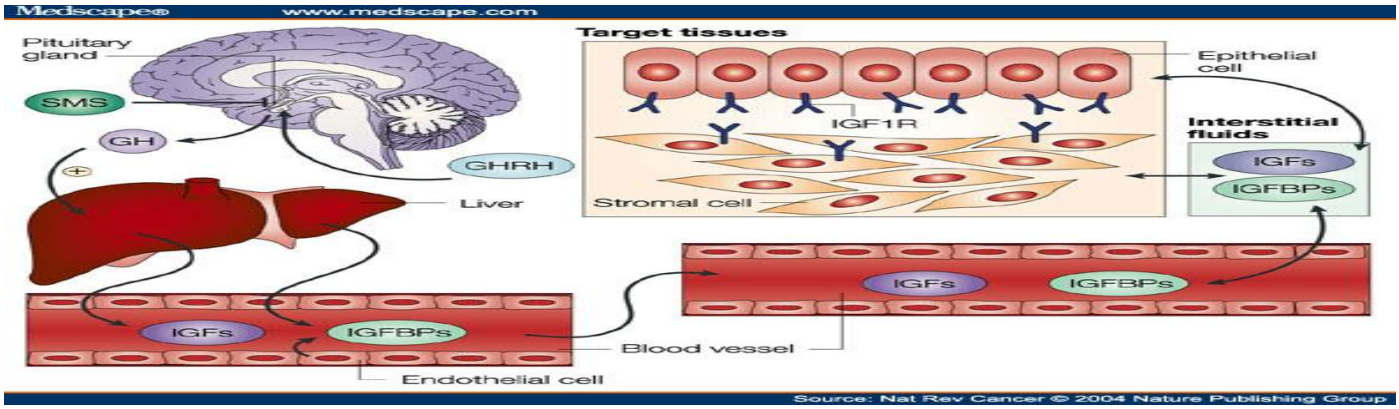
*Indicates hypothalamic releasing and inhibiting hormones:
GHRH = growth hormone–releasing hormone; GHIH = growth hormone–inhibiting hormone

ACTION OF GROWTH HORMONE

- **GH has 2 pattern of Action :**
- **1- Direct (before it modulated in the liver in other word → it still in original chemical form as it released).**
- **<u>It act on :</u> Skeletal muscles, liver and adipose.**



- **2- Indirect : (it called that after it modulated in the liver to somatomedine IGF) → which has better effect than GH .**
- **MW of somatomedine IGF : 4500-7500 MW.**
- **The most effective form of somatomedine IGF is : <u>Somatomedine C or IGF 1</u>**



The effect of GH in the human body :

1- EFFECT ON CARBOHYDRATE

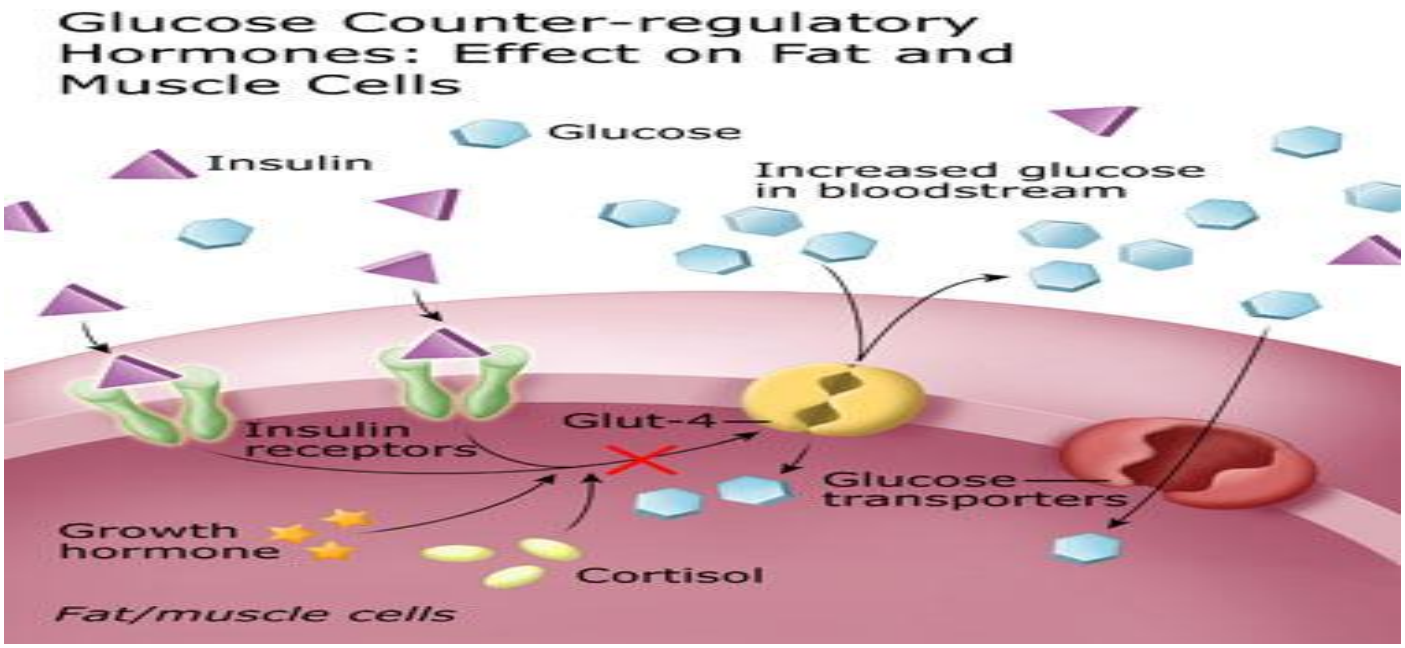
- **1- Increase blood glucose**
- **The GH Increase blood glucose by 2 ways :**

1- (Diabetogenic effect (prevent the cells from taking the Glucose from the blood)

2- (↑ gluconeogenesis)

2-Decrease glucose utilization in energy.

3-Increase in insulin. (it increase to match the rising of glucose level in the blood)



2- EFFECT ON PROTEIN

- Increase protein synthesis. By :

a- Increase AA uptake.

b- Increase DNA synthesis.

c- Increase RNA synthesis.

- Decrease protein catabolism.

3- EFFECT oN FAT

1- Increase FFA.

2- FFA Acetyl-CoA energy

4- EFFECT oN BONE AND CARTILAGE

1- Increase liner growth. (this only before the age of 21 – in other words : before the Epiphyseal plates calcified)

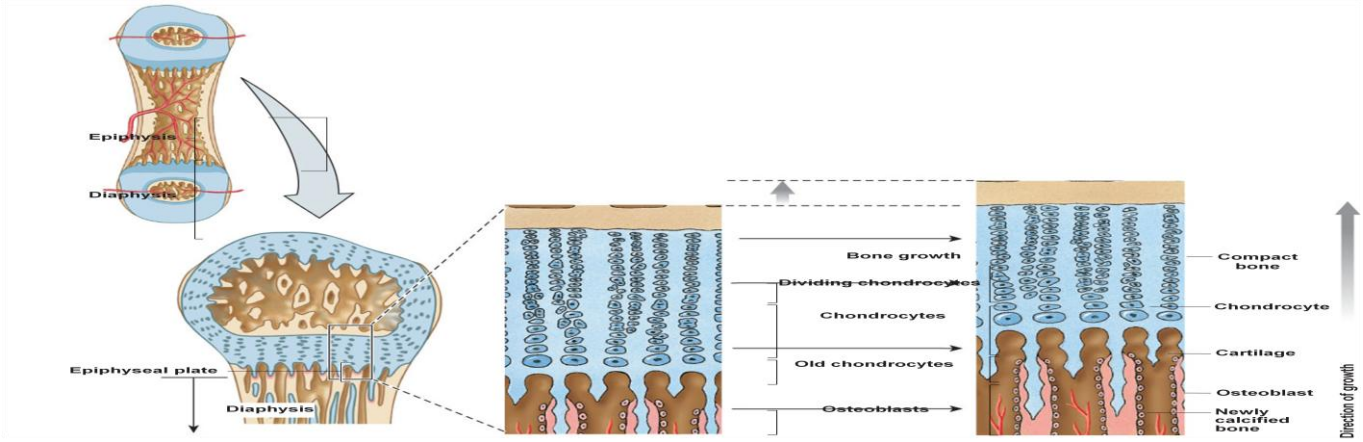
2- Increase metabolism in cartilage forming cells.

3- Increase proliferation of condrocytes.

4-Widening of the epiphyseal plate.

Note :

1) **the growth effect of growth hormone are mediated by somatomedins .**
2) **After the age of 21 the GH stimulate growing on sides النمو العرضي**



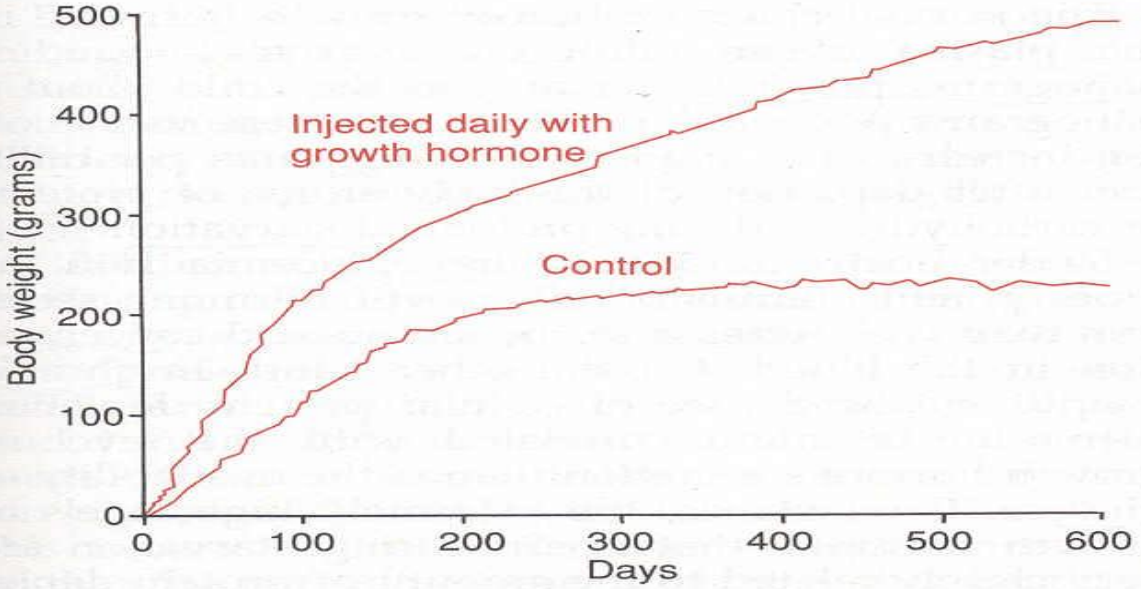
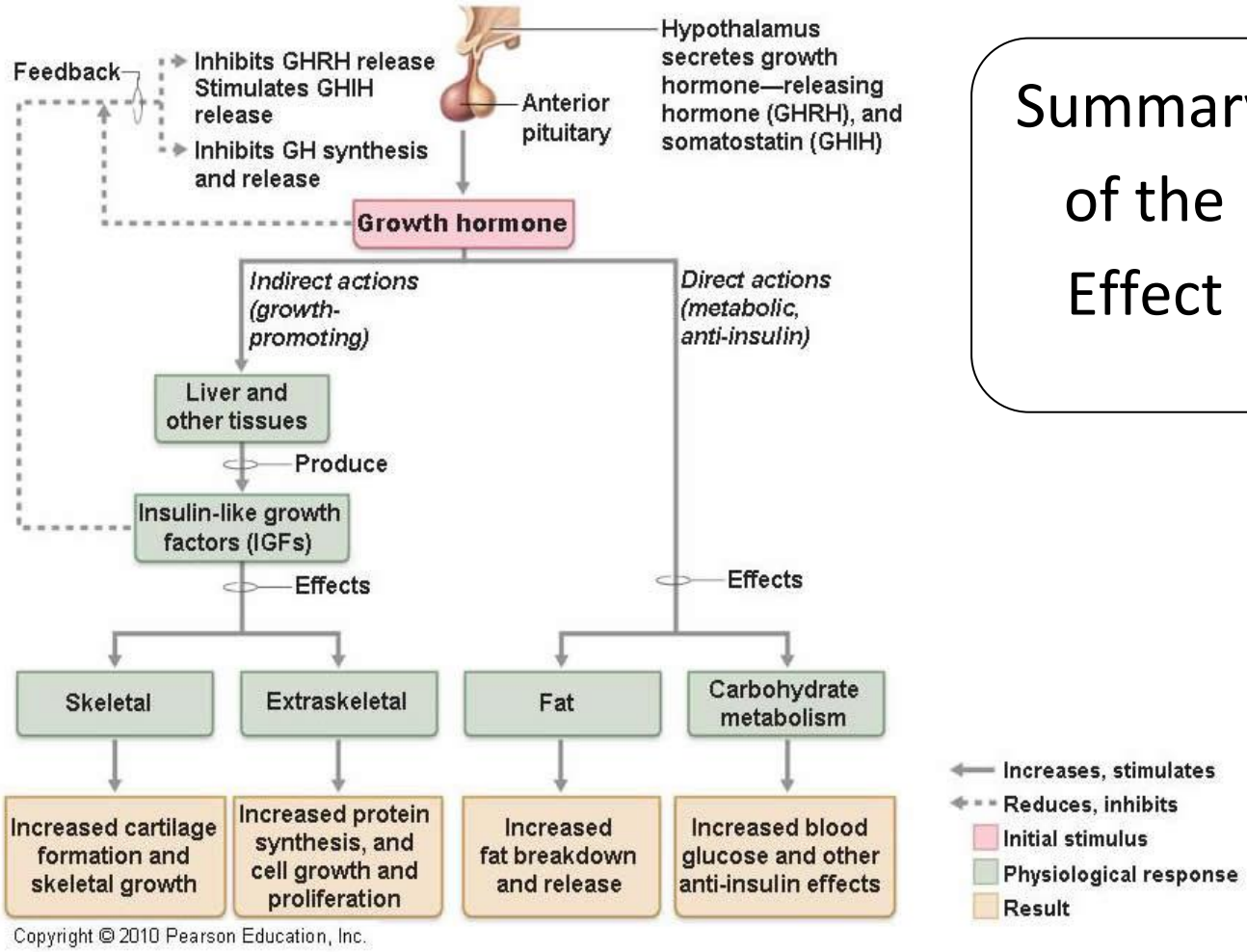


Figure 49–7 Comparison of weight gain of a rat injected daily with growth hormone with that of a normal rat.



Summary of the Effect

ABNORMALITIES

1- Hyposecretion of GH.

It cause Dwarfism.

Causes of Hyposecretion :

1- Problems in the hypothalamus (No GHRH)
2- Anterior pituitary (No GH)
3- Receptors (GH resistance)
4- liver (No conversion to somatomedins)

2- Hypersecretion.

- **Often associated with tumor.**
- **It cause Giganitsm (if the problem occure Before the age 21 (before Epiphyseal plates calcified .**

  Or Acromegaly (it occure after the Epiphyseal
- **plates calcified .**
- **treatment : Octreotride (mimic the natural IGF which tend to inhibit the secretion of growth hormone)**

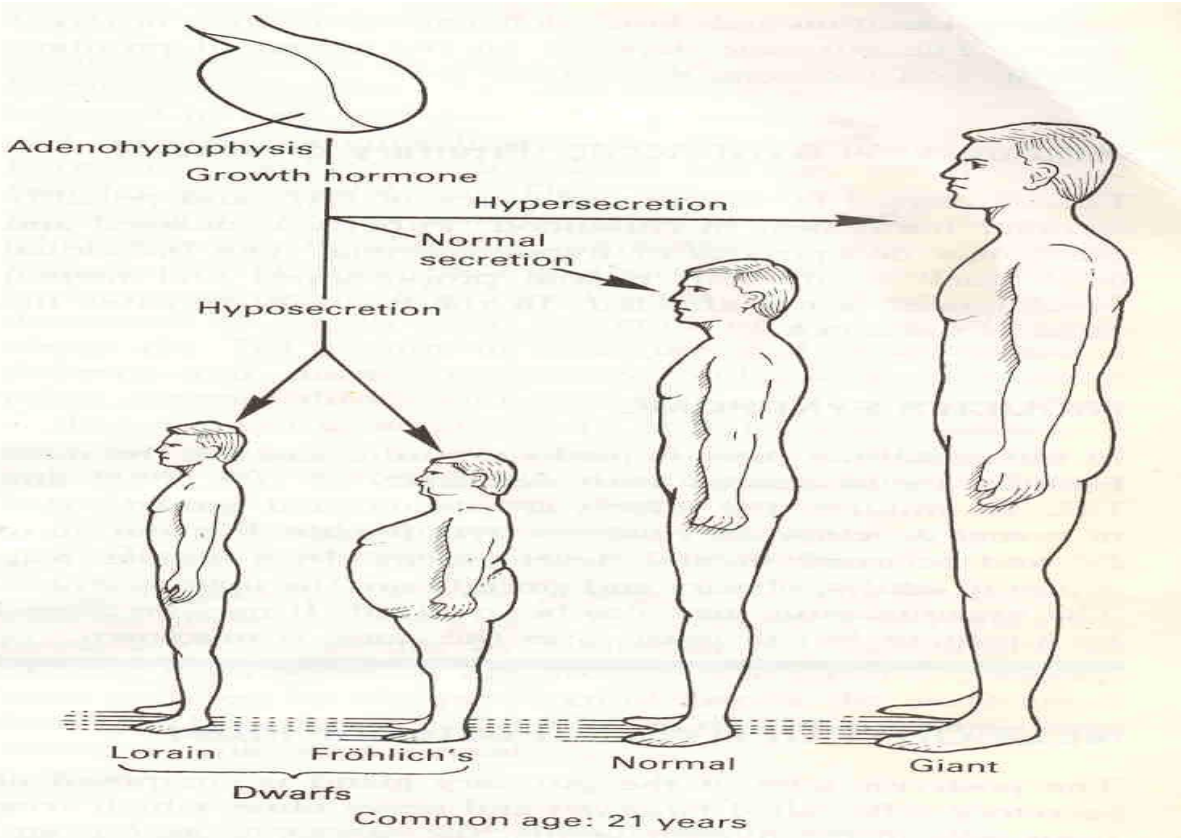


Figure 14:5 Effects of normal and abnormal growth hormone secretion.

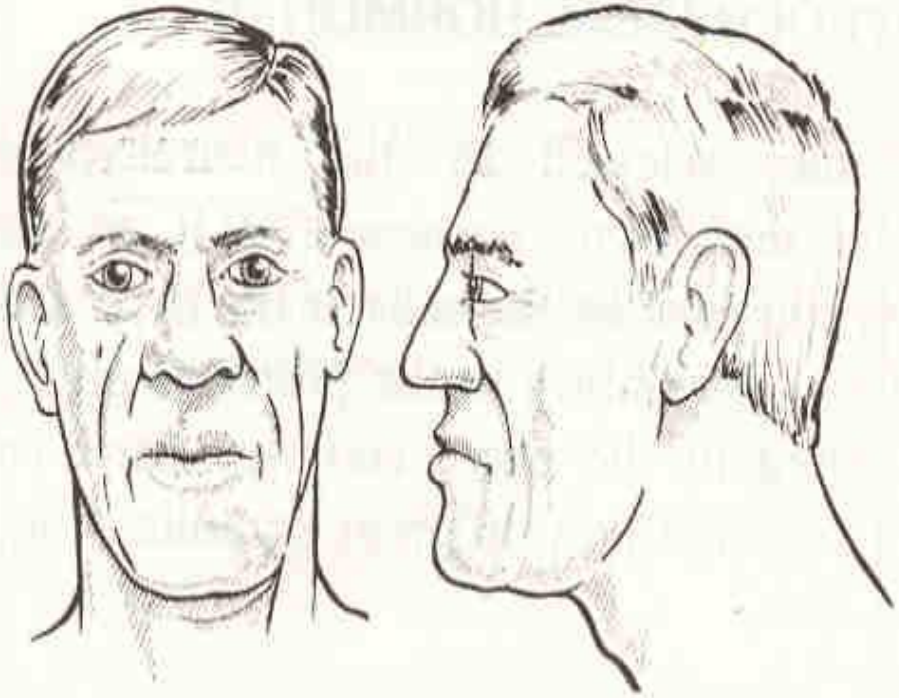


Figure 14:6 Acromegaly.

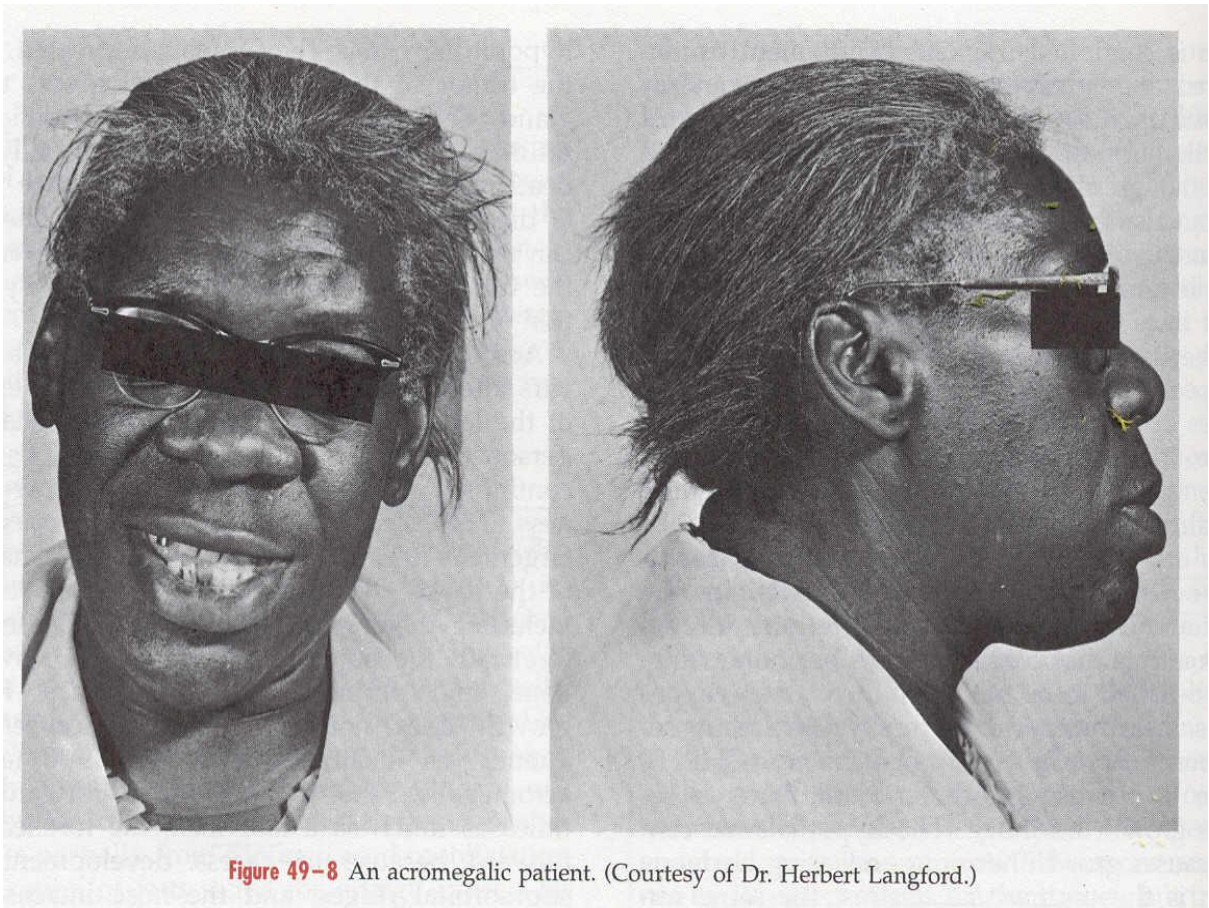


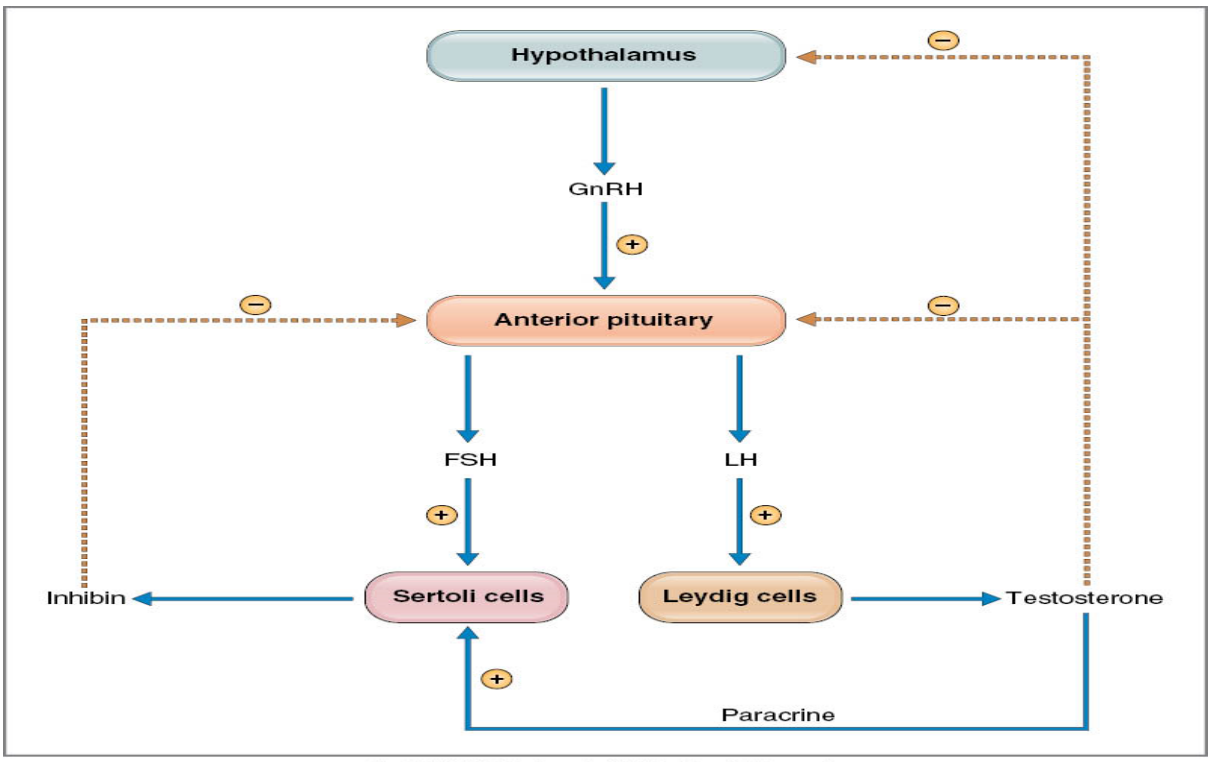
Figure 49–8 An acromegalic patient. (Courtesy of Dr. Herbert Langford.)

Fourth : FSH AND LH

الدكتور قال هذا انتم دارسينه البلوك اللي راح عشان كذا ما ركز عليه هنا

- **The chemical structure : Glycoproteins.**
- **These 2 hormos secreted from the cell ": Gonadotrophs (15%)**
- **α and β.**
- **Related to TSH.**

SECRETION



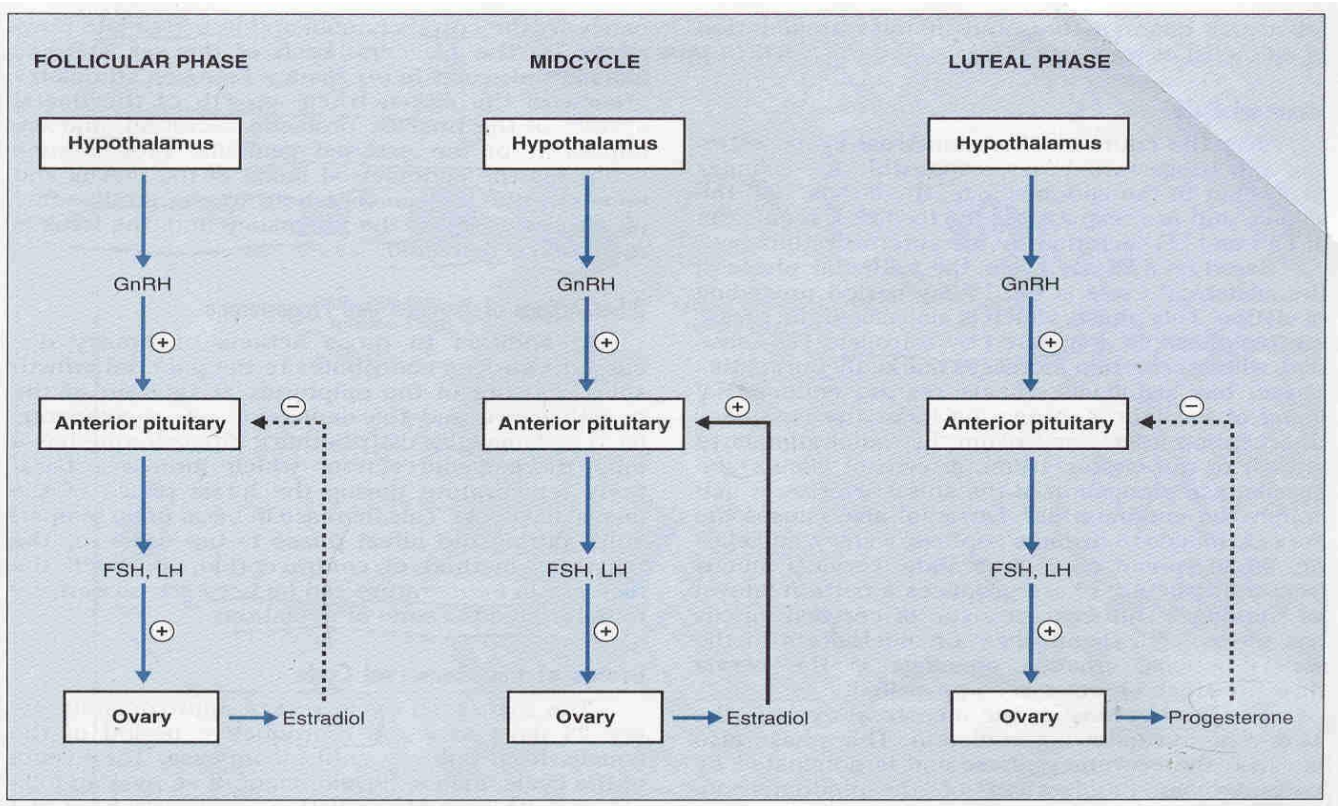
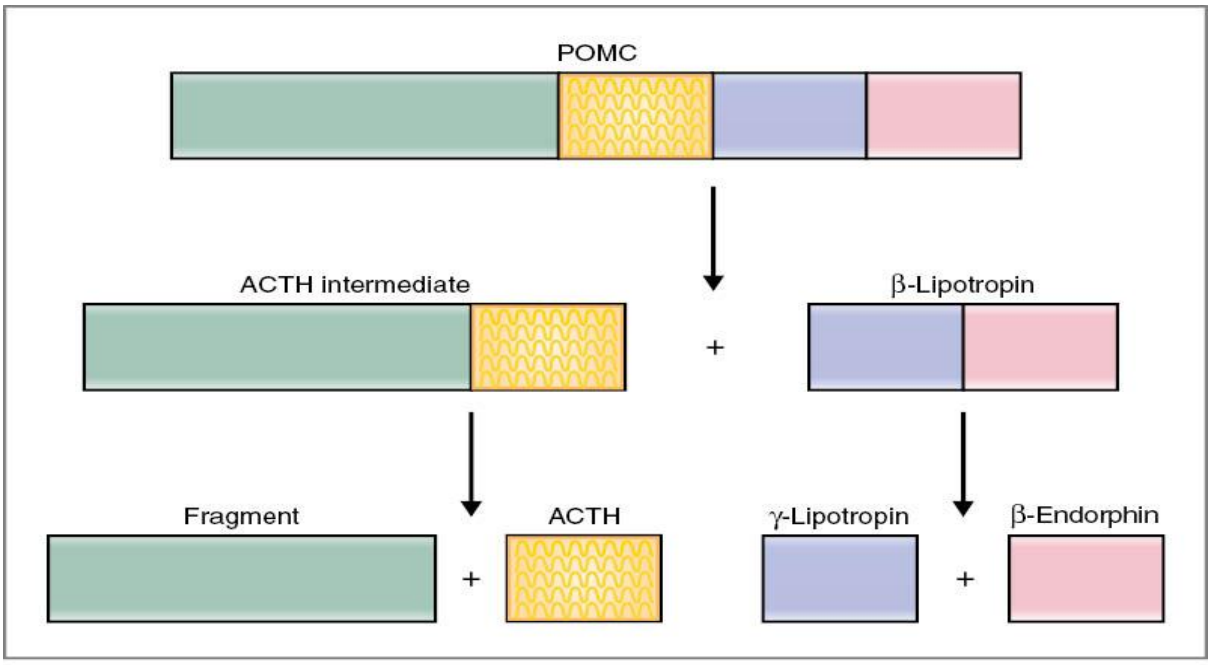


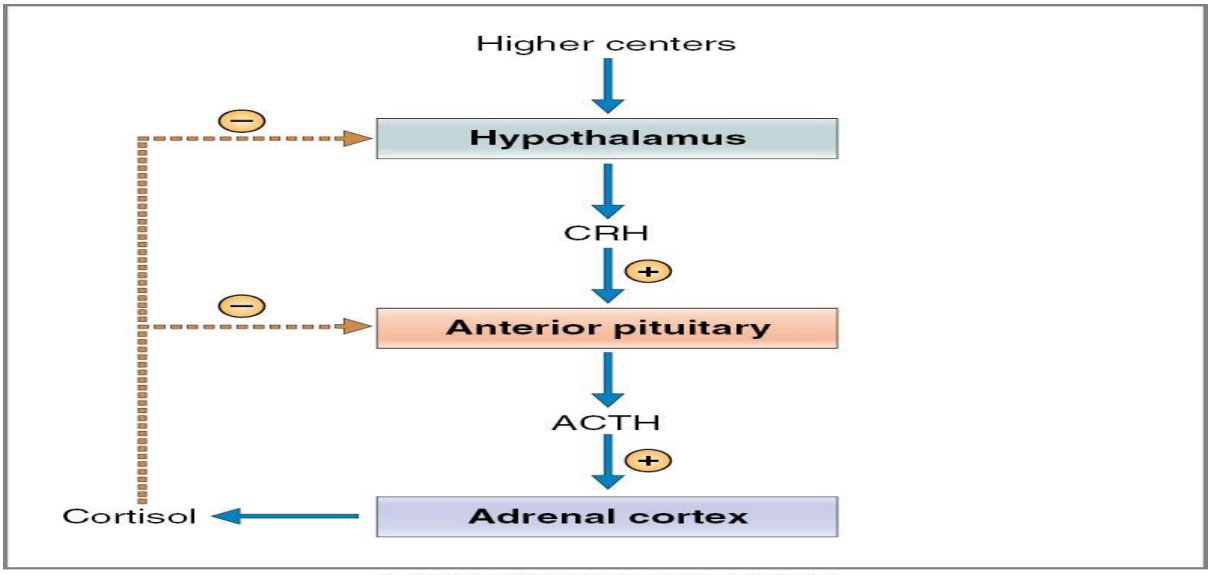
FIGURE 10–9. Control of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) secretion in females during the menstrual cycle. The follicular and luteal phases are characterized by negative feedback of estradiol and progesterone, respectively, on the anterior pituitary. Midcycle is characterized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

Fifth : ACTH

- **It secreted from the cell : Cortictrophs.(15%)**
- Synthisis :
- 1- This hormone come from prcurseoir structure called **Preproopiomelanocortin (POMC).**
- 2- the POMS cleavge into 2 parts then these two parts cleavage to give 4 structures :
- **Fragments " contain MSH " + ACTH + gamma lipotropin + B endorphin .**

  MSH : melanocyte-stimulating hormone which cause pigmentation if their level increase in blood . ex. : addison's disease





ACTION

- **Stimulate synthesis and secretion of adrenal cortical hormones.**

Table 20.19 Hormones in serum

Hormone	Reference range	Units
Adrenocorticotrophic hormone (ACTH) (plasma)	7–51 (07:00–10:00 h)	ng/l
Cortisol	150–550 (at 08:00 h) < 200 (at 22:00 h)	nmol/l
Follicle-stimulating hormone (FSH)		
Male	1.5–9.0	U/l
Female*	3.0–15 (early follicular) Up to 20 (mid-cycle) > 30 (post-menopausal)	U/l
Gastrin (plasma)	Up to 120	ng/l
Growth hormone (GH)	Very variable, usually less than 2, but may be up to 50 with stress	mU/l
Insulin	Highly variable and interpretable only in relation to plasma glucose and body habitus	mU/l
Luteinising hormone (LH)		
Female*	2.5–9.0 (early follicular) Up to 90 (mid-cycle) > 20 (post-menopausal)	U/l
Male	1.5–9.0	U/l
Oestradiol-17β		
Female	110–180 (early follicular) 550–1650 (mid-cycle) 370–770 (luteal) < 150 (post-menopausal)	pmol/l
Male	< 200	pmol/l
Parathyroid hormone (PTH)	10–65	ng/l
Progesterone		
Male	< 2.0	nmol/l
Female	< 2.0 (follicular) > 15 (mid-luteal) < 2.0 (post-menopausal)	nmol/l
Prolactin (PRL)	60–390	mU/l
Testosterone		
Male	10–30	nmol/l
Female	0.4–2.8	nmol/l
Thyroid-stimulating hormone (TSH)	0.15–3.5	mU/l
Thyroxine (free) (free T_4)	10–27	pmol/l
Tri-iodothyronine (T_3)	1.0–2.6	nmol/l
TSH receptor antibodies (TRAb)	< 7	U/l

* Luteal phase values similar to follicular phase.

Notes

1. A number of hormones are unstable, and collection details are critical to obtaining a meaningful result. Refer to local hospital handbook.
2. Values in the table are only a guideline; hormone levels can often only be meaningfully understood in relation to factors such as sex (e.g. testosterone), age (e.g. FSH in women), time of day (e.g. cortisol) or regulatory factors (e.g. insulin and glucose, PTH and [Ca^{++}]). Also, reference ranges may be critically method-dependent.

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	

قام بالمقارنه والتدقيق والمقارنه مع الكتاب المرجع
المعتمد من الدكتور حبيب الشعب :

محمد المومي

مشكورا