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ENDOCRYNE SYSTEM

The endocrine system and the nervous system coordinate the activity of the organism.
The endocrine system does it through chemical messengers called hormones that can have medium and long term effects and act at a distance.
Both endocrine and nervous systems produce chemical messengers but the main difference is the time of action, infati the nervous system is faster and has a short term.
Another difference is the type of intracellular communication.

- Endocrine
- Autocrine and paracrine
- Neurotransmitter
- Neurohormoneà directly released in the blood

The hormones can be steroid and nonsteroid hormones, non steroid can be proteins like insulin and glucagon and glycoproteins like FSH and LH.
We can also have hormones that are amino acids like epinephrine, melatonin ecc.
The hormones need to be in very low concentrations and also they are really selective, so there is no need to secrete a really high level of hormone.
The receptors of the hormones can be:
ON THE CELL SURFACE:

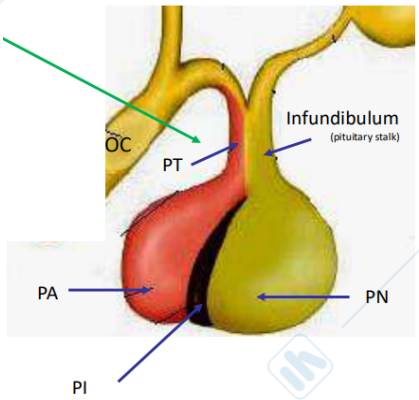
- Ion-channel: they have a ligand binding pocket and an opening where only specific ions can pass through.
- Membrane proteins: they bind external ligands and convert the signal into an intracellular signal.

INTRACELLULAR
They pass inside of the nucleus and bind the DNA to transcript a specific gene.
In particular the steroid organs have a genomic action and it takes at least more than ten minutes to take action.
Was discover that steroid hormones can also have a non genomic action where the ligand bind a receptor, and this type of action is really faster
ENDOCRINE GLAND:
They can originate from different germinal foglietti

- Ectoderm/neuroectodermà adenohypophysis, neurohypophysis, epiphysis, adrenal medullary
- Mesodermà Adrenal cortex tm test and ovary
- Endodermà Thyroid, parathyroid, pancreas islets

PITUITARY GLAND

Is inside of the sella turcica, body of the sphenoid bone and is in contiguous with the base of the brain called hypothalamus.
This gland is composed by two major parts: the pars anterior or distalis called also ADENOHYPOPHYSIS (dark stain) and the other is pars nervosa or posterior called also NEUROHYPOPHYSIS.
The other parts are called pars intermedia and pars tuberalis (directly connected with the hypothalamus)



PARS INTERMEDIA

Whe can see these structures in histochemistry and we can see some structures called follicles, structures with a cavity inside.
In other animals this structure is more developed.
These cells produce POMC that is a precursor of the MSH.

Turning back to the development of the embryo.
In the oral cavity we can see a sort of pouch called hypophyseal pouch also called Rathke's, this part has an ectodermal origin and has a sort of epithelial structure.

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Very close there is the brain that is developing and one part of the brain that is called neurohypophyseal bud moove in front of the pouch.
This part ended in contact, following the day the pouch in the oral cavity lose contact with it but stay in contact with the final part of the brain.
So there are two parts, one part from the brain and one part from the oral cavity.

ADENOHYPOPHYSIS

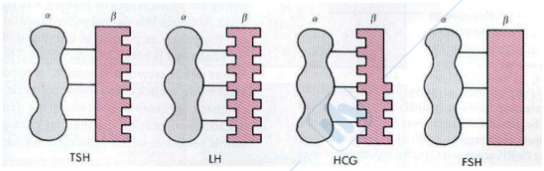
Cordonal structures with different types pf cells:

- alfa , acidophilus→ proteic hormones
- beta, basophils→ glycoprotein hormones

The precursor is POMC and depending on the region
every cells in the adenohypophysis produce only one type of hormone:

- GH→ Growth hormone
- ACTH→ Adrenocortical hormone, this hormone is responsible for the stress
- TSH→ Thyroid stimulating hormone, growth of the glands and production of the hormones by the glands
- LH , FSH→ Follicle stimulating hormone and luteinizing hormone , are gonadotropic hormones (only cells that produce 2 hormones)
  They were discovered before in the female sex and they maintain the name but they are also in the testis.
- Prolactin→ This hormone is important during pregnancy because increase the amount of milk

Glycoprotein hormones contain two subunits, a common α subunit and a distinct β subunit: TSH, LH, FSH and hCG.



❑ Secreting PRL	20%
❑ Secreting ACTH	15%
❑ Secreting GH	50%
❑ Secreting LH-FSH	10%
❑ Secreting TSH	5%

Mechanism→ negative feedback, The rise of the hormone levels produced by the target gland blocks the production of the corresponding pituitary hormone.
Also the hypothalamus produces adenohypophyseal regulating hormones

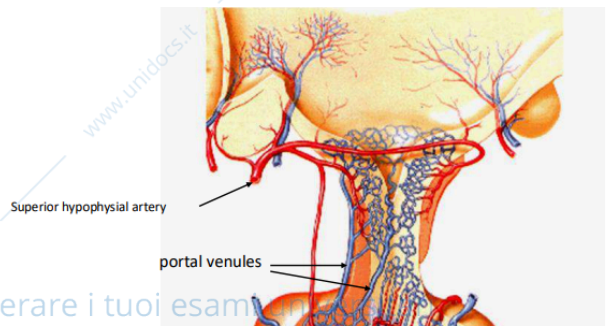
NEUROHYPOPHYSIS

Here there isn't a corodnal structures, so no endocrine cells, but there are nervous fibers arriving from the anterior region of the hypothalamus.
There are two nuclei:

- Supraoptic nucleus
- Paraventricular nucleus

The neurons here are neurons that produce a hormone that is released directly to the blood stream.
The hormones produced by these two nuclei are the vasopressin, also called the antidiuretic hormon (adh) and oxytocin (important during the contraction of the delivery and in the contraction of the mammary muscles to let the milk exit), these hormones are produced in the neurosecretory cells and are transported to the neurohypophysis.

There is a sort of axis, in the hypothalamus there are so many nuclei and each of that produces hormones.



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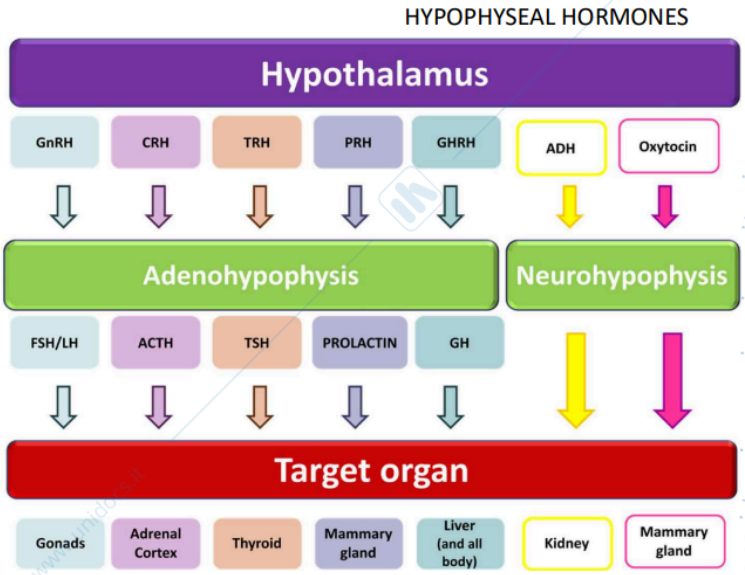
These hormones are called releasing or inhibiting factors and are able to regulate the activity of the pituitary cells.
They are released in the hypothalamus-pituitary portal circulation that leads them directly to the adenohypophysis.
They don't go everywhere in the body but just in this part of the body to regulate the adenohypophysis.

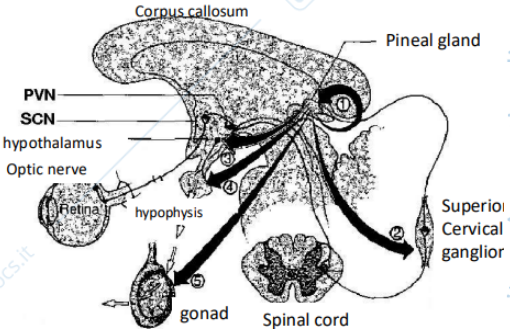


PINEAL GLAND

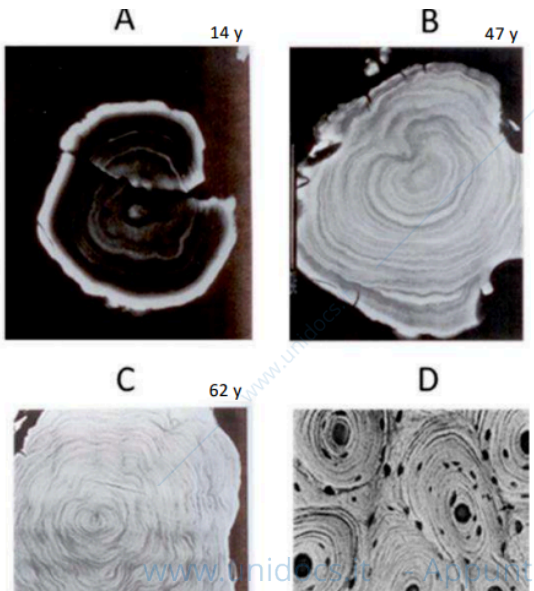
Also called epiphysis.
Is the part of the body connected to the epithalamus, part attached to the roof of the third ventricle.
During the fetal stage it is bigger but then goes to a devolution in adults, depending on the region on the wall the dimension is different, is bigger pole region.
Phylogenetically is derived from the pineal eye or parietal eye of the reptiles, infact this structure contains cells that can synthesize opsin.

The pineal gland produces MELATONIN, is an indole amine derived from Serotonin, is important for the regulation of the circadian rhythm and is mainly produced in the night hours.
This gland is near to the third ventricle, in fact the melatonin is released in the bloodstream but also in the CSF.
There are different types of cells:

- pinealocytes→ contain a lot of mitochondria, and the shape change
- neurons
- glial cells



The receptors for melatonin are not present everywhere, are in specific areas of the brain, pituitary and other organs that may be related to the control of reproduction.
But many structures of the body produce melatonin, because it is a sort of antioxidant direct and indirect.
direct scavenging the action of ROS and indirectly stimulating antioxidant enzymes.
Many tissues in fact use melatonin for this purpose.



In the pineal gland, if we see the coloured tissue there are some structures called corporal aranacea or brain sand, that are a sort of calcifications.
They increase in size during the development and are present also in fetus and in children.
They increase and have a structure that is similar to the bones.

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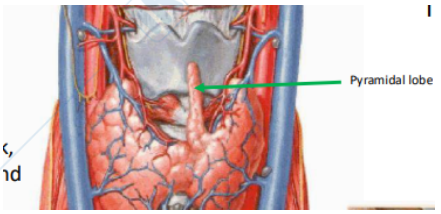
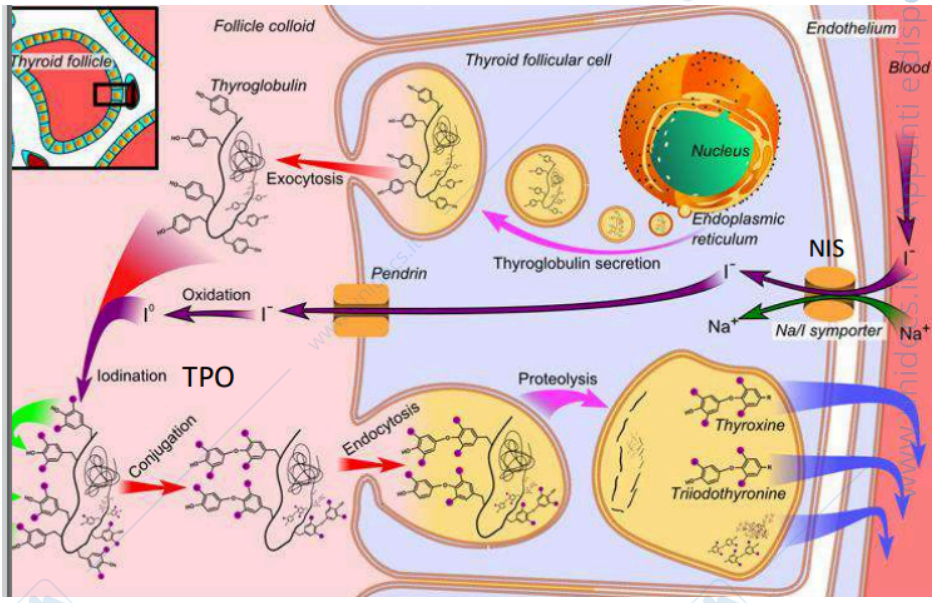
THYROID



Two bigger lobes connected by an isthmus, and located in the neck ventral to the larynx and the trachea.
Is surrounded by a fibrous lamina and the parenchyma has a follicular structure.
The follicles contain inside a liquid that is called colloid.
In 50% of the people there is another structure that is called pyramidal lobe.
In the origins, the thyroid migrates from the oral cavity, in particular in the tongue, and moves to the neck. They migrate through the thyroglossal duct , during this process part of this process part remains and the pyramidal lobe is what remains of the thyroglossal duct.
There are different types of cells:

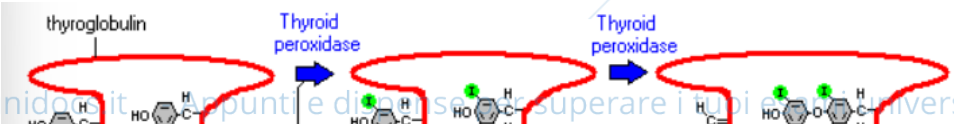
- follicular cells, are the proper cells of the thyroid , this cells form the wall of the follicle, the cavity contain a protein called colloid
- parafollicular cells

Each of these follicles is surrounded by capillaries, the hormones produced by these cells are T3 (Triiodothyronine) and T4 (Thyroxine) in base of the number of iodine that is present.
80% of the hormone released is T4 but the active form is the T3.



This cells are able to take iodine from the bloodstream and take it inside the cell using the Na+/I symporter
And also the iodin can exit the cell from another transporter that is called pendrine.
The cells produce proteins that stays in the colloid.
STEPS:

- The cell produce the protein called thyroglobulin
- The iodin that exit from the cell through the pendrin is oxidized and attached to the protein thanks to the thyroid peroxidase (TPO)
- Then this enzyme do the conjugation
- then there is the endocytosis (difference because in the thyroid the hormone is not directly release but is stored in the colloid)
- Then with a proteolysis there is the removing of the tyrosine and are release in the bloodstream



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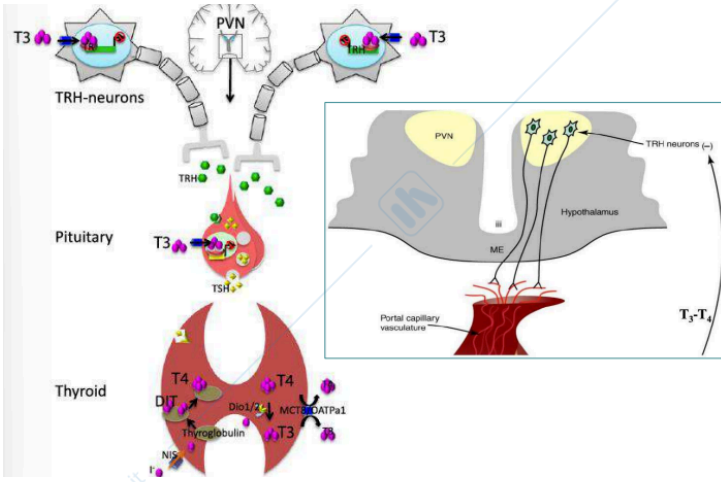
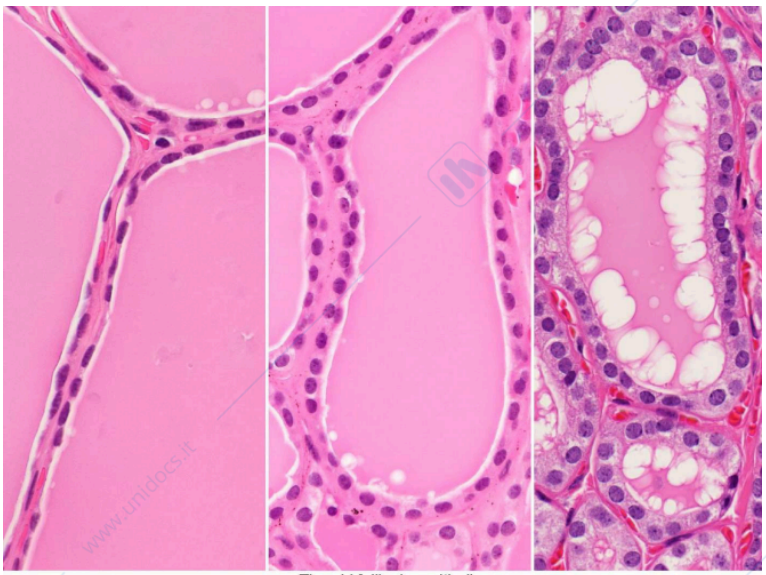
The correct pathway starts from the hypothalamus.
neurons release TRH and the pituitary gland releases TSH.
Some cells can uptake the hormones and portare them to astrocytes,where T4 can be converted to T3,
but can also be transported in neurons .
During development the thyroids are also important.
In the first growth the thyroid hormones are produced by the mother and allow the development of many parts of the body.
Like thyroid, pituitary and hypothalamus.



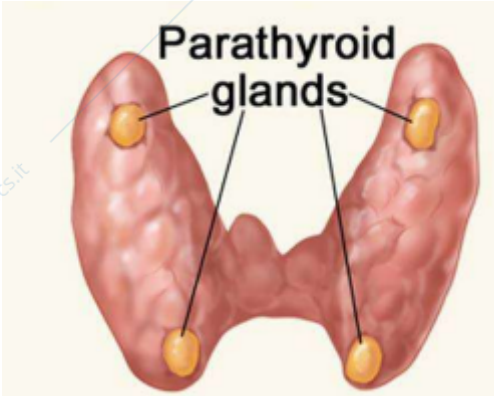
In many cases if the mother has some problems in the production of thyroids hormones in the development of the fetus can be some problems in the first stages of development.


Thyroid follicular epithelium:
flat, cuboidal, and columnar (H&E, high power)

- fist picture is a lot of colloid but not in action
- cuboidal structure is when is in action
- the colloid disappear when there is a lot of production of hormones

There are the three stages of the thyroid in life and also there is the condition when the thyroid is in overfunction or hypofunction.
HYPERTHYROIDISM→ increase of t3 and t4, suppression of TSH secretion also because there is a direct connection with the nervous system there are so many psychiatric disorders and behavioral disorders. In Fact if you have some problem the first thing is do the blood exam and check for the levels of T3 and T4.
HYPOTHYROIDISM→ drop of T3 and T4 and a decrease of the TSH levels.

The parafollicular cells or C cells in the thyroids, they are not directly regulated by the pituitary gland, they can't reach the lumen of the follicles and they secrete a peptide hormone called CALCITONIN, this specific hormone decreases the concentration of calcium in the blood.



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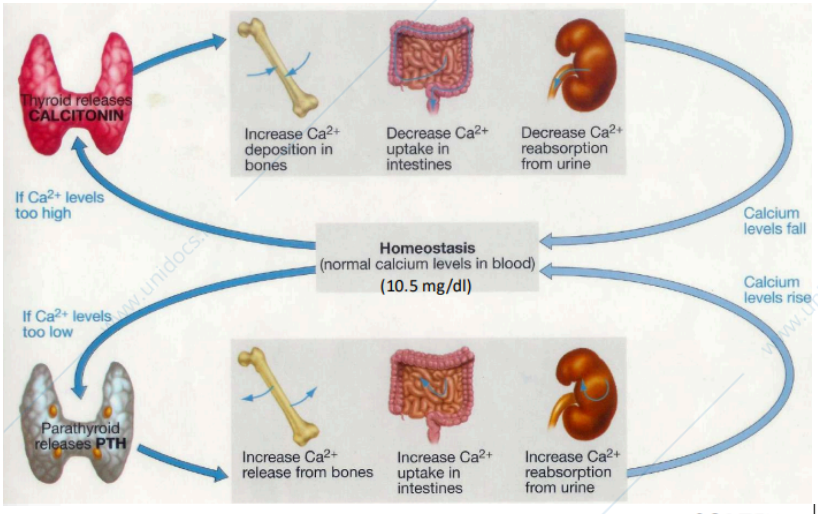
PARATHYROID GLANDS

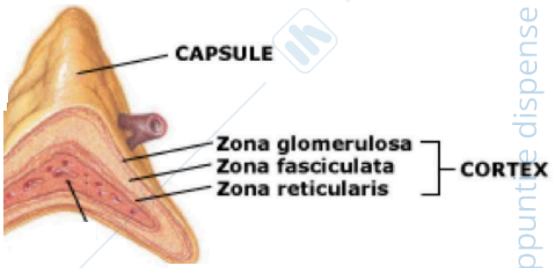
The parathyroid glands are four small glands located behind the thyroid lobe , they have a cordonal structure.
They are surrounded by a capsule, and the cells of this glands produce parathyroid hormone(PTH), this is a calcitonin ANTAGONIST.



The parathyroid glands and the c cells are necessary to maintain the homeostasis of the normal calcium levels in the blood.
The action of these two hormones is not involved in the action of the hypophysis.

ADRENAL GLANDS

They stay above the kidney, these glands are solid organs, there are a lot of arteries that reach the gland from different parts.



CORTEX

(ext)

ZONA GLOMERULOSA (15%):
mineralocorticoids (aldosterone)

ZONA FASCICULATA (75%):
glucocorticoids (cortisol)

ZONA RETICULARIS (10%): androgens

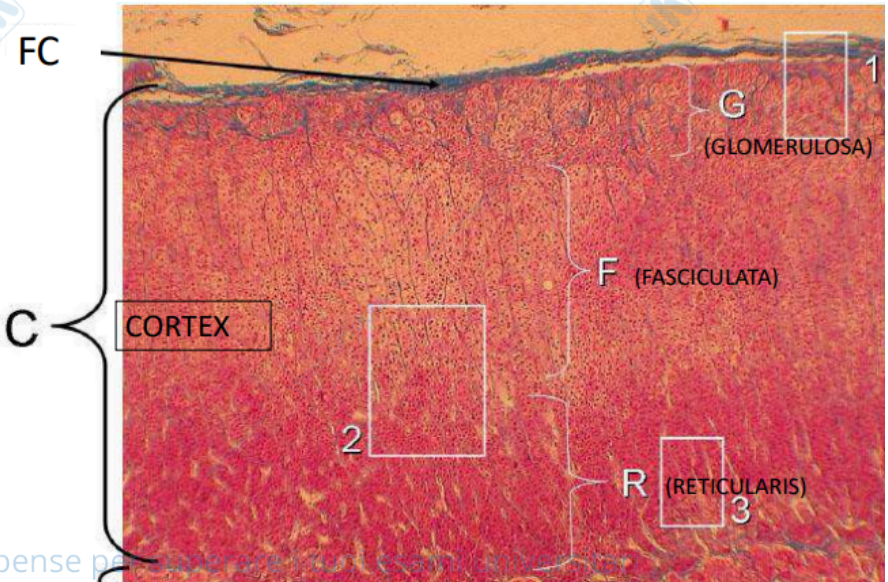
(int)

STRUCTURE:

Outside there is the connective tissue that forms a capsule and inside we have the parenchyma.
The parenchyma can be divided in two different parts : the cortex and the medulla.
The capsule also surrounds all the parts of the organ and receives the vessels.
In the cortex we can distinguish three different parts:

- zona glomerulosa→ produce the mineralcorticoids like aldosterone.
- zona fasciculata→ produce the glucocorticoids like the cortisol, the action is against some stress agents
- zona reticularis→ produce androgens that are involved in the development of secondary sexual characters.

The medulla and the cortex are literally two different glands, in particular the cells of the medulla originate from the neural crest and later are surrounded by the cells of the cortex.



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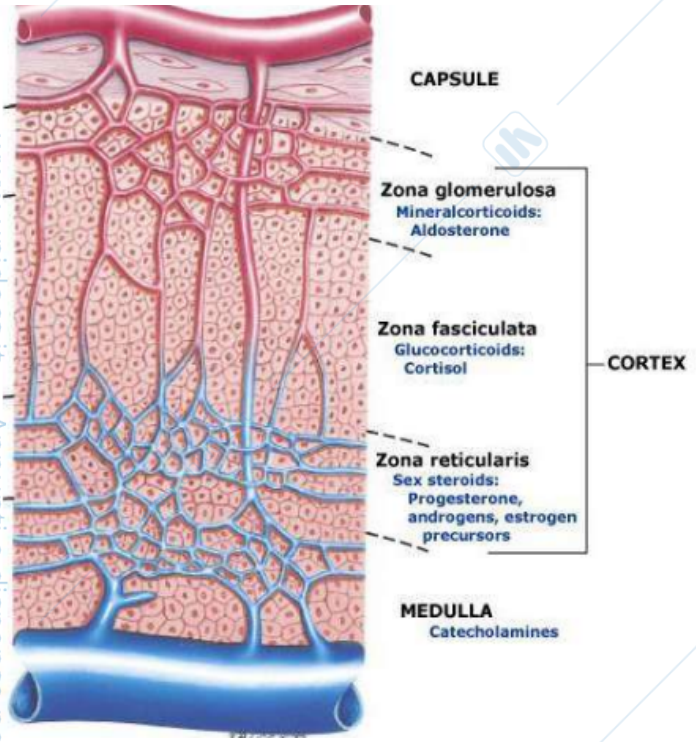
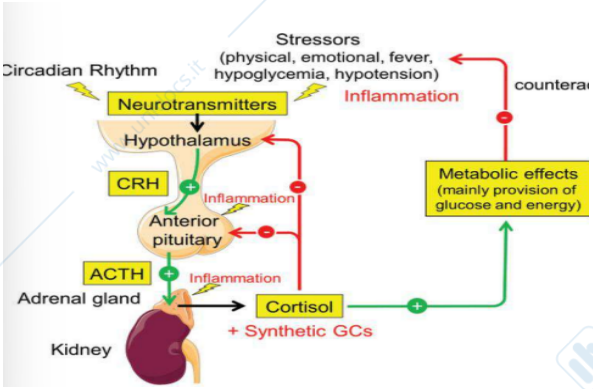
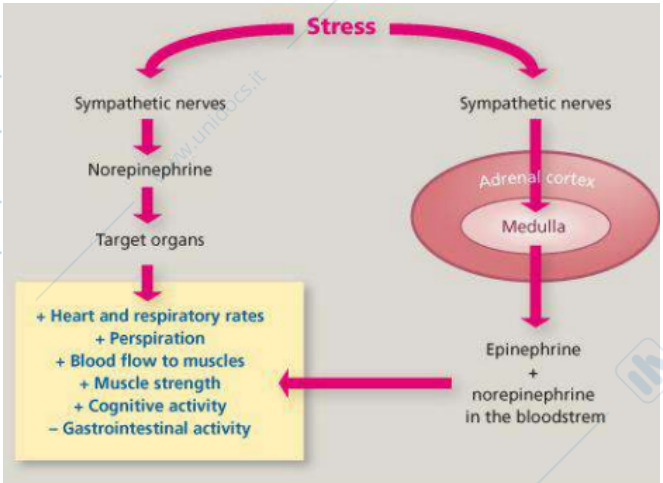
These glands produce the steroid hormones that are binded by the steroids receptors, the cytoplasmic activated receptors bind the dna and regulate the activity of certain genes, in fact these are long their effects.



All the hormones that are produced reach the medullary part where there is a big vein called suprarenal vein.
The major product of the adrenal glands is cortisol in fact; the main axis of these glands is called stress axis.
the secretion of the adrenal glands is regulatet by the ACTH, that is produced by the pituitary gland in response to CRF by the hypothalamus.



In this case the corticosteroids have several targets and stimulate the metabolism of the target.
Inside the cortex there is the medulla that produce different hormones:
CATECHOLAMINES: they are epinephrine for 80% and norepinephrine 20%, these two hormones derived from phenylalanine that goes to tyrosine dopamine and epinephrine.
The principal function of these two hormones is to be a neurotransmitter to the autonomic nervous system that can be described as sympathomimetic action.

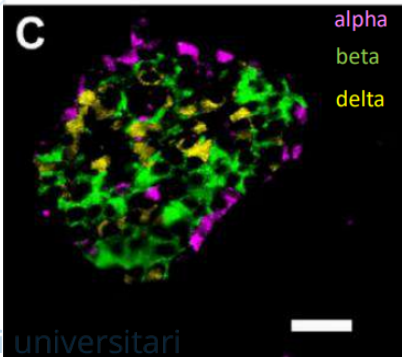


This region is also reached by neurons, and in case of stress a signal that reaches the glands and the cells in the glands start to produce epinephrine.

PANCREAS

In the parenchyma of this solid organ we can observe the presence of cells that can be described as langerhans cells.
In it we can distinguish three types of cells:

- alpha cells→ 20% and produced glucagon
- beta cells→ 75% and produce insulin and amylin



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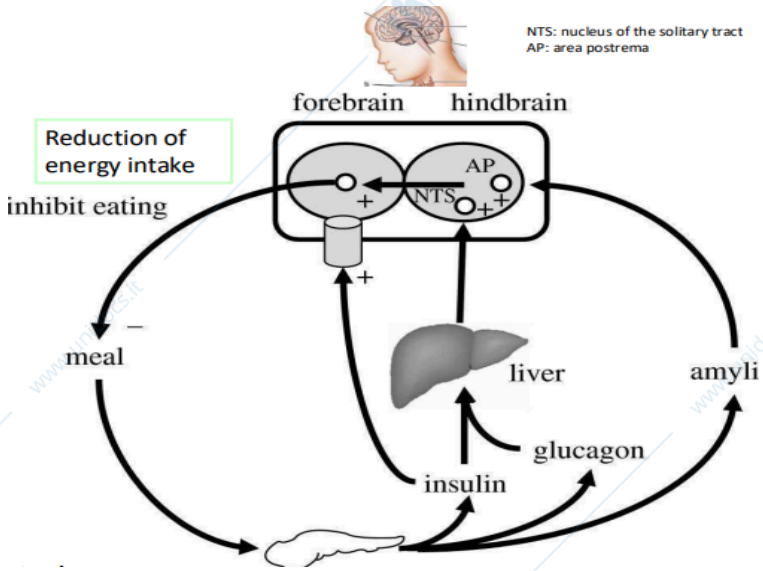
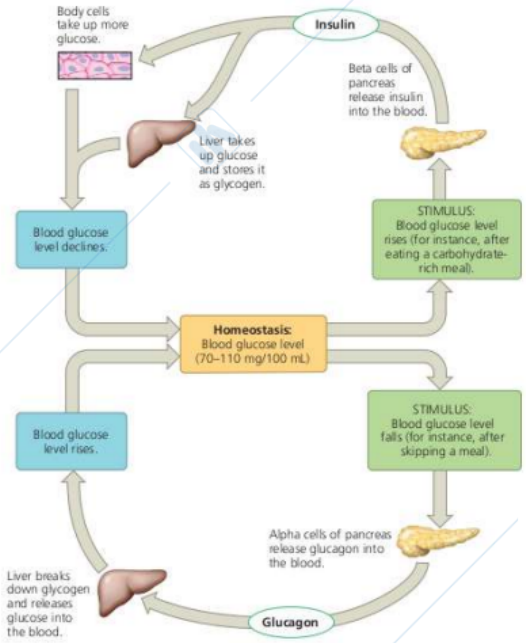
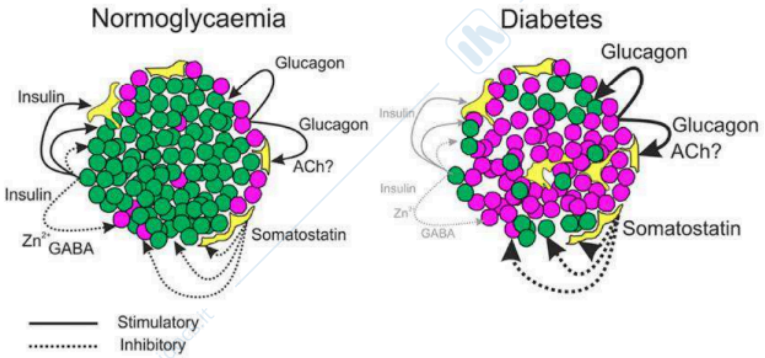
- delta cells→ 5% and produce somatostatin

If you observe an islet you can see how they are distributed and we can say that the majority of the beta cells are in the inner part of the island. And the other cells stays in front of the capillary network. They are not under the control of the hypophysis.
Insulin and glucagon are highly important for the homeostasis of blood glucose level.
the liver takes up the glucose and stores the glycogen.







alpha
beta
delta

Beta cells are not in contact with the capillary network so they act at the level of the other cells.
delta cells produce a hormone called somatostatin that is a sort of controller of the other cells.
In people that suffer from diabetes the beta cells disappear, and they are what produce insulin so the glucose is no longer taken under control.

GONADS

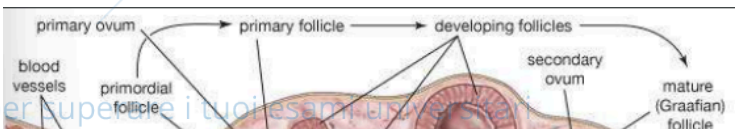
The gonads are important for the production of gametes and sexual hormones, male and female have different chromosomes and in the XY what brings the masculinization is the gene SRY.
What change in the development of the structure of the structure is the two ducts:

- wolf duct in male, in female goes to a total regression
- mullerian duct in female, in males goes to regression

the factor that is AMH in males, COUP-TFII in females (?).

Gonads produce sex hormones:
in particular the ovary produce estrogen and progesterone and the testis produce androgens but they are produced by two sex.

<u>OVARY</u>



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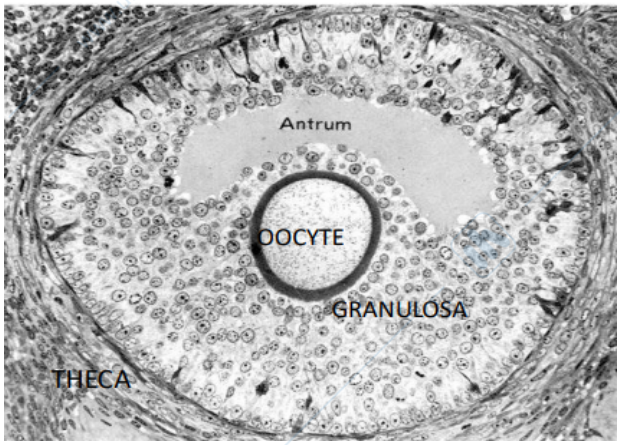
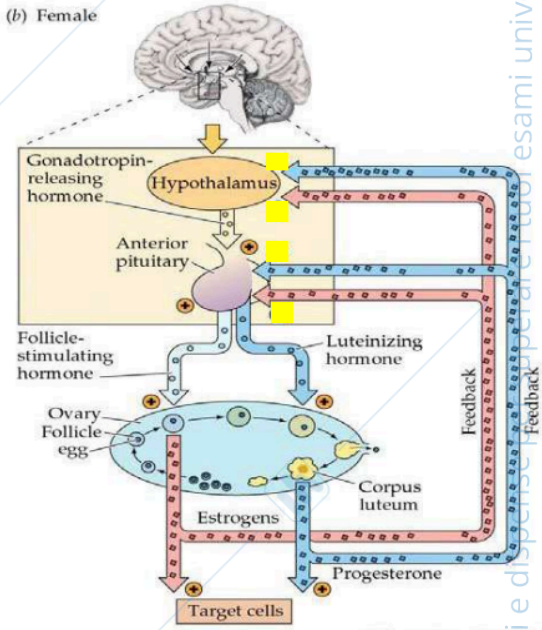
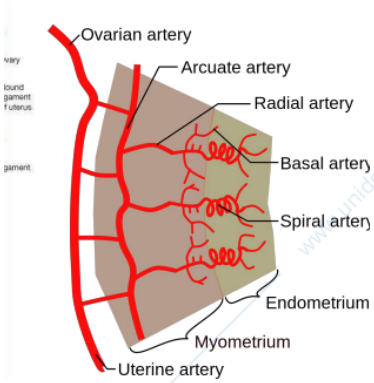
follicles that produces estrogen and after the release of the releasing of the oocyte if becomes coorspu luteus and start to produce progesterone.

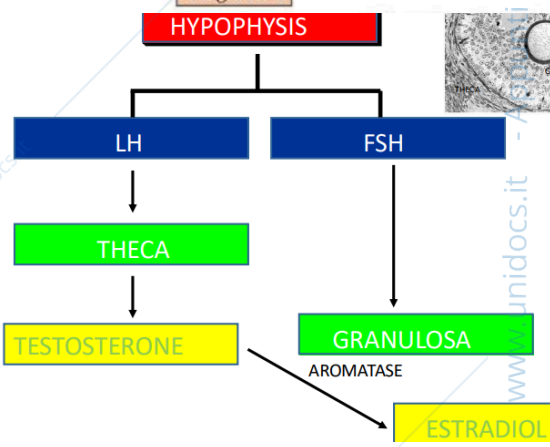


The follicle is formed by cells that surround the oocyte that are called granulosa and around the follicle is organizing a capsule called theca.
Both theca and granulosa produce hormones that are under the control of the hypothalamus that produce gonadotropin releasing hormones and the anterior pituitary produce FSH and LH.
In particular the aromatase enzyme that is located in the granulosa cells especially in the outer region depending on the cycle stage may vary the number of the positive granulosa cells.
Due to the presence of aromatase, granulosa cells convert testosterone, produced by the thecal cells, into estradiol.



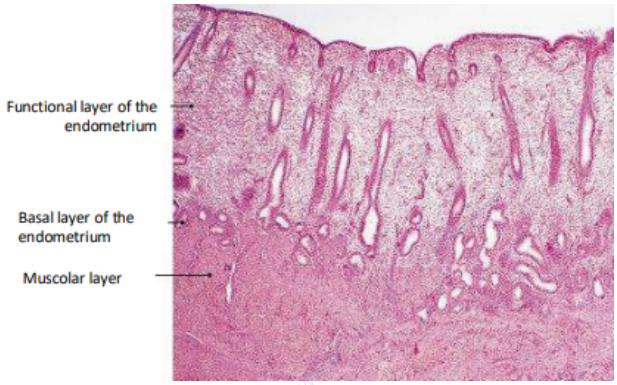
Corpus luteum is what is formed after the exit of the ovocyte and produces progesterone.





UTERUS
the spiral artery arrives to the more internal layer called endometrium.
The uterine wall consist of three layers:

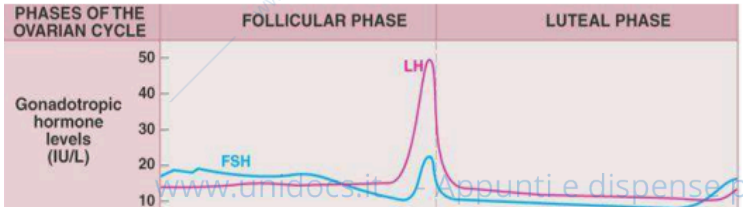
- mucosa or endometrium
- muscolar layer or myometrium
- serosa or perimetrium



We can distinguish between two parts in the endometrium: the basal layer and the functional layer.
The functional layer change in base of the menstrual period.

We can talk about an axis HYPOTHALAMIC-PITUITARY-OVARIAN AXIS and they control the menstrual cycle.

The first 14 days are called follicular phase because there is an increase of and increase in size of the follicles.



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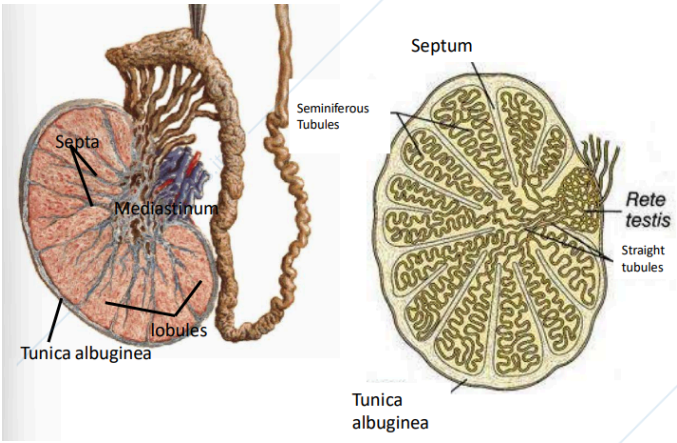
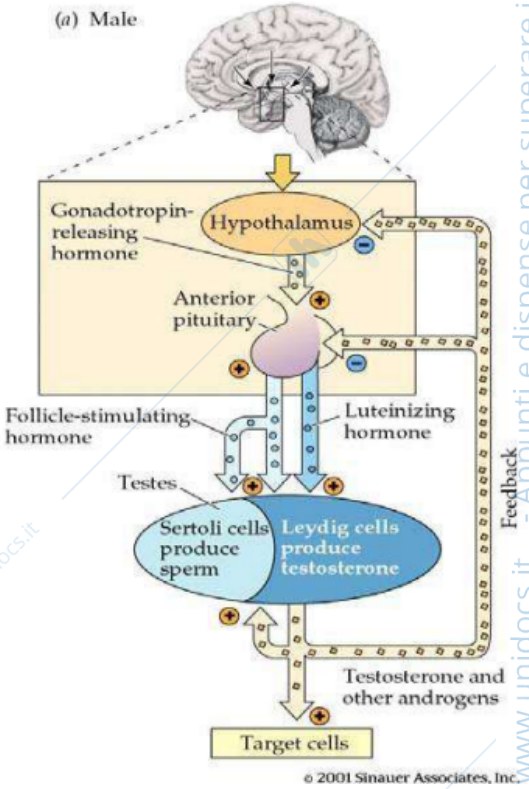
At 14 days the follicle arrives at the maximum of the size and the oocyte is expelled because the quantity of estrogen rises.
the LH increases and this is a signal to release the oocyte.
What remains transform in corpus luteus and start to produce progesterone and endometrium is regenerated.
After menses the endometrium regenerates and is called the proliferative stage where the spinal artery and glands start to regenerate.
In the secretory stage we have the maximum extension of the endometrium that is ready to receive a zygote.

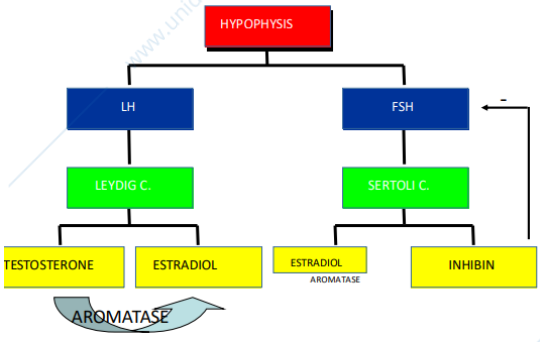
TESTIS



We have lobus with inside the presence of tubules, everything is surrounded by the tunica albuginea. Inside the tubules there are the sertoli cells and in the matrix there are the leydig cells.
the sertoli cells are able to produce inhibin and estrogens. They surround the proliferating and differentiating germ cells forming pockets around these cells
•They are controlled by the FSH pituitary hormone (follicle stimulating hormone) •They secrete inhibin, a glycoprotein which inhibits the secretion of FSH and regulate the rate of sperm production • They secrete the androgen binding protein (ABP) which makes the testis responsive to testosterone •They secrete small quantities of estradiol.



Sertoli cells during development have two important functions:



• Produces an Anti-mullerian factor (AMH) that determines the regression of the paramesonephric duct (Muller)
• block the meiosis so that the germ cells can multiply by mitosis
Estradiol is important for the development of the seminiferous tubules of the testis.

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