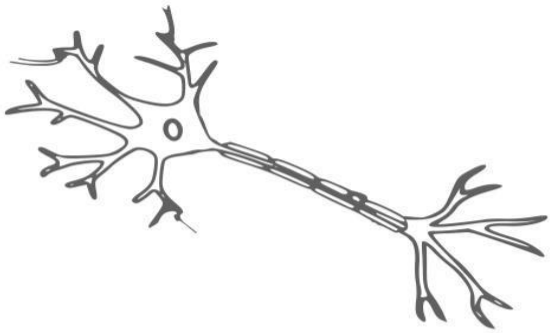
Sheet no. 10

Physiology



Writer: Osama zaareer
Corrector: Mohammad aladawi
Doctor: Dr. Ebaa Al Zayadneh

There are two main chemical classification for ligands(hormones) according to solubility, because this will determine the location of the receptors:

1-lipid soluble hormone, which are hydrophobic, and as a result, transporting these hormones in blood (which is here is the aqueous environment) will be very hard, so hormones will need transporting proteins in the plasma of the blood.

Main types of lipid soluble hormones:

✓Steroids: lipids derived from cholesterol(lipophilic hormones)

✓ Testosterone

✓ Estradiol

✓ Cortisol

✓ Progesterone

✓ Thyroid (amine but lipid soluble), ex. T1,T4 *note: some amines are water soluble.

✓ Nitric oxide (NO) : Due to its gaseous nature, it easily penetrates the plasma membrane,

(NO here is a hormone or a local mediator)

2-water soluble hormone, which are hydrophilic, so they don't require transporting protein even though transporting proteins are existing in some cases, and keep in mind that these water soluble hormones can't cross the plasma membrane due to multiple reasons such as: polarity, charge and size.

Main types of water soluble hormones:

AMINES: hormones derived from tyrosine and tryptophan. ❖

POLYPEPTIDES AND PROTEINS:

✓ Polypeptides: chains of < 100 amino acid length eg: ADH ✓ Protein hormones: polypeptide

chains > 100 amino acid eg: growth hormones.

❖ EICOSANOIDS(PROSTAGLANDUNS): local mediators derived from arachidonic acid-20 carbon 4 double bonds. In physiological level they are charged molecules so the cant enter inside the cell.

❖ GLYCOPROTEINS:

▪ Long polypeptides >100 bound to 1 or more carbohydrate (CHO) groups.

▪ They have alpha and beta subunits (alpha is common and beta is specific)

✓ FSH,LH,TSH and hCG (human chorionic gonadotropin).

*note: Some books divide the hormones to polar and nonpolar.

Polar = water soluble Nonpolar

= lipid soluble

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Usually hormones after it's synthesised are maybe not found in their final form, and in order to distinguish the active hormone (which is ready to bind with receptors and to act or cause a response in the cell) from the final form hormone, we simply give them names and here is the clarification:

Prohormones and Prehormones:

-The hormones are synthesized in the Nucleus then packaged in the ER, then into the Golgi apparatus for post-translational modification, packaged then released by exocytosis.

-Before the modification (precursor) = Prohormones

*prohormone: precursor is a longer chained polypeptide that is cut and spliced together to make the hormone

Proinsulin_ gives insulin

-Preprohormones: Larger precursor molecule that prohormones are derived from.

*for example :preproinsulin *prehormone:

molecules secreted by endocrine glands that are inactive until changed into Hormones by target cells.

T4 converted to T3 (tri-iodothyronin)

*note: the major difference between T4 and T3 is the iodine group which is missing from T3, T4 is a tetra-iodothyronin

In oder to form T3 from T4 we just need an enzyme which cuts an iodine group from T4.

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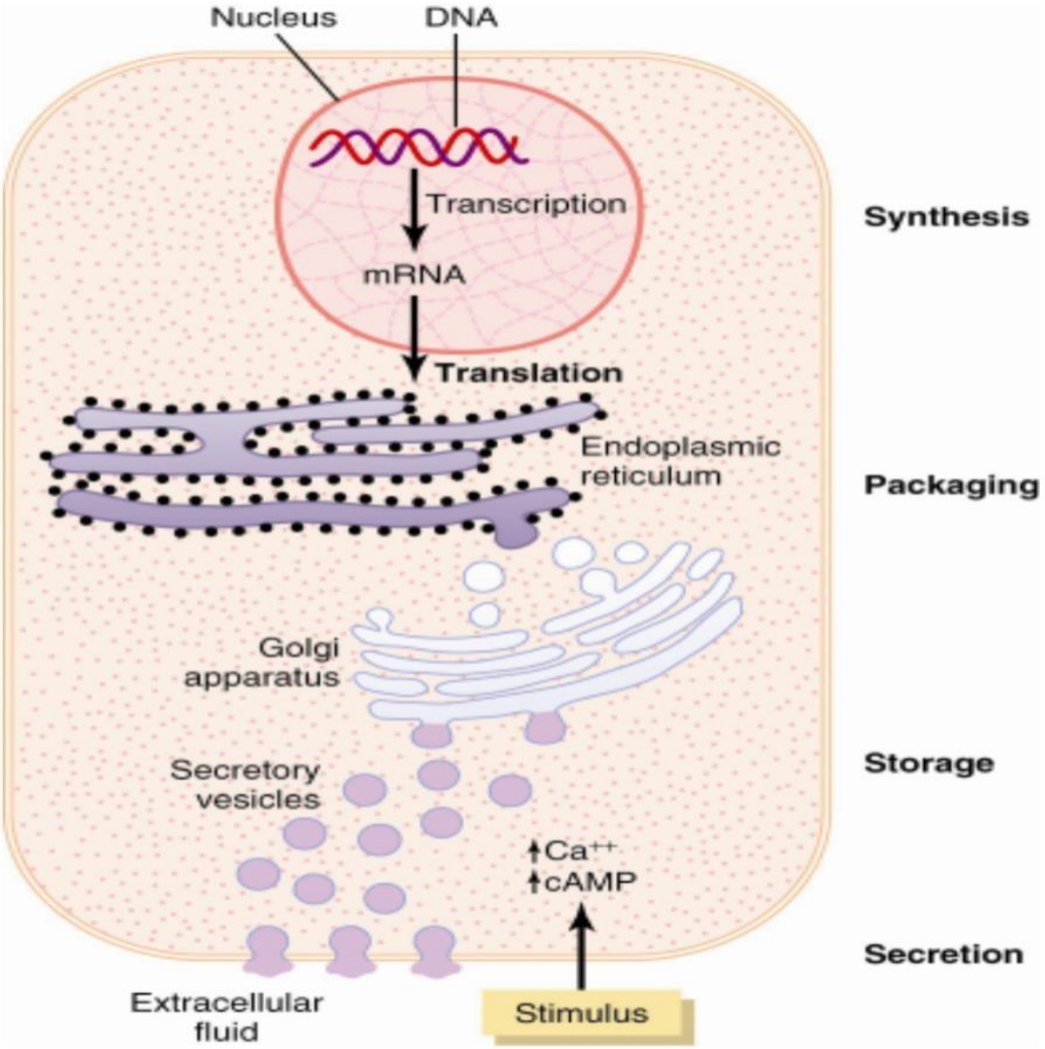
=Ponder the image here.



**Some notes:

-gene expression must be occurred

-golgi makes modifications

-packaging occurs in the secretory molecules

-there must be signalling to do secretion so vesicles can be released.

in the minute 13:50 Dr.Ebaa said: بتحتاجزinstead of بتحتاج and she laughed, and all student laughed and she said: بلّش تأثير الصيام, can you imagine!! It's the first time students laugh in a physiology lecture.(not funny I know)

……

The table below will help you:

Chemical classification of hormones

Table 10-4 Chemical Classification and Function of Hormones

Chemical Classification	Examples	Regulated Function
Endocrine Hormones		
Amino acid derivatives	Epinephrine (adrenaline) and norepinephrine (both derived from tyrosine)	Stress responses: regulation of heart rate and blood pressure; release of glucose and fatty acids from storage sites
	Thyroxine (derived from tyrosine)	Regulation of metabolic rate
Peptides	Antidiuretic hormone (vasopressin)	Regulation of body water and blood pressure
	Hypothalamic hormones (releasing factors)	Regulation of tropic hormone release from pituitary gland
Proteins	Anterior pituitary hormones	Regulation of other endocrine systems
Steroids	Sex hormones (androgens and estrogens)	Development and control of reproductive capacity
	Corticosteroids	Stress responses; control of blood electrolytes
Paracrine Hormones		
Amino acid derivative	Histamine	Local responses to stress and injury
Arachidonic acid derivatives	Prostaglandins	Local responses to stress and injury

-All peptides are water soluble

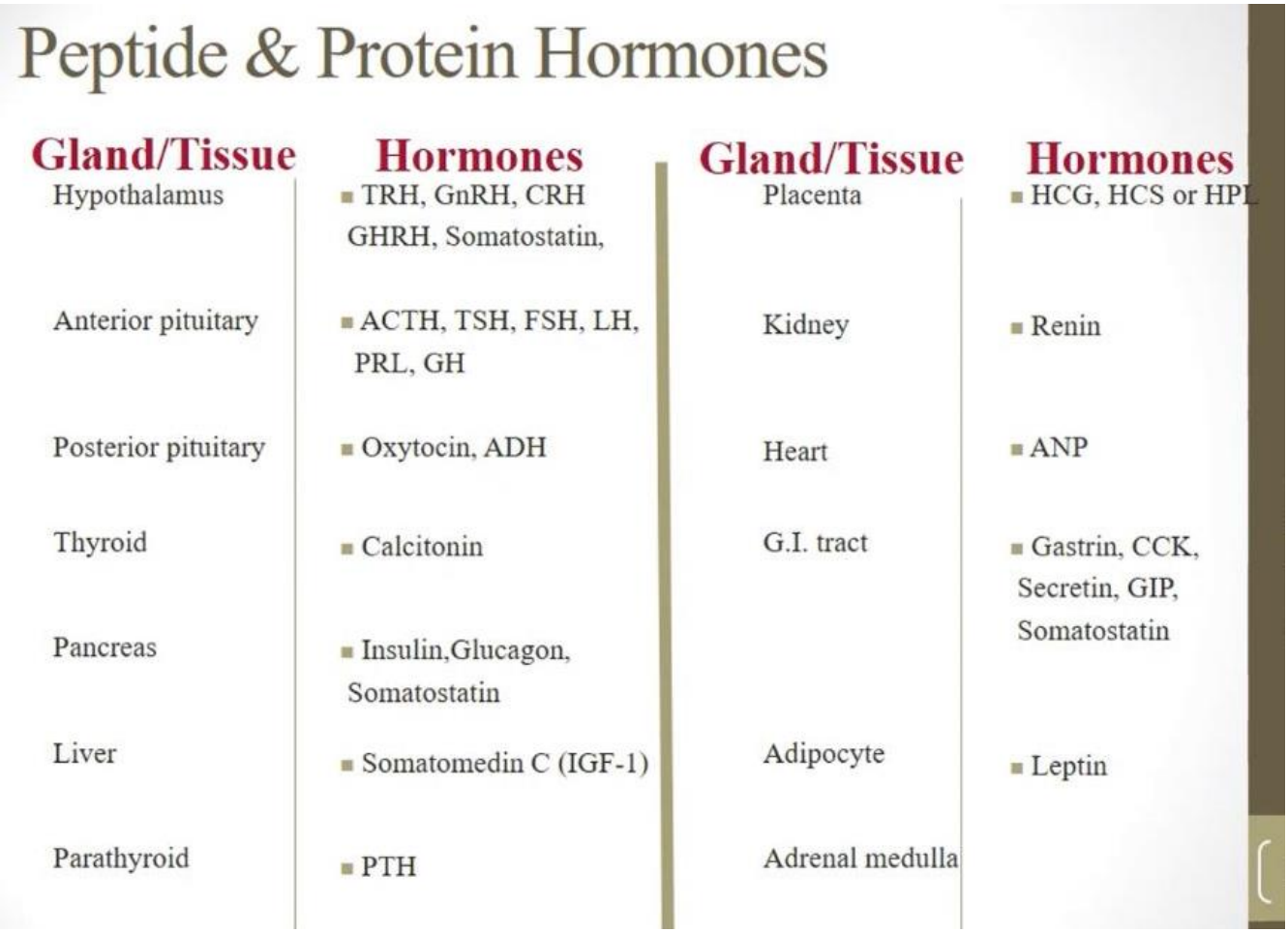
-All steroids are lipid soluble

But for the amino derivatives there is a deference so be careful:

Epinephrine and norepinephrine are water soluble, whereas thyroxine is a lipid soluble.

**Note: you don't have to memorize the regulated functions…

**Note: there are many types of prostaglandins, some cause vasoconstriction and some cause vasodilation.



Amine Hormones

Gland/Tissue	Hormones
Hypothalamus	▪ Dopamine
Thyroid	▪ T_3, T_4
Adrenal medulla	▪Epinephrine and Norepinephrine (NE, EPI)

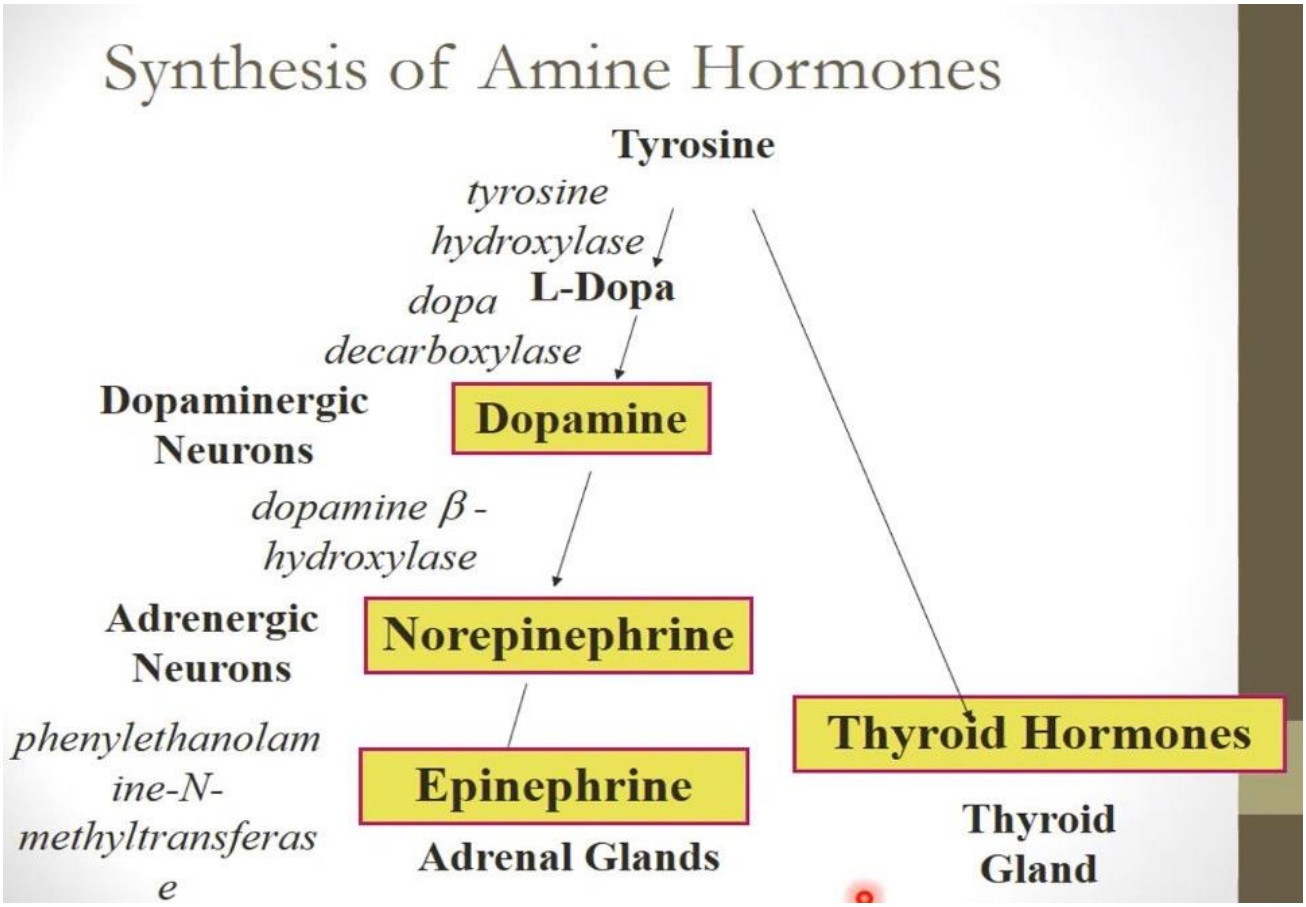
-the thing in common between protein and peptide hormones that they all share same pathways and same locations in the receptors.
We don't have to distinguish between protein and peptide hormones .

- the only amine hormones which are lipid soluble are T3 and T4.

Steroid Hormones

Gland/Tissue	Hormones
Adrenal Cortex	▪ Cortisol, Aldosterone, Androgens
Testes	▪ Testosteron
Ovaries	▪ Estrogens, Progesterone
Corpus Luteum	▪ Estrogens, Progesterone
Placenta	▪ Estrogens, Progesterone
Kidney	▪ 1,25-Dihydroxycholecalcife (calcitriol)(Vitamin D)

Ponder the plot here:



the only deference which determines the type of hormone which will be secreted, is the enzymes that reside in the cell.

-you don’t have to memorize the names, just understand the concept of the pathway.

Hormone Activity:

-Hormones only affect specific target tissues with specific receptors.

-Receptors are dynamic and can be either broken down or synthesised in the membrane, which means that they don't have a fixed number either in the membrane or inside the cell, and If there's no receptor for the hormone, it will not make any action, also Different density for hormones gives different response.

-Downregulation: decrease in the number of receptors and response.

➢ Downregulation decreases the activity of the hormone and causes desensitization caused from prolonged exposure to hormones, especially the polypeptide hormones. For example, insensitivity of insulin does not mean that the insulin is not there, it just means that it exists in high levels, so the cells are not sensitive to it anymore.

-Upregulation: increase in the number of receptors or activity Upregulation Increases the sensitivity and activity of the hormone which leads to a greater response, this is called the priming effect.

-Effects of Hormones in tissue response

*priming effect (upregulation): there will be a period we will not see any response, because the cell hasn't yet synthesis the receptors of a certain hormone.

➢ Increase the number of receptors formed on target cells in response to particular Hormone.

➢ greater response by the target cell

-desensitizations (downregulation): happens when the concentration of the hormone increases so much, and the cell has been affected by the hormone for a long period, this will justify that the response of the cell is decreasing by time, for ex. 80% in the first hour — 30% in the second hour (same concentration of hormone in the two hours).

➢ prolonged exposure to high polypeptide hormone

➢ Subsequent exposure to the same hormone produces less response.

➢ decrease in number of receptors on target cell

Example: insulin in adipose tissue (Diabetes type 2), there is a high concentration of insulin, but a low response to it.

**Note: pulsatile secretion may prevent downregulation.

—pulsatile means: not a continuous secretion of hormone all the time, but as a pulses each in a different time.

-Effects of hormone concertation in tissue response

-Hormone concertation in the blood depends on:

*the rate of secretion of the gland.

*half-life

The time required for the blood hormone concentration to be reduced to half reference level (normal physiological level).

**It may be minutes to days, it differs from hormone to another.

Note: I stopped in the middle of the slide because the doctor stopped here

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تصبُّ الخلّ في الزّيت

لها سبع دجاجات

وديك حسنُ الصّوت