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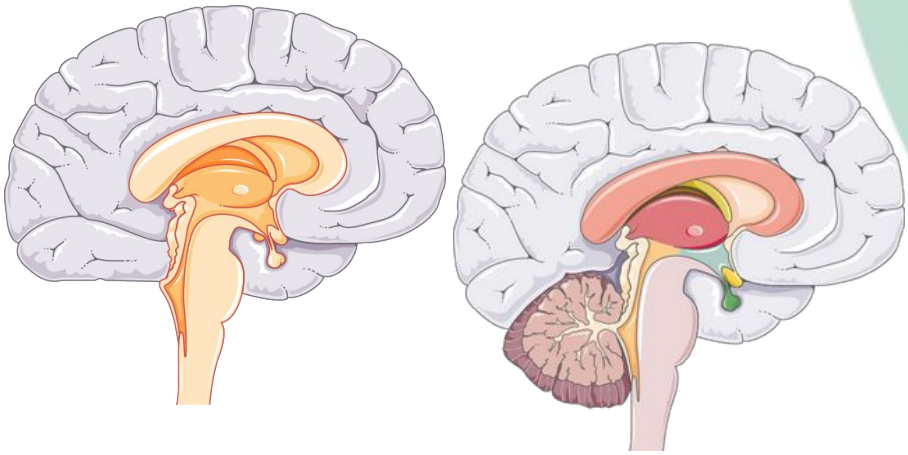
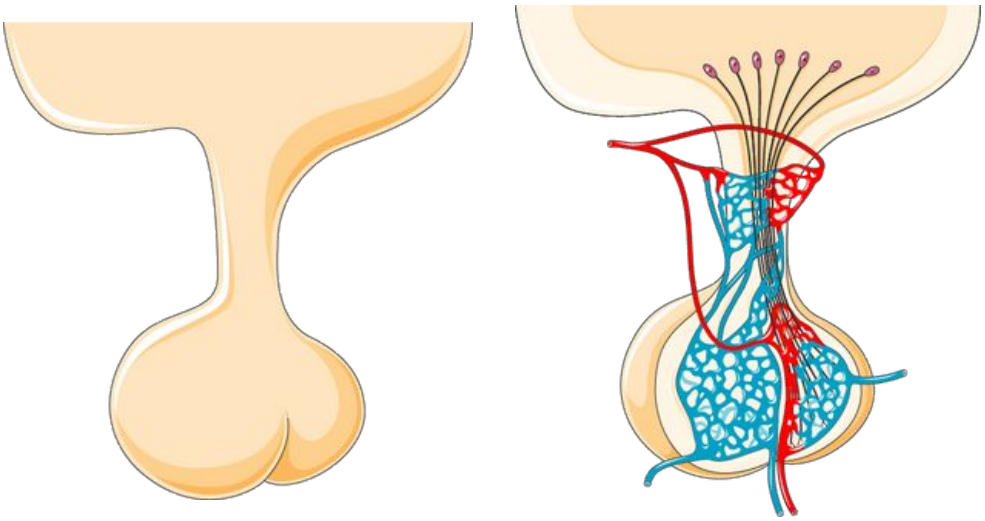




Anterior pituitary gland

ENDO Physiology

Editing File

Color Index :

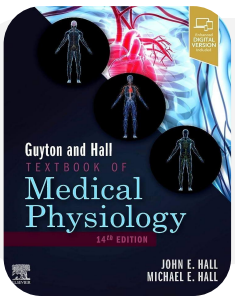
- Main Text
- Important
- Girls Slides
- Boys Slides
- Notes
- Extra

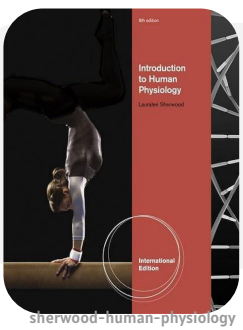
Objectives

- **List Anterior pituitary hormones:**
  - Know chemical structure / secretion
- **Describe action of Anterior pituitary hormones**
- **Know conditions related to hypo or hyper secretion of Anterior Pituitary hormones**
- **Know Mechanism of action of hormones**
  - Hormone receptors, down-regulation and up-regulation
  - Intracellular signaling
  - Second messenger mechanism

Resources

Only ENDO chapters included





sherwood-human-physiology

This lecture was presented by:
Dr. Hana Alzamil - Prof. Abdulmajeed Aldrees

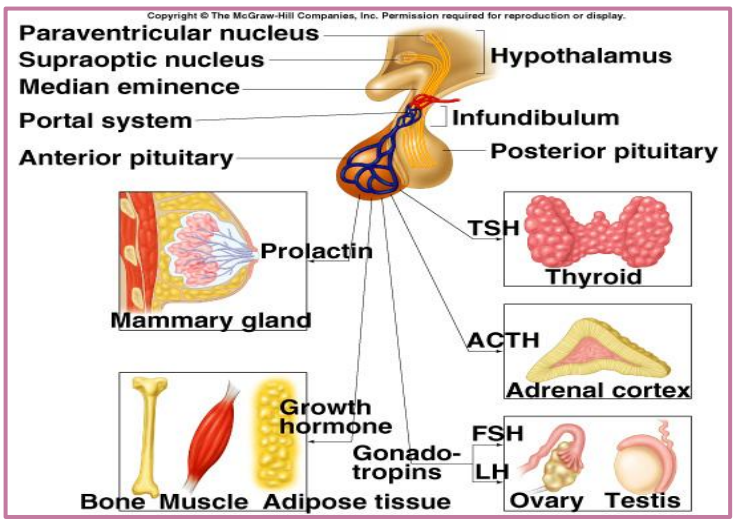
ANTERIOR PITUITARY HORMONES

Anterior Pituitary Gland Hormones

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

Anterior pituitary gland hormones

Hormone	Target tissue	Principle action	Secretion regulation
ACTH Adrenocorticotropic Hormone	Adrenal cortex	Stimulate secretion of glucocorticoids	(+): CRH (-): Glucocorticoids
TSH Thyroid stimulating Hormone	Thyroid gland	Stimulate Thyroid hormones secretion	(+): TRH (-): Thyroid hormones
GH Growth Hormone	Most tissue	Promote Protein synthesis, growth, lipolysis and increased blood glucose	(+): GHRH (-): Somatostatin (=GHIH)
FSH Follicle stimulating Hormone	Gonads	Promote Gamete production, and Stimulate estrogen production in female	(+): GnRH (-): sex steroids and inhibin (inhibin only inhibit FSH)
LH Luteinizing Hormone		Sex hormone secretion: Male: testosteron Female: ovulation, corpus luteum	
PRL Prolactin	Mammary glands, sex accessory organs	Promote Milk production in lactating females. Additional actions in other organs.	(-): PIH (=Dopamine)



Stimulated = (+)
Inhibited = (-)

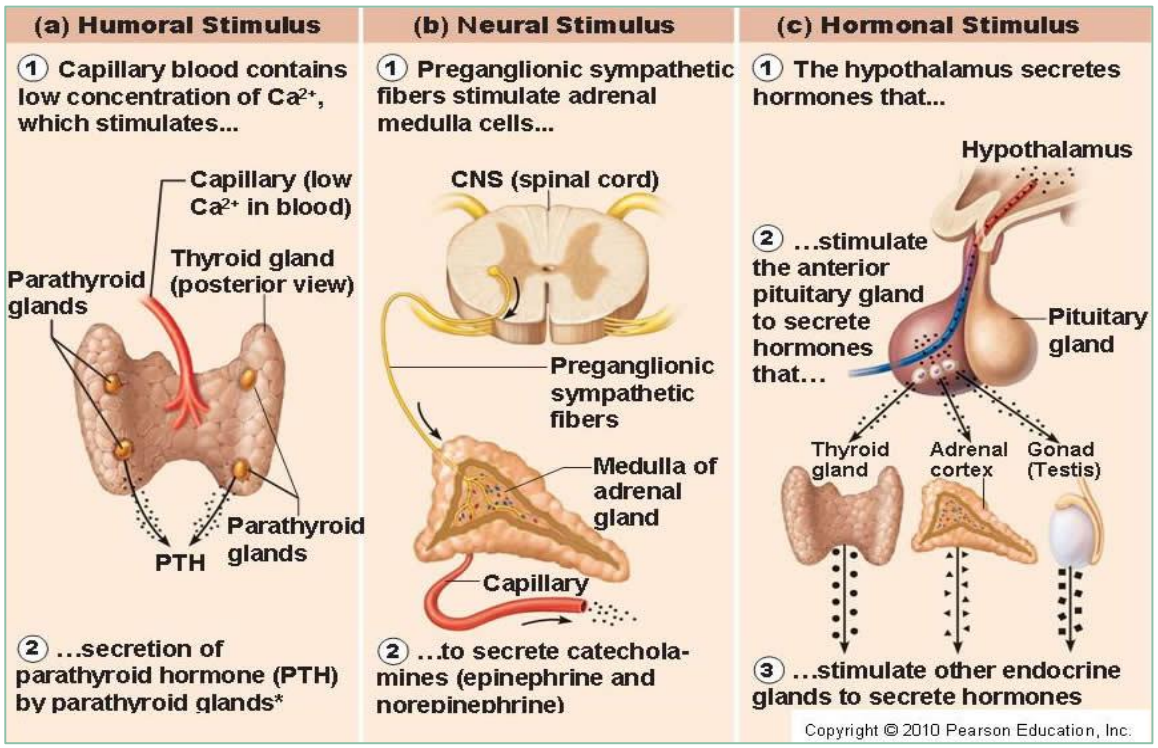
PITUITARY GLAND

Anterior pituitary hormones

1) GH
- Physiological functions
- Regulation of GH secretion
  - Feedback mechanism
  - Factors controlling secretion

2) Prolactin
- Physiological functions
- Regulation of prolactin secretion

Endocrine gland stimuli may be humoral, neural or hormonal

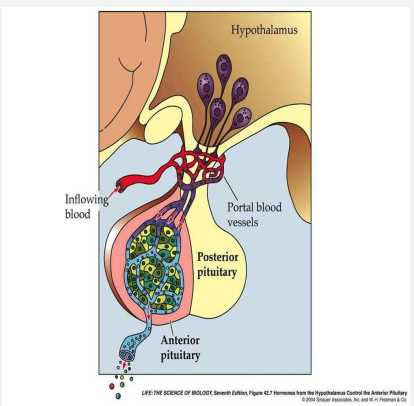


ADENOHYPOPHYSIS

Anterior pituitary gland (adenohypophysis)

Is connected to hypothalamus by portal system:

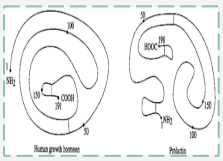
"hypothalamic hypophysial portal vessels".



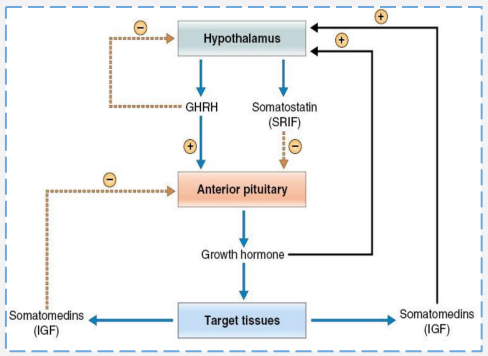
Growth Hormone (Somatotropin)

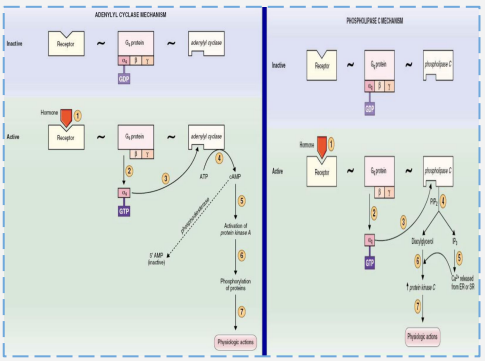
Growth Hormone | **Male slides**

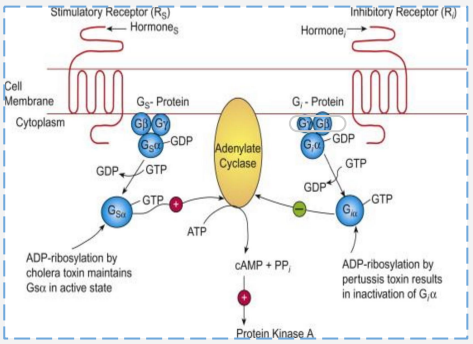
- Somatotropic hormone, somatotropin. • 191 AA.
- Somatotrophs.(20%) • MW 22000 kD. • GHRH .



GH and Prolactin are 75% similar in structure







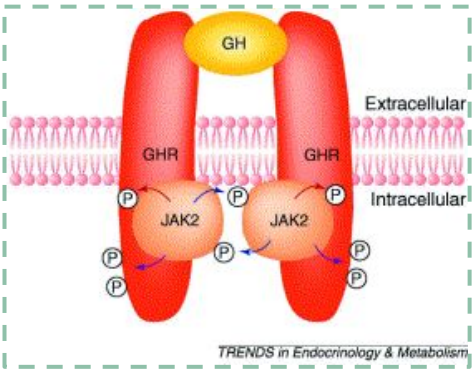
GHRH —> Receptor —> Gs protein —> AC & PLC —> cAMP & IP3/Ca —> secretion + synthesis

Somatostatin (SRIF) —> receptor Gi —> inhibit generation of cAMP —> Decrease secretion

1 Direct effect (Mechanism of Action)

- GH itself attaches on the dimers receptor "similar as insulin" and activates it
- Its activation will lead to approximation of these dimeres together, and this is called phosphorylation of the receptor → then action of that hormone will start

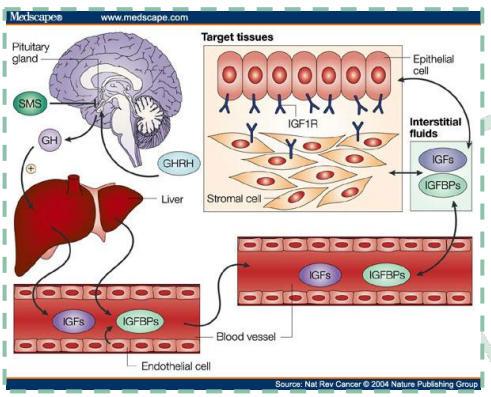
→ Example: Skeletal muscle, liver, adipose



2 Indirect effect (Somatomedins)

- Somatomedin C, 4500-6500 MW
- Anterior pituitary will release GH to act on the liver to release IGF (somatomedin C)
- GFs will be transported in the blood through IGF binding protein (IGFBP) then to the target tissue
- GH in this type of action depends on somatomedin
- somatomedin is responsible for effect of GH on bone & cartilage growth and increase the synthesis of protein in skeletal muscles.

→ Insulin-like growth factor (IGF): Somatomedin

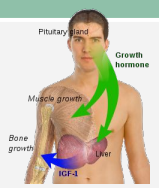


Growth Hormone (Somatotropin)

Functions of Growth Hormone

A) Long term effect Promotion of growth: Indirect effect

- ↑ cellular sizes & ↑ mitosis = ↑ tissue growth & organ size
- Depends on somatomedin 'insulin– like growth factor [IGF-I& II] secreted by the liver, which is responsible for effect of GH on bone & cartilage growth and increase the synthesis of protein in skeletal muscles.



Mechanism of bone growth

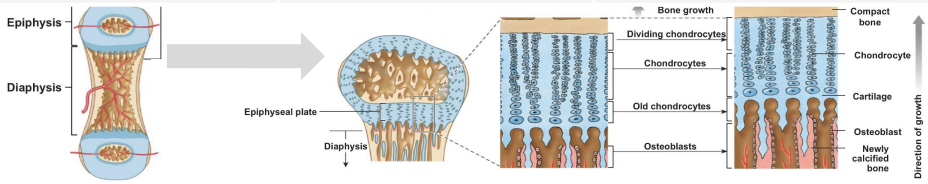
I. Linear growth of long bones:

- Long bones grow in length at epiphyseal cartilages, causing deposition of **New Cartilage** (↑collagen synthesis) followed by its conversion into bone.
- When bony fusion occurs between shaft & epiphysis at each end, no further lengthening of long bone occur.

1- Increase liner growth.
2- Increase metabolism in cartilage forming cells.
3- Increase proliferation of chondrocytes.
4- Widening of the epiphyseal plate.

2. Deposition of New Bone

- (↑ cell proliferation) on surfaces of older bone & in some bone cavities, ↑ thickness of bones
- Occurs hands, feets and in membranous bones, e.g. jaw, & skull bones, vertebrae.



B) Short term effects Metabolic effects: Direct effect

protein metabolism (Anabolic)

↑ rate of protein synthesis in all cells through:

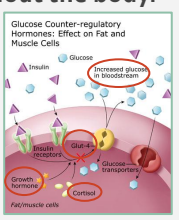
- ↑ amino acids uptake.
- ↑DNA synthesis / transcription= RNA synthesis.
- ↑RNA synthesis / translation= protein synthesis.
- ↓Protein catabolism "protein sparer"

Fat metabolism: (Catabolic)

- ↑mobilization of FFA from adipose tissue stores.
- Conversion of FFT to acetyl CoA to provide energy

CHO metabolism: Hyperglycemic

- ↓ Glucose uptake by tissues (skeletal muscles and fat).
- ↓ Rate of glucose utilization throughout the body.
- ↑Glucose production by the liver (↑ gluconeogenesis).
- ↑ Insulin resistance (due to↑FFA)
- ↑ Blood glucose (Diabetogenic)



*Cortisol & GH will inhibit glucose utilization causing increased glucose conc. extracellularly, thus cortisol should be used carefully for diabetic patients.

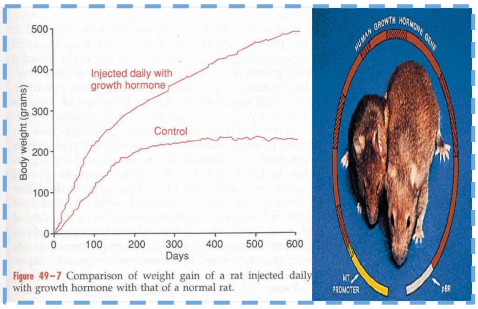
Other Effect of Growth Hormone GH

Female slides

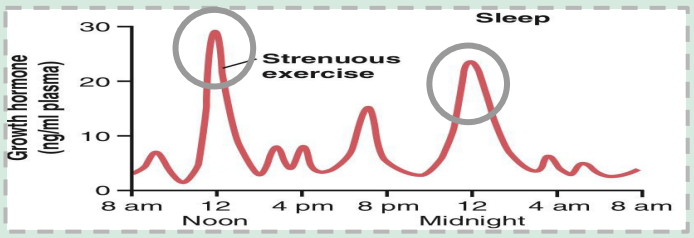
- Increases calcium absorption from GIT
- Strengthens and increases the mineralization of bone
- Retention of Na^+ and K^+
- Increases muscle mass
- Stimulates the growth of all internal organs excluding the brain
- Contributes to the maintenance and function of pancreatic islets
- Stimulates the immune system

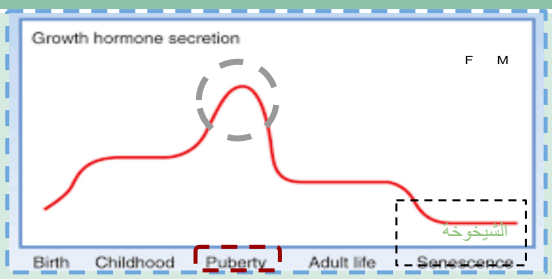
Growth Hormone (Somatotropin)

Here is a comparison between a rat injected with GH and another normal rat, you can see that in certain days, GH will not increase and will be balanced/controlled in the normal rat و هذا من حكمة الله, because in the injected rat we can see that the line is going up all days, this is basically what happened in case of Acromegaly.



Secretion





Typical Variations in growth hormone secretion through the day:

- Powerful effect during strenuous exercise.
- High rate during the first few hours of deep sleep.
- It is pulsatile every 2h.

During puberty, sex hormones will trigger the release of GH (estrogen, testosterone). That is why we grow mainly in puberty.

Important

↑GH secretion/ Stimulatory factors:

- Hypothalamus: GHRH
- Hypoglycemia (Fasting/starvation) =↓Glucose concentration
- Muscular exercise
- ↓FFAs concentration
- ↑Protein or AA intake (after meal)
- During sleep stage III & IV "deep sleep" in children
- Arginine
- Stress (emotions or trauma)
- Ghrelin (stomach)
- Hormones of puberty (estrogen)
- α-Adrenergic agonists

↓GH secretion/ inhibitory factors:

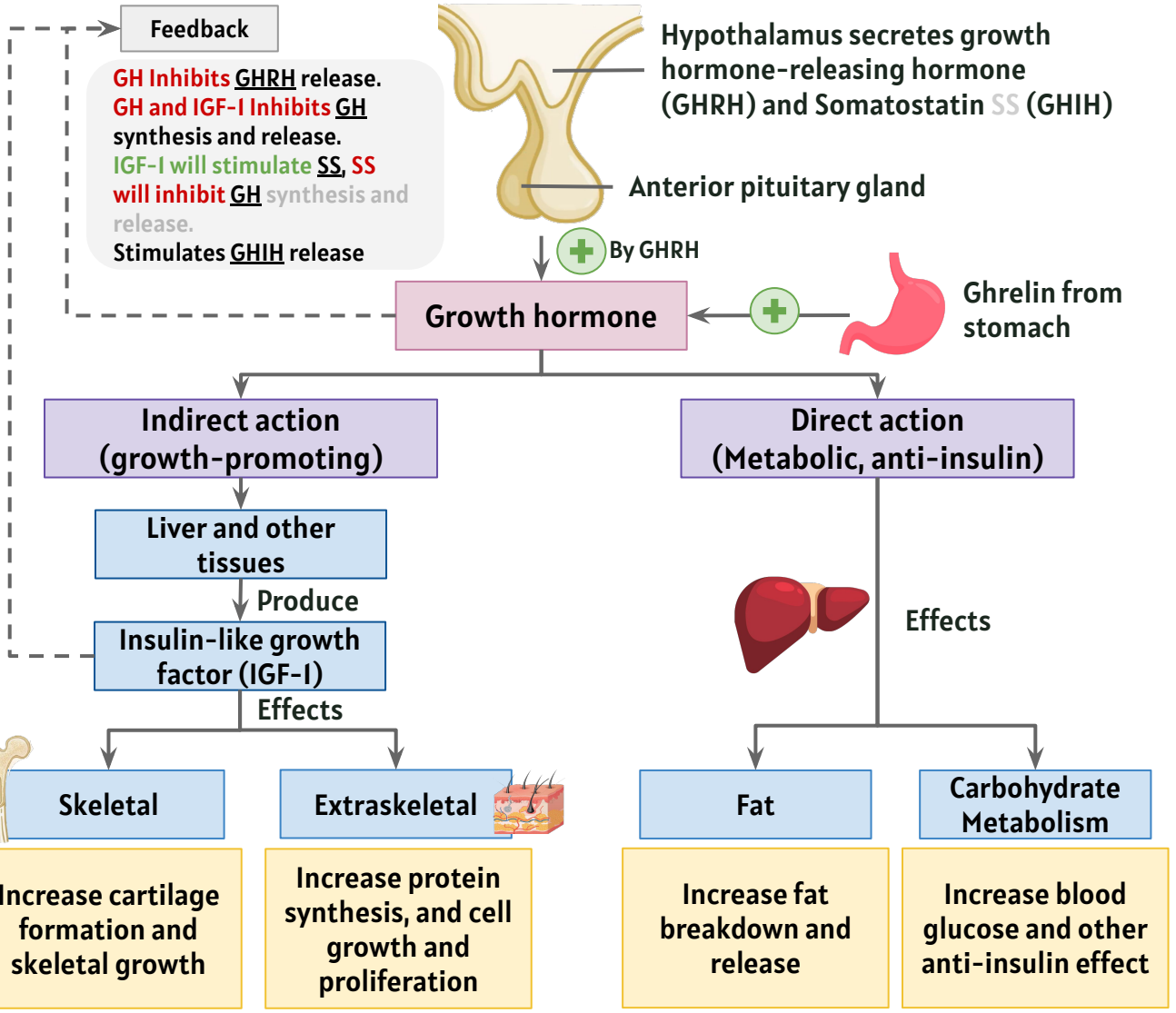
- Hypothalamus: GHIH (somatostatin)
- Hyperglycemia (↑Glucose intake) = ↑Glucose concentration
- Obesity
- ↑FFAs concentration
- Growth hormone
- Senescence
- Somatomedins (=IGF)
- Pregnancy
- β–Adrenergic agonists
- Emotional deprivation via either increased GHIH or decreased GHRH release

Growth Hormone (Somatotropin)

Increase, Stimulates
Reduces, Inhibits
Initial stimulus
Physiological response
Result

Feedback Mechanism

Female slides



Regulation & Effects

TABLE 16.1 Pituitary Hormones: Summary of Regulation and Effects

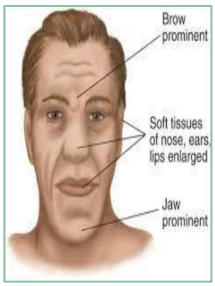
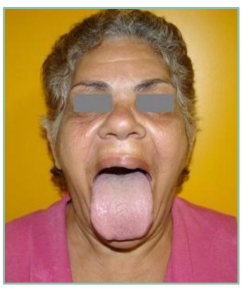
HORMONE (CHEMICAL STRUCTURE AND CELL TYPE)	REGULATION OF RELEASE	TARGET ORGAN AND EFFECTS	EFFECTS OF HYPOSECRETION ↓ AND HYPERSECRETION ↑
Anterior Pituitary Hormones			
Growth hormone (GH) (Protein, somatotroph)	**Stimulated** by GHRH* release, which is triggered by low blood levels of GH as well as 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

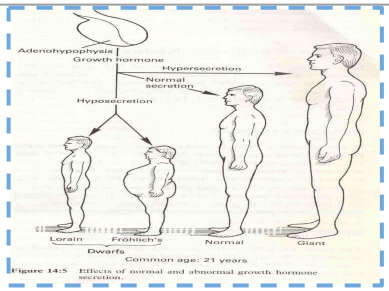
Growth Hormone (Somatotropin)

Abnormality of GH Secretion

GH/IGF-I hypersecretion

In childhood	In adult Important	In both
(Gigantism) ↑Height as it occurs before epiphyseal fusion of long bones with their shafts. • Often associated with tumor. • Octreotride.	**(Acromegaly)** Soft tissue continues 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, vertebrae. Protrusion of lower jaw. Hunched back (kyphosis) → vertebrae enlargement. Often associated with tumor. Treated by octreotide. Their height will not be changed.	Hyperglycemia (diabetes). + insulin resistance
 	 	

GH/IGF-I hyposecretion

In childhood	In adult
Pituitary dwarfism  - Causes? - Where?	Metabolism disorders Will not be shortened, but metabolic syndrome functions will be affected
 Figure 14:5 Effects of normal and abnormal growth hormone secretion.	

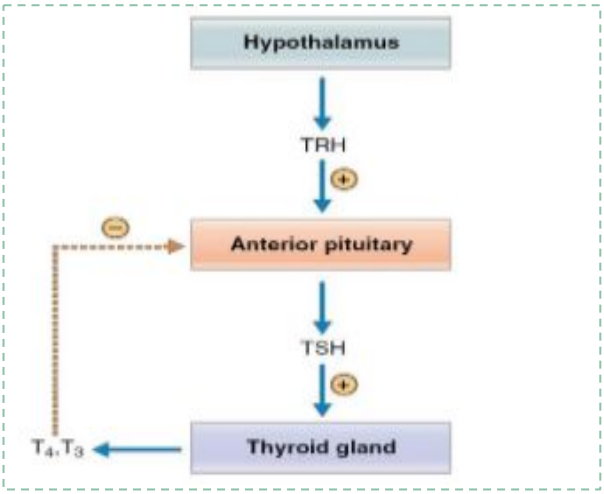
Other hormones produced by Anterior Pituitary gland

Hormone	Produced by	Chemical structure	
TSH	Thyrotrophs as glycoprotein (5%)	Related to FSH & LH	Have similar α subunit and different β subunit which is the active form of a hormone (functional subunit)
FSH	Gonadotrophs as glycoprotein (15%)	Related to TSH	
LH			
PRL	Lactotrophs (15%)	Related to GH	

TSH

Abnormalities

- Hyperthyroidism
- Hypothyroidism

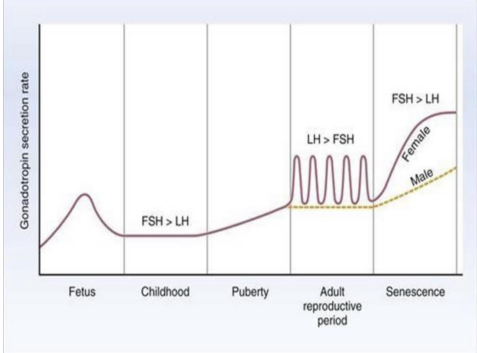


Action

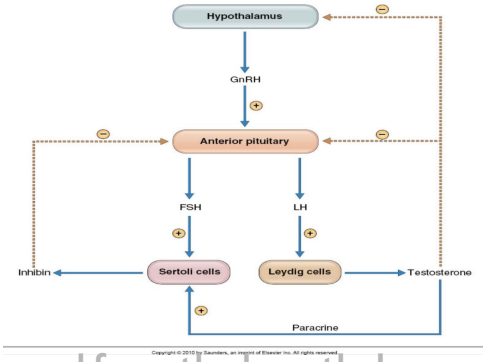
1- Increase synthesis and secretion of thyroid hormones.

2- Trophic effect.
Increase the size and the number of cells of the thyroid gland

FSH & LH



During childhood the FSH is more than LH but in the **adult reproductive period** it fluctuate and **LH will be more than FSH**, lastly during senescence FSH is more than LH(same as childhood)



GnRH released from the hypothalamus will stimulate the anterior pituitary gland to secrete FSH and LH.
LH will stimulate leydig cells to release testosterone, which will inhibit AP & hypothalamus and stimulate sertoli cells.
FSH will stimulate sertoli cells (which are also stimulated by testosterone) to secret inhibin which inhibits AP.

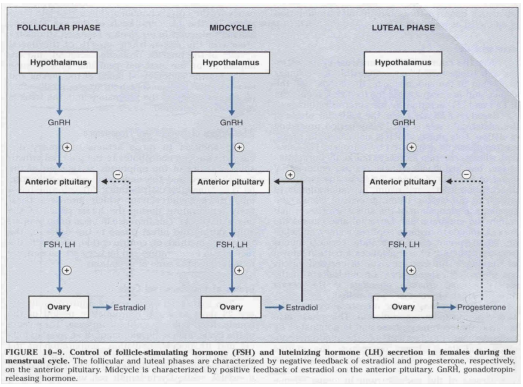
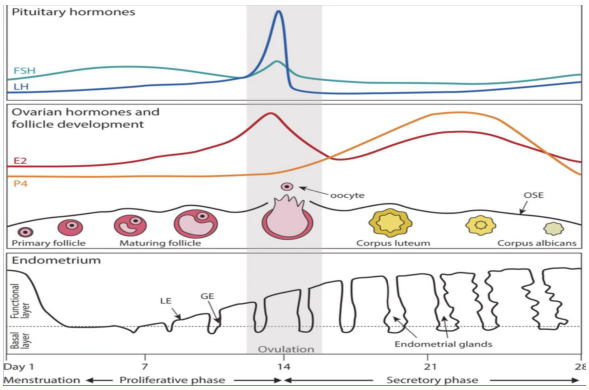


FIGURE 10–9. Control of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) secretion in females during the menstrual cycle. The follicular and luteal phases are characterized by negative feedback of estradiol and progesterone, respectively, on the anterior pituitary. Midcycle is characterized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

Follicular phase: estradiol inhibits AP (**negative** feedback)
Mid cycle: estradiol stimulate AP (**positive** feedback)
Luteal phases: progesterone inhibits AP (**negative** feedback)



During **ovulation** there will be a great **increase in LH and Estradiol** and minimal changes on FSH and Progesterone

Prolactin

Female slides

The major function of prolactin is **milk production.**

Related to GH

Produced by Lactotrophs(15%)

Composed of 198 amino acids

Effect on breast

- I- Breast development
- 2- ↑ mRNA
- 3- Lactogenesis: production of milk proteins: ↑ Casein, lactose, lipid and lactalbumin

Other effects

- I-Inhibits the effects of gonadotropins. ↓GnRH
  - Inhibits ovulation
  - ↑Parturition
- 2- ↑ Dopamine secretion in median eminence (Inhibit its own secretion)

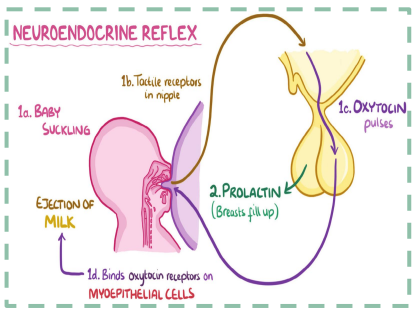
Control of Prolactin secretion

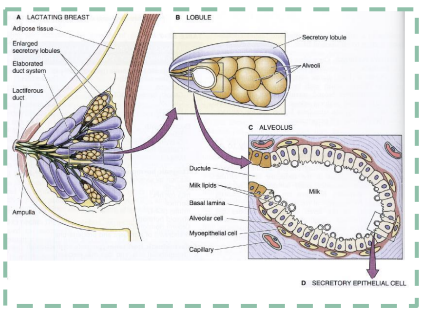
Stimulators

- Stimulation of the nippple (suckling)
- Sleep
- Surgical & psychological stress
- Exercise
- TRH: thyrotropin-releasing hormone
- Dopamine antagonist/inhibitors
- Pregnancy (estrogen)

Inhibitors

- PIH "Dopamine"
  - Source of dopamine:
    - Hypothalamus (major)
    - Posterior pituitary gland
  - There's small portal connection between posterior pituitary and anterior that why it affect prolactin release
  - Non-lactotrophs cells of anterior pituitary gland (minor)
- Dopamine agonist (bromocriptine)
- Prolactin (-ve feedback)
- Somatostatin





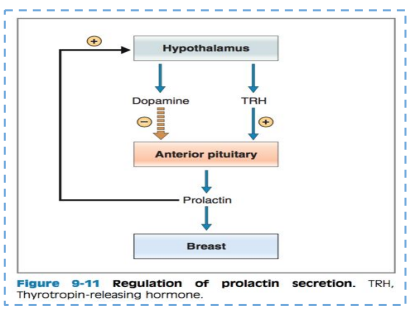
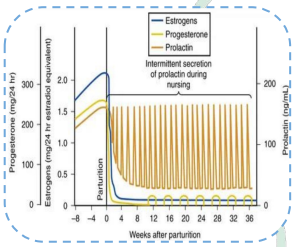


Figure 9-11 Regulation of prolactin secretion. TRH, Thyrotropin-releasing hormone.



Prolactin Abnormalities

Increase prolactin level prevents pregnancy

Hyperprolactinemia

↑ Prolactin excess
Galactorrhea (Amenorrhea) and Infertility.

Treated by **Bromocriptine**
(D2 Receptor Agonists)

Hypoprolactinemia

↓ Prolactin deficiency
Failure to lactate.

Girls Dr: Increase in prolactin level in pregnant women (that's why breasts increase in size during pregnancy) prolactin continue to rise until it reaches its highest level before childbirth immediately, after delivery it will decrease and suckling will increase its level again (439)

ACTH

Produced by Corticotrophs(15%)

Function: Stimulate synthesis and secretion of adrenal cortical hormones

Preproopiomelanocortin (POMC) is the pituitary precursor of circulating melanocyte stimulating hormone **(α-MSH)**, adrenocorticotropic hormone **(ACTH)**, **β-endorphin.**

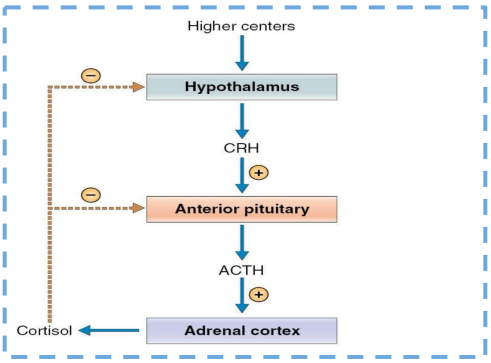
Control of ACTH Secretion

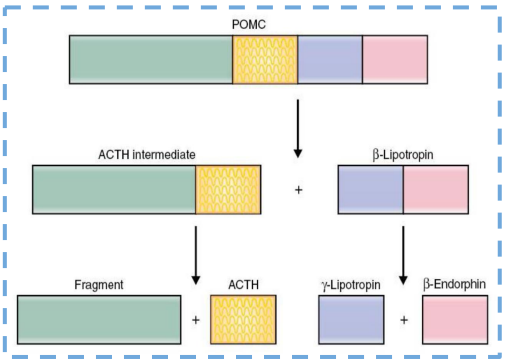
Stimulatory Factors

- ↓Blood cortisol level (Hypoglycemia)
- Stress (trauma-surgery)
- Sleep-wake transition

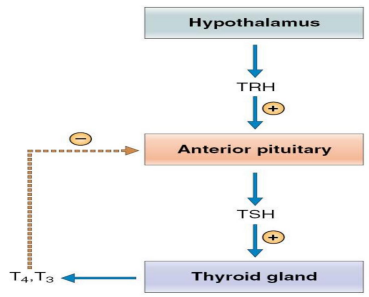
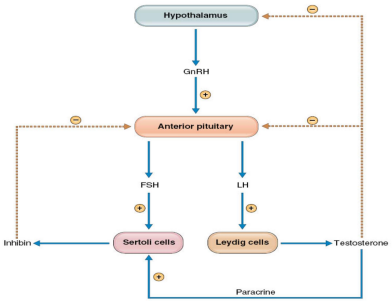
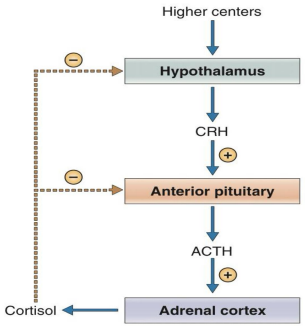
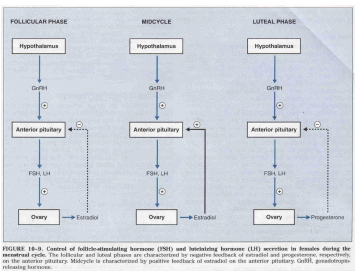
Inhibitory Factors

- ↑ Blood cortisol level





Other Hormones produced by A. Pituitary

	TSH	FSH & LH	ACTH
Introduction	- Thyrotrophs.(5%) - Glycoproteins. - (α and β) - Related to FSH and LH. (Due to similar structure, they have the same α unit but different β)	- Glycoproteins. - Gonadotrophs (15%) - α and β. - Related to TSH.	- Corticotrophs.(15%) - ACTH, MSH, β-endorphin. - Pre Proopiomelanocortin (POMC).
Actions	1- Increase synthesis and secretion of thyroid hormones. 2- Trophic effect (change in size of the gland, if we increase the stimulus of thyroid hormone but T3+T4 still low, the stimulation will increase even more causing increasing of the gland size)	**FSH:** promotes gamete production and stimulates estrogen production in females **LH:** stimulates sex hormone, ovulation, corpus luteum formation in females & testosterone secretion in males.	Stimulate synthesis and secretion of adrenal cortical hormones.
Regulation	 Hypothalamus secretes TRH stimulation thyrotrophs of anterior pituitary to secrete TSH acting on thyroid gland and this results in -ve feedback by releasing T4, T3	 Once anterior pituitary gets stimulated by GnRH coming from hypothalamus it releases: 1) LH stimulating leydig (adjacent to testicles tubules) cells to secrete testosterone resulting in -ve feedback. 2) FSH stimulating Sertoli cells (work on spermatogenesis in testicles) to secrete inhibin resulting in -ve feedback.	 CRH released from the hypothalamus and stimulate the Ant.pituitary gland to release another hormone(ACTH) that act on adrenal cortex so they release Cortisol ,and it will cause the negative feedback when it's increased to maintain it within the normal value .
Factors affecting the secretion	Stimulatory: TRH Inhibitory: T3, T4 Other factors including psychopathy, neuropathy and dopamine (dual effect)...	Stimulatory: GnRH Inhibitory: sex steroids and inhibin (for FSH)	Stimulatory factors: 1. Decreased blood cortisol level. 2. Sleep wake transition. 3. Stress. Inhibitory factors: 1. Increase blood cortisol level
Abnormalities	1) Hyperthyroidism (More hormones in circulation) 2) Hypothyroidism	-	-
Pictures	-		-

MCQs:

QI: Which of the following inhibit the release of ACTH

A- Decreased cortisol levels | B- Elevated cortisol levels | C- Psychological stress | D- Dopamine secretion

Q2: A patient presented to you with protrusion of the lower jaw which of the following could be the cause :

A- Increased prolactin levels | B- Decreased GH levels | C- Tumor of the anterior pituitary | D- Drug-drug interaction

Q3: Which of the following is a direct function of GH

A- Diabetogenic effect | B- Increases bone length | C- Milk production "lactation" | D- Causes tissue growth

Q4: Which one of the following has greater effect in stimulating GH

A- Exercise | B- hypoglycemia | C- Sleep | D- pulsatile effect

Q5: Which of the following is true about GH

A- Composed of 198 Amino acids | B- Composed 2 Amino acids | C- Composed 191 Amino acids | D- Composed 200 Amino acids

Q6: What is the major source of dopamine in prolactin regulation

A- Hypothalamus | B- Non-lactotrophs cells of anterior pituitary | C- Posterior pituitary | D- Drugs such as "bromocriptine"

Q7: Which one of the following is Not an action of GH on carbohydrates?

A.Anti-insulin activity | B.increase the number of insulin receptor. | C. Suppresses uptake of glucose in peripheral tissue. | D. Enhance hepatic glucose output

Answers: QI: B | Q2: C | Q3: A | Q4: A | Q5: C | Q6: A | Q9: B

SAQ:

- **Q:I. How growth hormone effects carbohydrates metabolism?**
- **Q:2.what is the role of somatomedin?**

AI:

- ↓Glucose uptake by tissues (Skeletal muscles & fat) → glucose level will be raised in blood (hyperglycemia)
- ↓Rate of glucose utilization throughout the body
- ↑Glucose production by the liver (↑Gluconeogenesis)
- ↑Insulin resistance (Diabetogenic)

A2: GH does not show any direct action on bones. It acts on the bones through a substance called somatomedin, which is secreted by the liver.

Team Leaders

Norah Al Mania

Ayedh Al Qantash

Sadeem Alyahya

Mohammed AlKodhari

Team Members

Remas Al Jeaidi

Layan Al Ruwaili

Reena Al Sadoni

Jana Al Mutlaqah

Renad M Al Shehri

Jouri Al Maymoni

Remaz Al Mahmoud

Aljoharah Al Wohaibi

Shoug Al Khalifa

Rafan Alhazzani

Milaf Al Otaibi

Shahad Al Zaid

Aseel Al Shehri

Almas Al Mutairi

Afnan Al Ahmari

Rawan Al Qahtani

Faisal Al Showier

Abdullah Al Assiri

Yousof Badoghaish

Zeyad Al Otaibi

Aban Basfar

Feras Mazen

Faisal Al Abdullah

Nazmi A Al Qutub

Nazmi M Al Qutub

Osama Al Mashjari

Hamad Al Ziyadi

Mohammed Al Qutub

Mansour Al Dossari

Abdulmalik Al Shammakhi

Waleed Al Rasheed

Faisal Al Ateeq

Ryan Al Ghizzi

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