Endocrine

434 Physiology team
presents to you:

Mid-Term Revision

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Transport of Hormones:

1- Water soluble hormones- hydrophilic (peptides & catecholamine) dissolved in plasma.

2-Fat soluble hormones – hydrophobic Steroids and thyroid hormones transported bound to plasma proteins (90%). binding to proteins helps to: -provide reservoirs -Slow hormones clearance.

Hormone Interactions Examples:

1-Permissiveness: Thyroid hormone has permissive effect on growth hormone action
•Deficiency of thyroid hormone in infants leads to dwarfism.

2-Synergism: Blood glucose levels & synergistic effects of glucagon, cortisol and epinephrine

3-Antagonism: Glucagon antagonizes the action of insulin, Calcitonin and parathyroid hormone have antagonistic actions

Adenylyl Cyclase Mechanism	Phospholipid Mechanism	Guanyl Cyclase	Tyrosine Kinase Mechanism
ACH, LH, FSH	GnRH	ANP, NO	Insulin, IGF-1, GH, Prolactin
TSH, GHRH	TRH		
Somatostatin	Angiotensin II		
ADH (V2), HCG	ADH (V1)		
MSH, CRH	Oxytocin		
Calcitonin			
PTH,Glucagon			

Hormones: Are secretions of ductless glands that are directly released into the blood stream. They can act on cells in the vicinity or on distant target cells.

Endocrine glands: pituitary, thyroid, parathyroid, adrenal, pineal, and thymus.

-The pancreas and gonads produce both hormones and exocrine products also Liver.

-The hypothalamus has both neural functions and releases hormones.

-Other tissues and organs that produce hormones: adipose cells, pockets of cells in the walls of the small intestine, stomach, kidneys, and heart.

L1-Introduction to Endocrine

Types of Hormones:

1-Proteins and Peptides: Including: - anterior and posterior pituitary - pancreas (insulin and glucagon) -parathyroid hormone stored in vesicles until needed (Synthesized as preprohormone > post-translational modification to prohormone > then hormone).

2-Steroids: Secreted by: - Adrenal cortex (cortisol and aldosterone) -Ovaries and placenta (progesterone and estrogen) –Testes (testosterone).

3-Derivatives of amino acid tyrosine (Amines): Secreted by: -Thyroid (thyroxin and triiodothyronine) -Adrenal medulla (epinephrine and norepinephrine)

Endocrine Hormone: Released by Glands or Specialized Cells into circulating Blood and influence the target cells.

Paracrine: Secreted by cells into extracellular fluid and affect neighbouring Target cells of Different Type.

Autocrine: Chemicals that exert their effects on same cells that secrete them.

Neurotransmitter: Released by axon terminals into the synaptic junction and act locally.

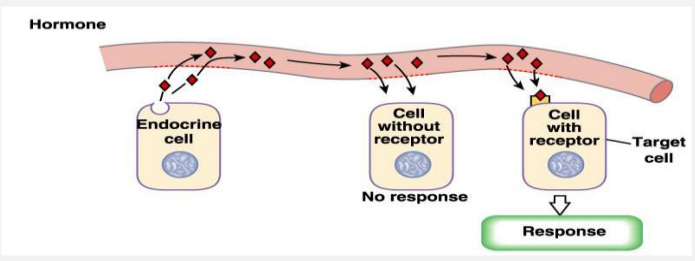
Neuroendocrine Hormones: Secreted by neurons into circulating blood and influence the target cells.

Cytokines: Peptides released by cells into the extracellular fluid and function as autocrine, paracrine or Endocrine Hormones (e.g: Interleukins, Lymphokines).

Target cells refer to cells that contain specific receptors (binding sites) for a particular hormone.

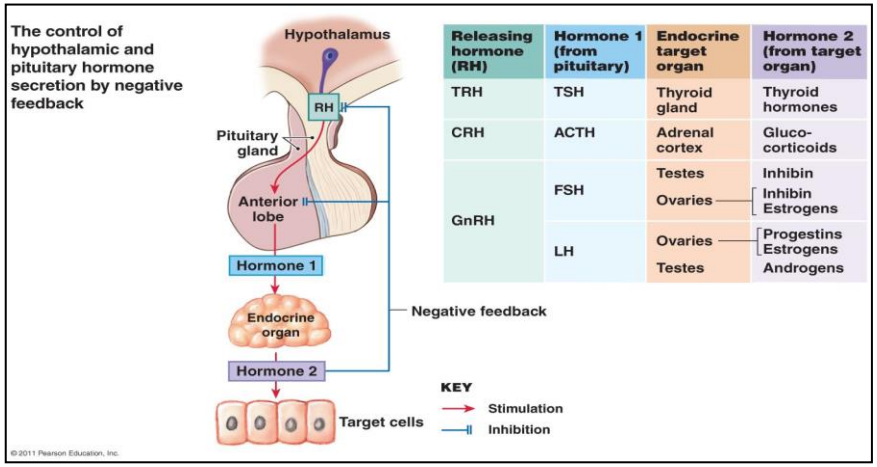
Target cell activation depends on:

1- Blood levels of the hormone
2- Relative number of receptors on the target cell
3- The affinity of those receptors for the hormone



L2-Hypothalamo-pituitary axis

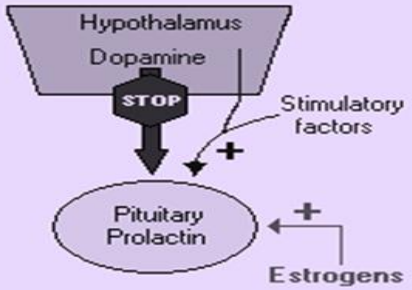
Anterior pituitary gland is connected to hypothalamus by:
Hypothalamic-hypophysial portal vessels



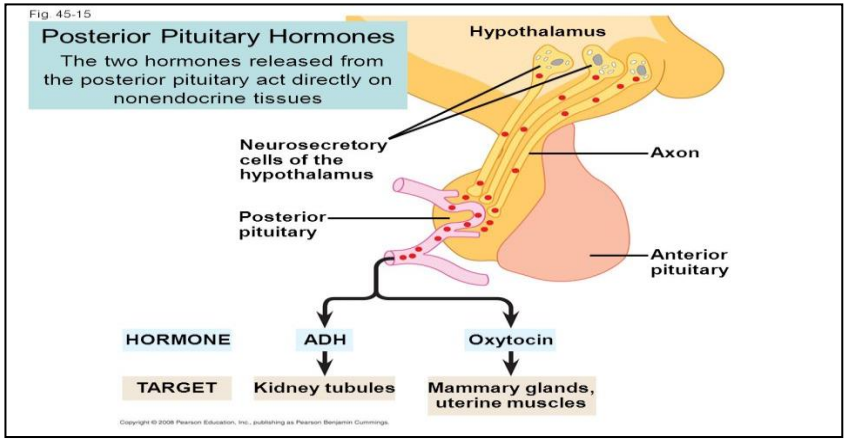
Releasing hormone (RH)	Hormone 1 (from pituitary)	Endocrine target organ	Hormone 2 (from target organ)
TRH	TSH	Thyroid gland	Thyroid hormones
CRH	ACTH	Adrenal cortex	Gluco-corticoids
GnRH	FSH	Testes	Inhibin
		Ovaries	Inhibin, Estrogens
	LH	Ovaries	Progestins, Estrogens
		Testes	Androgens

PIH

Prolactin inhibitory hormone (PIH) AKA Dopamine:
Inhibits prolactin secretion



Hypothalamic control of posterior pituitary gland:
Hormones are synthesized in the supraoptic (→ ADH) and paraventricular nuclei (→ Oxytocin) and released in posterior pituitary



GH

Growth hormone hypothalamic regulation:

- Growth hormone releasing hormone (GHRH)
  - Stimulates release of growth hormone
- Growth hormone inhibiting hormone (GHIH) AKA **somatostatin**
  - Inhibits release of growth hormone

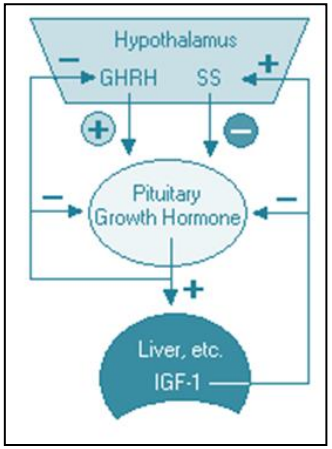
TH

Thyroid hormone hpothalamic regulation:

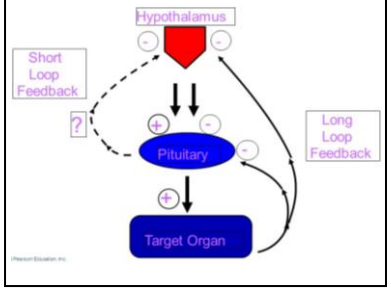
- Thyrotropin releasing hormone (TRH) → stimulates release of thyroid stimulating hormone (TSH) from the anterior pituitary → stimulates release of thyroid hormones by the thyroid gland
- T_3 & T_4 increase → negative feed back

CRH

Corticotropin-releasing hormone stimulates release of adrenocorticotropin hormone (ACTH) → stimulates release of cortisol by the adrenal cortex



Negative feedback mechanisms can be long or short loop reflexes



GnRH

Gonadotropin releasing hormone causes release of 2 gonadotropic hormones:
Luteinizing & follicle stimulating h.s

Feedback mechanisms can be:
Positive or negative

+ve

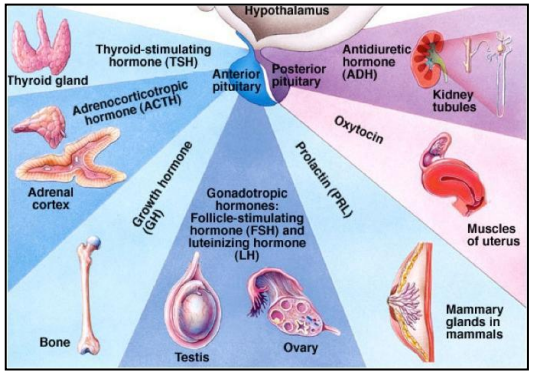
Positive feedback

- Release of hormone A stimulates the release of hormone B
- Hormone B stimulates further release of hormone A
- Example: Baby suckles at nipple → oxytocin release → milk ejection → baby continues suckling

-ve

Negative feedback

- Release of hormone A stimulates the release of hormone B
- Hormone B inhibits release of hormone A
- Example: rising blood glucose → insulin secretion → glucose uptake by liver and body cells → normal glucose level → insulin secretion stops



Gonadotropins:

FSH stimulates gamete (egg or sperm) production

LH in males: stimulates interstitial cells of the testes (leydig cells) to produce testosterone

LH in females: maturation of ovarian follicle

Synthesis & release of estrogens & progesterone

Factors increasing prolactin:

- Pregnancy
- Sleep
- Surgical & psychological stress
- Exercise
- Stimulation of the nipple
- TRH

Factors inhibiting prolactin:

PIH (dopamine)

Pituitary gland hormones mnemonic:

"GOAT FLAP"

Anterior pituitary: Growth hormone, Thyroid stimulating hormone, Follicle stimulating hormone, Luteinizing hormone, ACTH, Prolactin

Posterior pituitary: Oxytocin, ADH

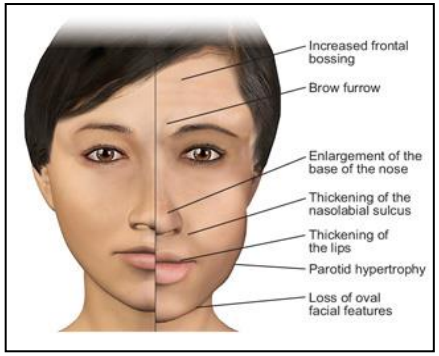
Prolactin

Stimulates milk production by the breasts

L3,4-Pituitary

Growth hormone:

- Produced by: somatotropic cells
- Stimulates most cells, mainly bone and skeletal muscles
- Promotes protein synthesis (anabolic effect)
- Encourages the use of fats for fuel
- Decreases glucose uptake in tissues, increases its production by liver
- Metabolic actions are **direct**
- Most effects are mediated **indirectly** by **somatomedins (IGF1)**

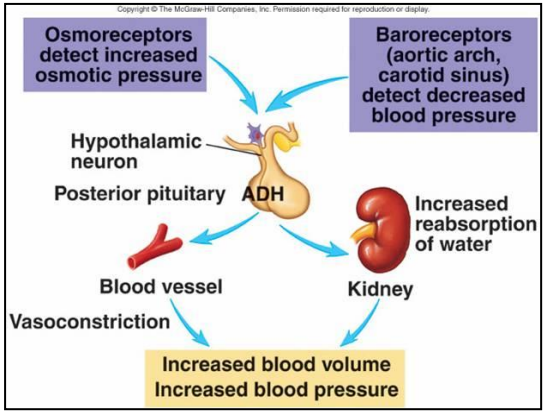


ADH Receptors

V_1 a → vasoconstri.

V_1 b → ↑ ACTH

V_2 → located in principle cells → increases water reabsorption in kidneys



ADH disorders

SIADH → hyponatremia and hypo-osmolality due to continued secretion of ADH

Neurogenic Diabetes Insipidus → failure of hypophysis to synthesize or secrete ADH

Nephrogenic diabetes insipidus → failure of kidney to respond to ADH

Factors stimulating GH:

↓Glucose

↓FFA

↑aminoacid (arginine)

Fasting, prolonged caloric deprivation stress, exercise, puberty, androgens, sleep

Factors inhibiting GH:

↑Glucose

↑FFA

Somatostatin

Somatomedins

GH senscence

↑GH leads to:

Acromegaly in adults

Gigantism in childhood

↓ GH leads to:

Dwarfism in childhood

Oxytocin

- Stimulates uterine contraction
- Triggers milk ejection

Oxytocin stimuli:

Hugging, touching, orgasm

In both sexes

Stress

Ejaculation

Inhibited by: alcohol

Remember!

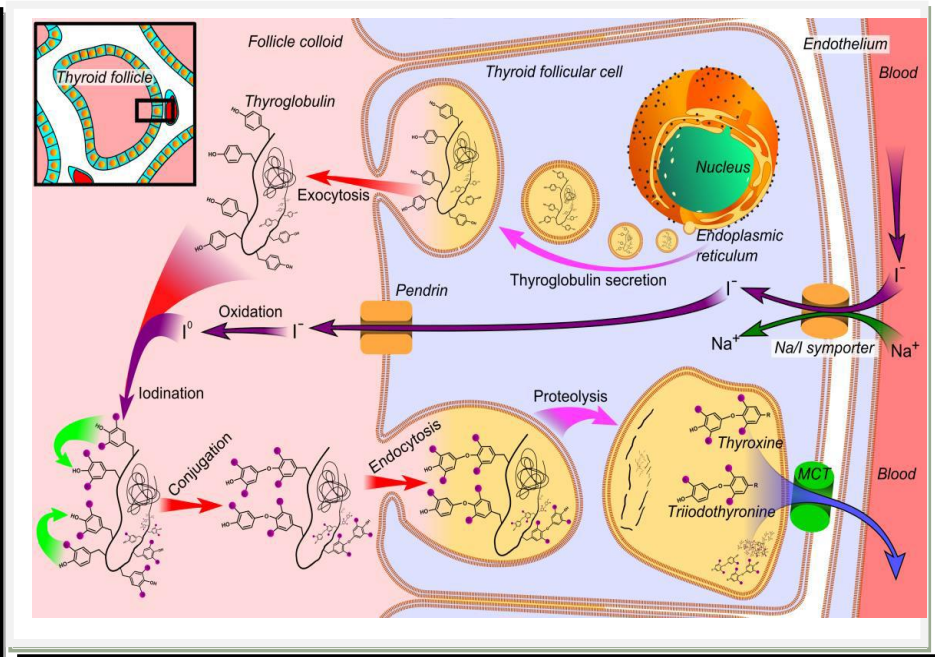
GH counteracts in general the effects of insulin on glucose and lipid metabolism, but shares protein anabolic properties with insulin.

Oxytocin and autism

Autistic group have significantly lower plasma oxytocin levels than in the non-autistic.

Steps of Synthesis:

1. Iodide pump.
2. Thyroglobulin synthesis.
3. Oxidation of iodide to iodine.
4. Iodination of tyrosine.
5. Coupling.
6. Endocytosis of thyroglobulin.
7. Fusion of lysosomes.
8. Hydrolysis of peptide bonds.
9. Release of T3 and T4
10. Deiodination of DIT and MIT by Thyroid deiodinase (Recycling).



L5,6- Thyroid Gland and thyroid Disorders

Cretinism:

A condition of severely stunted physical and mental growth due to untreated congenital deficiency of thyroid hormones (congenital hypothyroidism).

Causes:

1-Congenital lack of thyroid gland (congenital cretinism).
2-Genetic deficiency leading to failure to produce hormone.
3-Iodine lack in the diet (endemic cretinism).

Symptoms:

o Infant is normal at birth but abnormality appears within weeks - Protruding tongue - Dwarf with short limbs. Mental retardation.
o Often umbilical hernia.
o Delayed appearance of teeth.

Treatment: Changes are irreversible unless treatment is given early.

Effects of Thyroid Hormone:

1-CVS: increase pump.
2-CNS:
In Peri-natal Period >Maturation of CNS
In Adult > Hyperexcitability
3-Bones: bone formation, ossification, and bone maturation.
4-GIT: Increase in Appetite, increase motility > Diarrhea.
5-Respiratory: Increase ventilation rate - Increase dissociation of oxygen from Hb by increasing RBC 2,3-DPG (2,3 diphosphoglycerate).
6-Increase in BMR.

Metabolism Effects of Thyroid Hormone :

1-Carbohydrates: TH *stimulates* all aspects of carbohydrate metabolism:

- Increase glucose uptake by the cells.
- Increase glycogenolysis.
- Increase gluconeogenesis.
- Increase rate of absorption from the GIT.

2-Fats: Essentially all aspects of fat metabolism are also *enhanced* under the TH:

- Increase lipolysis.
- Decrease of Cholesterol in the blood (Hypocholesteremia).

3-Proteins: Overall effect is catabolic leading to decrease in muscle mass. In contrast to GH which has anabolic effect.

Thyroid Hormones Release to Tissues:

1. T4 & T3 readily diffuse through the cell membrane.
2. Stored in the targeted tissues (days to weeks). -not shown in image-
3. 90% of T4 is deionized to T3 by idoinase enzyme.
4. In the nucleus, T3 mainly binds to thyroid hormone receptor and influence transcription of genes.