Note: *First of all, I just want to say that I'm really sorry for any mistake or anything missing in this sheet. I really tried my best but the professor's voice would sometimes disappear just when he is about to say the main word in the sentence; so if there is a mistake it means I couldn't hear it well, sorry.* ^^

Last lecture, we talked about the adrenal gland; its function, its secreted hormones and how they're controlled, then about Cortisol and some of its functions.

Today we'll talk about Aldosterone.

- Aldosterone is the main and most potent mineralocorticoid hormone.

- ***Main function***: 1. is to mobilize the target fluid volume; consequently, blood volume, leading to normalizing blood pressure.
  2. It also binds weakly to the Cortisol receptors.

- 40% of it is free, while the remaining 60% is bound to proteins; 20% is bound to corticosteroid-binding protein and the other 40% is bound to albumin.

Mineralocorticoids hormones (or chemicals) can be; natural or synthetic.
Other mineralocorticoids (than Aldosterone) that are subsequently strong are:

1. Flurocortisone
2. Corticosterone
3-deoxycorticosterone
4-pregenolone and progesterone

Aldosterone secretion regulation:

When we talked about ACTH, we said it was the major stimulus for Cortisol. Aldosterone's main stimulus, beside the ACTH, is the reduction of blood volume or body fluids volume in the kidneys.

The kidneys produce hormones, like Renin ,that produce Angiotensin I from Angeotensinogen(from liver). Angiotensin I produces Angiotensin II under the influence of converting enzymes from the lungs (other tissues can also synthesis these converting enzymes, they make about 50% of them). *Angiotensin II* is the **main stimulus** for Aldosterone secretion from the adrenal cortex.

Another stimulus to produce Aldosterone is the increase in K^+ concentration or reduction of Na^+ in the blood, then third comes the ACTH. Aldosterone then causes Na^+ reabsorption from renal tubules.

As for Angiotensin II, in addition to stimulating Aldosterone secretion, it –directly and indirectly- stimulates the reabsorption of Na^+ in the renal tubules, mainly the proximal tubules, directly through the basolateral and luminal membrane.

For the next part, please refer to the picture of nephron's structure in the slides

- You can see the afferent and efferent arterioles.
- One of the functions of Angiotensin II is vasoconstriction of Efferent arterioles.
- When this happens, the fluid in the peritubular capillaries (seen in the picture) increases.
- Reduction in the hydrostatic pressure in these capillaries and, relatively, increase in protein concentration in them are the 2 factors that increase the reabsorption of water as well as Na^+.

There's another stimulant for Aldosterone secretion; Angiotensin III, which is potent as Angiotensin II.

We said that Aldosterone increases the reabsorption of Na^+ through renal tubules, it also increases it through other organs, such as intestines and sweat glands

Change in pressure, volume, sodium concentration or potassium concentration or B-adrenergic stimulation will stimulate an apparatus in the kidney(Glomerular apparatus) to produce Renin. Renin will produce Angiotensin I which will give us Angiotensin II & III.

Androgens & Estrogens:

- We have 2 weak androgens that are produced in the adrenal cortex; Dehydroepiandrosterone and Androstenedione, which produce (also in the adrenal cortex) potent androgens:
    1. Androstenedione gives Estrone.
    2. Testosterone produces Estradiol.

- Androgens & Estrogens are not that important in males in any stage of their lives (normally); they have Testosterone which is produced by the testis.

- On the other hand, Androgens & Estrogens are very important in females, in all stages of their lives –from childhood till death. They are very important especially after menopause, because then the adrenal cortex becomes the main source for them as the ovaries stop functioning.

- In females, Androgens function is for the growth of pubic and axillary hair, and Libido.
  In males, same as Testosterone.

- When the 2 enzymes producing Cortisol are deficient, the 2 weak androgens will be produced more.

Thyroid Gland

- Stimulated by TSH which is an anterior pituitary hormone. TSH is stimulated by the hypothalamic hormone; TRH.
  it is inhibited by Dopamine and Somatostatin, also affected by Cortisol and Growth hormone by stimulating Somatostatin(most probably) or dopamine release.

- TSH stimulates the growth as well as synthesis and secretion of the thyroid gland.

- TSH is composed of 2 subunits; alpha and beta. Alpha is non-specific while beta is specific and it doesn't function unless bound to alpha.

- The thyroid gland produces 2 hormones; T3 & T4, which exert a feedback control over thyroid level, pituitary level and hypothalamic level. This control exert its effect hour by hour, day by day.

Please, refer to the TSH structure in the slides, which shows the TSH 2 subunits.

- TSH has 2 types of 2nd messengers; c-AMP or IP3 and diacylic glycerol(for metabolism), leading to growth of cells and synthesis and secretion of the hormone.

- Thyroid gland is composed of 2 lobes (right and left) that are connected by an Ismuth and lie in front of the trachea. It weighs about 25-30 gm and has a rich blood supply.

Please, refer to the picture of thyroid follicles in the slides for the next couple of points.

- Thyroid gland has follicles that are full of fluid along with proteins, chemicals,hormones… etc.
- This colloid is surrounded by epithelial cells(Follicular cells). These cells are the ones that synthesis the hormone which they secret in the colloid.
- In between the follicular cells, there are other cells, known as parafollicular cells which secrete Calcitonin.

- In Fetus, the thyroid gland can produce its hormones by the 12^{th} week of gestation, under the effect of the hypothalamus and pituitary hormones. (From the fetus, ***not*** the mother; maternal TSH ***can't*** cross the placenta.)

- How did they know TSH can't cross the placenta?

Fetuses that can't synthesis T3 or T4 will be born with a disease called cretinism, when these newborns mothers' thyroid hormones are tested they show normal levels.

- T3 and T4 are essential for normal growth of all organs, but specifically the nervous and skeletal systems.

- The thyroid gland is unique in 2 aspects:
    1. It integrate inorganic and organic substances; Iodine and tyrosine
    2. The only gland that stores its secretions, the storage is sufficient for about 1 month. (On the slides it's 2-3 months, the prof. doesn't think so.)he thinks that there is mixing between iodine storage and hormone storage.

Please, refer to the image of the amino acid; tyrosine in the slides.

- Each hormone is composed of 2 tyrosine amino acids.
- When 1 Iodine binds with 1 tyrosine they'll give → 'monoiodothyrosine'.
- When 2 Iodine bind 1 tyrosine they'll give → 'diiodothyrosine'.
- When diiodothyrosine' and 'diiodothyrosine' bind, they'll give → 'tetraiodothyroidine'T4.
- When 'monoiodothyrosine' and 'diiodothyrosine' bind they'll give → T3 (triiodothyronine)

- There's another hormone; reverse T3 (inactive) which only differs from T3 by the location of the Iodine.

- Thyroid produces:

    1. T4 ***mainly*** (which is a pro-hormone) has Little activity.
    2. Little of T3 (which is *extremely* active)
    3. Little of Reverse T3 (which is totally inactive).

Someone asked the doctor a question, the doctor said it is not required from us , but we should know that the thyroid hormone doesn't pass the placenta, and that's why Cretinism occurs.

"Your time is limited, so don't waste it living someone else's life. Don't be trapped by dogma- which is living with the result of other people's thinking. Don't let the noise of other's opinions drown your own inner voice. And most importantly, have the courage to follow your heart and intuition, they somehow already know what you truly want to become. Everything else is secondary."

Steve Jobs