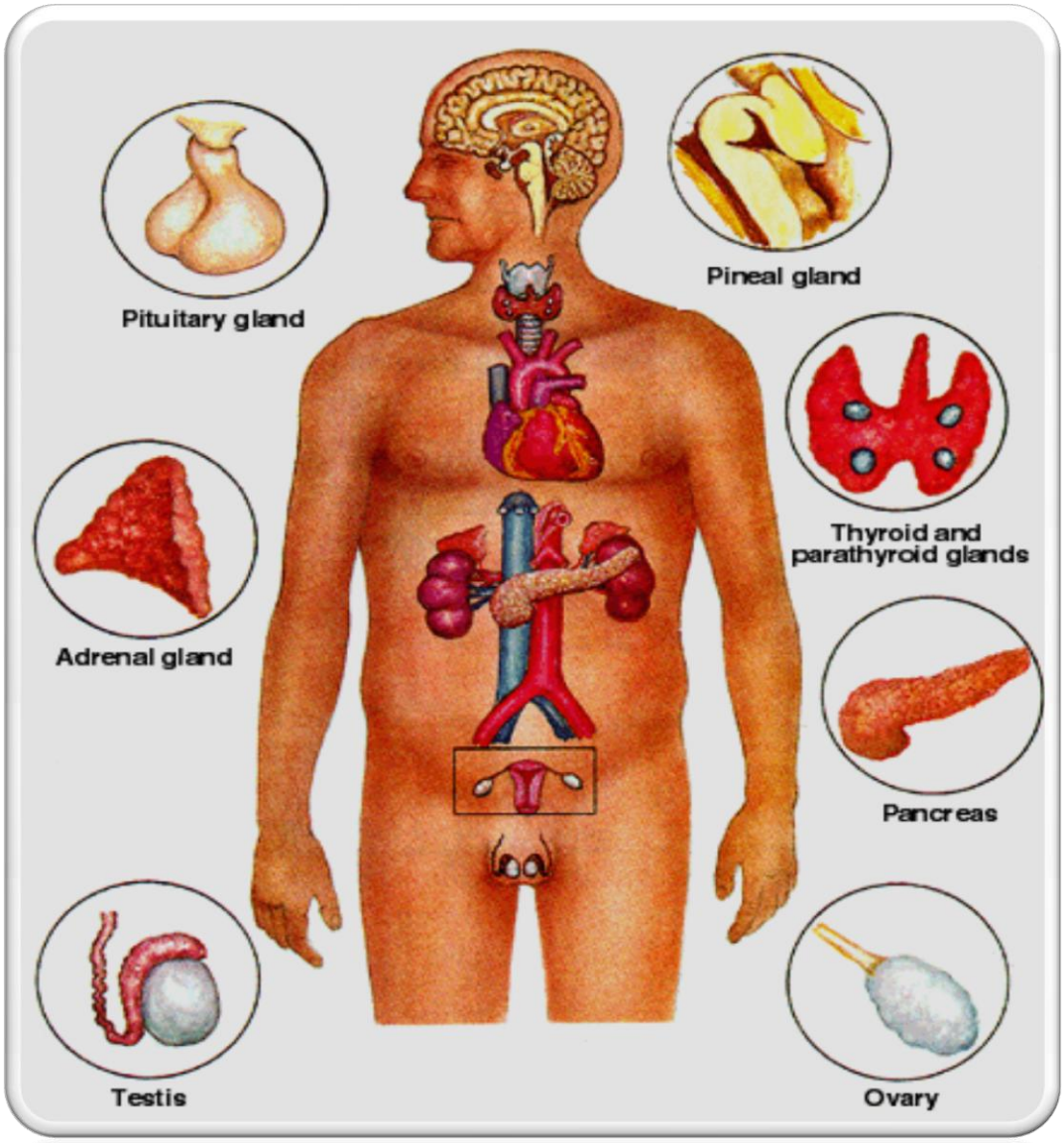
ENDOCRINE BLOCK

PHYSIOLOGY TEAM 431



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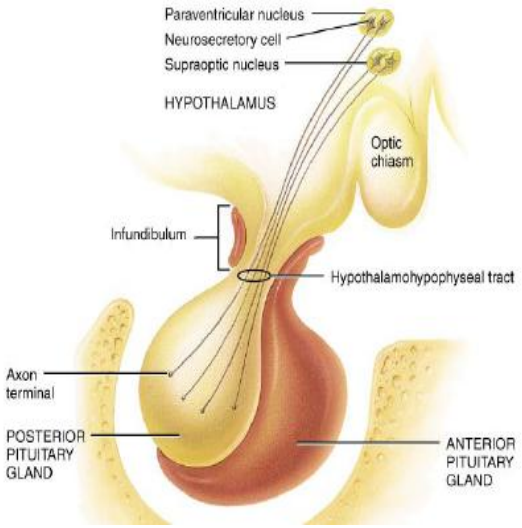
ADH (vasopressin) has 2 functions, that's why it has 2 names:
1. Vasoconstriction.
2. Water retention.

Posterior Pituitary

What controls posterior pituitary? Hypothalamic-hypophyseal tract

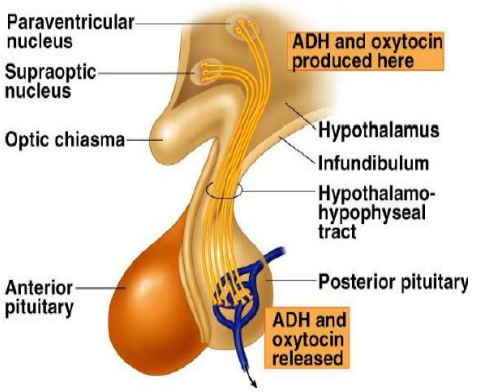
What controls anterior pituitary? Hypothalamic-hypophyseal portal system.

- Posterior pituitary gland stores and releases hormones that are synthesized by large neurons in the supraoptic above the optic chiasm and paraventricular nuclei of the hypothalamus.
- Consists of axon terminal of hypothalamic neurons.
- Hormones secreted by the posterior pituitary:
  1. ADH (vasopressin). 2. Oxytocin.



- ❖ Supraoptic nuclei of the hypothalamus synthesize mainly ADH, and 1/6 oxytocin.
- ❖ Paraventricular nuclei of the hypothalamus synthesize mainly oxytocin and 1/6 ADH.
- ❖ Then packaging and storage of these hormones (peptides) into vesicles.
- ❖ These vesicles can be transported in the axons till they reach the posterior pituitary.
- ❖ Posterior pituitary substance: is supporting cells called pitucytes. Their function is to support these axons (end terminal axons).
- ❖ When the hormone is needed, it will be released by an impulse which travels from these nuclei, helps in carrying the vesicles down the axon (hypothalamic-hypophyseal tract) and then they will be released.

N.B posterior pituitary gland does not synthesize hormones.



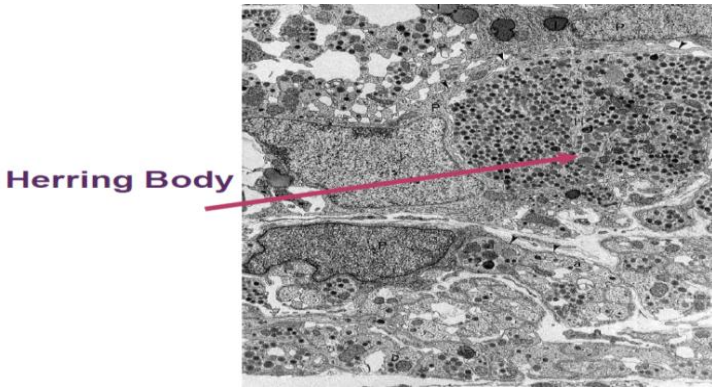
Hypothalamic control of pituitary secretions:

Secretions of the posterior pituitary are controlled by nervous signals from hypothalamus.

ADH: if there is any changes in the osmolarity there will be stimulation of some osmo receptors near the nuclei< these osmo receptors will send impulses to the nuclei and stimulate them to release ADH in the posterior pituitary

Paraventricular which secrets oxytocin:
-Also there are some impulses which will travel from either the uterus or the mammary gland (after sucking).
-Some mechano receptors will send impulses through the vagus and glossopharyngeal nerve and these impulses will travel till they reach the nuclei and cause stimulation to release oxytocin.

Electron microscopic photo shows Herring Body which stores hormones in the axons (terminal endings).



Antidiuretic Hormone (Vasopressin)

Synthesis of ADH:

- It's synthesized as pre-prohormone and processed into nonapeptide (nine amino acids).
- ADH synthesized in the cell bodies of hypothalamic neurons (supraoptic nucleus).
- ADH is stored in the neurohypophysis (posterior pituitary)- forms the ,most readily released ADH pool.

Receptors of ADH (vasopressin):

There are 2 types of receptors for ADH

1. $V1_A$ receptors: mediate vasoconstriction (on blood vessels). Also found in the liver mediate glycogenolysis (break down of glycogen into glucose).
2. $V1_B$ receptors: are specific for anterior pituitary and mediate increased ACTH secretions.
3. V2 receptors:
   Are located in the principal cells (epithelium) in distal convoluted tubule and collecting ducts in the kidneys. They are specific for water absorption.

That why sometimes when the ADH secretion is high in case of posterior pituitary tumor it might lead to increased ACTH which will release more cortisol and it will also affect the skin causing pigmentation.

Mechanism of action of ADH: Antidiuresis (retains and prevents excessive loss of water in urine (kidney) and sweating).

- ✓ ADH binds to V2 receptors on the peritubular (serosal) surface principal cells of the distal convoluted tubules and medullary collecting duct. (Serosal means near the blood vessel not the lumen).
- ✓ After the hormone binds to the receptor it stimulates the production of secondary messenger (adenylate cyclase) which will stimulate the conversion of ATP to cAMP.
- ✓ Once cAMP is formed it will activates protein kinase A leading to phosphorylation of some proteins that will cause production and insertion (movement) of aquaporin2 (channels for water absorption) into the luminal membrane and open pores to allow water to be reabsorbed from the tubules back to the blood.
- ✓ By this action it enhances the permeability of the collecting tubules to water only.
- ✓ Increased membrane permeability to water permits back diffusion of solute-free water, resulting in increased urine osmolality (concentrates urine). (Means that it will lead to production of concentrated urine and prevent water loss).
- ✓ When ADH is removed, the water channels withdraw from the membrane and the apical surface of the cell becomes impermeable to water once again. .

Plasma osmolarity is most important stimulator of ADH secretion because it's very sensitive.

- High solutes in the fluid (hyperosmolarity).
- Low solutes in the fluid (hypoosmolarity).

Secretion of ADH:

Osmotic and non-osmotic stimuli.

Osmotic stimuli: osmolality (amount of solutes in a fluid).

- ✓ Increase in the osmolarity will stimulate osmoreceptors in the ventral part of the hypothalamus, close to the supraoptic nuclei.
- ✓ If plasma osmolarity is directly increased by administration of solutes, only those solutes that do not 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.
- ✓ H_2O deprivation → high osmolarity of blood → stimulation of osmoreceptor → stimulate supraoptic nucleus → stimulate nerve ending → release ADH

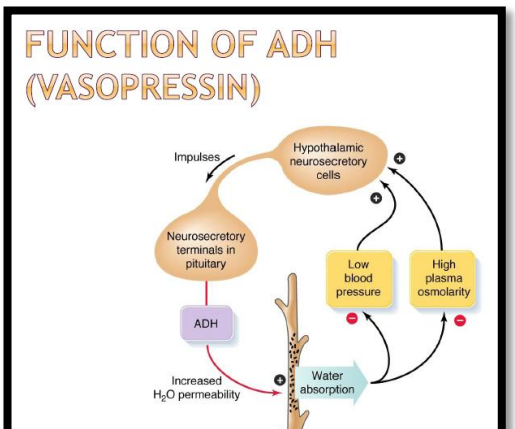
Non-osmotic stimuli: (Stimulus is change in the blood pressure).

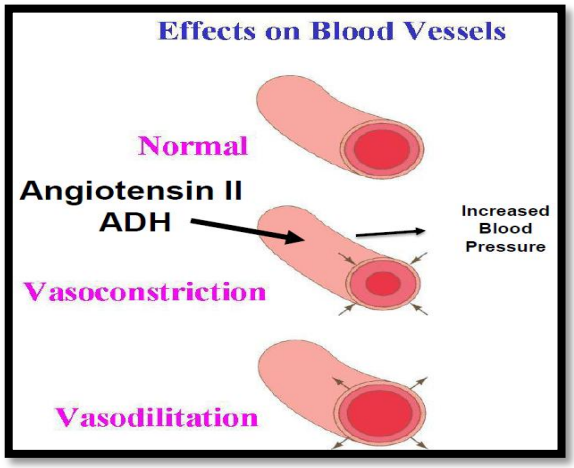
- ✓ Hypovolemia is perceived by (pressure receptors) carotid and aortic baroreceptors, and stretch receptors in left atrium and pulmonary veins.
- ✓ Normally, pressure receptors tonically inhibit ADH release.
- ✓ Decrease in blood pressure induces ADH secretion by reducing input from pressure receptors.
- ✓ 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. It senses 5-10% change in volume to be stimulated.

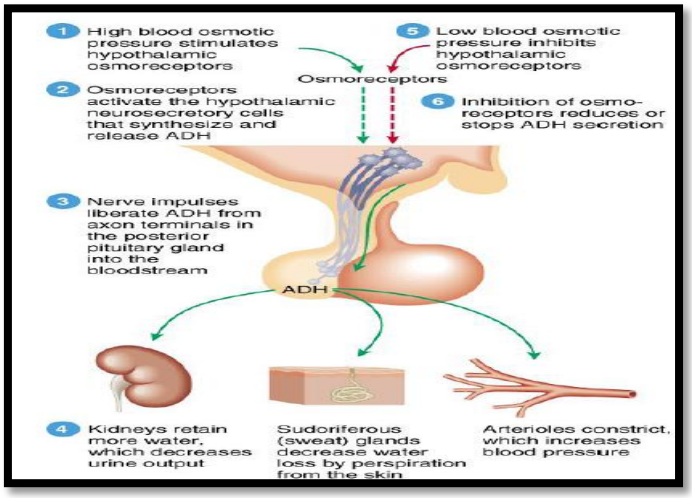
- In normal situation, when the blood pressure and volume is normal (sometimes high) the baroreceptors are stretched leading to inhibition of ADH release by sending impulses continuously to the brain.
- Once blood pressure or volume drops (shock, hemorrhage, excessive vomiting diarrhea, and severe dehydration) it removes this stretch causing stop of inhibitory impulses leading to increase in ADH secretion.
- Increased ADH causes water reabsorption and correct the low volume or blood pressure.
- Finally it will stop the release (negative feedback).

CONTROL OF ADH RELEASE

- **Osmotic pressure:**
  - Osmoreceptor mediated
  - ↑osmolality → ↑ADH secretion
  - ↓osmolality → ↓ ADH secretion
- **Volume effects**
  - Baroreceptor mediated (vagus nerve)
  - ↑blood pressure → ↓ ADH secretion
  - ↓blood pressure → ↑ ADH secretion







ADH actions:

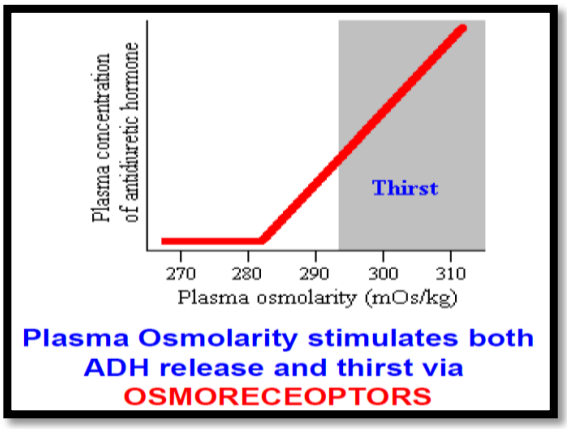
1. Most important on the kidney to conserve water.
2. Act on sweat gland and reduce sweating.
3. In higher concentration it will produce vasoconstriction.

Regulation of ADH:

- Dehydration: ADH released.
- Overhydration: ADH inhibited.

Minute increase in the osmolarity will lead to:

1. first high and rapid release of ADH
2. Then will stimulate the thirst mechanism to help take more water but it happens later when the osmolarity is above 290.



Plasma Osmolarity stimulates both ADH release and thirst via OSMORECEOPTORS

TABLE SUMMARIZES THE MAJOR CHARACTERISTICS OF OSMORECEPTORS AND BARORECEPTORS

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

Location of osmoreceptors: anterolateral or anteroventral hypothalamus
Location of baroreceptors: also found in the atrium.

Stimuli that increase ADH secretion: pain, nausea, surgical stress, emotional stress.

Stimuli that decrease ADH secretion: alcohol intake.

- The volume receptors also stimulate the sympathetic nervous system → which stimulates Renin release from Juxtaglomerular Apparatus of the kidney → this leads to activation of Angiotensin II that causes →
  - vasoconstriction → increase in BP
  - Thirst → which makes the person drink water → increase blood volume

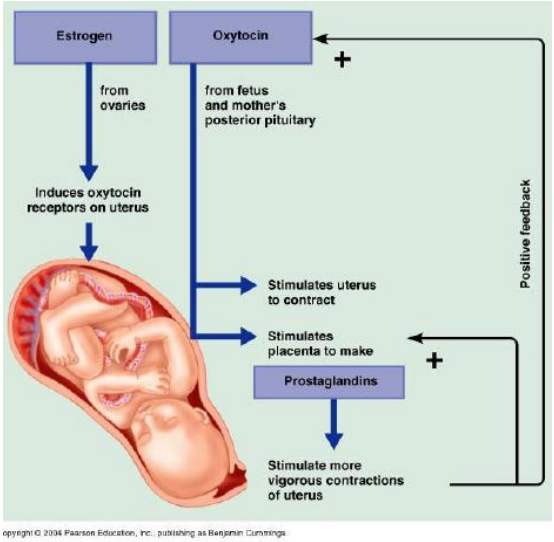
- Mechanical disruption or the neurohypohyseal tract by trauma, tumor, or surgery temporarily causes ADH deficiency.
- ADH will be restored after regeneration of the axons (about 2 weeks).
- But if disruption happens at a high enough level, the cell bodies die in the hypothalamus resulting in permanent ADH deficiency

Oxytocin

Function of oxytocin:

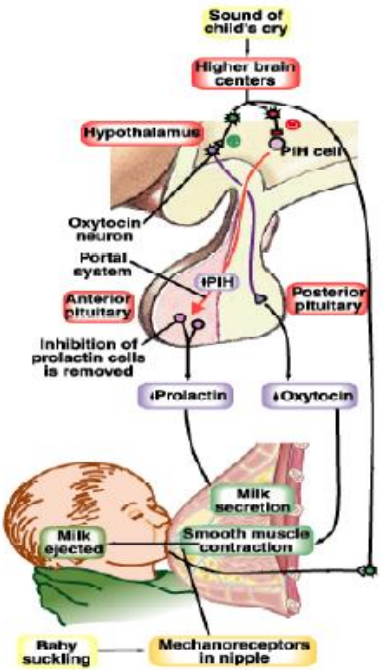
1. Breast Feeding (acts on the breast): positive feedback.
   Contracts the myoepithelial cells that surround the alveoli (Which is full of milk) so it will cause ejection of milk.
2. Childbirth (parturition): (act on the uterus)
   In late pregnancy, uterine smooth muscle (myometrium) becomes sensitive to oxytocin (positive feedback).
3. Also oxytocin can stimulate the release of prostaglandins because they are important in the uterus contraction.

- ✓ The fetus is pushed by the contraction of uterus towards the cervix, when the head of the fetus is pushed to the cervix, the cervix receptors will be stretched and will be stimulated.
- ✓ The impulse will travel through the nerve to the brain, and will stimulate release of oxytocin.
- ✓ Oxytocin will travel in blood cause more contraction which will push the head more towards the cervix.
- ✓ Cervix will be stimulated again and send impulses to release more oxytocin until the baby is delivered.
- ✓ Towards the end of pregnancy oxytocin increases and the oxytocin receptors up regulate.



- ✓ The nipple has mechanoreceptors.
- ✓ When the baby starts breast feed, these receptors will sense the sucking action and send impulses to the vagus.
- ✓ That goes to the brain to stimulate oxytocin and stop prolactin inhibitory hormone (PIH) which will increase prolactin secretion (When u stop the inhibitory mechanism the release of hormone will increase)

- Sometimes when the mother hears the baby crying the milk comes down psychologically (emotionally)
- Also the milk can come down cyclically (When the time comes for breast feeding).



Oxytocin sometimes is used as a drug to induce labor either by:

1. Stimulation of week contraction
2. Or when the mother exceeds the time of delivery (more than 42 weeks) and they have to stimulate the labor by oxytocin.

(And they start with prostaglandin to help make the cervix soft and then they give oxytocin).

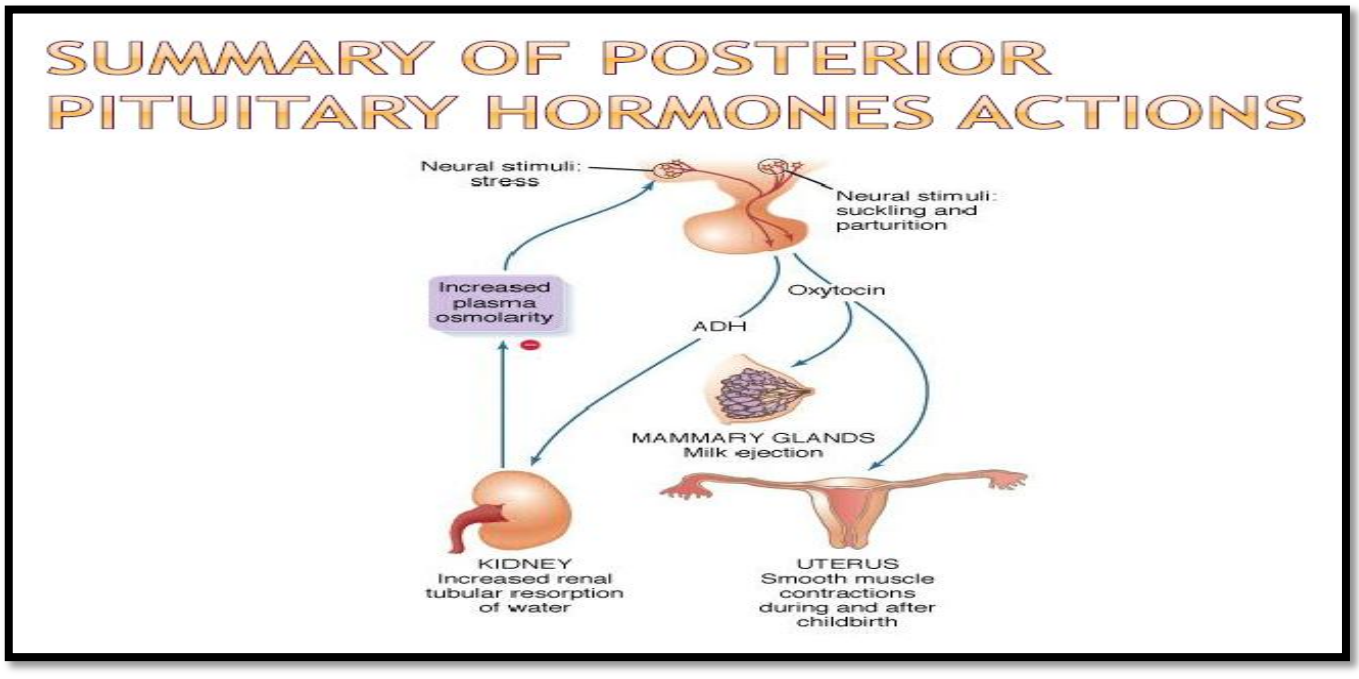
- Oxytocic drugs (e.g., Syntocinon) are used by obtetricians to induce labor in postmature pregnant women

Other stimuli that control release of oxytocin:

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

Oxytocin and Autism:

- Autistic group had significantly lower plasma oxytocin levels than in the non-autism group. (that's why when u hug an autistic child, he feels comfortable because it stimulates oxytocin release).
- Elevated oxytocin was associated with higher scores on social and developmental measures for the non-autistic children



SUMMARY

1) The Posterior Pituitary does NOT synthesize the hormones (ADH & Oxytocin) but only stores them after they are sent to it from hypothalamus

2) Thus ADH increases water retention by the kidney → decreased urine output (volume) → increasing the ECF volume → body water conservation .

3) Injection (administration) of solutes that do not freely or rapidly penetrate cell membranes , such as sodium (hypertonic saline) → increase the ECF osmotic pressure as compared to ICF of osmoreceptors → water diffuses out of osmoreceptors → ADH secretion is stimualted

4) On the other hand , injection of substances that enter cells rapidly, such as urea, do not change osmotic equilibrium and thus do not stimulate ADH release

5) Oxytocin release is stimulated by the infant suckling his mother's breast .

6) On the uterus : Oxytocin 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 breast-feeds him → baby suckling produces oxytocin release → milk let-down + uterine contraction (which prevents further blood-loss from the mother

Questions

1. Hypovolemia causes:
   a. Increase in ADH secretion
   b. Decrease in ADH secretion.
   c. Increase in oxytocin secretion.

2. ADH is synthesized mainly in:
   a. Paraventricular nuclei.
   b. Supraoptic nuclei.

3. Posterior pituitary is controlled by:
   a. Hypothalamic hypophyseal tract.
   b. Hypothalamic-hypophyseal portal system.

4- ADH increase by :
   a. Stimulation of baroreceptors
   b. Suppression of baroreceptors

Answers:

1(a) 2(b) 3(a) 4(b)