جامعة الملك سعود
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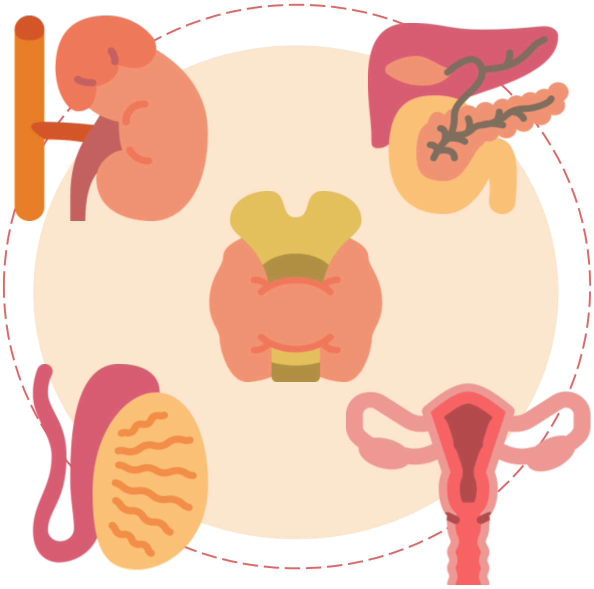

Anterior pituitary gland

Objectives:

- Anterior pituitary hormones
  - GH
    - Physiological functions
    - Regulation of GH secretion
      - Feedback mechanism
      - Factors controlling secretion
  - Prolactin
    - Physiological functions
    - Regulation of prolactin secretion

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Colour index:
- Important
- Numbers
- Extra

وَأَن لَّيْسَ لِلْإِنسَانِ إِلَّا مَا سَعَىٰ

Males

Anterior pituitary hormones

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

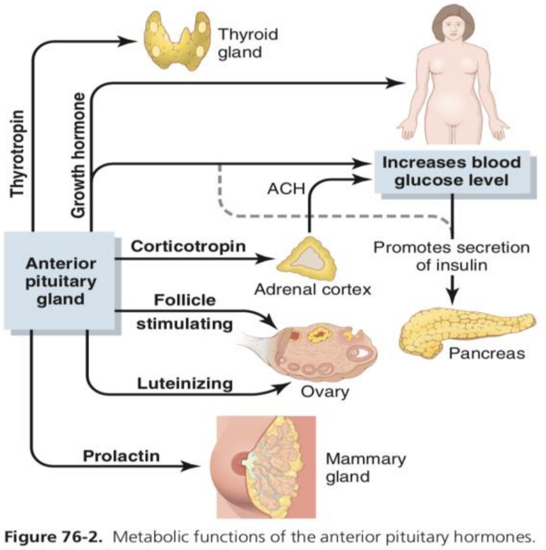


Figure 76-2. Metabolic functions of the anterior pituitary hormones. ACH, adrenal corticosteroid hormones.

Growth hormone

- Synthesized by Somatotrophs (20%)
- 191 AA
- Somatotropic hormone, Somatotropin
- MW 22000kD
- GHRH (ventromedial nucleus)

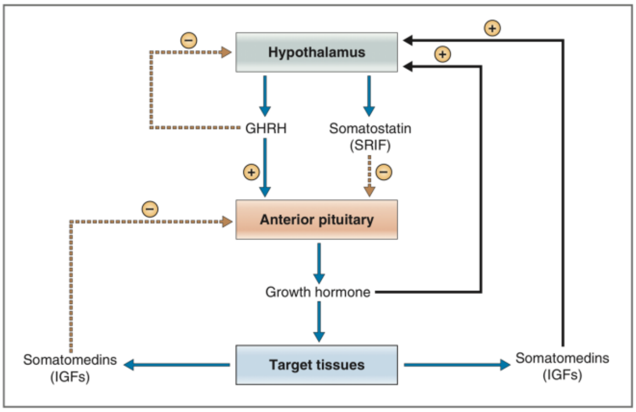


Fig. 9.11 Regulation of growth hormone secretion. *GHRH*, Growth hormone–releasing hormone; *IGF*, insulin-like growth factor; *SRIF*, somatotropin release–inhibiting factor.

Growth hormone

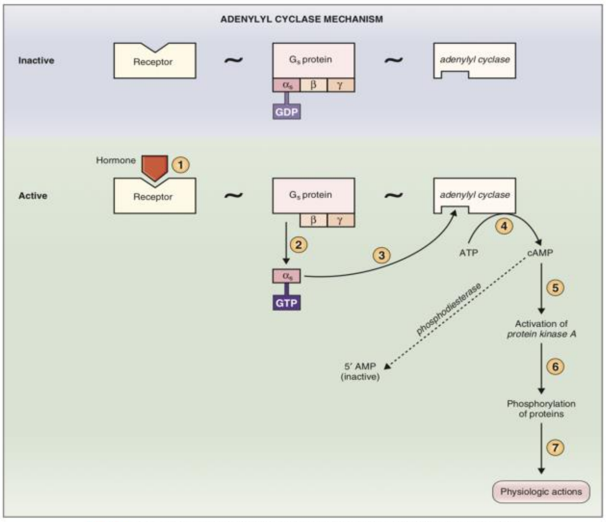


Fig. 9.4 **Steps involved in the adenylyl cyclase (cAMP) mechanism of action.** See the text for an explanation of the circled numbers. *AMP,* Adenosine monophosphate; *ATP,* adenosine triphosphate; *cAMP,* cyclic adenosine monophosphate; *GDP,* guanosine diphosphate; *GTP,* guanosine triphosphate.

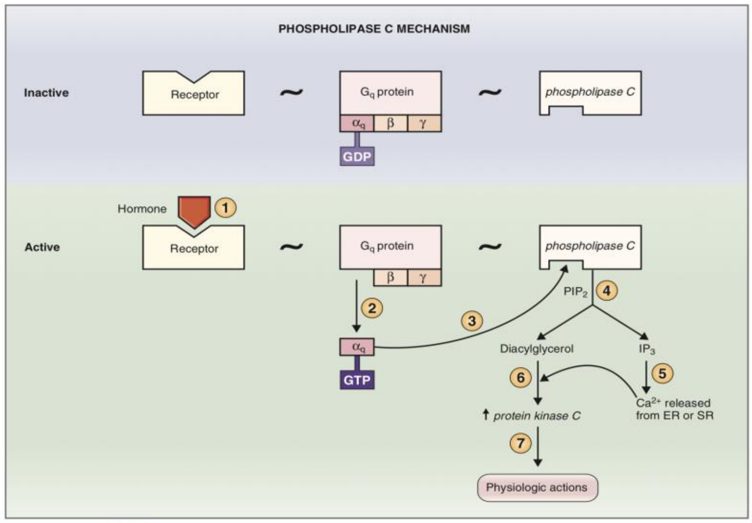


Fig. 9.5 **Steps involved in the phospholipase C (IP_3/Ca^{2+}) mechanism of action.** See the text for an explanation of the circled numbers. *ER,* Endoplasmic reticulum; *GDP,* guanosine diphosphate; *GTP,* guanosine triphosphate; *IP_3,* inositol 1,4,5-triphosphate; *PIP_2,* phosphatidylinositol 4,5-diphosphate; *SR,* sarcoplasmic reticulum.

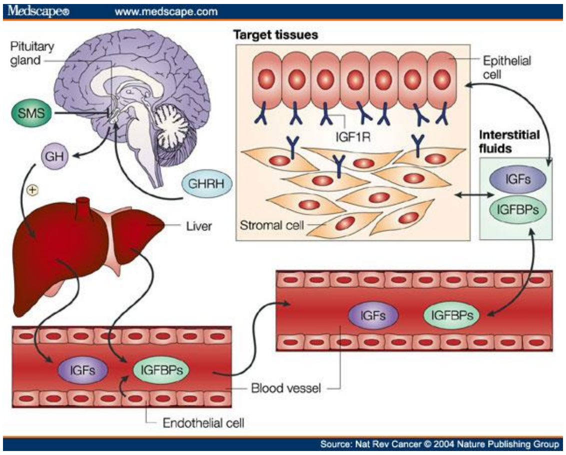
- GHRH → receptor → Gs protien → Adenylyl cyclase and phospholipase C → cAMP IP3/Ca → secretion + synthesis
- Somatostatin (SRIF) → receptor Gi → inhibit generation of cAMP →Decrease secretion

Males

Mechanism of action

Indirect effect (somatomedins)

Somatomedin C



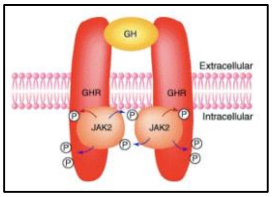
GH is long chain amino acid,

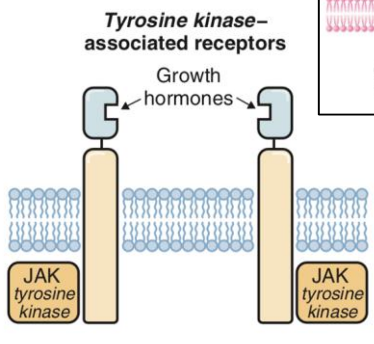
1. Dissolves in blood (doesn't need carrier), but it have fast clearance = 20 mins.
2. IGF (insulin like growth factor 1) binds to transfer protein (Insulin like growth factor binding protein), which protect IGF from the fast clearance and increase its time.
3. IGF binds to Its receptor (IGF-1 Receptor)

Direct effect

Skeletal muscles, liver and adipose.

GH is very long chain of amino acid so it need receptor.
{Enzyme linked ,one pass receptor}
Enzyme linked: When the hormone is attached to its receptor it will start stimulating enzymes inside the cell.





C **Growth hormone receptor**

Functions of Growth Hormone

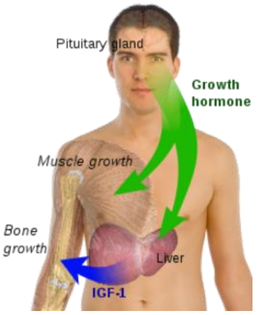
Long Term Effect

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

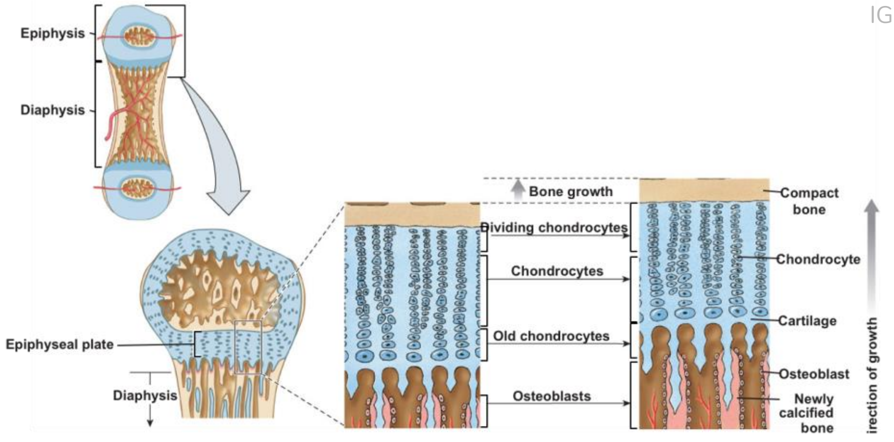
1. Linear growth of long bones:
- Long bones grow in length at epiphyseal cartilages between epiphysis and diaphysis, causing deposition of New Cartilage (↑ collagen synthesis) followed by its conversion into bone.
- When bony fusion occurs between shaft & epiphysis at each end, <u>no further lengthening</u> 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 (flat bone), e.g. jaw, & skull bones. and hands/ feet

Indirect effect
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.



IGF works on bones and muscles



Functions of Growth Hormone

Short Term Effect

Metabolic Effects

Protein metabolism (Anabolic)

↑ rate of protein synthesis in all cells through:

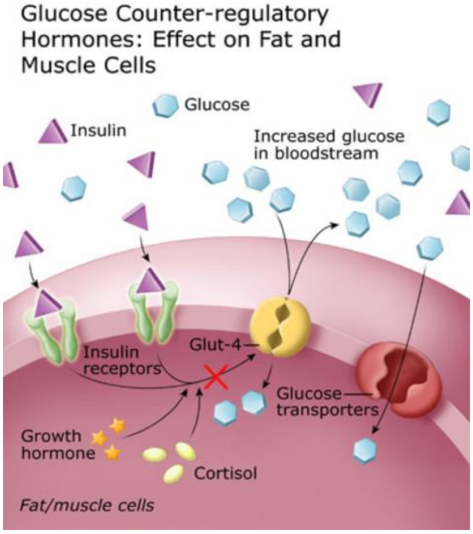
- ↑ Amino acids transport into cells
- ↑ DNA transcription= RNA synthesis
- ↑ RNA translation= protein synthesis
- ↓protein catabolism "protein sparer"

Fat metabolism (Catabolic)

- ↑ Mobilization of FFAs 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. (fat is the alternative of glucose for energy).
- ↑ Glucose production by the liver (↑ gluconeogenesis) production of glucose from noncarbohydrate origin
- ↑ Insulin resistance (↑ FFA) (**diabetogenic effect**)



Other effects of growth hormone

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

Controls of growth hormone secretion

Stimulate the secretion

- **The hypothalamus**:
  - GHRH
- **Hypoglycemia** (fasting)
- **Muscular exercise**
- **Intake of protein or amino acids** → (after meals).
- **During sleep** (more in children)
- **Stress conditions**, e.g. trauma or emotions
- **Grelin** (stomach) "hunger hormone"

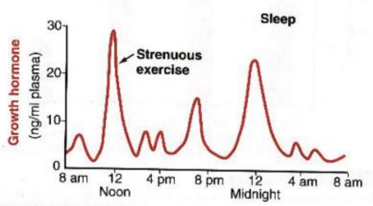


FIGURE 75-6
Typical variations in growth hormone secretion throughout the day, demonstrating the especially powerful effect of strenuous exercise and also the high rate of growth hormone secretion that occurs during the first few hours of deep sleep.

Pulsatile every 2H

Inhibit the secretion

- The **hypothalamus**:
  - GHIH (somatostatin)
- **Hyperglycemia** (glucose intake)
- **FFAs**

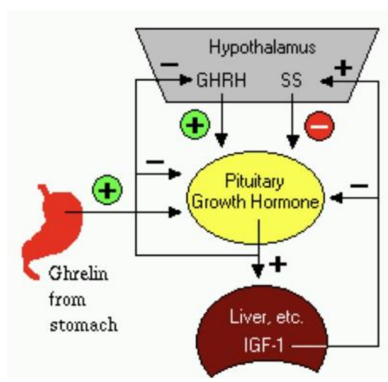


TABLE 9.4 Factors Affecting Growth Hormone Secretion

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

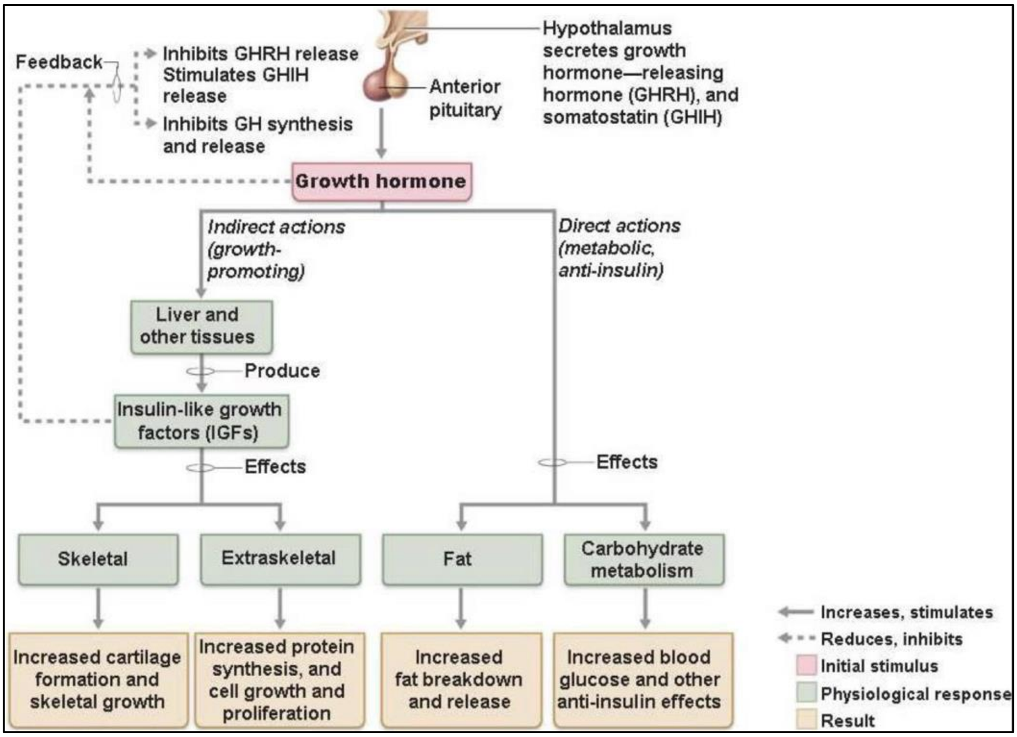
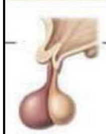


TABLE 16.1 Pituitary Hormones: Summary of Regulation and Effects

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 of GH secretion

Increased GH secretion

In adults

In children

Acromegaly

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).

Gigantism

- as all body tissues grow rapidly, including bones. Height increases as it occurs before epiphyseal fusion of long bones with their shafts.
- Hyperglycemia (diabetes).

Decreased GH secretion

Pituitary Dwarfism

where?:

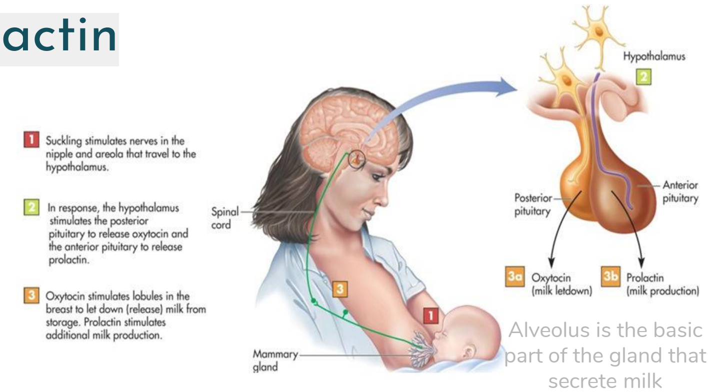
If the problem of the dwarfism is due to the thyroid gland he will be mentally retarded while if it is due to growth hormone deficiency the CNS will be then OK

Causes:

1. Decreased secretion of GHRH due to hypothalamic dysfunction
2. Primary deficiencies of GH secretion from anterior pituitary gland
3. Failure to generate somatomedins in the liver
4. Deficiency of GH or somatomedins receptor in the target tissue

Prolactin

- Synthesized by lactotrophs (15%)
- 198 AA
- Related to GH
- The major function of prolactin is milk production



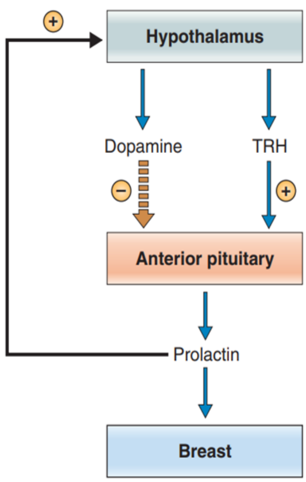
Alveolus is the basic part of the gland that secrete milk

Controlled:

*PIH: Prolactin Inhibiting Hormone
~ PRL: Prolactin

by Suckling response (inhibits PIH* release)

by PIH (dopamine) (Inhibits prolactin release)



[Prolactin Animation 2:33]

Sources of Dopamine

Males

1. Dopaminergic neuron in the hypothalamus
2. Dopaminergic neuron in the posterior pituitary gland
3. Non lactotrophs cells of the anterior pituitary gland

Prolactin Effect:

on Breast

1. **Increases mRNA**
2. **Breast development**
3. **Lactogenesis**

- Increases production of **Casein**, **Lactalbumin** and lipid.
- Parturition

Other effects

1. **Dopamine**

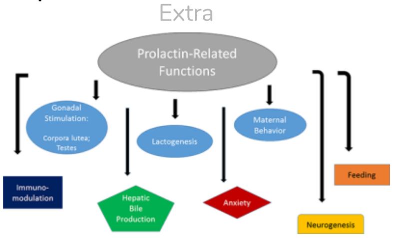
Stimulates the secretion of dopamine in median eminence (inhibits its own secretion)

2. **Inhibition of ovulation**

Inhibits the effects of gonadotropins, GnRH
no LH or FSH, work as contraceptives

Although prolactin level is high in pregnancy, lactation doesn't occur because the high level of estrogen and progesterone down regulating prolactin receptor in the breast and block the action of prolactin.

Extra



Control of Prolactin Secretion

- PIH (Dopamine) inhibit its secretion
- Exercise increases PRL secretion
- Surgical & psychological stress increases PRL secretion
- Stimulation of the nipple increases PRL secretion
- During Sleep Prolactin level rises
- During pregnancy prolactin level rises no milk ejection
- TRH increases PRL secretion

TABLE 9.5 Factors Affecting Prolactin Secretion

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

TRH, Thyrotropin-releasing hormone.

Abnormalities

Males

Prolactin deficiency

- Failure to lactate

Prolactin excess

- Galactorrhea
- Infillterty
- Bromocriptine

Males

TSH

- Synthesized by Thyrotrophs (5%)
- Glycoproteins
- α and β
- Related to LH and FSH

Abnormalities

- Hyperthyroidism
- Hypothyroidism

Actions

1. Increased synthesis and secretion of thyroid hormone.
2. Trophic effect (size)

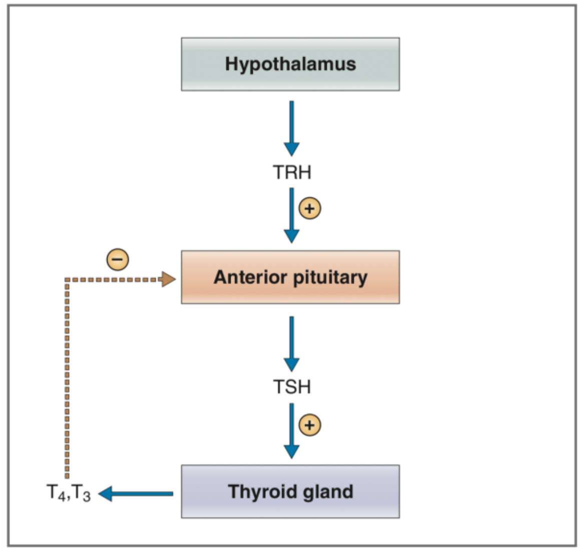


Fig. 9.19 Regulation of thyroid hormone secretion. *T_3*, Triiodothyronine; *T_4*, thyroxine; *TRH*, thyrotropin-releasing hormone; *TSH*, thyroid-stimulating hormone.

Males

FSH and LH

- Synthesized by Gonadotrophs (15%)
- Glycoproteins
- α and β
- Related to TSH

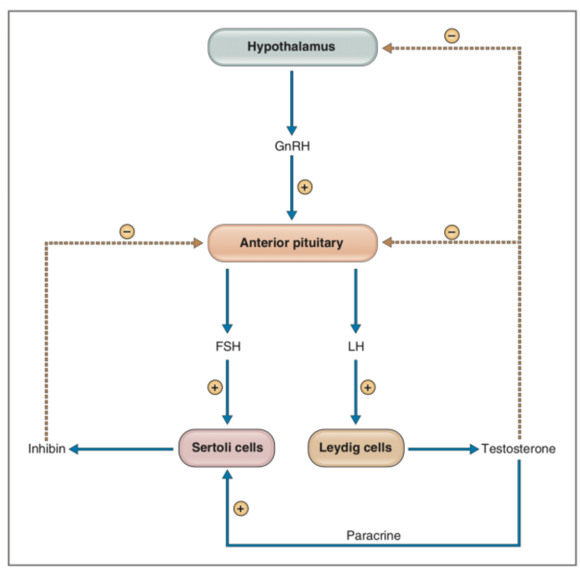


Fig. 10.6 Control of gonadotropin-releasing hormone (GnRH), follicle-stimulating hormone (FSH), and luteinizing hormone (LH) secretion in males.

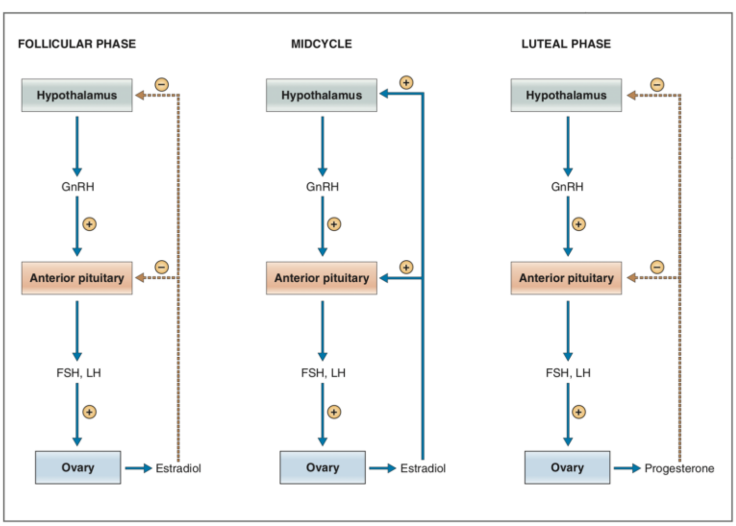


Fig. 10.9 Control of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) secretion in females during the menstrual cycle. The follicular and luteal phases are characterized by negative feedback of estradiol and progesterone, respectively, on the anterior pituitary. Midcycle is characterized by positive feedback of estradiol on the anterior pituitary. *GnRH*, Gonadotropin-releasing hormone.

ACTH

- Synthesized by Corticotrophs(15%)
- ACTH,MSH,β endorphin
- Preproopiomelanocortin POMC

β-Endorphin is an endogenous opiate.

Actions

- Stimulate synthesis and secretion of adrenocortical hormones

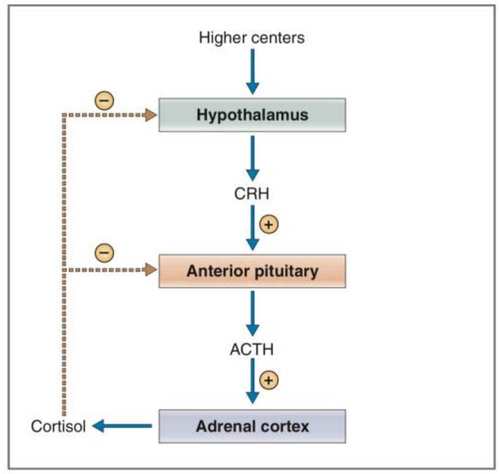


Fig. 9.25 Regulation of cortisol secretion. *ACTH,* Adrenocorticotropic hormone; *CRH,* corticotropin-releasing hormone.

TABLE 9.10 Factors Affecting ACTH Secretion

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

ADH, Antidiuretic hormone.

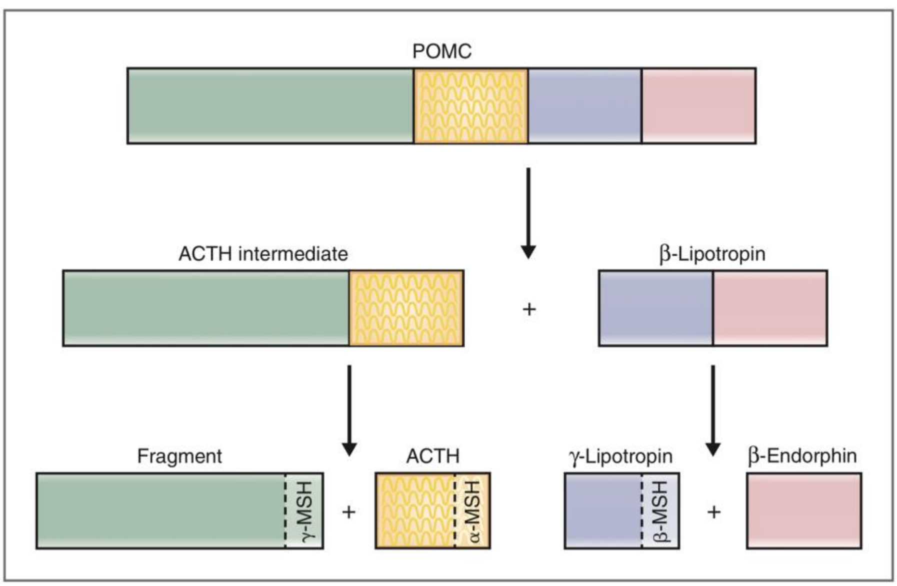


Fig. 9.10 The hormones derived from pro-opiomelanocortin (POMC). The fragment contains γ-MSH; ACTH contains α-MSH; and γ-lipotropin contains β-MSH. *ACTH,* Adrenocorticotropic hormone; *MSH,* melanocyte-stimulating hormone.

The preprohormone for this group, preproopiomelanocortin,is transcribed from a single gene.The signal peptide is cleaved in the endoplasmic reticulum,yielding POMC, the precursor to the ACTH family. Endopeptidases then hydrolyze peptide bonds in POMCand intermediates to produce the members of the ACTH family. The anterior pituitary in humans produces mainly ACTH, γ-lipotropin, and β-endorphin.It is noteworthy that MSH activity is found in POMCand in several of its products: The “fragment,” which is left over from hydrolysis of the ACTH intermediate, containsγ-MSH; ACTH contains α-MSH; and γ-lipotropin contains β-MSH. These MSH-containing fragments can cause skin pigmentation in humans if their blood levels are increased.

Points mentioned by Females' Doctor at the beginning of 2nd Lec. are in Bold

Summary

<table>
<tr><th colspan="3">Growth Hormone (GH)</th></tr>
<tr><td>Characteristics</td><td colspan="2">1. synthesized by somatotrophs
2. 191 amino acids
3. Pulsatile Secretions that vary during the day
4. has a direct and indirect effect.
Direct effect of GH on muscles, liver, and adipose tissue.
Indirect effect: GH stimulates liver to release (IGFs) (insulin like growth factors\ Somatomedins) along with (IGFBPs) (Insulin like growth factor binding proteins) which acts on bone, cartilage and muscles.
*GH is easily cleared from blood, unlike IGFs (somatomedins) since they're bound to proteins (IGFBPs)</td></tr>
<tr><td>Stimulation</td><td>-The hypothalamus:- GHRH
- Muscular exercise
- During sleep (more in children)
- Grelin (stomach)</td><td>- Hypoglycemia (fasting)
- Intake of protein
- Stress conditions</td></tr>
<tr><td>Inhibitio n</td><td colspan="2">- The hypothalamus:- GHI (somatostatin)
- Hyperglycemia (glucose intake)
- FFAs</td></tr>
<tr><td>Effects</td><td>Long Term: Promotes growth
1. Linear growth of long bones at epiphyseal plate by deposition of new cartilage, that's converted into bone.
2.Deposition of new bone on surface of old bones and in bone cavities, which increases thickness of membranous bones (jaw and skull).</td><td>Short Term: Metabolic effects
1. Anabolic protein metabolism) Increasing rate of protein synthesis in all cells
2. Catabolic (Fat Metabolism)
Release of fatty acids from adipose tissue
3.Hyperglycemic (CHO metabolism)
Inhibits glucose uptake by tissues, and increases its synthesis by the liver (Gluconeogenesis)</td></tr>
<tr><td rowspan="2">Abnormalities</td><td colspan="2">High GH secretions:
Acromegaly: occurs in adulthood, after epiphyseal plate closure, Thus NO linear growth of bones, but soft tissues and membranous bones will grow in thickness.
Gigantism: occurs in Childhood, before epiphyseal plate closure. All body tissues will grow rapidly, height will increase, + Hyperglycemia.</td></tr>
<tr><td colspan="2">Low GH secretions: Pituitary dwarfism</td></tr>
</table>

Summary

<table>
<tr><th colspan="3">Prolactin Hormone</th></tr>
<tr><td>Characteristics</td><td colspan="2">1. synthesized by lactotrophs
2. 198 amino acids
3. Related to GH structurally
4. Major function is milk production</td></tr>
<tr><td>Stimulation</td><td colspan="2">- Suckling response (stimulation of the nipple), which inhibits PIH secretion
- Exercise
- Surgical & psychological stress
- During sleep
- During pregnancy
- TRH</td></tr>
<tr><td></td><td colspan="2">Inhibition: PIH (Dopamine)</td></tr>
<tr><td>Effects</td><td>On Breast
1. Increases mRNA
2. Breast Development
3. Lactogenesis: increases production of Casein, Lactalbumin and lipid.</td><td>Other Effects
1. Dopamine: stimulates dopamine secretion in median eminence (to inhibit its own secretion)
2. Inhibition of ovulation: by inhibiting Gonadotropins, GnRH</td></tr>
<tr><td>Abnormalities</td><td>Prolactin excess
- Galactorrhea
- Infertility
- Treatment: Bromocriptine, a dopamine agonist</td><td>Prolactin deficiency
- Failure to lactate</td></tr>
</table>

MCQs

1.Which of the following hormones originates in the anterior pituitary?
A) Growth hormone–releasing hormone
(GHRH)
B) Somatostatin
C) Thyroid-stimulating hormone (TSH)
D) Oxytocin

2.Which of the following inhibits the secretion of growth hormone by the anterior pituitary?
A) Sleep
B) Stress
C) Puberty
D) Somatomedins

3.Which of the following metabolic substrates is preferentially metabolized by growth hormone?
A) Fats
B) Proteins
C) Glycogen
D) Glucose

4.Which one of the following is an inhibitory factor for ACTH secretion?
A) ADH
B) Opioids
C) B adrenergic antagonist
D) Serotonin

5.Which of the following explains the suppression of lactation during pregnancy?
A) Blood prolactin levels are too low for milk production to occur
B) Human placental lactogen levels are too low for milk production to occur
C) Blood levels of estrogen and progesterone are high
D) The maternal anterior pituitary is suppressed

6.Growth hormone secretion would most likely be suppressed under which of the following conditions?
A) Acromegaly
B) Gigantism
C) Deep Sleep
D) Acute hyperglycemia

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

8.The growth hormone receptor
A) activates Gs.
B) requires dimerization to exert its effects.
C) must be internalized to exert its effects.
D) resembles the IGF-I receptor.

Answers
1-C
2-D
3-A
4-B
5-C
6-D
7-C
8-B