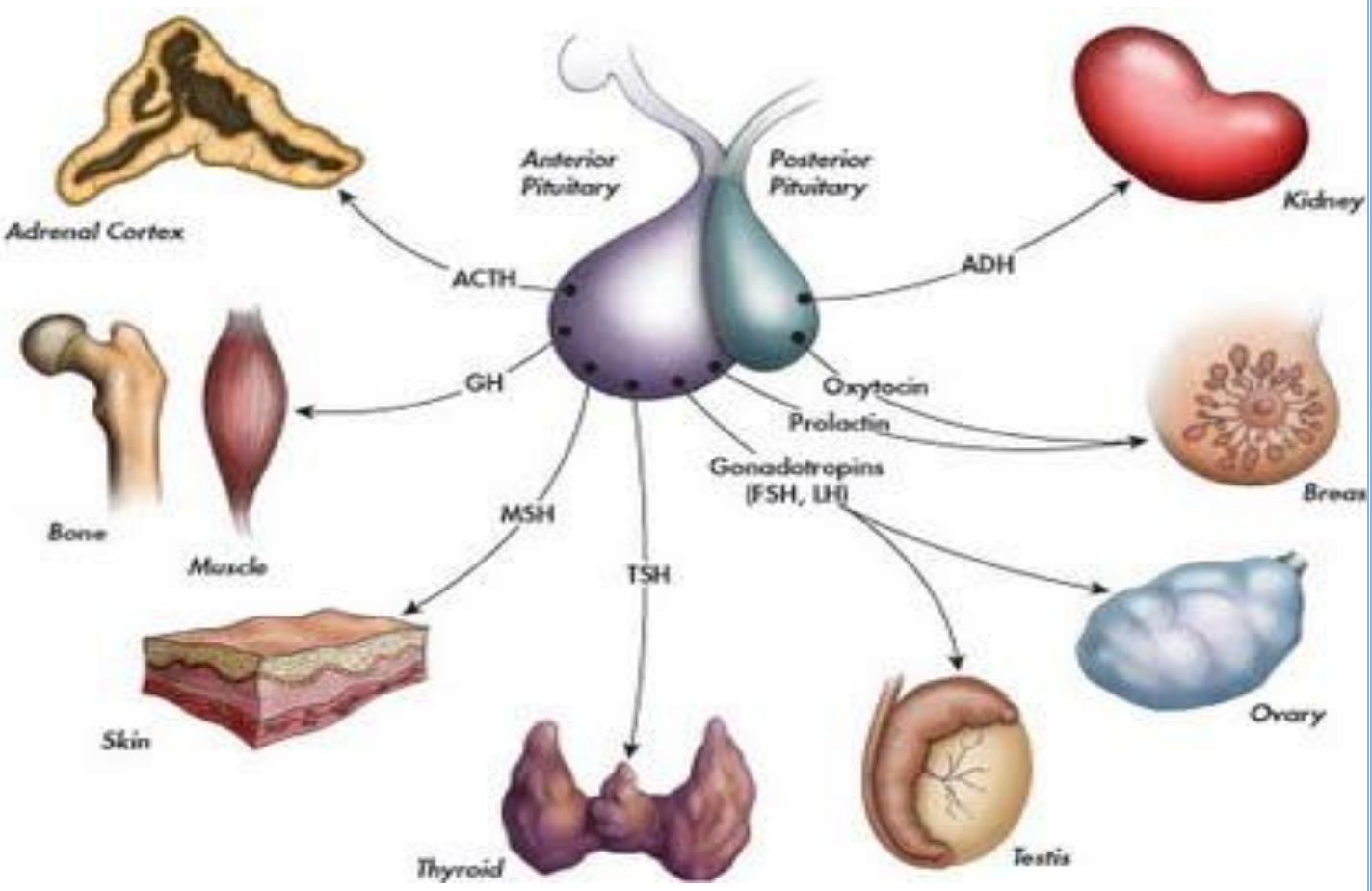
Endocrine Block

3rd & 4th Lecture

Pituitary Gland



PHYSIOLOGY TEAM – 430

Physiology Team Leaders:

Al-Waleed Al-Johar Layan Akkielah

This Lecture is done by:

Al-Waleed Al-Johar Layan Akkielah

Organized by : Layan Akkielah

Anterior Pituitary gland (adenohypophysis):

Regulation of the secretion of the anterior pituitary hormones :

1) Hypothalamic control :

- The secretion of the anterior pituitary hormones is controlled by hormones secreted from the hypothalamus (***releasing and inhibiting hormones***)
- Hypothalamic hormones travel through the ***hypothalamus- hypophyseal portal system*** to the anterior pituitary gland where they stimulate or inhibit the release of the anterior pituitary gland hormones.

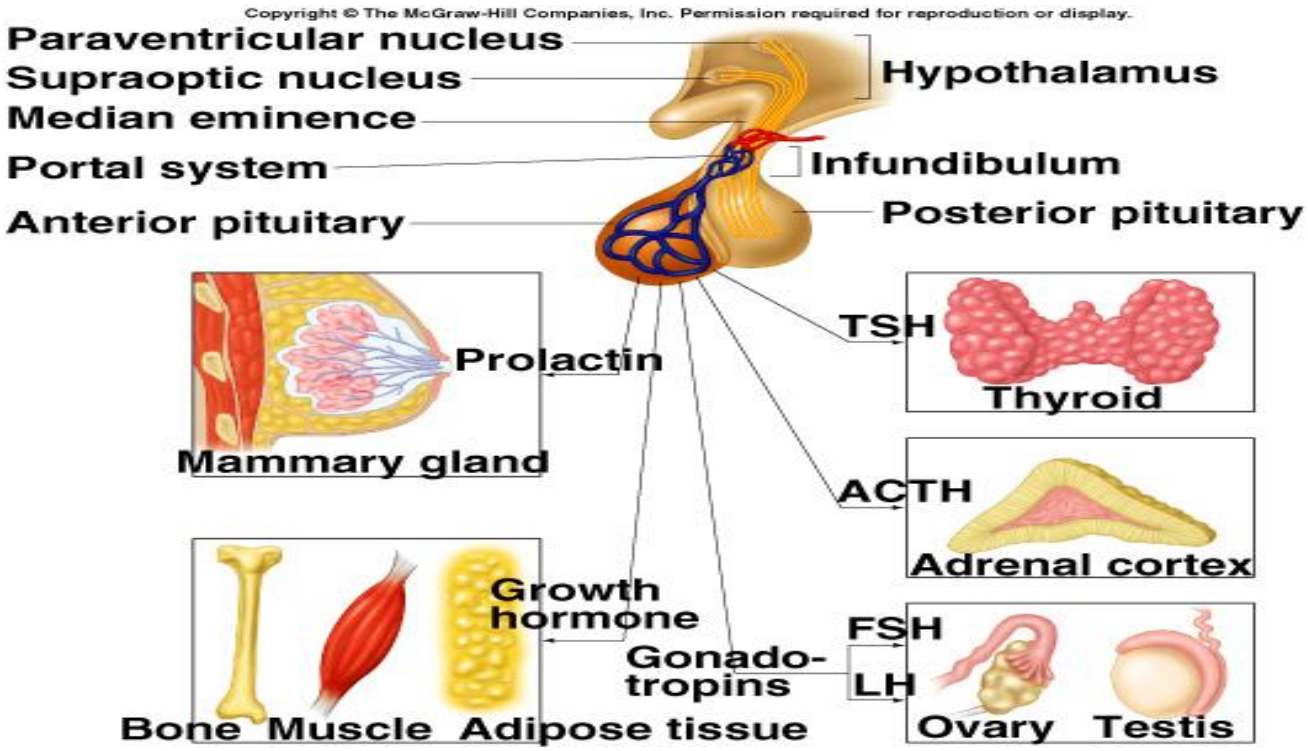
2) Feedback control :

- Anterior pituitary gland secretions are controlled by the target glands they regulate.
- Most of the hormones secreted from the Anterior pituitary gland are controlled by a ***Negative feedback*** inhibition (the hormone is inhibited by the rise in the secretion of the hormone of the gland its affecting)
- Some are regulated by a ***Positive feedback*** effect (the rise of the hormones secreted from the target gland stimulate the secretion of the Anterior pituitary gland hormone)

3) Higher brain centers :
Emotions and psychological stress affect the secretion of the anterior pituitary gland.

4) Humoral control

Anterior pituitary gland 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

❖ Growth Hormone *(somatotropin)*

Growth hormone (GH) stimulates body cells to ***increase in size and divide.***

Regulation of GH :

Stimulates GH secretion
Hypothalamic hormone : Growth hormone – releasing hormone (GHRH)
Muscular exercise
Intake of protein or amino acids(after meals).
Hypoglycemia (fasting)
Ghrelin (amino acid and a hormone produced from the lining cells of the stomach)
During sleep (more in children)
Stress conditions, e.g. trauma or emotions

Inhibits GH secretion
Hypothalamic hormone : Growth hormone – inhibiting hormone (GHIH – somatostatin)
FFAs
Negative feedback
glucose intake

Hypothalamic regulation :

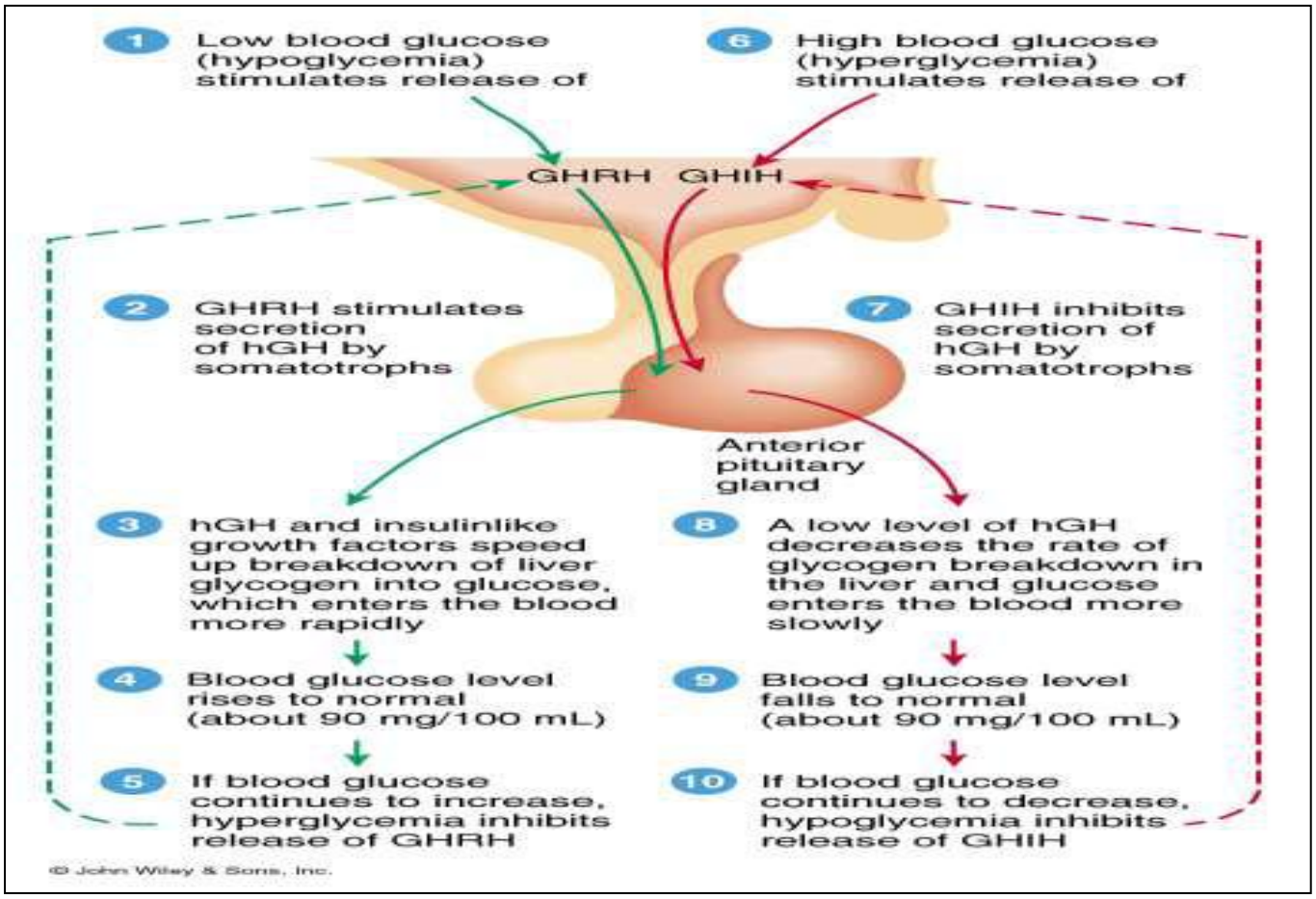


TABLE 16.1 Pituitary Hormones: Summary of Regulation and Effects

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

Mechanism of action :

– *Direct effect :*

- The action of GH on its receptors which are located on the target tissue

– *indirect effect :*

- The Liver produces and secretes *somatomedins* (*insulin –like growth factors*) in *response to GH stimulation*.
- IGF1's targets are *bone and cartilage and it stimulates cell division and growth*
- increase the *synthesis of protein in skeletal muscles*.

Functions of GH :

A) **Long term effect** : **Promotion of growth (due to the indirect effect) :**

- ↑ cellular sizes & ↑ mitosis &↑ tissue growth & organ size

Mechanisms of bone growth:

1. 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.
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:

– **Effects of GH on Protein metabolism (Anabolic) :**

↑ rate of protein synthesis in all cells through:

- amino acids transport into cells (increase amino acid concentration in cell → increase protein synthesis)
- ↑DNA transcription → RNA synthesis → protein synthesis
- ↑RNA translation → protein synthesis
- ↓protein catabolism "protein sparer"

GH enhances protein synthesis and reduces the breakdown of protiens

– **Effects of GH on Fat metabolism: Catabolic :**

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

– **Effects of GH on CHO metabolism: Hyperglycemic:**

- ↓ glucose uptake by tissues (skeletal muscles and fat).
- ↓ rate of glucose utilization throughout the body.
- ↑glucose production by the liver (↑ gluconeogenesis).

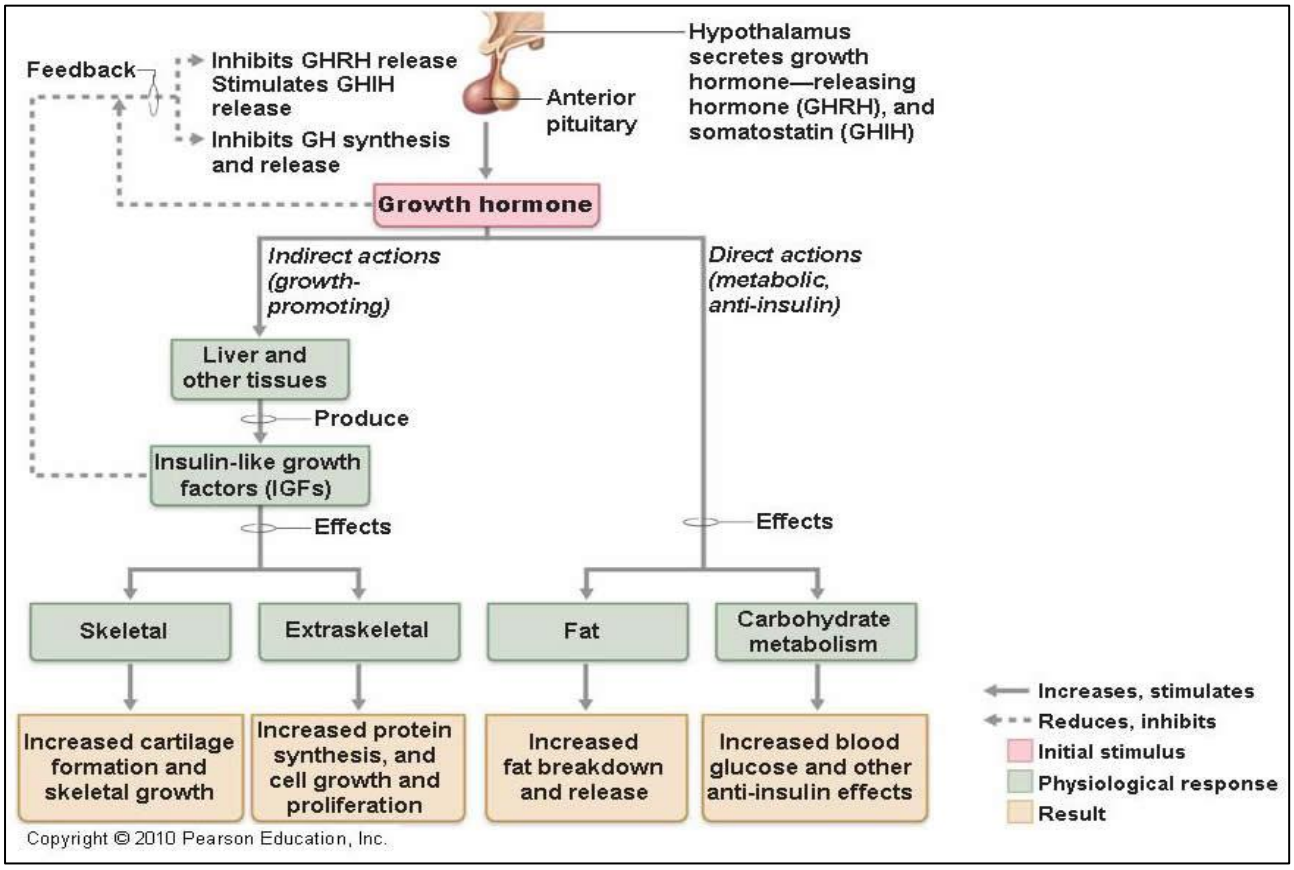
These changes are due to ↑insulin resistance (↑FFA) (diabetogenic)

As a result of insulin resistance, the person's body produces larger quantities of insulin to maintain normal levels of glucose in the blood therefore its effect is called diabetogenic.

– **Other effects include :**

- *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

Summary of GH functions :



Abnormalities of GH :

- **Hyposecretion** of GH in *childhood* → *Dwarfism*

- **Hypersecretion** of GH in *childhood* → *Gigantism*
  (all body tissues grow rapidly, including bones. Height ↑ as it occurs before epiphyseal fusion of long bones with their shafts. **Hyperglycemia** (diabetes))

- **Hypersecretion** of GH in *adults* → *Acromegaly*
  (elongation of the jaw, deformities in bones of face, hands and feet , growth of soft tissue and Hunched back (kyphosis) (enlargement of vertebrae)

❖ Prolactin :

secreted in both males and females

related to GH

Regulation of PRL :

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	

Functions of PRL :

- *stimulation of milk production* by mammary gland of lactating females .
- Effect on the breast :
  - *Increases* mRNA
  - *Increases* production of casein (proteins commonly found in mammalian milk) and lactalbumin
  - *Inhibits* the effects of gonadotropins
- Stimulates the secretion of *dopamine* in median eminence (inhibits its own secretion)

Sources of Dopamine:

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

Abnormalities:

1- PRL deficiency: failure to lactate

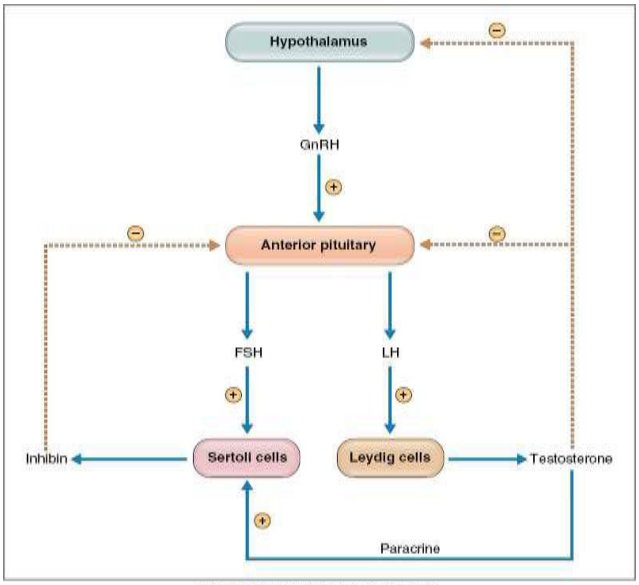
2- PRL Excess: Galactorrhea, Infertility

❖ FSH & LH :

Related to TSH

Secretion :

In male: they help in secreting Testosterone
In female: they help in secretion of Progesterone & Estrogen



❖ ACTH:

Formation :

To form this hormone, it requires a precursor named Preproopiomelanocortin (POMC), due to the cleavage of this precursor, it will produce along with the ACTH other hormones, they are: Melanocyte Stimulating hormone and β-endorphin

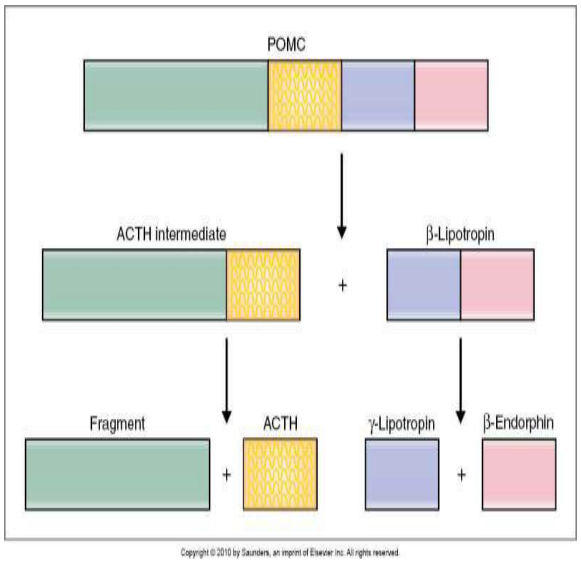


Table 9-10 Factors Affecting ACTH Secretion

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	

Posterior pituitary gland (neurohypophysis)

- Posterior pituitary gland stores and releases hormones that *are produced by large neuron in the supraoptic and paraventricular nuclei of the hypothalamus* .
- Consists of axon terminals of hypothalamic neurons
- Secretions of the posterior pituitary are controlled by *Nervous* signals from hypothalamus
- Hormones secreted by the Posterior Pituitary gland :
  ADH (anti-diuretic hormone – vasopressin) and **oxytocin**

❖ ADH (Anti-diuretic hormone):

- It is a polypeptide formed from *nine amino acids.*
- Synthesized in the *supraoptic* nuclei .
- Main function is to *control the rate of water excretion in the urine* and help control the *concentration of water* in the body.

Mechanism of action of ADH :

- The presence of ADH in the collecting ducts and tubules increases the permeability of water so most of the water gets reabsorbed results in → conserving water in the body and concentrated urine.
- ADH binds to V2 receptors on the peritubular (serosal) surface of cells (principle cells) of the distal convoluted tubules and medullary collecting ducts → activation of adnylyl cycalse and formation of cAMP → induces production and insertion of **aquaporin2** into the luminal membrane → there will be many new pores that allow free diffusion of water (enhances permeability of cell to water) → water is then absorbed by osmosis.

Aquaporins are special vesicles that have highly water-permeable pores

There are 3 types of receptors for ADH: V1A , V1B , V2

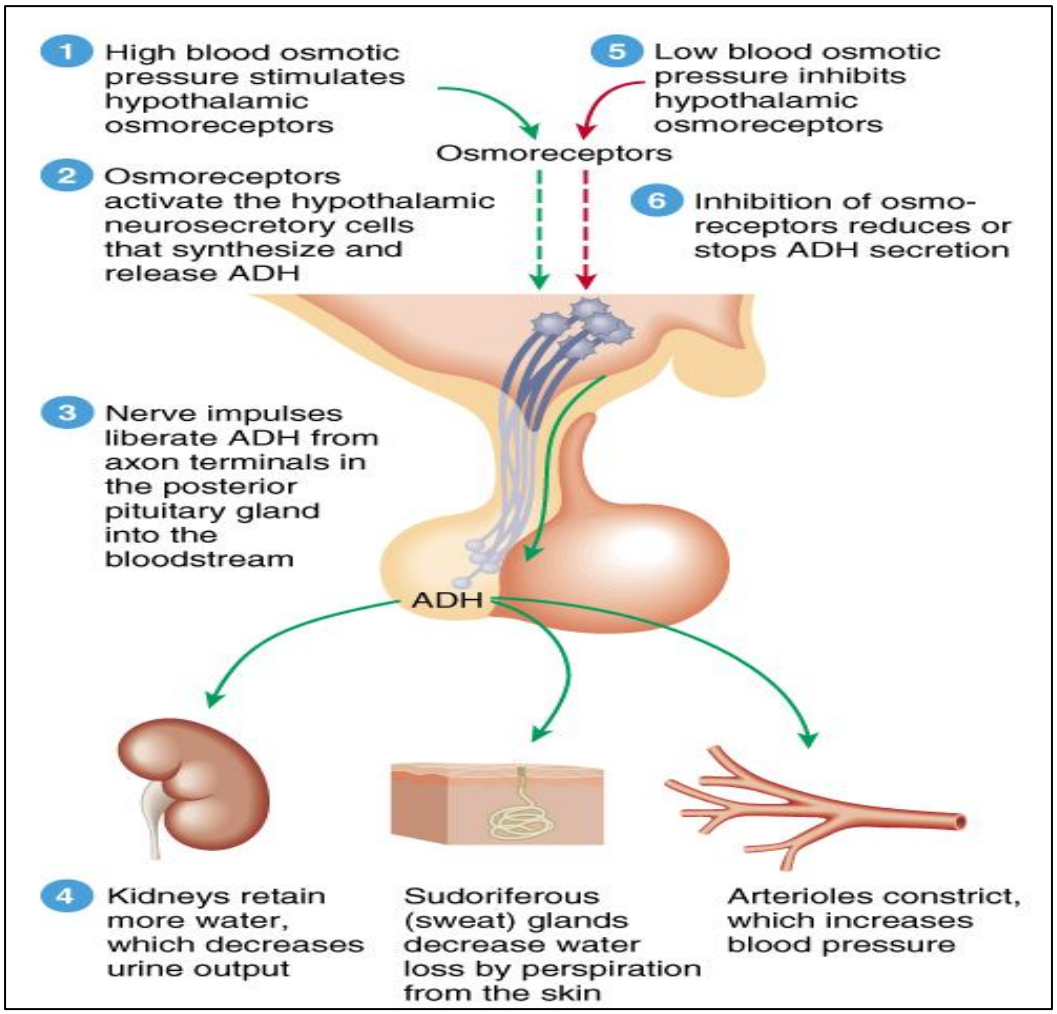
- V1A receptors mediate vasoconstriction
- V1A receptors also found in the liver glycogenolysis
- V1B receptors are unique to anterior pituitary and mediate increased ACTH secretion
- *V2 receptors are located in the principle cells in distal convoluted tubule and collecting ducts in the kidneys and its important for absorption of water.*

Regulation of ADH secretion :

- Osmotic regulation
- Non- osmotic regulation

Osmotic regulation :

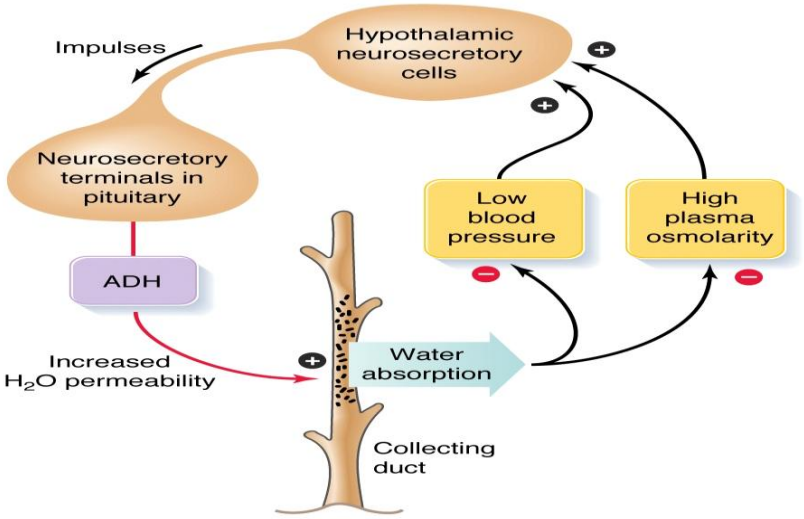
- ADH secretion is *very sensitive to changes in osmolality*.
- Injection of a concentrated electrolyte (electrolytes that do not penetrate cell membranes rapidly such as sodium) solution will *increase plasma osmolality* therefore it will *stimulate the secretion of ADH and thirst* via osmoreceptors
- Conversely, substances that enter cells rapidly, such as urea, do not change osmotic equilibrium and thus do not stimulate ADH release.
- Changes of 1-2% result in increased ADH secretion.



High blood osmotic pressure indicates ***dehydration*** → stimulation of ADH secretion ***Over hydration*** → inhibition of ADH secretion

Non- osmotic regulation :

- *Hypovolemia* causes *increase in ADH secretion*
- Hypovolemia is perceived by *Pressure receptors* such as carotid and aortic baroreceptors, and stretch receptors in left atrium and pulmonary veins .
- Normally, pressure receptors *tonically inhibit ADH release*
- When the atria's stretch receptors get *excited due to overfilling*, it sends signals to brain to *inhibit the ADH* secretion → *vasodilation* → regulate blood pressure and blood volume.
- Decreased stretch of baroreceptors → *reduced neural input* → *increased secretion of ADH* → *vasoconstriction* → regulate blood pressure and blood volume.
- Sensitivity to baroreceptors is less than osmoreceptors– senses 5 to 10% change in volume



Receptors	**Osmoreceptors**	**Baroreceptors**
Location	Anterolateral hypothalamus	Carotid sinus & aortic arch
Value Measured	Plasma osmolality	Circulating volume
ADH Release Stimulated By	Activation of receptor	Suppression of receptor
Change Required for Action	1% above 280 mosm/kg	10-15% decrease
Resulting Amount of ADH	Small	Large (vasoconstriction)
Override Other?	No	yes

Stimuli that increase ADH secretion: Pain , Nausea , Surgical stress , Emotional stress.

Stimuli that decrease ADH secretion: Alcohol intake

❖ Oxytocin:

Functions : -

1) Milk ejection:

- Targets the female breast of lactating women to release milk .
- Note that milk formation is by the hormone Prolactin , but milk release (when the infant suckles the mother) is by Oxytocin
- Oxytocin release is stimulated by the infant suckling his mother's breast
- Then oxytocin acts on myoepthelial cells (specialised contrctile smooth muscle cells that surround milk storage cavities) → contraction → expression of milk from its site of synthesis into larger ducts of the breast → milk excretion
- Thus, milk is then made available to a suckling infant.

2) Uterine Contraction:

- Stimulation of mechanoreceptors in the uterine cervix and vagina during labor (parturition) cause a rise in oxytocin levels → uterine contraction
- This helps in:

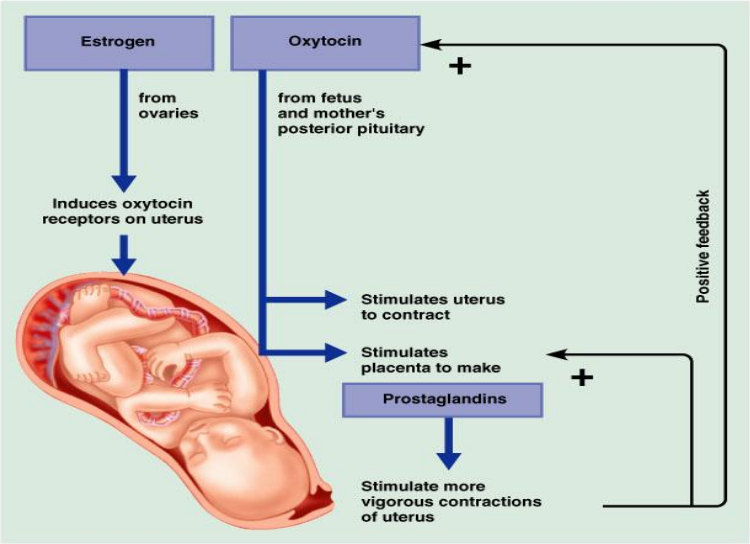
1) Expulsion of the baby during labor
2) Stopping bleeding after delivery
3) Also, after the baby is born & as the mother breastfeeds him → baby suckling produces oxytocin release → milk let-down + uterine contraction (which prevents further blood-loss from the mother) .

- Oxytocic drugs (e.g., Syntocinon) are used by obtetricians to induce labor in postmature pregnant women

Regulation:

– Regulated by higher brain centers and positive feedback .

– In humans, oxytocin is thought to be released during hugging, touching, and orgasm in both sexes.
– Release increased during stress
– Release inhibited by alcohol
– In males secretion increases at time of ejaculation (contraction of smooth muscle of vas deferens)



Oxytocin and autism

– Autistic group had significantly lower plasma oxytocin levels than in the non-autism group
– Elevated oxytocin was associated with higher scores on social and developmental measures for the non-autistic children

That's why when you hug an autistic child, he feels comfortable