ENDOCRINE BLOCK

PITUITARY GLAND

Correction File

Case..

28 year-old woman reports a history of oligomenorrhea, and infertility for 10 months. She reports some breast tenderness and headaches, but denies any galactorrhea. Her last menstrual period was May 30th; she denies the possibility of pregnant

Which hormone is incresed in this case ? Prolactin hormone

Mention some differential diagnosis of elevation this hormone ?

- Nipple stimulation or sex
- History of chest wall surgery or trauma
- Primary hypothyordism due ⬆in TRH
- Excessive exercise
- Renal failure
- Cirrhosis

Mention other symptoms can be found in this case ? breast enlargment

Mention the main funtion of prolaction hormone ? Stimulats milk Production

Mention the cause of inferilty in this case ?
Because of hyperprolactinemia inhibts the GnRH that leads to ⬇ in FSH and LH

What is the proper teatment of elevation this hormone ? Dopamine agonist

Mention some factors that stimulate the release of Prolactin and some inhibit it?
Factors ⬆:Suckling response inhibits PIH release
Sleep , Surgical & psychological stress , Exercise Stimulation of the nipple ,TRH & Pregnancy
Factors ⬇: Release is inhibited by PIH (dopamine)

What are the Causes of Hyperprolactinemia ?

Hypothalamic Dopamine Deficiency	Defective Transport Mechanisms
- Diseases of the hypothalamus(including tumors, arterio-venous malformations,& inflammatory processes - Drugs (e.g. alpha-methyldopa and reserpine)	- Section of the pituitary stalk - Pituitary or stalk tumors

Lactotroph Insensitivity to Dopamine Stimulation of Lactotrophs	Stimulation of Lactotrophs
- Dopamine-receptor-blocking agents	- Hypothyroidism- increased TRH production (acts as a PRF) - Estrogens: stimulate lactotrophs - Injury to the chest wall: abnormal stimulation of the reflex associated with the rise in prolactin that is seen normally in lactating women during suckling.

Mention the type of regulatory feedback in the following:

- Baby sucking milk from the breast and prolactoin⇒ Positive
- Prolactin Inhibtin hormone (dopamine) and prolactin⇒ Negative

What are the functions of the hypothalamus?
Linking the nervous system to the endocrine system by :
1-secretion of regulatory hormones to control the activity of ant. lobe of pituitary gland
2-production of ADH and oxytocin
3-control of sympathetic output to adrenal medulla

Case..

A 58-year-old carpenter attended an orthopedic surgeon because he had difficulty in holding the tools of his trade. For the previous 12 years, he had seen his primary care physician repeatedly complaining of 'pins and needles' and numbness in both hands. The orthopedic surgeon confirmed the clinical diagnosis of bilateral carpal tunnel syndrome and performed bilateral decompression of the median nerve at the wrist. Clinical examination showed the hands to be broad and spatulate. From the clinical examination and investigation patient has large tongue with deep furrows, deep voice and imparied glucose tolerance (insulin resistance) ?

What is the most likely the diagnosis ? Acromegaly

What is typically cause of this disease ? Hyperfunctioning mass (pituitary adenoma)

Mention the hormone that will be elevated in this case? and mention the hormone that stimaulates and inhibts this hormone ?
Growth hormone / stimulated by GHRH and inhibted by somatostain.

Mention some changes that can be found in this patient ?
1-High serum IGF-1 due faliure to suppress serum GH
2-Increase in blood glucose level
What is the name of this disease in Chlidren ? Gigantism
If the patient is child and has low level of GH, What is the name of the diseases that results ?
Growth hormone deficiency in childrean → dwarfism

Mention the manegment of this patient ?
Pitutary adenoma resection follwed by somatstain analog

What is the Blood supply of the Pituitary gland ?
Arteries which are branched from internal carotid artery.:
superior hypophyseal (for infundibulum and anterior lobe)
inferior hypophyseal(for posterior lobe) arteries
Veins: hypophyseal veins drain into cavernous sinuses.

Where does pituitary gland lie?
It lies in the middle of cranial fossa in hypophyseal fossa of the body of sphenoid bone and protected by sella turcica.

GROWTH HORMONE:
1-Produced by somatotropic cells in pulsatile fashion.
2-Its secretion is :

Increased by[SSS]	Decreased by[SOS]
1-Stress(exercise) 2-Starvation(hypoglycemia) 3-Sleep 4-Increase grelin stomach secretion 5-Intake of protein or amino acids (after meals)	1-Somatostatin 2-Obesity (⬆ Glucose ⬆ Free fatty acid) 3- Somatomedins & GH

Pituitary relation :
Superiorly : Diaphragma sellae
inferiorly : Sphenoidal air sinuses
laterally : Cavernous sinus , structures Passing through cavernous sinus: 6 th CN internal carotid artery
Lateral to the cavernous: 3rd, 4th and 5th(only maxillary & ophthalmic branches)
Anteriorly : Optic chiasm
posteriorly: Mammillary bodies

Mechanism of Insulin action :

1- Insulin binding activates receptor tyrosin kinase activity in the intracellular domain of the beta subunit of the insulin receptor

2- Tyrosine residues of the beta subunit are autophosphorylated.

3- Receptor Tyrosine kinase phosphorylates other proteins.eg: insulin receptor substrates (IRS)

4- Phosphorylated IRS promote activation of other protein kinases & phosphoates ,leading to biologic actions of insulin.

Biologic Effects of Insulin:

- Glucose uptake
- Glycogen synthesis
- Protein synthesis
- Fat synthesis

- Gluconeogenesis
- Glycogenolysis
- Lipolysis

Altered gene expression

Abortion of Hormonal Stimulus:

1. Release of hormone from its receptor (unbound receptor)
2. Dephosphorylation of protein substrate by phosphatase
3. Degradation of cAMP into AMP by phosphodiesterase
4. Inactivation of protein kinase A by a decrease of cAMP
5. Hydrolysis of GTP into GDP
6. Binding of α-subunit to βγ-subunits
7. Inactivation of adenylyl cyclase

General features of hormone classes :

	Group I	Group II			
Receptors	intracellular	Binds to surface (Plasma Membrane)			
	Lipophilic	Hydrophilic			
signal generation	Intracellular receptors (Receptor-Hormone Complex)	cAMP	cGMP	Ca+ & phosphatidylinanostisol	Tyrosine kinase
Example	1. Steroids (Sex hormones) 2. Thyroid hormones T3 , T4 & 3.calcitriol 4. Retinoic Acid	1.Catecholamine α2 & beta.(Act as protein) 2.Ant.pituitary hormones (ACTH, FSH, LH, TSH) 3. ADH : V2 4. Calcitonin 5. PTH 6. Glucagone 7. CRH	1. Atrial natriuretic peptide 2. nitric oxide	1. Ach 2. α1-adrenergic 3.angiotensin II 4.ADH: V1 5.TRH 6. Oxytocin	1. GH, 2.prolactin 3. insulin 4.erythropoietin

Thyroid Hormone is an amino-acid derivatives but behaive like Steroid

Mention the Types of hormones ?

1-Proteins and polypeptides such as- (anterior & posterior pituitary hormones & parathyroid hormones)
2-Derivatives of amino acid tyrosine such as -(thyroxin and epinephrine & norepinephrine)
3-Steroids such as- (cortisol & aldosterone rogesterone estrogenes tosterone)

Hormones alter target cell activity by one of the following mechanisms:

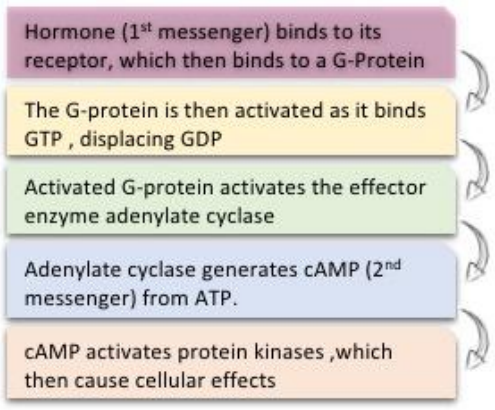
1-Ion Channel-Linked Receptors. 2-G Protein-Linked Hormone Receptors.
3-Enzyme-Linked Hormone Receptors. 4-Intracellular Hormone Receptors & Activation of Genes (steroid and thyroid hormones)

Mention the location of receptors ?

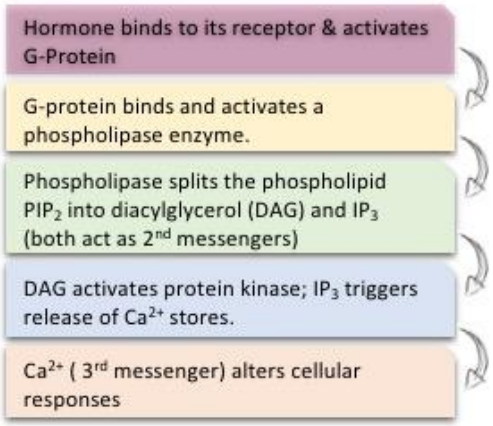
1. On the surface of cell membrane (proteins, peptides and catecholamines).
2. In the cell cytoplasm (Steroids).
3. In the cell nucleus (thyroid hormones).

Check the 'correction file' for more explanation.

★ **Cyclic Adenosine Monophosphate (cAMP) Second messenger mechanism:**



★ **Cell membrane phospholipid Second messenger system:**



- **Up- regulation :** The hormone induces greater than normal formation of a receptor or intracellular signaling proteins
- **Down-regulation :** ↑ hormone concentration leads to ↓ in the number of active receptors

Examples of negative feedback: (Most common)

1.The release of cortisol inhibit the release of ACTH and CRH.
2.T3 "release by the thyroid " inhibit the release of TRH and TSH.
3. Sex steroid hormones (estrogens and androgens) inhibit the the secretion of GnRH and inhibit the the response of anterior pituitary to GnRH.

Examples of Positive feedback

1-Estrogen (Estradiol) stimulate LH during ovulation. 2-Oxytocin During Pregnant Delivery.

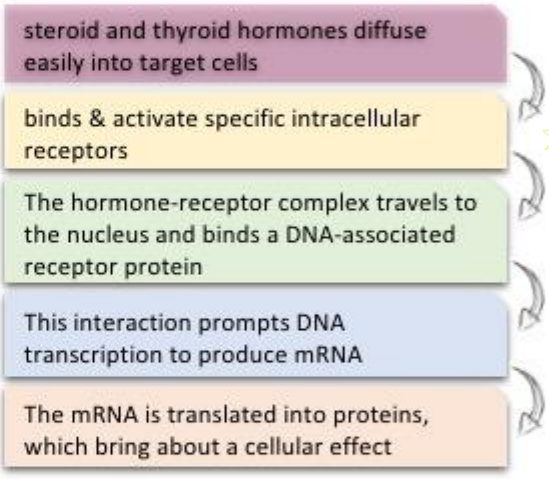
Calcium-Calmodulin Second Messenger System

1- On entering a cell, calcium ions bind with the protein calmodulin
2- the calmodulin changes its shape and initiates multiple effects inside the cell, including activation or inhibition of protein kinases
3- Activation of calmodulin-dependent protein kinases causes, via phosphorylation, activation or inhibition of proteins involved in the cell's response to the hormone

Activation of target cells depend on

1-Blood levels of hormone (depends of Rate of releasing and rate of removing)
2-number of recepotrs (as increases will increase the activity)
3- the affinity of hormone receptors

Steroid & Thyroid Hormones



Hormones are removed from the blood by:

1- Degrading enzymes
2-The kidneys
3-Liver enzyme systems

clearance of protein bound hormones is slower than clearance of peptide hormones

What are the types of stimulus in human body?

- Neural:pregangilionic symp. fibers stimulate adrenal medulla cells to secrete catecholamines (epinephrine norepinephrine)
- Humeral "Ionic". Capillary blood contains low conc. of Ca^{+2} which stimulate secretion of PTH by parathyroid gland.
- Hormonal: the hypothalamus secretes hormones stimulate the ant. pituitary gland to secrete hormones that stimulate other endocrine glands to secrete hormones

Mention the types of hormone interactions :

- Permissiveness : one hormone cannot exert its effects without another hormone being present .

Eg: Thyroid hormone have permissive effect on growth hormone action .
Deficiency of thyroid hormone in infants leads to dwarfism.

- Synergism : the total effect of two hormones together is greater than the sum of their individual effects

Eg: like Blood Glucose level & synergistic effects of glucagon, cortisol & epinephrine

- Antagonism : one or more hormones opposes the action of another hormone.

Glucagon antagonizes the action of insulin .
Eg: Calcitonin and parathyroid hormone have antagonistic actions.

Mohammed an athlete male, keep on exercising daily..
What do you expect to see when you monitor his hormone levels?

⬆ GH ⬆ Vit D (remember vit D can considered as a hormone)

Patient complains of Gigantism,. When you checked her blood glucose, you found that she has insulin resistence(Hyperglycemic), What is the possible mechanism for her high glucose level?

High growth hormone level leads to:
⬇ Glucose uptake in tissues
⬇Glucose utilization by target tissues such muscles and adipose tissue
⬆ Gluconeogenesis by the liver

Pituicytes function:

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

Herring Bodies function: Antidiuretic hormone (ADH) and oxytocin are both stored in Herring bodies,

Mention the Factors that increase and decrease in secretion of both oxtocin and ADH?

Factor ⬆ ADH : Pain,nausea, high serum osmolarity, hypoglycemia and low blood pressure (standing)
Factor ⬇ ADH : high blood pressure, low serum osmolarity ,ANP, Alpha agonist and Ethanol (Alcohol).
Factor ⬆ oxytocin : Hugging، touching,orgasm in both gender ,stress, time ejaculation in male , sucking nipple and time of delivery in pregnancy
Factor ⬇ oxytocin: Alcohol

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 nonautistic children

Triggers	Hypothalamic hormones	Ant.Pit cell	Secretion	Target	Actions
1-sleep 2-starvation 3-stress	GHRH (+) GHIH (Somatostatin) (-)	Somatotropes	GH	Most cells, but mainly 1-bone 2-skeletal ms.	⬆ 1-lipolysis 2-protein synthesis 3-production of IGF 4- use of fat for fuel. ⬇ glucose uptake
1-breast feeding 2-dopamine antagonists	PIF" dopamine" (-) TRH(+)	- Mammotropes, - Lactotropes	prolactin	Mainly the breast Mammary glands	1-milk production 2-inhibit ovulation
Low levels of thyroid hormones	TRH(+)	Thyrotropes	TSH	Thyroid glands	⬆ T3,T4
Puberty	GnRH(+)	Gonadotropes	-LH -FSH	Gonads	LH: 1\ovulation 2\Sex hormones FSH: Maturation of **F**ollicle
1-stressor 2-hypoglycemia 3-Fever	CRH(+)	Corticotropes	ACTH	Adrenal cortex	production of glucocorticoids & androgens

Mention the hormones of posterior pituitary gland, origin and main functions?

- **ADH :** from supraoptic nucleus / V1a : vasoconstriction & glycogenlysis. V1b : mediate ⬆ in ACTH secreation. V2 : located in priciple cells in distal convolated tubule & collecting ducts in kidneys that leads to fluid retention

•Via adenylate cyclase/cAMP induces production of specific proteins into the luminal membrane & enhances permeability of cell to H_2O.
• ⬆ membrane permeability to H_2O permits back diffusion of free H_2O, resulting in ⬆ urine osmolality (concentrates urine).

- **oxytocin :** Paraventriuclar nucleus / stimulates uterine contarction ending in birth(postive feedback)+ Milk ejection (letdown reflex) contacts myoepithlial cells of alveoli

Summary of ADH Pathophysiology

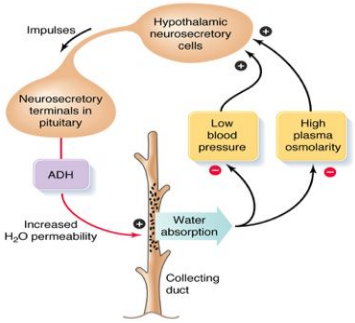
Disease	Serum ADH	Serum [osmolarity] & [Na]	[Urine osmolarity]	Urine flow rate
Central Diabetes insipidus	⬇	⬆ (because of excretion of too much H2O)	Hyposmotic	⬆
Nephrogenic Diabetes insipidus	⬆ (Because of ⬆ plasma osmolarity)	⬆ (because of excretion of too much H2O)	Hyposmotic	⬆
SIADH	⬆⬆	⬇ (because of reabsorption of too much H2O)	Hyperosmotic	⬇

Function of Growth hormone.

Direct	Indirect (somatomedin IGF)
Short term effect Metabolic effects	Long term effect Promotion of growth
Protein metabolism: Anabolic ⬆rate of protein synthesis in all cells through: ⬆AA transport into cells ⬆DNA transcription= RNA synthesis ⬆RNA translation= protein synthesis ⬇protein catabolism"protein sparer"	⬆ cellular sizes ⬆mitosis ⬆tissue growth ⬆Organ size
Fat metabolism: Catabolic ⬆Mobilization of FFAs from adipose tissue stores Conversion of FFA acetyl CoA (provide energy)	Linear growth : Long bones grow in length at epiphyseal cartilages
CHO metabolism: Hyperglycemic ⬇glucose uptake by tissues ⬇rate of glucose utilization throughout the body ⬆Gluconeogenesis insulin resistance (⬆FFA) (Diabetogenic)	Deposition of New Bone • cell proliferation on surfaces and cavities of older bone • ⬆the bone thickness • Occurs in membranous bones, e.g. jaw, & skull bones.

How Does Osmotic pressure Control ADH Release

Osmoreceptors in the hypothalamus:
⬆osmotic pressure →⬆ ADH secretion
⬇osmotic pressure →⬇ADH secretion



How Does Blood volume Control ADH Release

•Baroreceptor in carotid artery and aortic arch, & Stretch receptors in left atrium and pulmonary vein
⬆blood pressure →⬇ADH secretion
⬇blood pressure →⬆ADH secretion

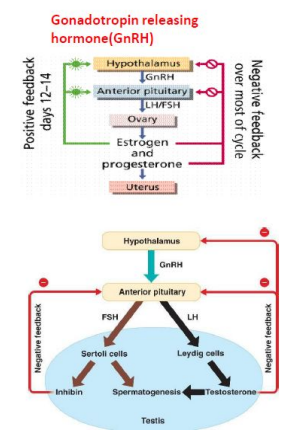
Mention two of ADH Disorders?

- Diabetes Insipidus:

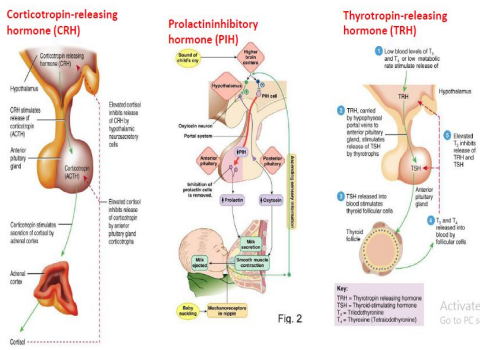
-Neurogenic (central): (failure of neurohypophysis to synthesize or secrete ADH)
-Nephrogenic: (failure of the kidney to respond appropriately to ADH)

- SIADH:

The syndrome of inappropriate antidiuretic hormone (ADH) secretion (SIADH) is defined by the hyponatremia and hypo-osmolality resulting from inappropriate, continued secretion or action of the hormone despite normal or increased plasma volume, which results in impaired water excretion



Important illustration of hyppothalamic control of Anterior Pituitary



List some of Anterior pituitary disorders:

- Non-functional pituitary tumor & mass-effect: hypopituitrism
- Prolactin secreting cell disorder: prolactinoma
- Growth hormone secreting cell disorder: acromegaly
- ACTH secreting cell disorders: cushing's
- TSH secreting cell tumor: TSH-secreting adenoma
- Gonadotropin secreting adenoma

THANK YOU FOR CHECKING OUR TEAM..

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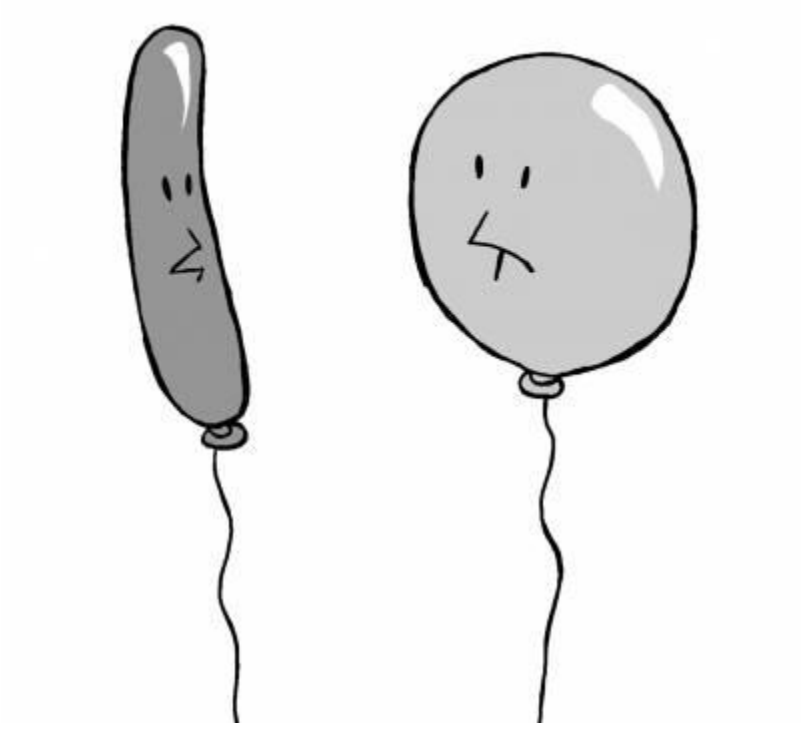

"It's probably hormonal thing"