Firstly the doctor give "Jumana" a slide the most important things in this slide are:

**ACE inhibitors** have been available for many years and are among the safest and best -tolerated of all antihypertensive medications.

**ACE inhibitors** have two main problems:

1-These drugs don’t function in all people,some people don’t response to these drugs.

2- Some others have side effects ,such as cough, ranging from mild to severe, which means that these people don’t tolerate these drugs.

They found some drugs don’t inhibit (angeotensin II) but they inhibit the receptors they also they found that these drugs don’t have any side effects "when we inhibit the receptors of (angeotensin II)".

**Thyroid Gland**

It is not essential for life so you still alive even when it removed or damaged, but it affect all metabolism operations in the body mainly the nervous system as well as the skeleton.

Now please look at fig 40-4 ,page115 in the booklet.

Thyroid gland stimulated by (**TSH**) which is an anterior pituitary gland hormone.

You have to know that (**TSH)** stimulated by (**TRH)** which is hypothalamic hormone and had peptide structure stored in the median eminence then it will be released from the median eminence to stimulate **(TSH)** in the anterior pituitary**.**

**TSH** stimulates the growth of cells of the thyroid gland as well as synthesis and secretion of the hormones.

**TSH** composed of two subunits:

 1- **α-subunit :** nonspecific because it’s also found in other three hormones (**LH** ,**FSH** ,and **CGH**).

2- **β-subunit :** it is the specific or active subunit, but it doesn’t function unless it bound to  **α-subunit.**

**TSH** is glycoprotein hormone and its receptor on the cell membrane.

**TSH** inhibited by mainly **dopamine**, **somatostatin** as well as **cortisol** and **GH**.

Tow hormones of thyroid gland (T4,T3) exert feedback on pituitary level as well as hypothalamic level.

Now please look at fig 40-5 ,page117 in the booklet.

**TSH** produces some compounds as second messengers:

1. **cAMP** most probably for the synthesis of hormones.
2. By activationof **phospholipase C** it produces **IP3** and diacylglycerol , Most probably for phospholipid metabolism and growth of the cells.

TSH produces **cAMP** for the synthesis of hormones,and also TSH produces the two second messengers (**cAMP** and **IP3** ) Most probably for phospholipid metabolism and growth of the cells.

Now please look at page118 in the booklet.

Thyroid gland is composed of two lobes: right and left, joined by isthmus these two lobes (thyroid gland) lies in front of trachea.

Thyroid gland weighs about 25-30 g and it’s richly blood supply (5ml/g/min) that means it’s very important.

Now please look at fig 48-1,page119 in the booklet.

When we take section for Thyroid gland we find that it composed of follicles, these follicles lined up by follicular cells (epithelial cells), these cells synthesize the thyroid hormones, and each follicle is full of colloid which contains proteins and hormones.

Now please look at page118 again in the booklet.

In between those cells there’s parafollicular cells (**C cells**) which produce unrelated hormone (**calcitonin)** plays role on calcium .

Thyroid hormones are essential for normal development of the nervous system and skeleton during the fetal life, therefore, the secretion of these hormones begins even by 12 week of human gestation (before the12th week) affected by fetal TSH and TRH because none of these hormones pass from the maternal blood to the fetal blood.

Now please look at fig 5.3.4 ,page121in the booklet.

 Thyroid gland produces an amino acids called **tyrosines**, which carry **iodine**, so it called iodinated tyrosines; therefore, thyroid gland is unique in two aspects:

First, incorporates (binds) inorganic substance with organic substance, like (iodine+tyrosine).

Second, synthesize and stores hormones sufficient for the human being for about one month.

When one tyrosine binds one iodine, this called **Monoiodotyrosine (MIT)**.

When one tyrosine binds two iodine, this called **Diiodotyrosine (DIT)**.

MIT and DIT together called>> tyrosine carrying iodine (iodotyrosines).

When two diiodotyrosines bind with each others, this produces **tetraiodothyronine** (**Thyroxine** or **T4**), this means that T4 is composed of two tyrosines carrying 4 iodine so maximally in the structure of the hormone there are 4 iodine ,But when one (DIT) binds with one(MIT), (**T3**) **triiodothyronine** will be produced**.**

T4 activity either very low or no activity, that means it is active but doesn’t functioning properly similar to the activity of T3 .

T3 is the active form.

There’s a third type totally inactive called reverse T3 (**rT3**), same as T3 in structure, but there’s change in the iodine position on tyrosine.

(T4, T3 and rT3) all called iodothyronines.

Thyroid gland mainly produces T4 which produces T3 and rT3, therefore, this hormone (T4) called **prohormone**.

Now please look at fig 76-2 ,page126 in the booklet.

Iodine taken from plasma into the follicular cells then into the colloid by a carrier that carry also (Na) ,"pendrin carrier" caries the iodine inside the colloid. Then it will modified inside the colloid to be utilized under the effect of peroxidase and binds with the tyrosine "this is called **iodination** (binding of iodine with tyrosine) or **organification** (binds with the amino acid)"

**\*** Iodination produce either (MIT) or (DIT).

**Coupling** is the production of T3 or T4.

In the thyroid gland there’s MIT and DIT, those bind each other in two ways, and this is called coupling:

**1-MIT+DIT=T3**

**2-DIT+DIT=T4**

**\*\*the doctor give another slide to Jumana!!.**

 Iodination and coupling don’t occur on free tyrosines, they occur on iodinated tyrosine in a protein structure called **Thyroidglobulin** (**TG**).

TG produced by thyroid gland, it contains about 70 tyrosine amino acids" but in some books like gytone they said 134", so we can conclude that there is variation in the structure of TG, all of them the same but this means that the amino acids which they leave the essential structure aren’t active , some hormones differ in the site which has the most activity, some in the middle and some others in the first part and some others in the last part; an e.g.: the TG is composed of amino acids 70 tyrosines but 4-8 just can incorporate iodine.

TG can carry MIT, DIT, T3, rT3 and T4, by **pinocytosis,** they are taken back into the follicular cells (epithelial cells) into the colloid , there’re enzymes in the follicular cells split T3 and T4, and those two hormones will be secreted into the blood "may be not all of them" then the remaining iodine reutilized.((this is the synthesis and secretion of thyroid hormone)).

Normally, just T3 and T4 are released into the blood, but abnormally T3,T4,MIT,DIT and TG are released into the blood.

Now please look at page131 in the booklet.

There’s storage of iodine in the body sufficient for the human being for 2-3 months, differ from one person to another depending on the diet.

Now please look at fig 32-4 ,page124 in the booklet.

T3 could produce Diiodothyronine, but why we said diiodothyronine instead of diiodothyrosine?

Due to diiodothyronine comes from a hormone (T4).

Please memorize table 53-1, page 130 in the booklet. ☹

\*\*we can notice from this table that T3 and rT3 are produced from T4.

Now please look at fig 48-45,page131 in the booklet.

More than 99.5 %of the thyroid hormones are bound to proteins, like T3, but (99.98%) of T4 is bound to proteins.

Now please look at table 5.3.3 ,page133 in the booklet.

There’re 3 types of proteins binds thyroid hormones**, thyroxin binding-globulin**, **Albumin** and **thyroxin binding-pre-albumin**, **what** the advantage from this binding?

To prevent filtration through the kidney and prolong the half-life of the thyroid hormones.

**Why** T3 more active and more effective than T4?

Because it can binds receptors and the affinity is more.

