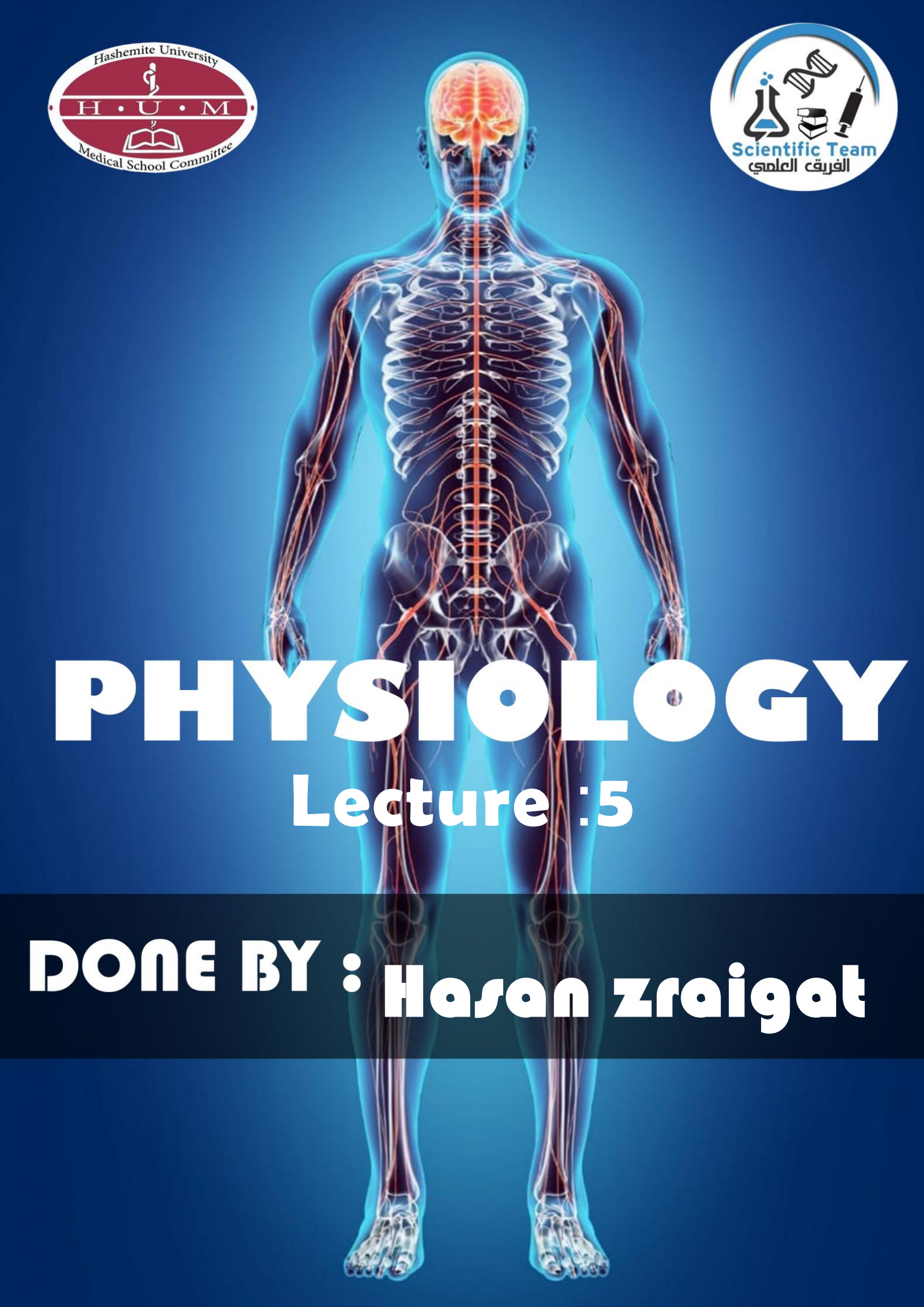

PHYSIOLOGY

Lecture :5

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Posterior Pituitary Hormone

Target organs of ADH : Uterus and Mammary glands

Oxytocin: Kidneys, Sudoriferous (sweat) glands and Arterioles

Hormones of the posterior lobe of the pituitary

▪ The posterior pituitary gland store and release antidiuretic hormone (ADH) and oxytocin

. ▪ These hormones are synthesized in hypothalamic nuclei

▪ Both hormones are packaged in secretory granules with their respective neurophysins

. ▪ Both hormones are homologous nonapeptides.

▪ ADH and oxytocin are synthesized by neurosecretory neurons in the supraoptic (SO) and PVN of the hypothalamus

▪ Hormones travel down the nerve axons for storage and secretion by the posterior pituitary.

▪ ADH is the primary hormone secreted by SO nucleus ▪ Oxytocin is the primary hormone secreted by PVN nucleus

pituitary has two parts: gland secretory part and neural part (anterior and posterior part)

*Posterior part: secret anti-diuretic hormone so, neurons from hypothalamus ends at posterior pituitary, they release chemical material (hormones) .

*anterior pituitary: it is glandular part we have at least 5-6 type of cells (function: to regulate other endocrine and exocrine glands)

other endocrine glands as: thyroid, adrenal gland(top of kidneys), we have 2 hormones to regulate testes and ovaries(all before are endocrine), hormone to regulate breast development and milk secretion(exocrine), hormone regulate body growth.

growth :for specific small tissue , larger tissue, or total body

طبعا يختلف الهدف من النمو حسب النسيج مثال في ال breast بهدف انتاج الحليب,بينما لما نحكي عن الأطراف ما فيها هدف لإفراز وإنما مجرد total body growth

What is anti-diuretic hormone?

Anti-diuretic hormone is made by special nerve cells found in an area at the base of the brain known as the hypothalamus. The nerve cells transport the hormone down their nerve fibres (axons) to the pituitary gland where the hormone is released into the bloodstream. Anti-diuretic hormone helps to control blood pressure by acting on the kidneys and the blood vessels. Its most important role is to conserve the fluid volume of your body by reducing the amount of water passed out in the urine. It does this by allowing water in the urine to be taken back into the body in a specific area of the kidney. Thus, more water returns to the bloodstream, urine concentration rises and water loss is reduced. Higher concentrations of anti-diuretic hormone cause blood vessels to constrict (become narrower) and this increases blood pressure. A deficiency of body fluid (dehydration) can only be finally restored by increasing water intake.

Actions of ADH

Regulates serum osmolarity by increasing the H2O permeability of the late distal tubules and collecting ducts

It increases H2O permeability via a V2 receptor and an adenylate cyclase– cAMP mechanism) which increase synthesis of water channels (aquaporin 2, AQP2) of the principal cells of the late distal tubule and collecting duct

Constriction of vascular smooth muscle (via a V1 receptor and an IP3/Ca2+ mechanism). This action increases the TPR

Regulation of ADH secretion

• Osmoregulation

• An increase of only 1% in the osmolality of the ECF bathing the hypothalamic osmoreceptors evokes an increased in ADH secretion.

• A similarly sized decrease in osmolality decreases ADH secretion.

• In this manner, ECF osmolality is kept very close to 285 mOsm/Kg.

• Osmoreceptor cells are located in hypothalamus, primarly in organum vasculosum in the third ventricle)

• Osmoreceptors are neurons that respond to increased plasma osmolarity, (principally plasma sodium concentration).

• They synapse with neurons of the SO and PVN and stimulates the release of ADH from neurosecretory cells and posterior pituitary

• Osmoreceptors also stimulate thirst hypothalamic centers that regulate water intake.

• Volume Regulation
• 15-25% blood volume reduction will severely stimulate ADH secretion.
• Decline in blood volume cause a drop in blood pressure
• Amount of blood volume is detected by atrial stretch receptors, and the drop in blood pressure is detected by baroreceptors of carotid, aortic receptors
• A signal transmitted via the baroreceptor afferents to the hypothalamus and increase ADH secretion
• This mechanism is especially important for restoring ECF volume following a hemorrhage.

Increased Plasma Osmolarity and Decreased Blood Volume Stimulate ADH Release

Increasing plasma osmolarity and decreasing blood volume independently increase ADH release .Osmoreceptors in the anterior hypothalamus tonically stimulate magnocellular neurons to secrete ADH. Lowering the osmolarity reduces ADH secretion and increasing plasma osmolarity increases it. This forms a negative feedback loop, as ADH retains water by action on the kidneys. Briefly, ADH engages a G_s mechanism through V2 receptors that increase the water and urea permeability of principal cells of the collecting duct, by recruiting latent aquaporin-2 water channels to the apical membrane. High ADH increases reabsorption of water and produces a low volume of highly concentrated urine; low ADH is associated with a high volume of highly dilute urine. Lowered osmolarity decreases ADH secretion, causing loss of water over salt in the kidney and the blood osmolarity returns toward normal. Increased osmolarity increases ADH secretion, leading to reabsorption of water. Salt can be excreted in excess of water, leading to a return toward normal plasma osmolarity.

Pathophysiology of ADH
▪ Diabetes insipidus ▪ Central DI ▪ Nephrogenic DI ▪ SIADH
▪ Gestational diabetes insipidus. Is rare. It occurs only during pregnancy when an enzyme made by the placenta destroys ADH in the mother.

Diabetes Insipidus Central diabetes insipidus (CDI) Causes
▪ Deficiency of Plasma ADH synthesis or section
• Hypothalamic destruction by stroke, hypoxia, head trauma, infection,
• Tumors (craniopharyngioma) Signs and symptoms
• Increased serum osmolarity
• Dehydration • Polyuria • polydepsia • Colourless urine instead of pale yellow. • Dry skin. • Constipation . • Weak muscles. • Bedwetting.

Nephrogenic diabetes insipidus

▪ The posterior pituitary and hypothalamic secretory neurons are normal

▪ Principal cells of the collecting duct are unresponsive to ADH due to a defect in the V2 receptor, Gs protein, or adenylyl cyclase.

▪ Genetics Autosomal recessive aquaporin-2 channel gene alterations X-linked recessive V-2 receptor gene alteration

▪ ADH levels are elevated in nephrogenic diabetes

▪ Other Causes: • Hypokalemia Hypercalcemia • Lithium, low potassium, and high calcium all diminish ADH's effectiveness on principal cells. The precise mechanism is still unclear, but it may involve disruption in the ability to traffic aquaporins to the luminal membrane of principal cells of the kidney • Chronic kidney disease or renal infarction Management : Thiazide diuretic

Syndrome of Inappropriate ADH Secretion (SIADH)

• Excessive secretion of ADH causes an inappropriate increased reabsorption of water in the renal collecting duct.

• hypoosmotic volume expansion.

• The osmolarity of ECF decreases because excess water is retained. • ECF and ICF volumes increases because of the water retention volume increases.

• Plasma protein concentration decreases because of the increase in ECF volume

• Increased water retention leads hyponatremia, normal sodium stores)

• Inappropriate concentration of urine, often greater than plasma osmolarity

• Causes

• Ectopic production of ADH by tumors (for example small cell lung)

• Drug induced: carbamazepine

Management

▪ Syndrome of Inappropriate ADH Secretion (SIADH)

• Fluid restriction but not salt restriction

• Only mild hyponatremia from SIADH can be managed with fluid restriction.

• Severe disease needs 3% hypertonic saline or V2 receptor antagonists.

• Nonpeptide V2 vasopressin antagonists (Conivaptan and tolvaptan)

• Demeclocycline it acts on collecting tubule cells to diminish their responsiveness to ADH

▪ Central diabetes insipidus DDAVP

▪ Nephrogenic diabetes insipidus

• Thiazide diuretics

Primary functions of oxytocin

Milk Let down and labor Milk let down reflex Afferent fibers carry impulses from the nipple to the spinal cord. Relays in the hypothalamus trigger the release of oxytocin from the posterior pituitary

Oxytocin nine a.a secreted by the POSTERIOR BITUTARY in response to terminal of neurons from the hypothalamus (particularly the paraventricular nuclei) if we cut this region btw the hypothalamus and the posterior pituitary what will happen?

Everything will decrease except the prolactin would increase and oxytocin →(we have synthesis the oxytocin and the transport them through this area any cut in the nerve ending of the hypothalamohypophysial tract this region will cause a neural shock at the beginning (stop of the synthesis and secretion) and later on WHAT HAPPEN IS :

in any neuron IF the cut closer to the soma (cell body neuron) the soma will degenerate and if the cut was far from the soma the axon will regenerate i.e. it will take few days then it will come back ,regenerate and start to release neurotransmitters again which we call them HORMONES NOW

Effects of Oxytocin

• The Milk Ejection through the milk neuroendocrine reflex Reflex

• Oxytocin causes contraction of the myoepithelial cells that line the ducts of the breast.

• This squeezes the milk out of the alveoli of the lactating breast into the large ducts (sinuses) and thence out of the nipple (milk ejection)

• Can also be released before suckling (anticipatory) causing spontaneous milk ejection.

• The sight or sound of the infant may stimulate the hypothalamic neurons to secrete oxytocin, even in the absence of suckling.

• in males, circulating oxytocin increases at the time of ejaculation, and it is possible that this causes increased contraction of the smooth muscle of the vas deferens, propelling sperm toward the urethra.

Oxytocin functions

• Oxytocin causes contraction of the smooth muscle of the uterus and involved in labor and parturition.

• The sensitivity of the uterine musculature to oxytocin is enhanced by estrogen and inhibited by progesterone.

• In late pregnancy, the uterus becomes very sensitive to oxytocin coincident with a marked increase in the number of oxytocin receptors

• Oxytocin secretion is then increased during labor likely due to dilation of the cervix

• Oxytocin can be used to induce labor and reduce postpartum bleeding.

• Oxytocin may also act on the nonpregnant uterus to facilitate sperm transport. The passage of sperm up the female genital tract to the uterine tube

• in males, circulating oxytocin increases at the time of ejaculation, and it is possible that this causes increased contraction of the smooth muscle of the vas deferens, propelling sperm toward the urethra

• the secretion of oxytocin is believed to increase during orgasm

• The secretion of oxytocin is also increased by stressful stimuli and, like that of vasopressin, is inhibited by alcohol

• stimulates various types of positive social interaction

• What is the function of Oxytocin???

To increase: - Contractility of myoepithelial cells why?? Since they do the milk let down or milk ejection so going back to the last information we talked about:

- Milk synthesis in the alveoli: depend on prolactin

Note: -

this dilation of the cervix will feedback to the paraventricular nuclei to increase the oxytocin so it will lead to increase uterus contractility leading to baby more pushing down which lead to more dilatation and more dilatation mean more stimulation to oxytocin (THIS IS A POSITIVE FEEDBACK which is temporary to achieve a certain concentration to full fill a function once this function is performed no more need for this positive feedback) the process continue until the baby get to the outside (of course there is a sequence for the placenta) - when the baby get out there is no more distention of the cervix - every time nipple stimulation occur it will lead to uterus contraction since through the nipple stimulation we stimulate the oxytocin secretion which won't only go to the myoepithelial cells in the breast , it will go to the whole body wherever it has a receptor it will function - What is the value of the nipple stimulation after delivery on the uterus? Now when the mother has the baby inside the size the baby was large and the uterus of course will

compensate with the baby size. so uterus after the delivery will decrease in size in addition the contraction of uterus will do kind of constriction of blood vessels found in this region (and finally عن الرحم المشيمة انسالخuterine wall) that will decrease the bleeding caused by the return the uterus back to pre-pregnancy size - So females who don't perform the breast feeding is susceptible more for the bleeding and the return of the uterus to the normal size would take a longer duration (it will get back but with longer duration) since we don't stimuli for the uterine contractility