Endocrine system
Biochemestry #1
Dr.Faisal Al-khateeb

- Some notes before we start :

1. Because we are talking about the same system in different subjects you might find some contradicts between one subject and another, so don't get confused and ask the Dr about them.
2. The reference in this lecture and the next ones is Harper's illustrated biochemistry, you can find it on this link *I am not sue if this is the last edition* http://www.4shared.com/get/F7ln9vKo/harpers_illustrated_biochemist.html (slide #1)
3. The Dr said his slides and the lecture notes (sheets) are enough enshallah.

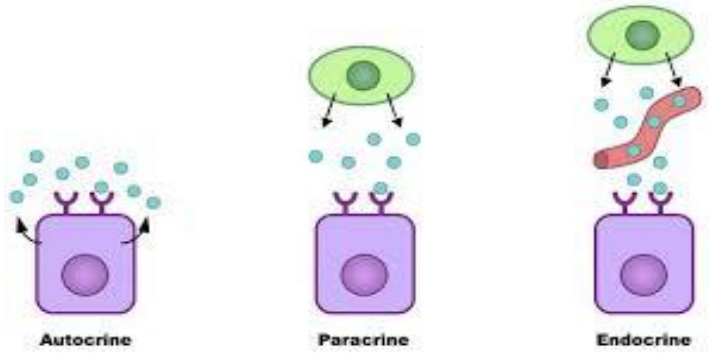
- Now let's start the lecture:
  - (Slide #2)

Humans as well as animals are multi cellular organisms, and survival of humans requires the ability to adapt to the environment that is contentiously changes, and cells needs to communicate in order to make the adaption (intercellular communication) .

- (Slide #3)

There are two systems in which accomplish this communication:
1. The nervous system (by electrical signals)
2. The endocrine system (By chemical signals).
   - ✓ These systems do not work separately there is overlapping between them. How?
     - ❖ The endocrine system is controlled by the central nervous system.
     - ❖ Many neurotransmitters resemble hormones. For e.g.: norepinephrine is neurotransmitter but it has many similarities to adrenalin or epinephrine (hormone).
     - ❖ Many hormones are synthesized in the central nervous system.

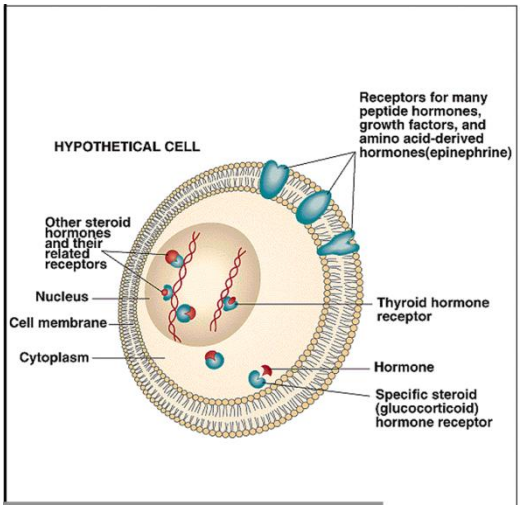
**Originally "hormone" means any substance produced in one part of the body, and affects cells in other parts of the body by transporting them through blood. "Which is wrong"?
**But the current definition is any substance that produced in a part of the body and carries a signal to affect the other cells (target cells) and produce a response. That leads us to 3 types of hormones: (slide #4)
1. Endocrine: the classical hormones that is secreted by endocrine glands in the blood to reach the target cells.
2. Paracrine: this types of hormones affect the neighborhood cells and it's not necessarily for this type to be secreted from a gland, it can be secreted from specialized cells.
3. Autocrine: this type affects the cells that produce them.



- (slide #5)
- ❖ In order to affect cells and generate a response the hormones need to interact with receptors.
- ❖ In our body there are more than 200 types of cells, few of them produce hormones and the other ones are the target cells.
- ❖ There are more than 50 hormones that are discovered till now and the no. is increasing continuously and these affect almost all cells of our body.
- ❖ Hormones are found in the blood or in the extracellular fluid in very low concentration (10^-15-10^-9 mole/L). In this low conc. How do they affect almost all cells of the body? That is the purpose of our lecture.
- ❖ Same hormone can affect several types of cells and the cell could be affected by different types of hormones.

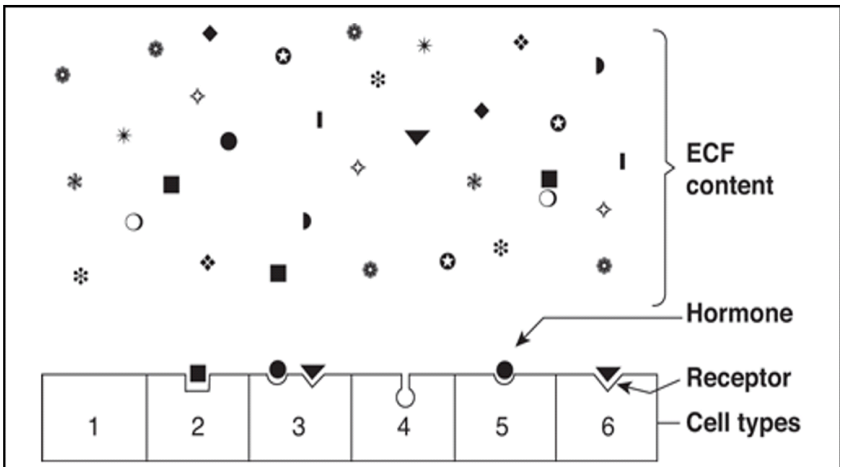
☒ In this picture we notice two types of receptors either:

1. On the cell surface in the plasma membrane.
2. In the cytosoplam or the nucleus.



☒ In the next picture shows that the cell receptors should be able to recognize and bind to different types of hormones and differentiate between hormones and similar molecules even if they(hormones)were found in low conc. and similar to each others. All of this because receptors have 2 important characteristics: <u>specificity</u> and <u>selectivity</u>.

☒ As we said target cells can distinguish between different hormones. And distinguish between a given hormone and a similar molecule produced at much higher conc. Like CO_x which is present in the plasma at much higher conc. Than some hormones, however the receptors of the hormone are able to distinguish them.



- (slide #7)

So binding hormone to its receptor should be:

- ✓ **Specific**: each receptor is specific for its hormone even if the hormone was in low conc. and a similar molecule was in high conc.
- ✓ **Saturable**: the amount of hormones can bind all receptors so after that increasing the amount of the hormone won`t affect the increasing of the response.
- ✓ **Within the conc. range**: this means that the amount of hormone in negligible in binding, if we have a hormone in the physiological range and its receptor they will bind even if the hormone was not in high amounts. Because the amount decides the response not the occurrence of binding.
  Which leads us to the next slide

- (slide #8)

- Extent of binding depends on hormone concentration.
  This is illustrated by this equation:

$$H + R \underset{k-1}{\overset{k+1}{\rightleftharpoons}} H\text{-}R$$

(It is similar to the substrate-enzyme relationship)
H: hormone
R: receptor
H-R: hormone-receptor complex
k+1: constant rate of association (Ka)
k-1: constant rate of dissociation(Kd)

- The binding is reversible.
- The affinity of receptor to bind to a hormone is represented by Ka & Kd.
- If we increase the conc. of a hormone we`ll increase the formation of H-R complex , but if we increase it to much higher levels the response won't be affected as we said earlier because all the receptors are occupied. (The receptors are saturated.)

- (slide #9)

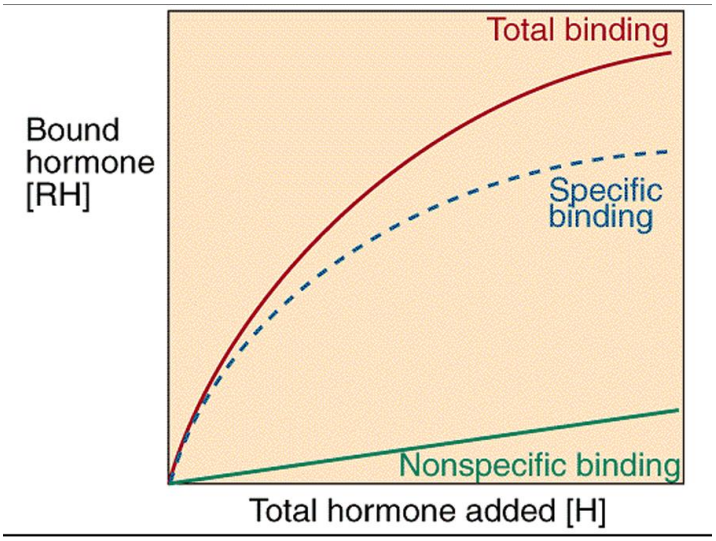
- ❖ Association constant : $K_a = [H\text{-}R] / [H]^* [R]$
- ❖ Dissociation constant: $K_d = [H]^* [R] / [H\text{-}R]$

  * Note: $K_a = 1/ K_d$
- ❖ 20x dissociation constant is enough to saturate the receptors. Which means that the receptor is saturated by a conc. of a hormone that is equal to 20 times Kd, so before we consider a receptor is the receptor for certain hormone we need to measure the Kd if Kd was much higher than the actual conc. that means that this receptor is not the one for this hormone.

(slide #10)

There is some nonspecific binding and it has nothing to do with the hormone-receptor binding, so we have to subscribe it from the total binding and the result will be the specific binding.

Kd: gives us an idea about what is the conc. of a hormone that is required to saturate 50% of the receptors. (Like the enzyme's Km).



(slide #11)

- Receptors are proteins.
- Several classes of receptors have been identified:
  - Insulin receptor for e.g is tetramer made of 2 alpha subunits and 2 beta subunits.
  - One polypeptide chain: epidermal growth factor
  - Seven helices that span the plasma membrane
  - Intracellular receptors: steroid and thyroid hormones
- Receptors are made of at least 2 domains :
  - Recognition: for recognizing the hormone and binding to it.
  - Coupling: after hormone binding →it leads to alteration of function of the cell, sending a signal as a response to binding. (transduction)
- Can be down or up regulated.

(slide #12)

❖ Hormones types :

- Polypeptide hormones (most hormones). e.g.:
  *pituitary hormones
  **hypothalamic releasing hormones
  ***insulin and growth factors
- Amino acids derivatives
  *adrenaline (derived from phenylalanine or tyrosin)
  **thyroid hormones
- Steroids

(slide #13)

❖ Classification of Hormones by mechanism of action

- <u>Hormones that bind to the intracellular receptors:</u>

1. Steroids
2. Thyroid hormones
3. Calcitirol (the active form of vit.D)
4. Retinoic acid (the active form of vit.A)

- Their receptors are inside the cell which means that they can penetrate the membrane so they are →**hydrophobic/lipophilic**

- They need carriers (transport proteins) to move through the plasma (blood)/extracellular fluids.
  The active form of the hormone is the free form, so the activity of the hormone depends on its association affinity to the transport protein and that is why hormones must have a certain affinity of dissociation and binding reversibly to the carriers.(not free).
- Their biding to proteins prevents them from degradation so they have long half life.

- <u>Hormones that bind to cell surface receptors:</u>
- They are free
- They have short half life
- They can NOT enter the cell , so they use 2nd messengers, like:

1. cAMP(glucagon, ACTH, β-adrenergic factor)
2. cGMP (atrial natriuretic factor , nitric oxide)
3. Calcium or phosphatidyl inositol (oxytocin,TRH)
4. kinase or phosphatase cascade (insulin, GH)

(slide #14)
The dr read this slide as it is.

General Features of Hormone Classes		
	Group I	Group II
Types	Steroids, iodothyronines, calcitriol, retinoids	Polypeptides, proteins, glycoproteins, catecholamines
Solubility	Lipophilic	Hydrophilic
Transport proteins	Yes	No
Plasma half-life	Long (hours to days)	Short (minutes)
Receptor	Intracellular	Plasma membrane
Mediator	Receptor-hormone complex	cAMP, cGMP, Ca^{2+}, metabolites of complex phosphinositols, kinase cascades

(slide #15)
The Action of polypeptide hormones:
- May cause the release of other substance from the cell

- Increase the flux of ions into cells
- Activation of enzymes or proteins
- Suppression of activities of enzymes and proteins.

(Slide #16, 17) the Dr read them.

Anterior Pituitary Hormones

- GROWTH HORMONE (GH)
  - Regulates growth
  - Affects protein, fat and carbohydrate metabolism.
- THYROID STIMULATING HORMONE (TSH) – controls secretion of thyroxin.
- ADRENOCORTICOTROPIC HORMONE (ACTH)
  - controls secretion of hormones released by adrenal cortex.
- MELANOCYTE-STIMULATING HORMONE (MSH)
  – along with ACTH, affects pigment release in skin

Anterior Pituitary Hormones Cont.

- FOLLICLE-STIMULATING HORMONE (FSH) –
  In females: stimulates maturation of egg cells
  estrogen secretion by ovaries.
  In males: spermatogesis
- LUTENIZING HORMONE (LH) –
  In females: stimulates release of ovum by ovary.
  In males: stimulates secretion of testosterone.
- PROLACTIN (PRL) – stimulates milk production.

❖ Some notes:

1. The previous slides we just have to know that they originate from the ant. Pituitary gland.

2. We have to know that these hormones affect the releasment of other hormones.
3. We just need to memorize their name, without their actions.
4. add to them β-endocrine

- (slide #18)

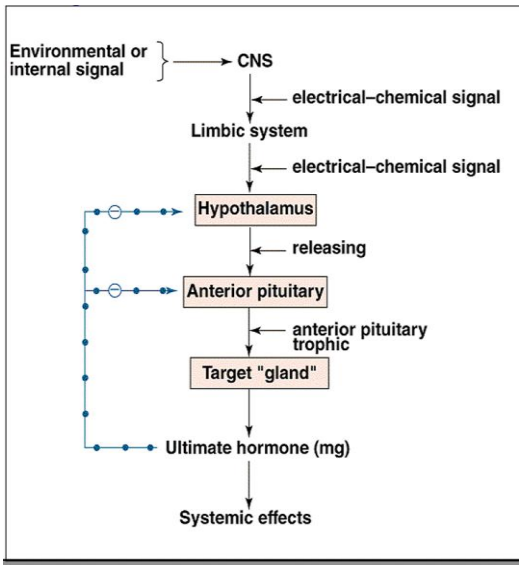
We need to know from this slide the next things:
1. we need to know that the function of these hormones is only stimulation of releasing other substances.
2. TRH (the smallest peptide hormone-3 a.a-) affects the release of TSH.
3.GnRIF is a large hormone with about 100 a.a.

Some Hypothalamic Releasing Hormones

Hormone		A.Acids
Thyrotropin Releasing Hormone	(TRH)	3
Gonadotropin Releasing Hormone	(GnRH)	10
Gonadotropin Release-inhibiting Factor	(GnRIF)	12kDa
Corticotropin- Releasing Hormone	(CRH)	41
Arginine Vasopressine	(AVP)	9
Angiotensin II	(AII)	8
Prolactin-Releasing Factor	(PRF)	
Prolactin-Release Inhibiting Factor	(PIF)	

- (slide # 19)

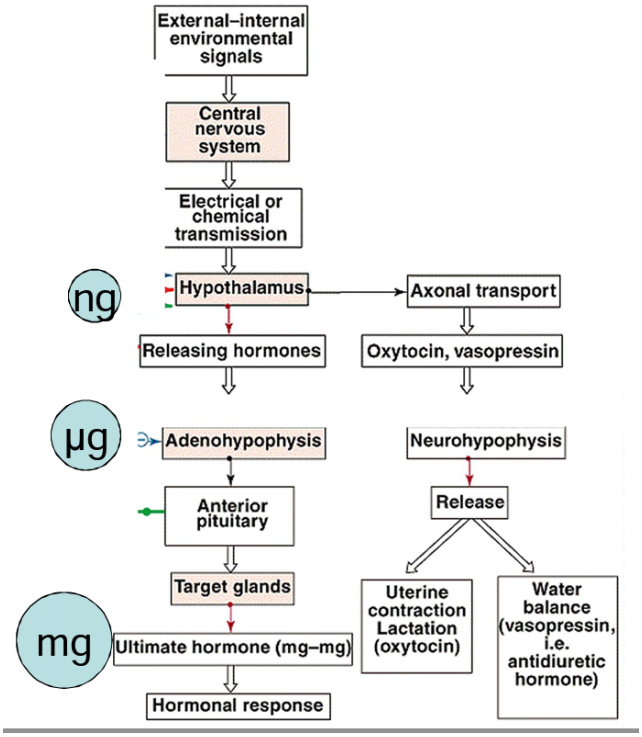
These hormones work through a system that amplifies specific signals.
Either an environment or internal signal
1.will make the CNS generates and sends an electrical signals
2.these signals transfers down to the hypothalamus(a region in the inferior part of the brain).
3. the hypothalamus release hormones that reach to the ant. Pituitary gland.
4. the ant. Pituitary release hormones that affect other cells (target cells).
5.the ultimate hormone affect many cells in the body which means a small signal from it could produce a systemic affect .
6. it was named by a cascade system because increasing amount of hormones at successive level→ increasing half-life of the hormone.



- (slide #20)

To make things clearer lets take a look at this slide:

- The hypothalamus as you can see release hormones in <u>nano-grams</u> amounts
- Then the adenohypophysis release hormones in micro-grams amount (1000x the one before).
- And then it reaches the target cells which release hormones in mili-grams amount. (10^6 the hypothalamus release)



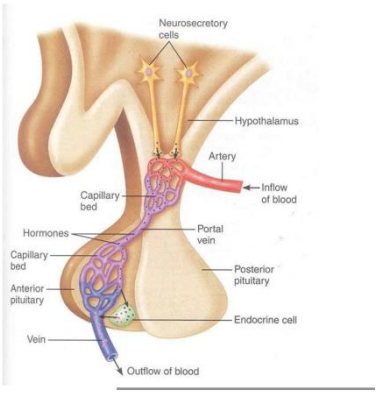
☒ How can we control this release?

- The control of the amount of the hormones occurs by **<u>feedback inhibition</u>**
- Each hormone affects the cells that release it.
- Like the releasing hormones affect their own secretion from the hypothalamus (we name this ultra-short feedback loop). (negative feedback)
- There is a short feedback loop in which the hormone affects on a previous step, like the ant. Pituitary hormones affect the hypothalamus.
- Or finally the long feedback loop in which the final hormone acts negatively to inhibit the releasing of the previous hormone and the releasing hormone, like the ultimate hormone here that affect the hypothalamus.

- (slide # 21,22) the Dr said that they have the same info as this one , so check them.
- (slide # 23)
- All pituitary hormones are made of a single polypeptide chains **<u>except</u>** : TSH, FSH, LH (they are dimmers with similar alpha subunits).

- (slide #24)

We notice here that the hypothalamus is very close to the ant. Pituitary gland .



- How the hormones transfer from the hypothalamus to the pituitary?
  Hypothalamus hormones are formed in a very low concentration so they will not be transferred through the systemic circulation.
- In case of the ant. Pituitary →They use a **portal circulation**(which is the circulation that comes from an organ(hypothalamus) and goes directly to another (ant. pituitary)).

- In case of the post. Pituitary it has a hormone that is transferred directly through axons so it seems like a part of the nervous system so it has another name which is "neurophysis".

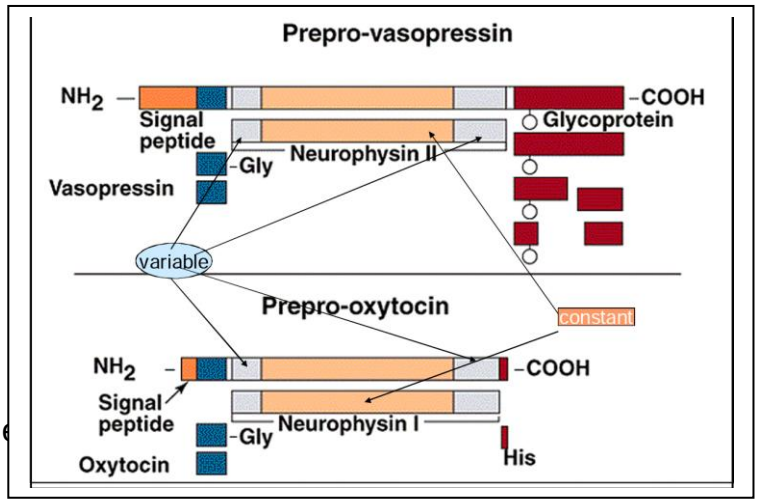
(slide #25)

- Synthesis of polypeptide hormones (occurs as precursor polypeptides ACTH, MSH,etc) .
- ACTH is synthesized by a large polypeptide synthesized by a single gene.
- This gene`s name is " سمّوا بالله " proopiomelanocortine (POMC).
- Pro: before
- Opio: opioid (anesthetic drug related to morphine)
- Melano: melanocyte/melanin
- Cortine : gene
- Forget the name and focus here: this polypeptide is cleaved at several places.
- The cleavage depends on the presence of specific enzymes; each cell has specific enzymes cuts the compatible part for it at specific sites of this polypeptide. That why we have polypeptides in variable lengths→ variable functions→ variable hormones.
  So this is why cells are different in their hormone secretions, because each type of cells has different kind of cleavage enzymes.
- ACTH (adrenocorticotrophic hormone) that stimulate adrenal cortex, and a part of the polypeptide gives us the MSH (melanocyte-stimulating hormone), so production of ACTH in high amount leads to pigmentation. (and if it was produced in higher level it leads to hyperpigmentation).

(slide #26)

- One gene may code more than one peptide
- Vasopressin and Oxytocin
- These are secreted by the post. Pituitary gland.
- They synthesized in separate cell bodies of hypothalamic neurons
- Vasopressin in response to baroreceptors or osmoreceptors
- Oxytocin in response to suckling.(the sucking action from the baby on the breast is the stimulation of this hormone).

(slide



This slide represents a gene that will produce a hormone and a long with the hormone accompanying peptides.
So neurophysin 1 and 2 are peptides that accompany vasopressin and oxytocin.

-The end-

Never be bullied into silence. Never allow yourself to be made a victim.

Accept no one's definition of your life; define yourself ^_^

Done by: Wala'a Al-salhi