Physiology Team 439

MED439
KING SAUD UNIVERSITY

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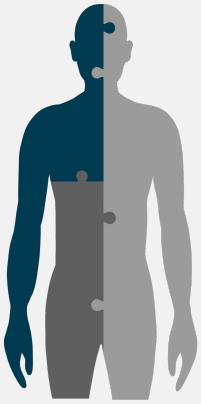


Anterior pituitary gland

Objectives:

- List Anterior Pituitary Hormones (Chemical structure Secretion)
- Describe actions of Anterior Pituitary hormones
- Mechanism of action of hormones (Hormone receptors, down-regulation and up-regulation, Intracellular signaling, Second messenger mechanism)
- Know conditions related to hypo or hyper secretion of Anterior Pituitary hormones

Color index:

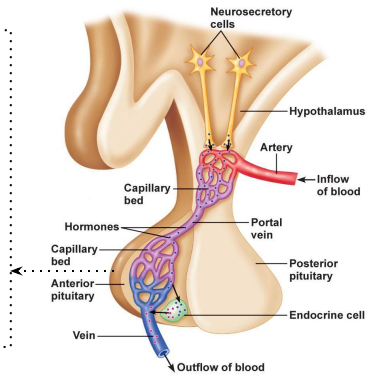
- Important.
- Girls slide only.
- Boys slide only.
- Dr's note.
- Extra information.

Editing File

Anterior pituitary gland

Anterior Lobe of pituitary gland is called " Adenohypophysis":
Adeno = Glandular part
Hypophysis = Pituitary gland

Anterior pituitary gland is connected to hypothalamus by portal system: " hypothalamic-hypophyseal portal vessels ".



Portal vessels are vessels that connect two capillary beds

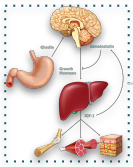
GH | Prolactin | TSH | LH | FSH | ACTH

Growth Hormone

useful video

Actions

In childhood & Adolescent — Regulates growth & metabolism



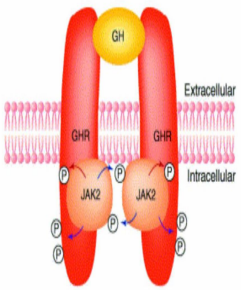
GHRH is produced by the hypothalamus it works on the anterior pituitary gland and stimulates the release of GH , GH goes to the liver and promotes the secretion of IGF-1 , IGF-1 works on the muscles , bones and adipose tissue for growth.
Ghrelin is released by the stomach and intestine it has a positive feedback on growth , which makes sense for example , when someone eats , the anterior pituitary gland will release GH to use these nutrients in growth

In Adults — Energy metabolism

- Somatotropic hormone, somatotropin. ▪ Somatotrophs.(20%). ▪ 191 AA. ▪ MW 22000 kD. ▪ GHRH
- The effect on growth is mediated through: [Insulin-like growth factor – IGF-1]/ [somatomedin C], which is secreted by the liver.
- Growth stops with the closure of the epiphysis epiphysis: growing plates in long bones

MOA

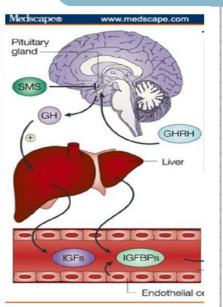
Direct



Skeletal muscles, liver and adipose.

GH is a protein hormone it doesn't enter the cell it connect to the receptor on the cell surface
Second messenger:phosphorylation

Indirect



4500-7500 MW.
Somatomedin C.
SOMATOMEDINS (IGFs)

Anterior pituitary gland releases GH which acts on the liver to secret IGFs(insulin like growth factor), then IGFs works on the muscles , bones and adipose tissue for growth

Growth Hormone

Functions

Growth

Increase cellular sizes, mitosis , tissue growth and organ size

Long term effect

Indirect effect

Depends on somatomedin C "insulin–like growth factor" [IGF- I&II] secreted by the liver, which is responsible for effect of GH on bone & cartilage growth & increase the synthesis of protein in skeletal muscles.

Mechanism of Bone growth*

Linear growth of long bones :
When bony fusion occurs between shaft & epiphysis at each end, no further lengthening of long bone occur.

Deposition of New Bone (cell proliferation of chondrocytes) on surfaces of older bone & in some bone cavities, it increase the thickness of bone : Occurs in membranous bones, e.g. jaw & skull bones.**Widening of the epiphyseal plate.**

Protein

Anabolic metabolism
Increase rate of protein synthesis in all cells through:

1. Increase amino acids transport into cells
2. Increase DNA transcription = RNA synthesis.
3. Increase RNA translation = protein synthesis.
4. Decrease protein catabolism "protein sparer".
   To save the already formed protein.

Short term effect

Fat

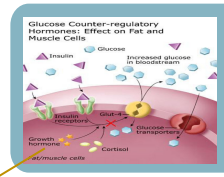
Catabolic metabolism

Mechanism

Stimulate mobilization of FFAs from adipose tissue stores.

Conversion of FFT to acetyl CoA to provide energy.
(FFA → Acetyl-coA→ Energy.)

CHO



Hyperglycemic metabolism

Most of the hormones can cause hyperglycemia (insulin antagonist) , while Insulin is almost the only one that causes hypoglycemia so when there is no insulin hyperglycemia will appear because there is no any hormone that do insulin's function.

Growth hormone Stops absorption of glucose in cell by inhibiting Glut

Mechanism

Decrease Glucose uptake by tissues (skeletal muscles & fat).

Increase glucose production by the liver (gluconeogenesis)

Insulin resistance Insulin antagonist (Diabetogenic)

Growth Hormone

Other effects*

- Increases calcium absorption from GIT.
- Strengthens & increases the mineralization of bone.
- Retention of Na+ and K+.
- Increases muscle mass.
- Stimulates the growth of all internal organs excluding the brain.
- Stimulates the immune system.

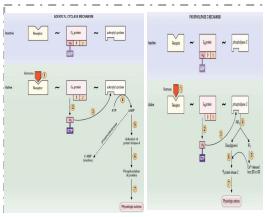
Control of secretion

Increase the secretion

- GHRH
- Hypoglycemia (fasting)
- Muscular exercise
- Intake of protein/amino acids (after meals).
- sleep
- Stress conditions, e.g. trauma or emotions defense mechanism
- Ghrelin (stomach) more nutrients more growth

Decrease the secretion

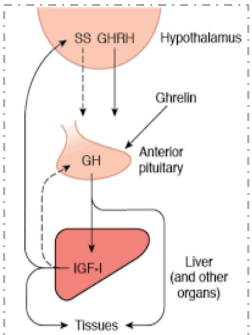
- GHIH (somatostatin)
- hyperglycemia (high glucose intake)
- FFAs GH increases FFAs and FFAs decrease GH secretion



GHRH-> receptor->Gs protein->Adenylyl cyclase and phospholipase C->cAMP and IP3/Ca->secretion +synthesis.

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

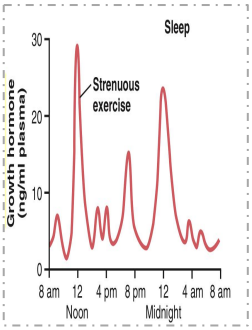
Typical variations in growth hormone secretion throughout the day, demonstrating the especially powerful effect of strenuous exercise and also the high rate of growth hormone secretion that occurs during the first few hours of deep sleep it is pulsatile every 2 hours GH is secreted in a pulsatile pattern



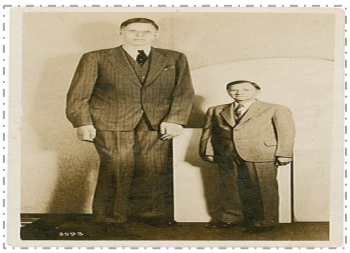
- Hypothalamus releases two hormones:
  1-GHRH which increase GH secretion
  2- SS (GHIH) which decrease GH secretion
- An increase in IGF-1 will cause negative feedback on GH and positive feedback on SS

Table 9–4 Factors Affecting Growth Hormone Secretion

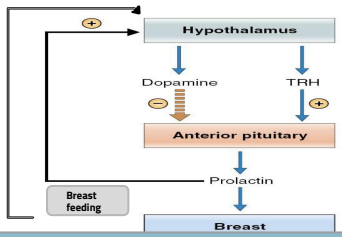
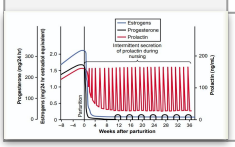
Stimulatory Factors	Inhibitory Factors
Decreased glucose concentration	Increased glucose concentration
Decreased free fatty acid concentration	Increased free fatty acid concentration
Arginine	Obesity
Fasting or starvation	Senescence
Hormones of puberty (estrogen, testosterone)	Somatostatin
Exercise	Somatomedins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

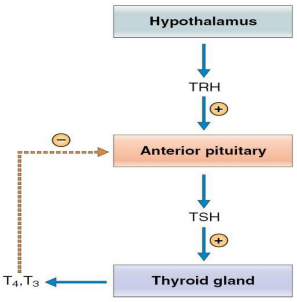
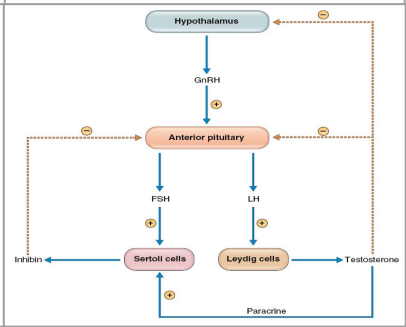
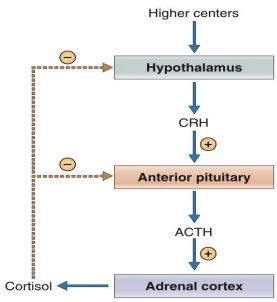
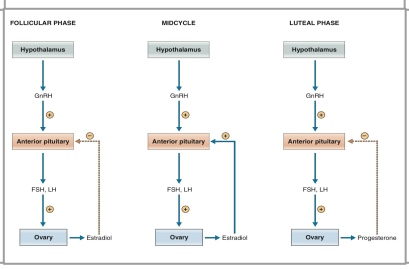


Abnormalities details from girls slides only

Childhood	**Gigantism** (Hypersecretion)	❖ the acidophilic, growth hormone-producing cells of the anterior pituitary gland become excessively active. ❖ All body tissues grow rapidly, including the bones. ❖ If the condition occurs before adolescence, height increases so that the person becomes a giant-up to 8 feet tall. ❖ Increased Height as it occurs before epiphyseal fusion of long bones with their shafts. ❖ Hyperglycemia (diabetes).	
	Dwarfism (Hyposecretion)	❖ Usually results from generalized deficiency of anterior pituitary secretion (panhypopituitarism) Decrease in all anterior pituitary hormones during childhood. ❖ Body parts develop in appropriate proportion to one another, but the rate of development is decreased. ❖ panhypopituitary dwarfism does not pass through puberty. ❖ However, only growth hormone is deficient; these persons do mature sexually and occasionally reproduce. If decreased production in adulthood will result in metabolic effects only ❖ where and causes? 1- Hypothalamus: lack of GHRH 2- Anterior pituitary: lack of GH 3- Target tissue: lack of receptor	
Adults	**Acromegaly** (Hypersecretion)	❖ Acidophilic tumor occurs after adolescence (after closure of the epiphyses of long bones) i.e. the person cannot grow taller, but the bones can become thicker and the soft tissues can continue to grow. ❖ 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, vertebrae. ❖ Protrusion of lower jaw ❖ Hunched back (kyphosis)(enlargement of vertebrae). ❖ Hyperglycemia (diabetes). ❖ Hypersecretion Often associated with tumor ▪ Gigantism. ❖ ▪ Acromegaly. ❖ ▪ Octreotride.	 

Prolactin

Overview	▪ Lactotrophs.(15%) ▪ 198 AA. ▪ Related to GH. ▪ Highest level is found at term.	
Actions*	**Effect on the breast**	- The major function of prolactin is milk production - Breast development. (Increase in all factors that make mammary glands produce milk) - Lactogenesis. (Lactose, lipid, casein) Parturition. - Increases mRNA and Increases production of casein and Lactalbumin. **- Other effects:** Stimulates the secretion of dopamine in median eminence (inhibits its own secretion).
	During Pregnancy	Growth of mammary glands. (no milk production due to the inhibitory effect of placental hormones) (The high levels of estrogen and progesterone, which are required to maintain pregnancy, will inhibit milk production)
	After delivery	PRL initiates and maintains milk production. (suckling stimulation . PRL release) The placenta detaches -> estrogen and progesterone levels will decrease -> Prolactin will increase.
	Gonadotropins	Inhibits the effects of gonadotropins (Inhibition of ovulation "GnRH"). Decreases the sensitivity of ovaries to gonadotropins FSH / LH leading to suppression of menstrual cycle. Occurs in 50% of lactating women, physiological birth control. As long as she is lactating their will be no ovulation and no menstruation because of the gonadotrophins inhibition, but this is not sufficient for birth control, abolishing of gonadotrophins inhibition can occur and ovulation happens while the menstruation is absent and she gets pregnant because ovulation appears before menstruation. Why will it lead to infertility? Increase in Prolactin -> Inhibit the release of GnRH from hypothalmus -> derease in LH and FSH -> No ovulation or menstrual period.
	Limbic system	Producing the characteristic maternal and nursing behavior.
Regulation of secretion*	- TRH → stimulates the production of prolactin - Dopamine → inhibits the production of prolactin. - Prolactin Stimulates the secretion of dopamine in median eminence (inhibits its own secretion) (negative feedback). - other than breastfeeding, the hypothalamus continuously secrets dopamine (Tonic inhibition) - Breastfeeding→ will inhibit the inhibitor which is Dopamine.	
Control of secretion	**Increase the Secretion (Stimulatory factors)** ❖ Pregnancy (Estrogen) ❖ Breast feeding (Suckling inhibits PIH release leading to increase prolactin release.) ❖ TRH ❖ Stress ❖ sleep/exercise ❖ Dopamine antagonists ❖ Chest wall stimulation or truma	**Decrease the Secretion (Inhibitory factors)** ❖ Dopamine ❖ Dopamine agonist (bromocriptine, metoclopramid) ❖ Somatostatin ❖ PRL (negative feedback))
Source of Dopamine*	- Dopaminergic neuron in the hypothalamus (major). - Dopaminergic neuron in the posterior pituitary gland. - Non lactotrophs cells of the anterior pituitary gland (very small amount).	
Abnormalities*	- Prolactin deficiency → Failure to lactate. - Prolactin excess → Galactorrhea and Infertility.	Excessive prolactin Treated by Bromocriptine (Dopamine agonist).
	All these hormones increase during parturition(pregnancy) After parturition prolactin levels will be increased cuz it's not blocked by estrogen and progesterone 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	

In male slides only	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)	**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 stimulating thyrotrophes 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 inhibin (for FSH)	**Stimulatory factors:** Decreased blood cortisol level Sleep wake transition Stress **Inhibitory factors:** Increase blood cortisol level  Table 9–10 Factors Affecting ACTH Secretion Stimulatory Factors: Decreased blood cortisol levels; Sleep-wake transition; Stress; hypoglycemia; surgery; trauma; Psychiatric disturbances; ADH; α-Adrenergic agonists; β-Adrenergic antagonists; Serotonin Inhibitory Factors: Increased blood cortisol levels; Opioids; Somatostatin
Abnormalities	1) Hyperthyroidism (More hormones in circulation) 2) Hypothyroidism	-	-
Pictures			

Summary

Hormones	Action	Control of secretion	Abnormalities
Growth Hormone	1- Regulates growth (by Insulin-like growth factor) through linear growth of long bone and deposition of new bone 2- Anabolic metabolism (Protein) 3- Catabolic metabolism (Fat) 4- Hyperglycemic metabolism (CHO) 5- Energy metabolism 6- Increases calcium absorption from GIT. 7- Strengthens & increases the mineralization of bone. 8- Retention of Na+ and K+. 9- Increases muscle mass. 10- Stimulates the immune system.	**Increase the secretion**: - GHRH - Hypoglycemia (fasting) - Muscular exercise - Intake of protein/amino acids (after meals). - sleep - Stress conditions, e.g. trauma or emotions - Ghrelin (stomach) **Decrease the secretion** - GHIH (somatostatin) - hyperglycemia (high glucose intake) - FFAs	**In childhood:** **Gigantism** (Increase Secretion) **Dwarfism** (Decrease Secretion) In Adult: **Acromegaly** (Increase Secretion)
Prolactin	1- **During Pregnancy** (Growth of mammary glands) 2- **After delivery** (PRL initiates and maintains milk production) 3- Decreases the sensitivity of ovaries to **gonadotropins** 4- **On Limbic system** (Producing the characteristic maternal and nursing behavior)	**Increase the secretion** - Estrogen - Breast feeding - TRH - Stress - sleep/exercise - Dopamine antagonists - Chest wall stimulation or truma **Decrease the secretion** - Dopamine - Dopamine agonist - (bromocriptine, metoclopramid) - Somatostatin - PRL	Prolactin deficiency → Failure to lactate. - Prolactin excess → Galactorrhea, Infertility,
TSH	1- Increase synthesis and secretion of thyroid hormones. 2- Trophic effect.	**Stimulatory:** TRH **Inhibitory:** T3, T4	1) Hyperthyroidism 2) Hypothyroidism
FSH	promotes gamete production and stimulates estrogen production in females	**Stimulatory:** GnRH **Inhibitory:** sex steroids inhibin (for FSH)	-
LH	stimulates sex hormone, ovulation, corpus luteum formation in females & testosterone secretion in males		-
ACTH	Stimulate synthesis and secretion of adrenal cortical hormones.	**Stimulatory factors:** Decreased blood cortisol level Sleep wake transition Stress **Inhibitory factors:** Increase blood cortisol level	-

MCQ & SAQ:

Q1: What's acromegaly?

A. generalized deficiency of anterior pituitary secretion during childhood.
B.Basophilic tumor occurs after adolescence
C. Acidophilic tumor occurs after adolescence
D. Increased Height .

Q2: which of the following stimulates LH secretion?

A. Testosterone
B. TRH
C. GnRH
D. Low FSH

Q3: Which one of the following is a metabolic effect caused by GH

A. Protein catabolism
B. Fat breakdown
C. ↓blood glucose level
D. None

Q4: What is the role of T4,T3 in regulating TSH secretion?

A. Act on thyroid gland as a negative feedback
B. Act on thyroid gland as a positive feedback
C. Act on anterior pituitary as a negative feedback
D. Act on anterior pituitary as a positive feedback

Q5: Short-term effect of GH ?

A.Increase cell size
B.Increase organ size
C. Increase glucose uptake
D. Increase glucose production

Q6: **Which of the following anterior pituitary hormones plays a major role in the regulation of a nonendocrine target gland?**
A. Prolactin
B. Adrenocorticotropic hormone
C. Thyroid-stimulating hormone
D. Follicle-stimulating hormone

answer key:
1: C
2: C
3:B
4: C
5: D
6:A

1- What increase the secretion of Growth Hormone?

2- List the functions of GH

3-What is the Physiological action of TSH ?

4- What is the role of prolactin on Gonadotropins

A1: GHRH /Hypoglycemia (fasting)/Muscular exercise/Intake of protein/amino acids (after meals)./sleep/Stress conditions, e.g. trauma or emotions/Ghrelin (stomach)

A2: increases skeletal growth / increases muscular growth / increased use of lipids for energy (slide 5)

A3: 1- Increase synthesis and secretion of thyroid hormones. 2- Trophic effect.

A4: decreases the sensitivity of ovaries to gonadotrophins leading to suppression of menstrual cycle.

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