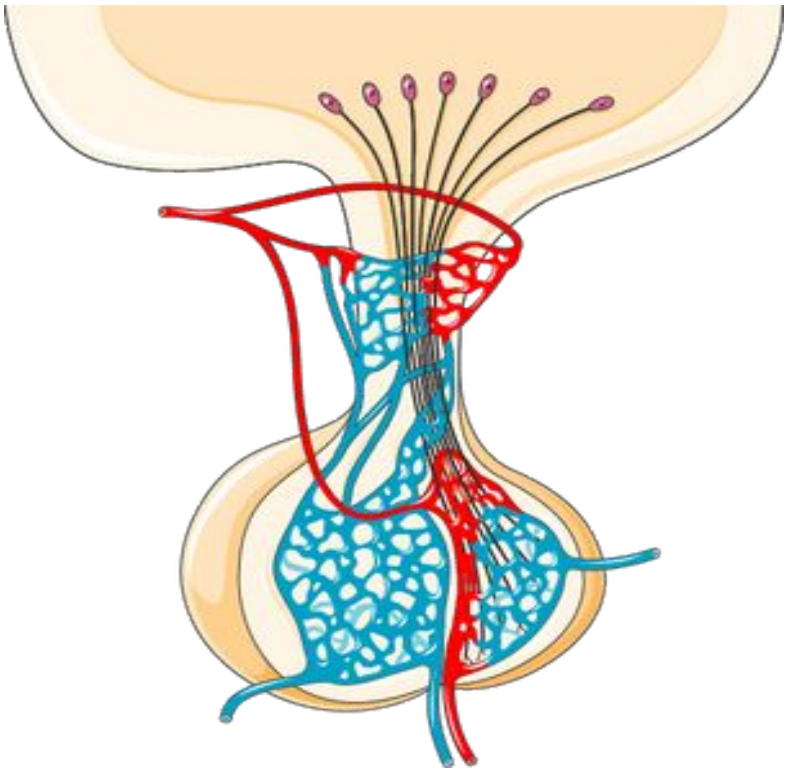
5



Posterior pituitary gland

ENDO Physiology

Editing File

Color Index :

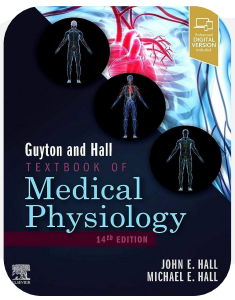
- Main Text
- Important
- Girls Slides
- Boys Slides
- Notes
- Extra

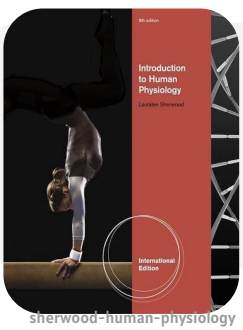
Objectives

- 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 ADH and explain why ADH is also known as vasopressin.
- Describe the stimuli and mechanisms that control ADH secretion.
- Identify disease states caused by a) over-secretion, and b) under-secretion of ADH and list the principle symptoms of each.

Resources

Only ENDO chapters included





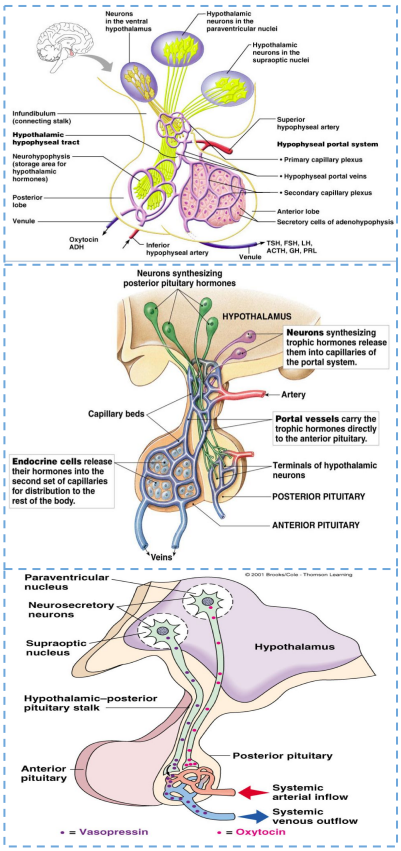
sherwood-human-physiology

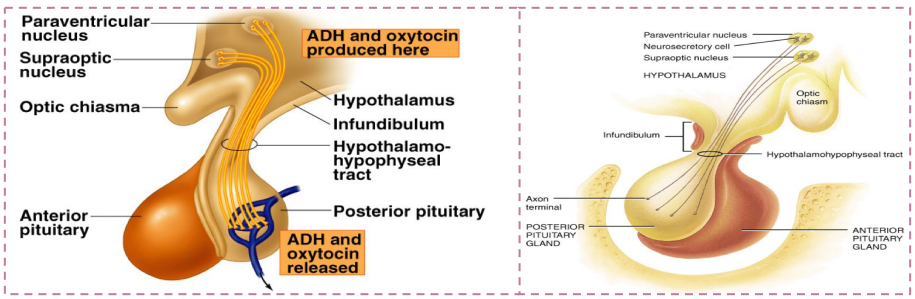
This lecture was presented by:
Dr. Hana Alzamil - Prof. Dr. Khalid Al Regaiey

Posterior pituitary

Posterior pituitary

- The posterior pituitary gland is composed mainly of glial-like cells called pituicytes.
- Has a neural connection with the hypothalamus **(hypothalamic-hypophyseal tract)**
- Nuclei of the hypothalamus synthesize oxytocin and antidiuretic hormone (ADH)
- Their axons pass through the pituitary stalk to the neurohypophysis and terminate in the posterior pituitary.
- Secretions of the posterior pituitary are controlled by nervous signals from hypothalamus (under hypothalamic control)
- Does not synthesize hormones , Consists of axon terminals of hypothalamic neurons





Posterior pituitary hormones

1 Vasopressin (ADH)

Cys-Tyr-**Phe**-Gln-Asn-Cys-Pro-**Arg**-GlyNH2

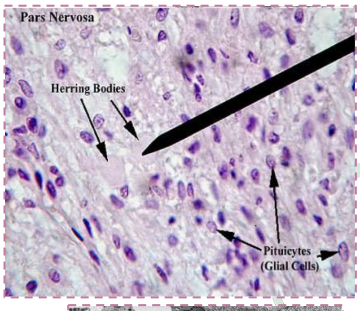
2 Oxytocin

Cys-Tyr-**Ile**-Gln-Asn-Cys-Pro-**Leu**-GlyNH2

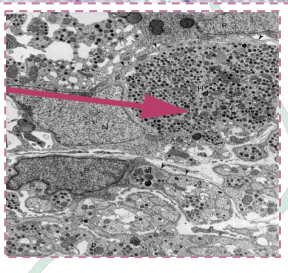
- Osmotic and non osmotic stimuli

Female slides

Pituicytes	Herring Bodies
Forms physical & chemical barrier between nerve terminal and blood vessels → amplify auto receptor negative feedback. Pituicytes are supporting cells, they form pods "finger-like projections", when the hormone isn't needed they will isolate chemically and physically the nerve ending from the blood vessel. Once there's a stimuli they'll allow the hormone to pass, and they do the action of amplification by retracting and allowing high amount of the hormone to release, therefore once the hormone reaches its high-threshold it will stimulate the negative feedback loop.	Neurosecretory terminal ends of axons from hypothalamus, hormones are temporarily stored in them.



Herring bodies



Oxytocin (Introduction)

Synthesis

Oxytocin is synthesized in the cell bodies of hypothalamic neurons (paraventricular nucleus)

Storage

Oxytocin is stored in the Herring bodies at the axon terminals in the posterior pituitary.

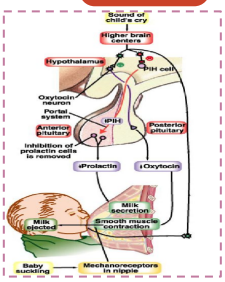
Important

Function of oxytocin

1 Breast feeding

Important

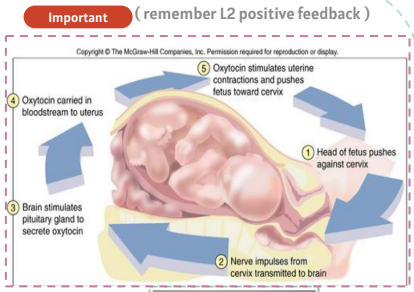
- Contracts the myoepithelial cells of the alveoli (classic neuroendocrine reflex)
- Oxytocin triggers milk ejection ("letdown" reflex) Contracts the myoepithelial cells of the alveoli
- Mechanosensory information from the nipple reaches the magnicellular neurons, causing the release of oxytocin into the general circulation. Oxytocin acts on receptors on myoepithelial cells in the mammary gland acini leading to the release of milk into the ductal system and, ultimately, the release of milk from the mammary gland.



2 Childbirth (parturition)

Important (remember L2 positive feedback)

- In late pregnancy, uterine smooth muscle (myometrium) becomes sensitive to oxytocin (positive feedback)
- Oxytocin is a strong stimulant of uterine contraction
- Regulated by a positive feedback mechanism
- This leads to increased intensity of uterine contractions, ending in birth



They use it in clinical, in the third stage of delivery when the head of the baby come out give the patient injection of oxytocin help her in contraction, لأن الرحم وقت عملية الولادة ممكن يحصل له ارتخاء في اللحظة الأخيرة ويصير نزيف حاد يؤدي لمضاعفات خطيرة

3 Ejaculation

- In males secretion increases at time of ejaculation (contraction of smooth muscle of vas deferens)

4

- In humans, oxytocin is thought to be released during hugging, touching, and orgasm in both sexes
- Release increased during stress
- Release inhibited by alcohol

5

- Oxytocin also acts on other regions of the brain, such as the medial preoptic area, ventral tegmental area, nucleus accumbens, and amygdala, to affect social behavior (particularly parental behavior) by reducing the stress response and increasing empathy.

Oxytocin Secretion, Control & Regulation

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
- Similarly, oxytocin has been proposed to be involved in the pathophysiology of autism, as indicated by a reduction in plasma oxytocin levels, as well as improved social interactions and reduced repetitive behaviors following intranasal oxytocin administration in autistic patients.
- A potential therapeutic role for oxytocin in the treatment of autism has been proposed.

Oxytocin and schizophrenia

Male slides

- Oxytocin receptor gene polymorphisms have been identified in schizophrenia and major depressive disorder, and some patients have shown improvement following administration of nasal oxytocin (including cognition in schizophrenic patients) and a decrease in depressive and anxiety symptoms in patients with major depressive disorder.

Clinical application : What will happen if pituitary stalk is cut above pituitary gland?

Female slides

- Secretion of hormones stop totally.
- Secretion of hormones will not be affected.
- **Secretion of hormones decreases then return to normal level after few day ✔**

Because initially there are no signals received from the hypothalamus to stimulate the release of hormones, but later on the nerve will form new synapses which will return the hormone to its normal level.

For better understanding

Extra Summary

Stimulate secretion

In Both Sexes:

1. Hugging, touching & orgasm
2. Stress

In female:

1. Sounds of baby cry
2. During delivery when the head of the baby reaches the cervix

In male:

1. Contraction of smooth muscle of vas deferens (ejaculation)

Inhibit secretion

In Both Sexes:

Alcohol

Effect

Uterus: Childbirth / Parturition:

Late pregnancy: uterine smooth muscle (myometrium) become sensitive to oxytocin (*strong stimulant of contraction*) → ↑ intensity of uterine contractions →ending in birth regulation by positive feedback

Mammary Gland: Breastfeed:

Contracts myoepithelial cells of alveoli → trigger milk ejection "Classic neuroendocrine (letdown) reflex" Mechanosensory information from the nipple reaches the magnicellular neurons, causing the release of oxytocin into the general circulation. Oxytocin acts on receptors on myoepithelial cells in the mammary gland acini leading to the release of milk into the ductal system and, ultimately, the release of milk from the mammary gland.

Vas Deferens (Ejaculation):

↑ smooth muscle contraction of vas deferens → help in ejaculation process.

Ejection is more different than release of synthesis

Antidiuretic Hormone (Introduction)

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)

Storage

- ADH is stored in the neurohypophysis (posterior pituitary)

Details are just in female slides but it's very important

Important **ADH (Vasopressin) Receptors**

V1A	V1B	V2
• Mediate vasoconstriction (with Angiotensin II). • Also found in the liver (glycogenolysis) → increased blood pressure.	• Mediate increased ACTH (adrenocorticotropic hormone) secretion. • Unique to anterior pituitary. If there's a tumor that causes excessive secretion of ADH, it will in parallel stimulates increased secretion of ACTH. So high ADH comes in parallel with high Cortisol.	• Are receptors located in the Principal cells in distal convoluted tubule & collecting ducts in kidneys.

Single Most Important Function of ADH: Conserve body water by reducing urine output.
They work on sweat gland to decrease water loss

Extra

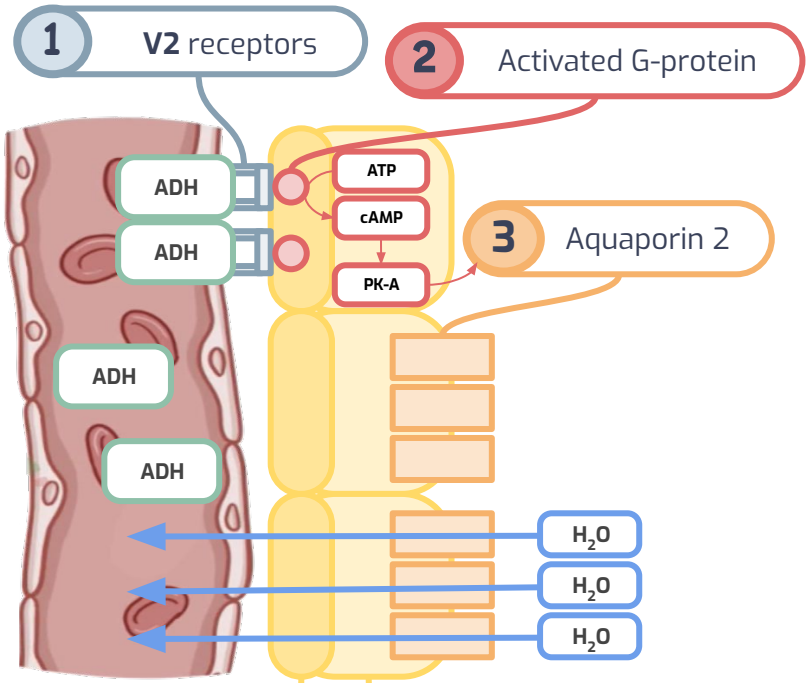
(442)

Osmotic pressure (oncotic pressure)	'Flashback from cardio' Baroreceptors
• Is the pressure that keeps the fluids in the capillaries. • One cause of its decrease is lossage of water faster than electrolytes → ↑electrolytes & ↓ water → ↑ ADH	• Baroreceptors are a type of osmotic receptors located in the arch of aorta & carotid arteries, they fire in response to a high BP (↑firing ↑BP = ↓firing = ↓BP)

Important

Antidiuretic hormone (mechanism of action)

(Special thanks to Sarah Alhamlan (439) for this amazing slide!)



Original Picture

AQP
Type 2= apical
Type 3,4= basolateral

Capillaries

Peritubular (serosal) surface
(basal membrane)

Lumen of Ducts

Principal cells of distal convoluted tubules & medullary collecting ducts
(Apical membrane)

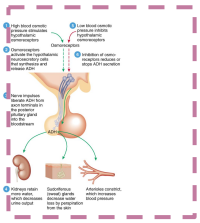
1 ADH binds to V2 receptors (step I in pic) on peritubular (serosal) surface of cells (principal cells) of distal convoluted tubules & medullary collecting ducts.

2 Via adenylate cyclase/cAMP ↑ induces production & **insertion of aquaporin 2** into luminal (apical) membrane + enhances permeability of cell to water. (step 2&3 in pic)
When ADH binds to its receptor,it activates the translocation of vesicles containing aquaporins to the apical cell membranes.

3 ↑ increased membrane permeability to water → permits back diffusion of **solute-free water** → ↑ urine osmolality (concentrates urine).

N.B In the absence of ADH → collecting tubules & ducts are almost impermeable to water → which allows extreme loss of water into urine.

Antidiuretic Hormone Secretion, Control & Regulation



Very Important

Dehydration → ADH released.
Overhydration → ADH inhibited.

Osmotic Stimuli

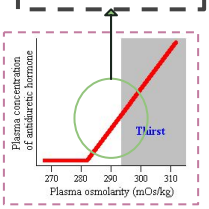
➢ **Stimuli:** Administration of solutes (Na+) will lead to ↑ in plasma osmolality which **will** stimulates both **ADH release** and **thirst** via:

➢ **Receptors:** osmoreceptors in or near the hypothalamus.

➢ **Sensitivity:** changes of 1-2% → ↑ ADH secretion, so it's very sensitive to changes in osmolality.

➢ **Effect:**
- ↑ Osmotic pressure/osmolality → ↑ ADH secretion:
- ↓ Osmotic pressure/osmolality → ↓ ADH secretion.
- Substances that enter cells rapidly, such as urea, do not change osmotic equilibrium →no simulation to release → no ADH secretion

Plasma osmolarity stimulates both ADH & thirst via Osmoreceptors



Non-osmotic stimuli: Volume effects

➢ **Stimuli: low blood volume (hypovolemia) & low blood pressure.**

➢ **Receptors:** baroreceptors in carotid artery & aortic arch (pressure receptors) mediated by vagus Nerve + stretch receptors in left atrium and pulmonary veins.

➢ **Normally: pressure receptors tonically inhibit ADH release.** Prolactin is as well tonically inhibited by dopamine.

➢ **Sensitivity:** senses changes 15 - 25% in volume → ↑ ADH secretion, sensitivity to baroreceptors is less than osmoreceptor

➢ **Effect:**
- ↑ **blood pressure** or ↑ blood volume → ↓ **ADH secretion.**
- ↓ **blood pressure** or ↓ blood volume → ↓ neural input from baroreceptors (pressure receptors) → relieves the source of tonic inhibition on hypothalamic cells → ↑ ADH secretion.

Non-osmotic stimuli: Others

➢ **Stimuli that increase ADH secretion (Physiological Stress):**
- Pain, nausea, trauma, surgical stress, emotional stress and fear.

➢ **Stimuli that decrease ADH secretion:**
- **Alcohol** intake (they lose their ability to control urination → urinate on themselves due to decreased ADH)

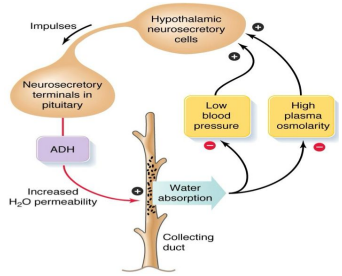
Male slides

Hypothalamus Receives feedback from:

- Osmoreceptors
- Carotid baroreceptors
- Aortic arch baroreceptors
- Atrial stretch receptors

Any increase in osmolality or decrease in blood volume will stimulate ADH secretion from posterior pituitary.

Function of ADH (vasopressin)



Pic was in both male and female slides

Antidiuretic hormone (Disorders)

Male slides

↑↑↑ ADH→ ↑ water retention (volume) + ↓ Na^+ conc. in ECF (osmolarity)
(blood → hyponatremia + urine → hyperosmolarity)
It might result from **bronchogenic** tumor, pneumonia or drugs
Treatment: hypertonic saline

ADH Disorders

- **SIADH** (Syndrome of Inappropriate Antidiuretic Hormone)
- **Diabetes Insipidus**

Disorders: Diabetes Insipidus

Very Important

A disorder resulting from deficiency of ADH or its action.
Characterized by: passage of copious amounts of dilute urine.
(a urine that has a lot of water and little electrolytes).

1- Neurogenic (central): failure of hypothalamus or neurohypophysis to **synthesize** or secrete ADH.
(The amount of ADH is abnormal, but the receptors are intact)

2- Nephrogenic: failure of the kidney to respond appropriately to ADH.
When the renal tubules of the kidney fail to respond to circulating ADH.
(The amount of ADH is normal, but it's unable to act on the receptors)
If you have increase ADH= nephrogenic
If you have decrease ADH/ neurogenic

Must be differentiated from other **polyuric states**, such as: primary **polydipsia** (عطش شديد) leading to increase consumption of fluids →↑urine volume & **osmotic diuresis.**

The resulting renal concentration defect → loss of large volumes of dilute urine→ cellular & extracellular dehydration & hypernatremia. Na is normal but the water is low

Treatment	Nephrogenic DI Treatment
Desmopressin (DDAVP): a synthetic analog is superior to native AVP (ADH) **because** : ➢ **Longer duration of action:** ○ **DDAVP:** 8 - 10 h ○ **AVP:** 2 - 3 h ➢ **More potent:** 3000 x greater antidiuretic activity than its pressor activity.	➢ Correction of underlying cause ➢ Provision of adequate fluids & calorie ➢ Low sodium diet ➢ Diuretics (thiazides) ➢ High dose of DDAVP

Antidiuretic Hormone

Extra Summary

Important

For better understanding

Stimulate secretion

- **↓ Baroreceptor:**

↓ blood pressure → ↑ ADH secretion.

- **↑ Osmoreceptors:**

↑ blood osmolality → stimulated hypothalamic osmoreceptors.

Extra explanation: when osmolality of blood is high, the receptors for osmolality (osmoreceptors) will send signals to the hypothalamus to increase the secretion of ADH
When the blood pressures (blood volume) is low, the receptors (baroreceptors) sense the change in blood and send signals to stop the inhibition (usually baroreceptors send signals to inhibit the secretion and in this case will inhibit the inhibition)

Inhibit secretion

- **↑Baroreceptors:**

↑ blood pressure → ↓ ADH secretion.

- **↓Osmoreceptors:**

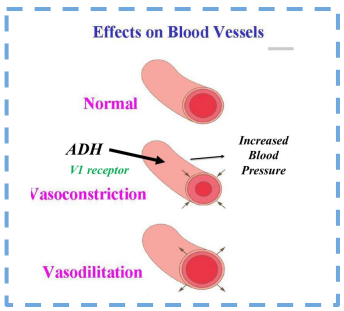
↓ blood osmotic pressure → inhibited hypothalamic osmoreceptors.

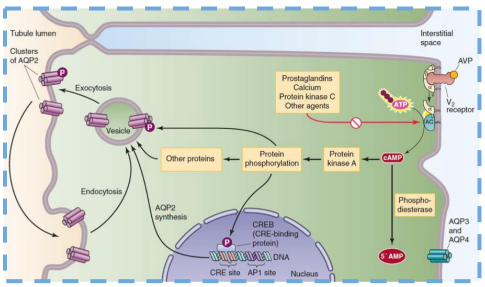
- **↑Alcohol**

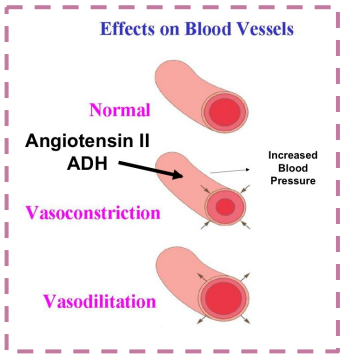
Effect

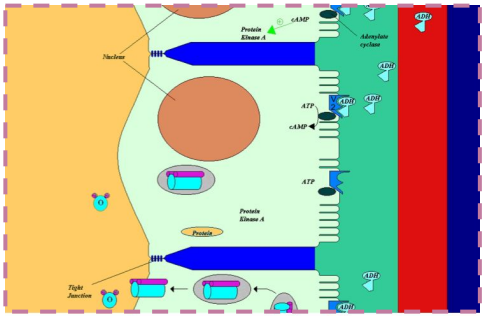
Kidney;
Kidneys retain more water which decrease urine output.
Sweat gland:
Sudoriferous glands ↓ water loss by perspiration from skin.
Arterioles:
Arterioles constrict →↑ blood pressure.

Pictures were in the lec

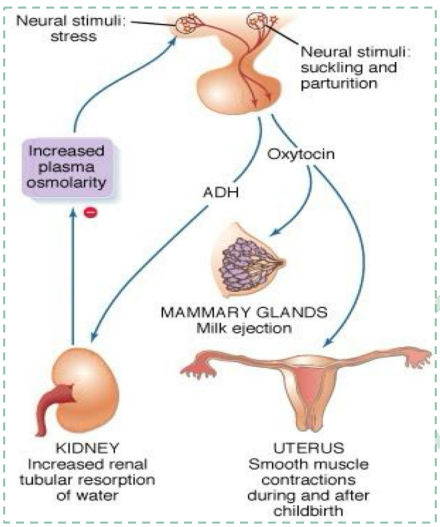








Summary of posterior pituitary hormones actions



Antidiuretic hormone (Summary from slides)

Very Important

When ADH levels are high, it leads to water absorption (due to antidiuretic action) and vasoconstriction.
When ADH levels are low, water is absorbed solely due to the antidiuretic effect.

Female slides

Receptors	Osmoreceptors	Baroreceptors
Location	Anterolateral hypothalamus	Carotid sinus, aortic arch, pulmonary veins, atria
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	15-25% decrease
Resulting Amount of ADH	Small (antidiuretic)	Large (vasoconstriction)
Override Other?	no	yes

Male slides

Control of Antidiuretic hormone secretion	
What causes ↑ ADH	**What causes ↓ ADH**
↑ plasma osmolarity	↓ plasma osmolarity
↓ blood pressure	↑ blood pressure
↓ blood volume	↑ blood volume
Nausea	Alcohol
Drugs: morphine - nicotine - cyclophosphamide.	**Drugs:** clonidine (*antihypertensive*) - haloperidol (*dopamine blocker*).
Hypoxia	------

MCQs:

QI: which of the following ADH receptors act on blood vessels?

A- $V1_A$ | B- $V1_B$ | C- V2 | D- V3

Q2: which of the following decrease ADH secretion?

A- high osmolarity | B- low blood pressure | C- low blood volume | D- alcohol intake

Q3: activation of osmoreceptor affect the ADH release in which way?

A- no effect | B- inhibit ADH release | C- stimulate ADH release | D- baroreceptor function

Q4: where is ADH synthesized?

A- Posterior pituitary | B- Anterior pituitary | C- pituicytes | D- supraoptic nuclei

Q5: DI characterized by failure renal tubules of kidney to respond appropriately to circulating ADH.

A- neurogenic | B- nephrogenic | C- SIADH | D- central

Q6: The hormone involved in the ejection of milk :

A- GH | B- Prolactin | C- Oxytocin | D- FSH

Answers: Q1:A | Q2:D | Q3:C | Q4:D | Q5:B | Q6:C

SAQ:

- QI. list five stimuli that increase ADH secretion?
- Q2. Explain the mechanism of action of ADH?

AI:↑ plasma osmolarity,↓ blood pressure ,↓ blood volume,Nausea,Hypoxia

A2: page 7

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

Special thanks to notes taker Lama Al Mutairi and Yazeed Al Sulaim and Fahad Al Mughaiseeb