

Posterior Pituitary

Objectives:

- ❖ Describe the posterior pituitary relationship with the hypothalamus
- ❖ List the target organs and functional effects of oxytocin.
- ❖ Name the stimuli for oxytocin release in relation to its reproductive and lactation functions.
- ❖ List the target cells for vasopressin and explain why vasopressin is also known as antidiuretic hormone.
- ❖ Describe the stimuli and mechanisms that control vasopressin secretion.
- ❖ Identify disease states caused by a) over-secretion, and b) under-secretion of vasopressin and list the principle symptoms of each.

Done by :

- **Team leaders:** Rahaf AlShammari, Abdulelah AlDossari
- **Team members:**
 - ◆ Fahad Alfaiz, Ali shehadah
 - ◆ Ghaida Saad Alsanad, Rawan mishal
 - ◆ Rakan Alsalhy, Wejdan albadrani
 - ◆ Faisal AlQarni, Afnan AlMustafa
 - ◆ Abdulaziz Al dukhayel, Sultan alaqil

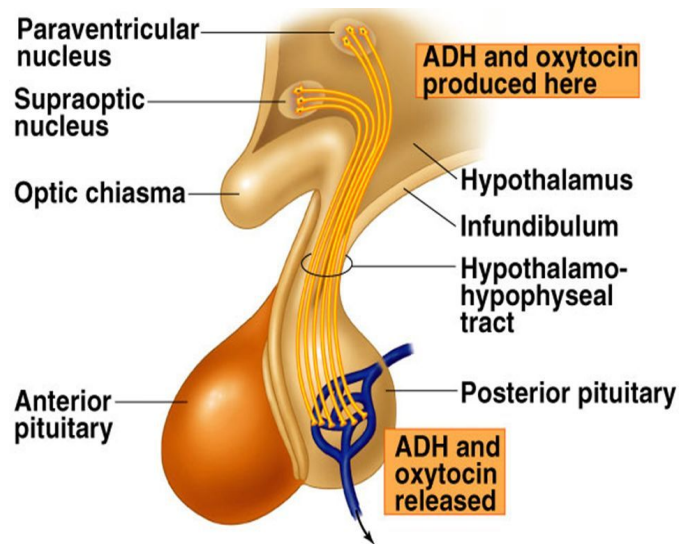


Colour index:

- Important
- Numbers
- Extra

The Posterior Pituitary and Hypothalamic Hormones

- Secretions of the posterior pituitary are controlled by **nervous signals** from hypothalamus. "Since its origin is from neuronal tissue"
- Has a neural connection with the hypothalamus (**hypothalamic- hypophyseal tract**).
- Nuclei of the hypothalamus synthesize oxytocin and antidiuretic hormone (ADH).
- These hormones are transported to the posterior pituitary.



Oxytocin and Vasopressin

In pigs it will be lysine instead of arginine and it's used in human to treat diabetes insipidus.

- Vasopressin: Cys-Tyr-**Phe**-Gln-Asn-Cys-Pro-**Arg**-GlyNH₂
- Oxytocin: Cys-Tyr-**Ile**-Gln-Asn-Cys-Pro-**Leu**-GlyNH₂

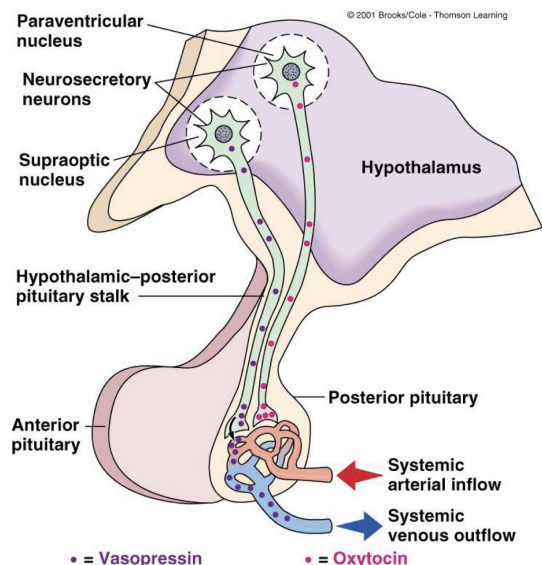
ADH has three names:
-ADH.
-Vasopressin.
-Arginine vasopressin.

Vasopressin and oxytocin has 9 amino acids

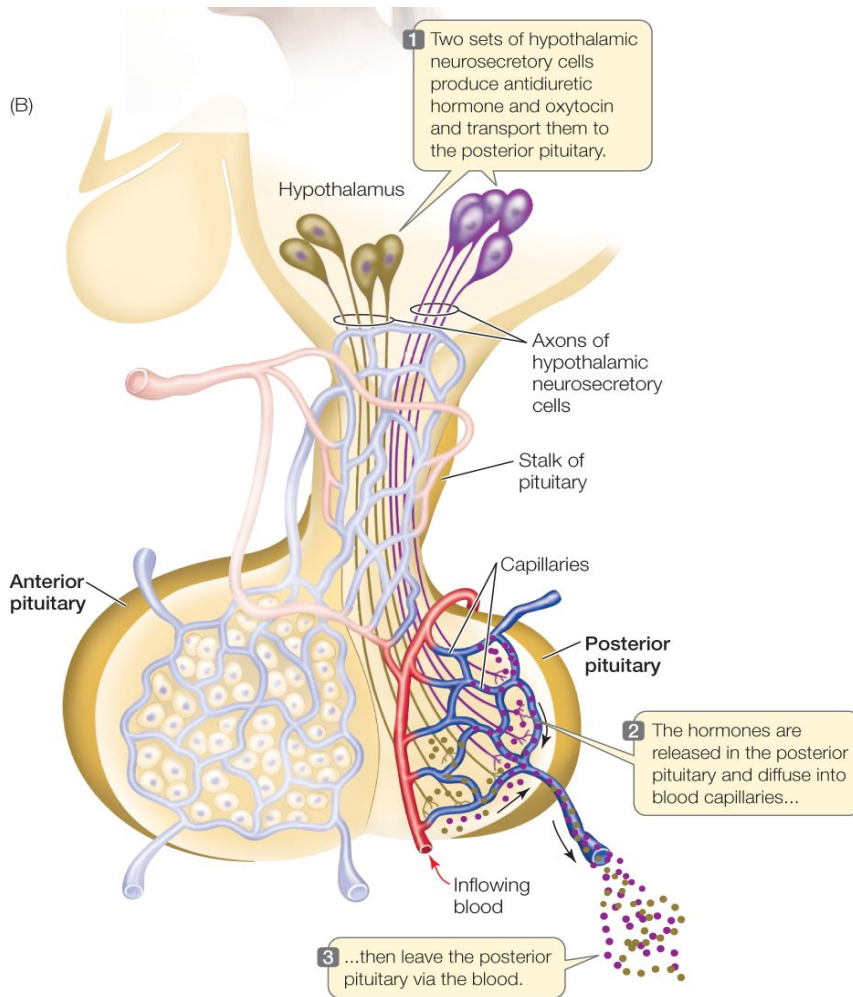
Posterior pituitary

- Does not synthesize hormones.
- Consists of axon terminals of hypothalamic neurons.

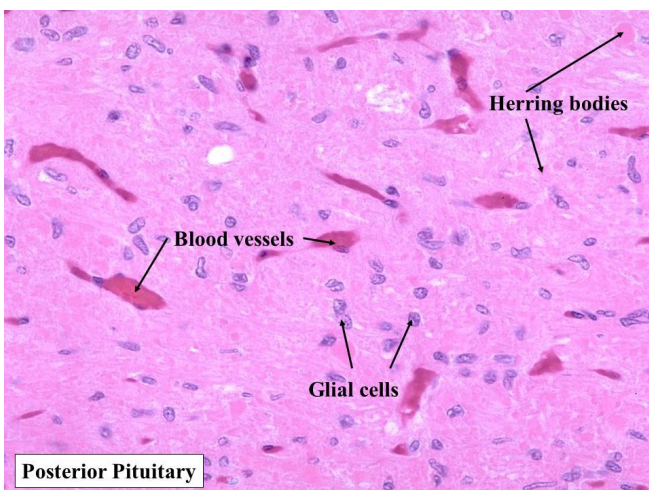
Synthesis of the hormones occur in:
1-paraventricular nucleus (mainly oxytocin + 1/2 ADH)
2-Supraoptic nucleus (mainly ADH + 1/2 oxytocin).



Secretion Of Posterior Pituitary Hormones



Pituicytes function



- It forms physical and chemical barrier between nerve terminal and blood vessels.
- Amplify auto receptor negative feedback.

Pituicytes regulate hormone secretion by releasing their processes to engulf the axonal endings and prevent the hormone secretion. If there is stimulation it retract its processes and the hormone will be released.

ADH

Synthesis

- It is synthesized as pre-prohormone and processed into a nonapeptide (nine amino acids).
- ADH synthesized in the cell bodies of hypothalamic neurons (**supraoptic nucleus**).
- ADH is stored in the neurohypophysis (posterior pituitary)

Receptors

V1A receptors

mediate **vasoconstriction**, also found in the **liver** glycogenolysis.

V1B receptors

are unique to **anterior pituitary** and mediate ACTH secretion.

V1 receptors are Gq coupling receptors.

V2 receptors

IMPORTANT

are located in the principle cells in distal convoluted tubule and collecting ducts in the **kidneys**.

Mechanism of action of ADH : antidiuresis

1- ADH binds to V2 receptors on the peritubular(serosal) surface of cells (principle cells) of the distal convoluted tubules and medullary collecting ducts.

2- Via adenylate cyclase/cAMP induces production and insertion of **aquaporin2** into the luminal membrane and enhances permeability of cell to water.

3- Increased membrane permeability to water permits back diffusion of solute-free water, resulting in increased urine osmolality (concentrates urine).

- The ADH hormone binds to its receptor V2 in the basolateral membrane.
- Activate the second messenger cAMP.
- cAMP activate Protein kinase A which phosphorylate another protein.
- The phosphorylated protein results in the movement of the vesicle containing the aquaporin to the luminal membrane.

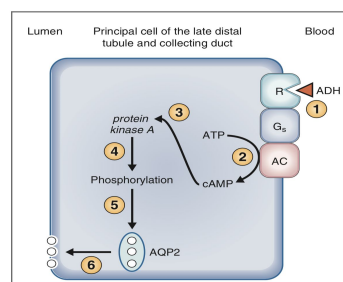


Fig. 6.41 Cellular mechanism of action of antidiuretic hormone in the principal cell of the late distal tubule and collecting duct. See the text for an explanation of the circled numbers. AC, Adenylate cyclase; ADH, antidiuretic hormone; AQP2, aquaporin 2; ATP, adenosine triphosphate; cAMP, cyclic adenosine monophosphate, or cyclic AMP; G_s, stimulatory G protein; R, V₂ receptor.

Secretion of ADH

osmosis stimuli

- If **plasma osmolality** is directly increased by administration of solutes, only those solutes that don't freely or rapidly penetrate cell membranes, such as sodium, **cause ADH release**.
- Conversely, substances that enter cells rapidly, such as urea, do not change osmotic equilibrium and thus don't stimulate ADH release.
- **ADH secretion is very sensitive to changes in osmolality.**
- Changes of 1-2% result in increased ADH secretion.

Experiment in animals:

They inject highly osmotic solutes near the hypothalamus. This result in direct release of ADH. Because of the presence of osmoreceptors near or inside the hypothalamus. When we inject highly osmotic solutes, water moves out, osmoreceptor shrinks, and this stimulates the release of ADH.

non-osmosis stimuli

- Hypovolemia is perceived by **"pressure receptors"** -- carotid and aortic baroreceptors, and stretch receptors in left atrium and pulmonary veins.
- Normally, pressure receptors tonically inhibit ADH release.
- Decrease in blood pressure induces ADH secretion by reducing input from pressure receptors.
- The reduced neural input to baroreceptors relieves the source of tonic inhibition on hypothalamic cells that secrete ADH.
- **Sensitivity to baroreceptors is less than osmoreceptors senses 5 to 10% change in volume.**

If we have low blood volume and low osmolality ADH will be activated because blood volume dominate on osmolality.

TABLE 9.6 Factors Affecting Antidiuretic Hormone Secretion

Stimulatory Factors	Inhibitory Factors
Increased serum osmolality	Decreased serum osmolality
Decreased ECF volume	Ethanol
Angiotensin II	α -Adrenergic agonists
Pain	ANP
Nausea	
Hypoglycemia	
Nicotine	
Opiates	
Antineoplastic drugs	

- Other Stimuli that increase ADH secretion: pain, nausea, surgical & emotional stress
- Stimuli that decrease ADH secretion: Alcohol intake



Summary of ADH secretion

osmotic pressure

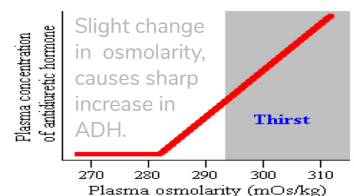
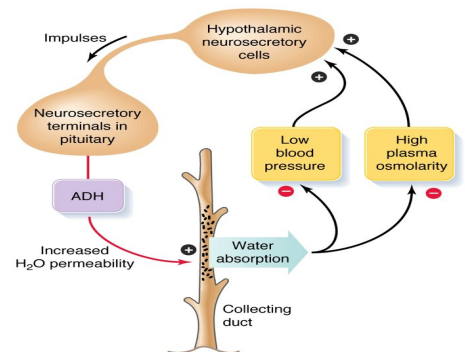
Osmoreceptors in the hypothalamus:

- \uparrow osmotic pressure \Rightarrow \uparrow ADH secretion.
- \downarrow osmotic pressure \Rightarrow \downarrow ADH secretion.

Volume effects

Baroreceptor mediated (vagus nerve):

- \uparrow Blood pressure \Rightarrow \downarrow ADH secretion.
- \downarrow Blood pressure \Rightarrow \uparrow ADH secretion.



ADH Disorders

Diabetes Insipidus

Syndrome of Inappropriate Antidiuretic Hormone (SIADH)

What is it?

Types

Treatment

DI is a disorder resulting from deficiency of antidiuretic hormone (ADH) or its action and is characterized by the passage of copious amounts of dilute urine.

It must be differentiated from other polyuric states such as: primary polydipsia & osmotic diuresis.

1 Neurogenic (central)

2 Nephrogenic

Desmopressin (DDAVP) a synthetic analogue is superior to native AVP because:

- It has a longer duration of action (8-10h vs 2-3h)
- More potent (it's antidiuretic activity is 3000 times greater than its pressor activity)

Nephrogenic

Neurogenic (central)

(failure of the kidney to respond appropriately to ADH)

Nephrogenic DI results when the renal tubules of the kidneys **fail to respond** to circulating ADH.

- The resulting renal concentration defect leads to the loss of large volumes of dilute urine. This causes cellular and extracellular dehydration and **hypernatremia**.

Treatment:

- Provision of adequate fluids and calorie
- Low sodium diet
- Diuretics
- High dose of DDAVP
- Correction of Underlying cause

(failure of hypothalamus or neurohypophysis to synthesize or secrete ADH)

Central DI is due to **failure of producing** adequate ADH.

Why we give Diuretics in patient with diabetes insipidus ?

Because these patient are suffering from hypernatremia and we will correct it by giving them Diuretics that will enhance Na excretion and water will follow Na.

Oxytocin

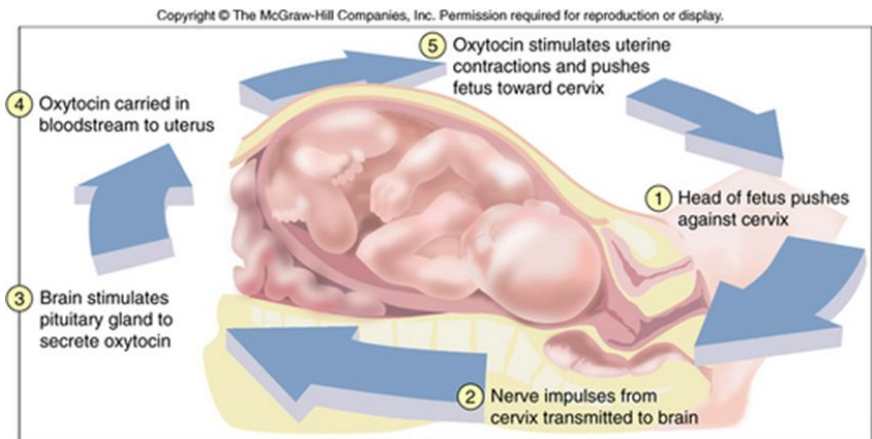
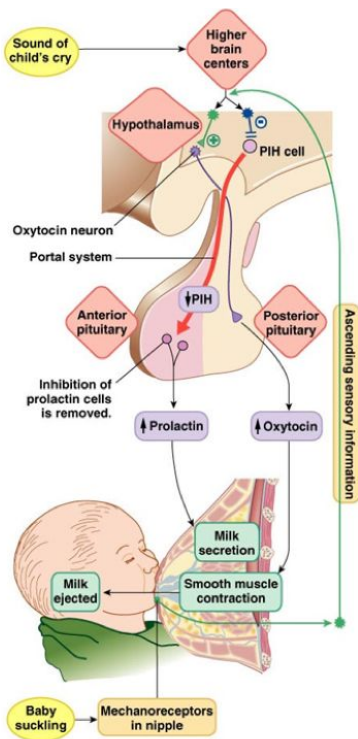
Oxytocin's Functions:

★ **Breast-feeding:** contracts the myoepithelial cells of the alveoli (classic neuroendocrine reflex)

★ **Childbirth (parturition):** In late pregnancy, uterine smooth muscle (myometrium) becomes sensitive to oxytocin (positive feedback)

Because in late pregnancy, more receptors will be formed (Upregulation of receptors)

The more contraction of the uterus and pressure on the cervix, the more oxytocin released.



Other stimuli that control release of oxytocin:

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

Tactile (touching) of baby to nipple sends impulses to hypothalamus, hypothalamus release Oxytocin. Stretch of uterine wall and cervix during labor cause positive feedback and widening of cervix (more stretch of cervix more oxytocin released).

TABLE 9.7 Factors Affecting Oxytocin Secretion

Stimulatory Factors	Inhibitory Factors
Suckling	Opioids (endorphins)
Sight, sound, or smell of the infant	
Dilation of the cervix	
Orgasm	

Summary

- Secretions of the posterior pituitary are controlled by **nervous signals**
- Nuclei of the hypothalamus synthesize oxytocin and antidiuretic hormone (ADH), and then transported via axons to the posterior pituitary gland and then stored there.
- Does not synthesize hormones.

	ADH	Oxytocin
Synthesis	<ul style="list-style-type: none"> • Synthesized as pre-prohormone in the cell bodies of hypothalamic neurons (supraoptic nucleus). • Has 3 type of receptors: 1- V1a 2-V1b 3-V2 	<ul style="list-style-type: none"> • Synthesized in the cell bodies of hypothalamic neurons (paraventricular nucleus).
Secretion	<p>1-Osmosis stimuli: \uparrow osmolarity \rightarrow \uparrowADH \downarrow osmolarity \rightarrow \downarrowADH</p> <p>2-Non-osmosis stimuli: via pressure receptors \downarrowVolume \rightarrow \uparrow ADH \uparrowVolume \rightarrow \downarrow ADH</p>	<p>Increased by:</p> <ul style="list-style-type: none"> - Hugging, touching, orgasm in both sexes - Stress - In males at ejaculation <p>Inhibited by:</p> <ul style="list-style-type: none"> - Alcohol
Function	<ul style="list-style-type: none"> • ADH binds to V2 receptors on the peritubular(serosal) surface of cells (principal cells) via cAMP <u>which</u> induces production and insertion of aquaporin2 <u>leads to</u> Increased permeability to water in cell membrane will <u>lead to</u> increased urine osmolality. 	<ul style="list-style-type: none"> • Breast feeding • Childbirth
Disorders	<ul style="list-style-type: none"> - Syndrome of inappropriate diuretic hormone (SIDH). - Diabetes insipidus <ul style="list-style-type: none"> a- <u>Neurogenic</u>(Central): Failure of hypothalamus or neurohypophysis to synthesize or secrete ADH b- <u>Nephrogenic</u>: Failure of the kidney to respond appropriately to ADH <u>Treatment</u> for both: Desmopressin 	<ul style="list-style-type: none"> - Autism relation: Autistic group had significantly lower plasma oxytocin levels than in the non-autism group

Pituicytes: It forms a barrier between nerve terminal and blood vessels, which Amplifies auto receptor negative feedback.

MCQs

1. Which statement about antidiuretic hormone (ADH) is true?

- A) It is synthesized in the posterior pituitary gland
- B) It increases salt and water reabsorption in the collecting tubules and ducts
- C) It stimulates thirst
- D) It has opposite effects on urine and plasma osmolality

2. Which of the following decreases the pressure in the pulmonary artery after birth?

- A) An increase in systemic arterial pressure
- B) Closure of ductus arteriosus
- C) An increase in left ventricular pressure
- D) A decrease in pulmonary vascular resistance

3. Why is milk produced by a woman only after delivery, not before?

- A) Levels of LH and FSH are too low during pregnancy to support milk production
- B) High levels of progesterone and estrogen during pregnancy suppress milk production
- C) Her alveolar cells of the breast do not reach maturity until after delivery
- D) Oxytocin is not secreted until the baby stimulates the nipple

4. Which one of these ADH receptors is located in the kidney?

- A) V1A
- B) V1B
- C) V2

5. What will happen if the pituitary stalk cut above the pituitary gland?

- A) Secretion of hormones stop totally.
- B) Secretion of hormones will not be affected.
- C) Secretion of hormones decreases then return to normal level after few days.

6. A 30-year-old woman is breastfeeding her infant. During suckling, which hormonal response is expected in the woman?

- A) Increased secretion of ADH from the supraoptic nuclei
- B) Increased secretion of ADH from the paraventricular nuclei
- C) Increased secretion of oxytocin from the paraventricular nuclei
- D) Decreased secretion of neurophysin

7. What is the consequence of sporadic nursing of the neonate by the mother?

- A) An increase in PRH
- B) An increase in oxytocin
- C) Lack of birth control
- D) Lack of prolactin

Answers

- 1. D
- 2. D
- 3. B
- 4. C
- 5. C
- 6. C
- 7. D