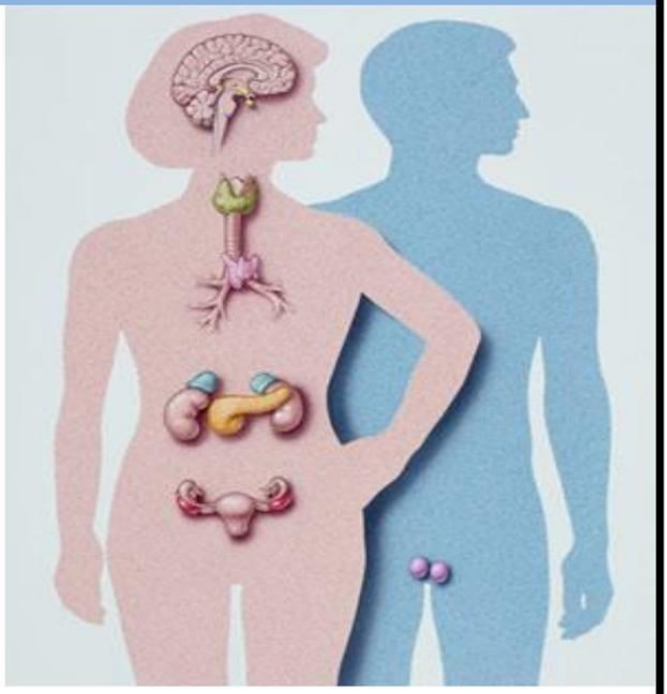
University of Jordan - Faculty of Medicine
(2013-19)

Medical Committee
The University of Jordan

Endocrine System



- [x] Anatomy/Embryology/Histology
- [ ] Biochemistry
- [ ] Physiology
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Lecture #: 3-Parathyroid Glands Date:

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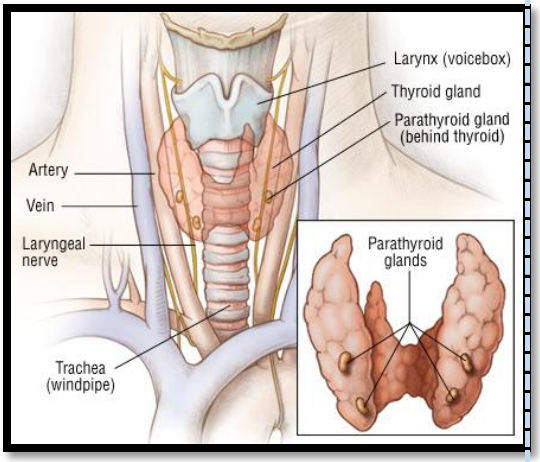
Designed by: Zakaria W. Shkoukani

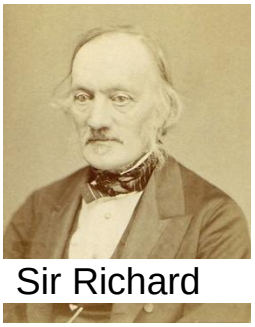
PARATHYROID GLANDS

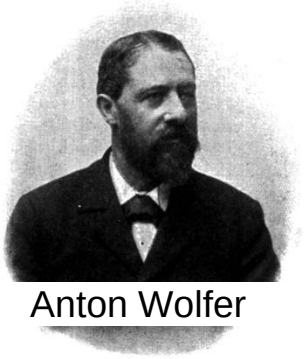
What are Parathyroid glands?

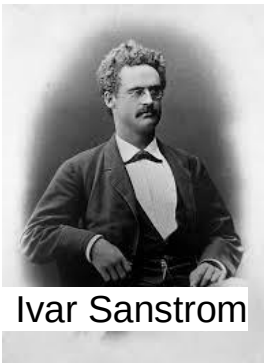
Any of usually four small kidneyshaped glands that lie in pairs near or within the posterior surface of the thyroid gland and secrete a hormone (Parathyroid hormone) necessary for the metabolism of calcium and phosphorus.



History of discovery of the Parathyroid glands (Taken from slides) :


Sir Richard


Anton Wolfer


Ivar Sanstrom

1849: Sir Richard Owen provided the 1st accurate description of normal parathyroid glands after examining an Indian Rhinoceros in London Zoo.

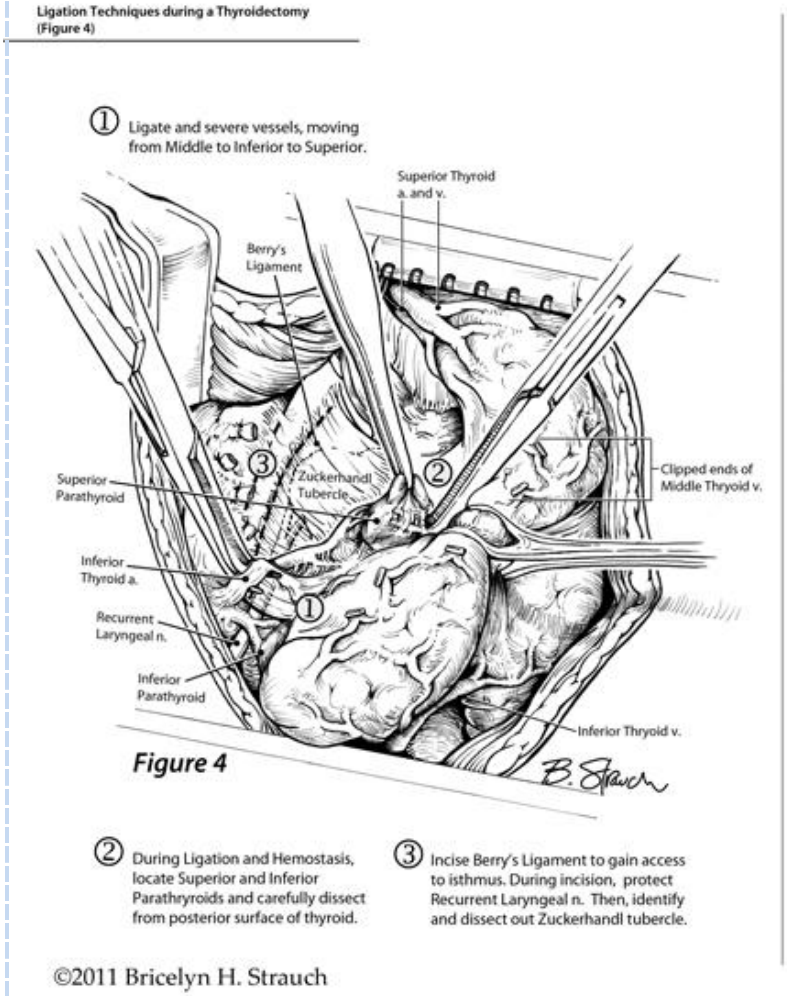
1879: Anton Wolfer described Tetany in patient after total thyroidectomy

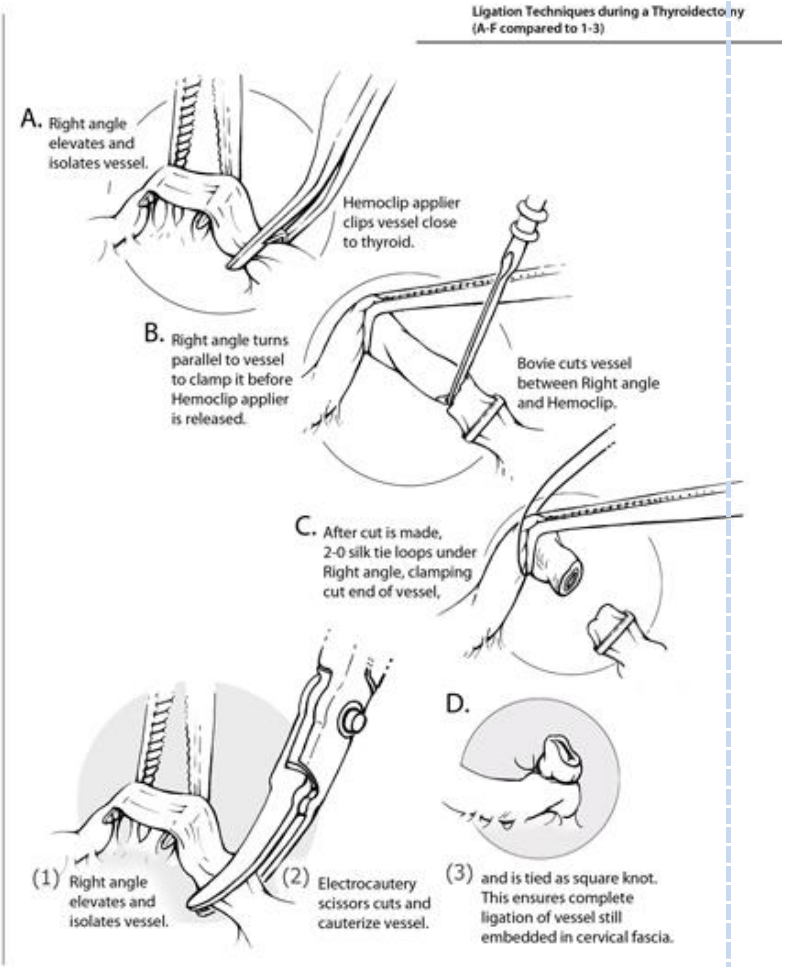
1880: Ivar Sanstrom, a Swedish medical student grossly and microscopically described parathyroid glands.

1909: Calicum measurements was possible in and association with parathyroids established / 1925: The 1st successful parathroidectomy on a 38 years old man with severe bone pain secondary to osteitis fibrosa cystica

EXTRA INFO (not required):

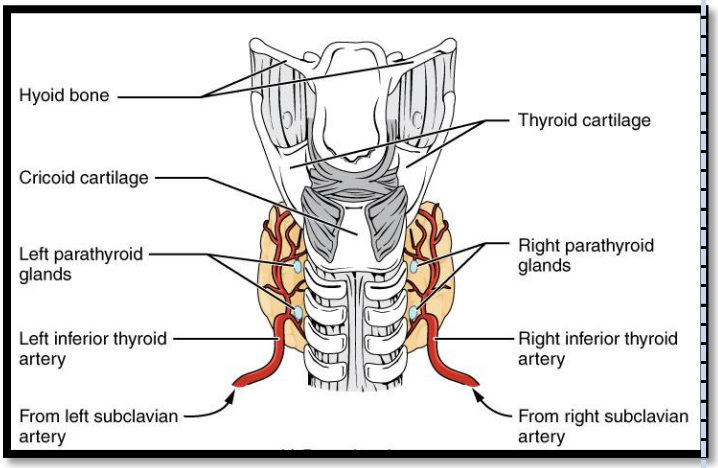
Thyroidectomy (an operation that involves the surgical removal of all or part of the thyroid gland) is a **bloodless surgery**, which means it's a surgery that makes no use of blood or blood transfusion. As noticed, The thyroid gland is placed in a critical place since it's surrounded by many blood vessels and nerves in which you must pay attention to upon operating on the thyroid/parathyroid glands. Thus, blood vessels should be ligated in order to secure them and even to avoid bleeding while operating. The picture below shows some techniques to ligate vessels during a thyroidectomy or a parathyroidectomy.





Remember: structures that are in posterior relation to the thyroid gland: Common carotid artery in front of the longus Coli Muscle/ Parathyroid Glands/ Inferior thyroid artery.

Can you describe what you see when you look at the posterior aspect of the Thyroid gland? (you can use the pictures below for help)



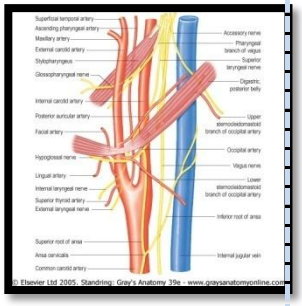
1) Hyoid bone

2)Epiglottis- Not shown in the picture-

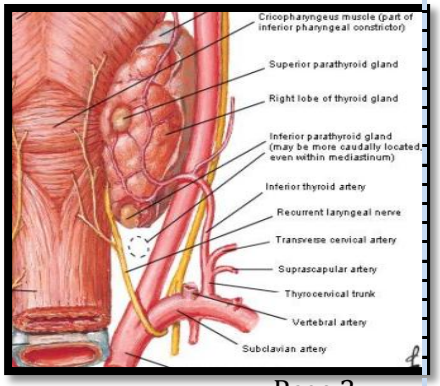
3) Parathyroid glands (4 in number, 2 superior and 2 inferior)

3)Inferior constrictor muscle (its 2 parts; Circopharyngeus & Thyropharyngeus muscles) – Not shown in the picture-

Side note: fibers of Circopharyngeus muscle are horizontal and continuous with the circular fibers of the esophagus, That's why when you examine the histology of the upper part of the esophagus, you'd notice 4 layers (Mucosa, Submucosa, muscularis, adventicia). Regarding The muscularis layer of the upper 1/3 of esophagus, it contains skeletal muscle fibers without any smooth muscle fibers and those skeletal muscle fibers belong to the Circopharyngeus muscle)

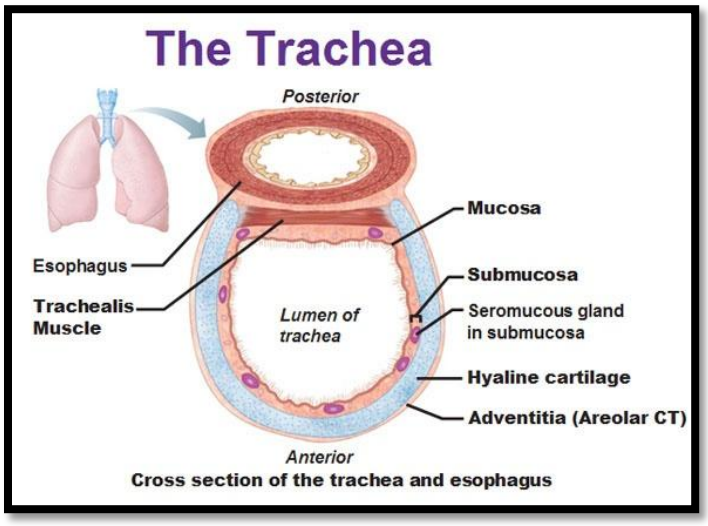


4) Common carotid artery, lateral to it the Internal jugular vein, and in between them the vagus nerve.



5) Superior thyroid artery (the 1st branch of the anterior aspect of the external carotid artery) & The inferior carotid artery(a branch of the thyrocervical trunck of the first part of the subclavian artery). Note the loop that the inferior carotid artery makes before reaching the Thyroid gland!

6) Trachealis muscle:



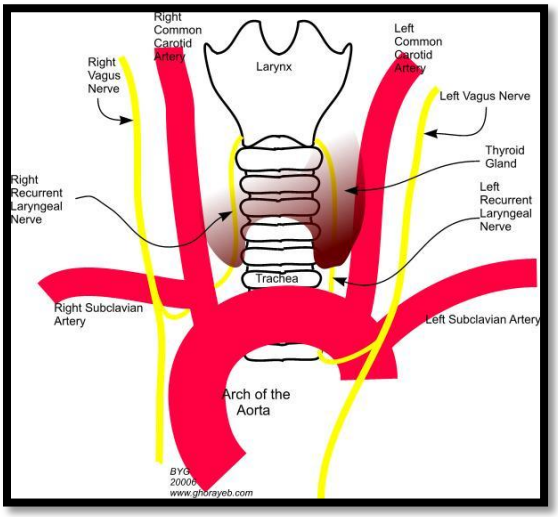
Trachealis Muscle is a smooth muscle that bridges the gap between the free ends of C-shaped cartilages at the posterior border of the trachea, adjacent to the esophagus.

The primary function of the trachealis muscle is to constrict the trachea, allowing air to be expelled with more force, e.g. Coughing. Also, The Trachealis muscle allows the esophagus to dilate upon the movement of the bolus of food on the expense of Trachea; If all trachea was made of cartilage then the esophagus would face some difficulty to dilate and expand upon the movement of the bolus of food.

7) Recurrent Laryngeal nerve:

The recurrent laryngeal nerve is a branch of the vagus nerve that supplies all the intrinsic muscles of the larynx, with the exception of the cricothyroid muscles.

There are two recurrent laryngeal nerves, right and left, in the human body. The nerves emerge from the vagus nerve at the level of the arch of aorta, and then travel up the side of the trachea to the larynx.



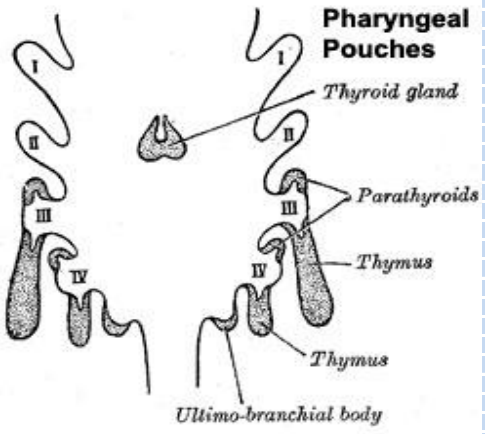
Note: The right and left nerves are not symmetrical; how come? (1) with the left nerve looping under the arch(In fetus, it loops under the ductus arteriosus, which is is a blood vessel that connects the pulmonary artery to the proximal descending aorta, and it later on becomes the ligamentum arteriosum after approximately 3 weeks of birth) and (2) the right nerve traveling directly upwards after looping under the subclaivian artery

Extra information (Not required): Why are they called recurrent laryngeal nerves? Because these nerves are one of few nerves that follow a *recurrent* course, moving in the opposite direction to the nerve they branch from.

Embryology of the parathyroid glands.

They start to develop at the 6th week of development of the fetus and they migrate caudally at 8 weeks (Different than the thyroid gland which develops after approximately 24 days of development). Meaning that endocrine glands almost take double the time the thyroid gland needs to develop.

Remember that all endocrine glands have two embryonic origins. Therefore, the parathyroid glands originate from the interaction of the endoderm of the third and fourth pharyngeal pouch and neural crest mesenchyme. The inferior parathyroid originates from the third pharyngeal pouch along with the thymus gland (a ductless butterfly-shaped lymphoid organ of the immune system, situated in the anterior mediastanium in the thorax, and also becomes much smaller upon approaching puberty) and the superior parathyroid glands arise from the fourth pharyngeal pouch.



What happens? During embryological development, the third pouch migrates downwards, dragging the thymus gland along with the inferior parathyroid glands. The superior pair are not dragged downwards by the fourth pouch to the same degree. So the glands are named after their final, not embryological, positions.

Clinical Note: Sometimes, The descend of the 3rd pharyngeal pouch is exaggerated to an extent where you could find the inferior glands have descended to a lower level away from the thyroid gland. In some cases, you might find them inside the thymus gland in the anterior mediastinum. Rarley, they fail to migrate, remaining in the high neck.

What to understand from this? Just know that the superior parathyroid glands are more fixed in their position than the inferior parathyroid glands.

The descend of the inferior parathyroid glands to a lower level to reach the thymus gland isn't really a bad thing. How come? Well, if the surgeon decided that the patient needed a thyroidectomy operation and during the operation, he removed the thyroid and the parathyroid glands, the patient WILL NOT develop tetany after the operation since he would still have his inferior parathyroid glands conserved in the thymus gland. The human body needs only one functional parathyroid gland to prevent hypoparathyrodism and tetany from happening, so how about still having two of them? ;)

Describe the Parathyroid glands?

1) Anatomical description?
   -Superior glands usually dorsal to the external laryngeal nerve at level of cricoid cartilage / Inferior glands located ventral to the recurrent laryngeal nerve. Note: There are variations in their location, especially in the location of the inferior parathyroid glands.

   Medicial skill: The parathyroid glands are in relation to the nerves (Recurrent and external laryngeal nerves) And these nerves are in relation with the the superior and inferior Thyroid arteries. So how would you find your way to the parathyroid glands during a surgery?
   Couldn't be any more simple; You trace the arteries to find the nerves (You'd usually look for the recurrent laryngeal nerve) and then you trace the nerves to find the glands.

2) These glands are small, 25-30 mg for each (average total weight is about 130/150mg)/ They're essential for life.

3) Each parathyroid gland is surrounded by a thin connective tissue capsule, which trace into the substance of the gland forming irregular small compartments.

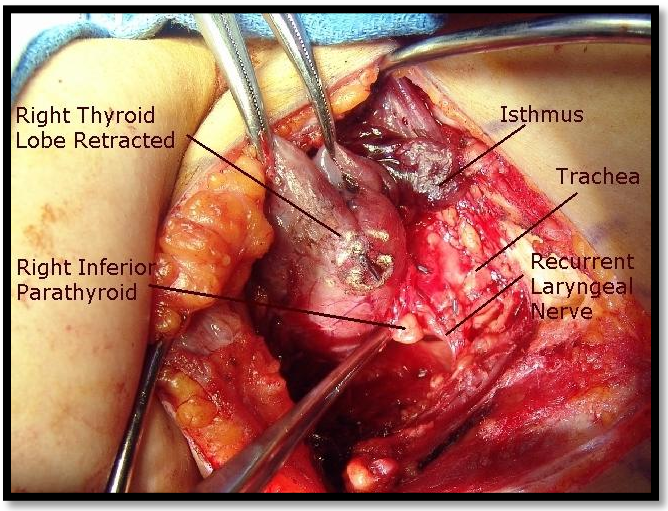
4) Blood Supply? Branches of the superior thyroid artery and the inferior thyroid artery anastamose frequently inside the substance of the Thyroid gland and most of the anastamoses is present at the site of the parathyroid gland, the cells try to arrange themselves around the branches of the arteries to release their hormones to circulation. Remember that Capillaries are abundant and fenestrated.
Medical skill: If Parathyroid glands are located some where outside the thyroid glands, you can simply trace the anastamoses between the superior and the inferior thyroid artery which will directly lead you to the Parathyroid gland. However, if The parathyroid glands are embedded within the substance of the Thyroid glands, tracing the anastamoses would be hard to achieve.

Note: Most of the blood supply of the Thyroid gland and the parathyroid gland, Approximately 80% of their blood supply, comes from The inferior Thyroid artery whereas branches from the superior thyroid artery form 20% of the blood supply of the superior glands (Which means that the main and the larger blood supply of the superior Glands comes from the inferior thyroid artery) – This will mostly be an exam question. Also, if you occlude one of the arteries, the blood supply won't be compromised since the collateral blood circulation found within the gland is enough to provide the blood supply in case one of the major arteries branches was affected.

5) Venous Drainge? Glands drain ipsillaterally by superior, middle, and inferior thyroid veins (right goes to the right side and left goes to the left.)

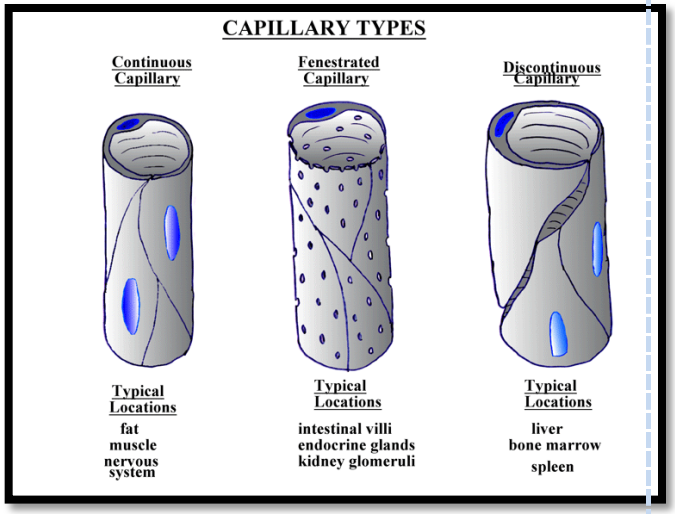
6) Color of the Parathyroid glands (Normally, it's Spicy yellow Mustard color) is an indication of their fat content, vascularity, and percentage of oxyphil cells within the glands.

Medical Note: The yellow color of the Parathyroid gland may be confused with the surrounding fat, especially in obese and old patients. Thus, New imitating techniques have been used to solve this problem. One of these techniques is Nuclear imaging where you can exactly specify the location of the gland before the surgery instead of playing a guessing game during the surgery.



Histology Of the Parathyroid glands:

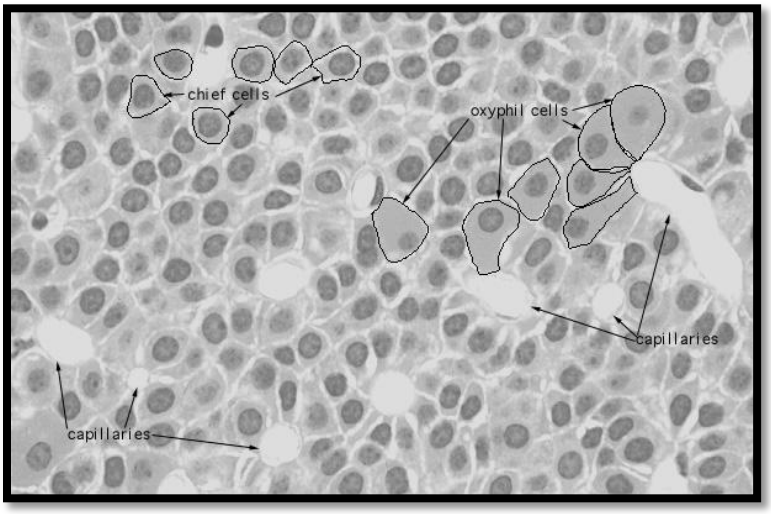
- Examining them under the microscope, you'd see that they're invaded by blood vessels to make sure their secretions would reach the circulation. Remember that these capillaries are of the fenestrated type like all the capillaries supplying endocrine glands. So the endothelium of the blood capillaries would be fenestrated and placed over an intact continuous basal lamina.

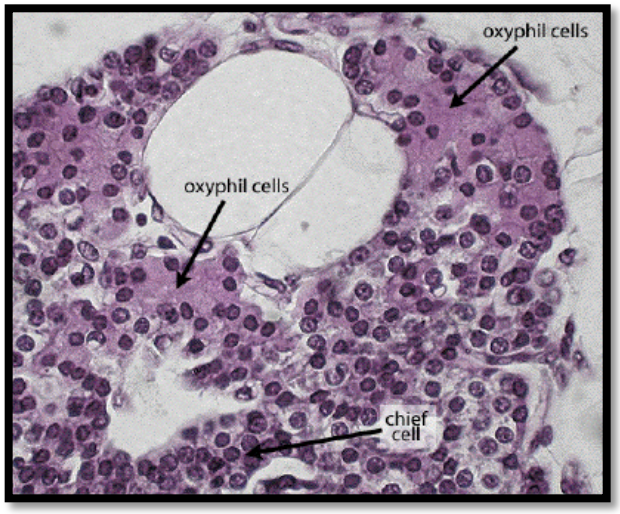


They're composed of two types of cells: Chief Cells & Oxyphil cells (Oxyphil cells are derived from chief cells and increase as one ages). Parathyroid hormone is secreted from both of them but mainly from Chief cells; Oxyphil cells, on the other hand, show low level of PTH activity.

1) Characteristics of Chief Cells: More frequent and numerous/ Polygonal cells/ Small size/ large centrally placed nucleus/ Weakly stained Basophilic nucleus/ And weakly stained acidophilic Cytoplasm/ They synthesize and secrete large amounts of parathormone (PTH) which regulates calcium and phosphate levels in the blood/ They can replicate when chronically stimulated by changes in blood calcium levels

2) Characteristics of Oxyphil cells: usually occur in clusters/ Larger in size/ the nucleus is small and uniformly intense basophilic/ Variable in position/ cytoplasm is strongly acidophilic/ They contain large amounts of abnormally shaped mitochondria/ minimal Secretion of parathyroid hormone.





Doubtable Issue? Some think that Oxyphil cells are stem cells that will later on differentiate into chief cells and others believe that Oxyphil cells are retired Chief cells and that's why they show low level of PTH activity.

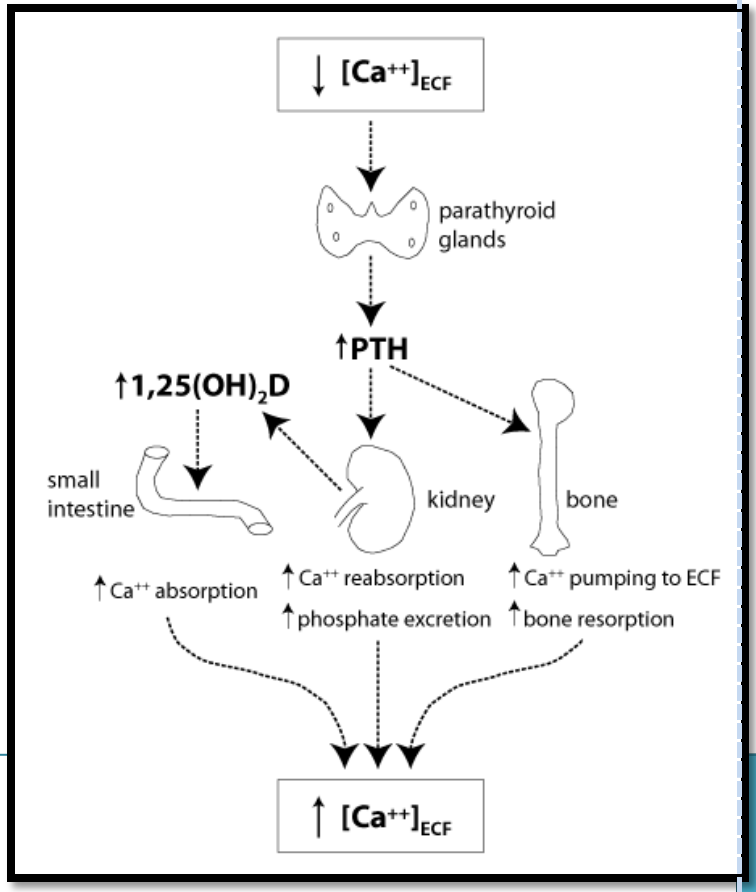
Since Chief cells are chronically stimulated by Calcium level in the blood;This stimulation would push the Chief cells to divide and produce PTH! Since they're able to divide then they can't possibly need stem cells. Also, Oxyphil cells are't present at birth, the start to appear after 4-7 weeks from birth so that's another evidence that they can't be stem cells since stem cells exist from birth. Thus, more likely they're retired chief cells.

- A good amount of adipose tissue would be noticed inside the parathyroid glands, especially in inferior parathyroid glands. it's safe to say that structures that arise from the 3rf pharyngeal arch of the embryo, including thymus gland in addition to the inferior parathyroid glands, would have a huge amount of adipose tissue as the age increases.

What to know from this? You'd see adipose tissue in both the superior and the inferior parathyroid glands but it's a lot more in the inferior ones.

What does the Parathyroid Hormone Do?

- The best Stimulus to secret parathyroid hormone from chief cells is CALCIUM LEVEL IN THE BLOOD; If the blood calcium level is too low, the parathyroid glands release more PTH. This causes the bones to release more calcium into the blood(By stimulating bone resorption by osteoclasts) and reduces the amount of calcium released by the kidneys into the urine, while excreting



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more phosphate to maintain the calcium-phosphorus balance. Also, vitamin D is converted to a more active form, causing the intestines to absorb more calcium. If the calcium level is too high, the parathyroid glands release less PTH, and the whole process is reversed (inhibited) as more Calcium would be deposited in bone inhibiting the action of osteoclasts.

Scoop With Rashid

Did you know that the celebrity Dr.Darwesh talked about during class is actually the Colombian-American actress, Sofia vergara? She was diagnosed with Thyroid Cancer in 2000 and this picture was taken for her on her first appearance after she had Thyroid gland removed.

Now, we're next to a new topic;

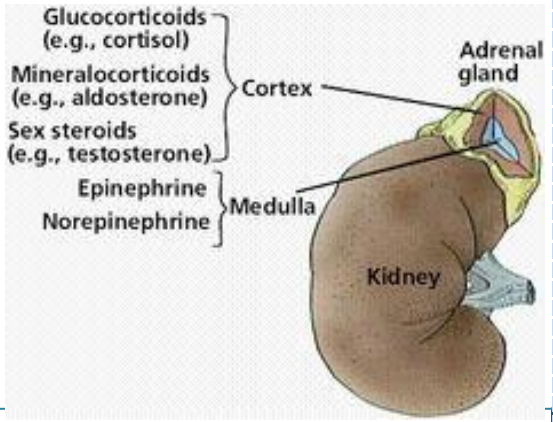
THE SUPRARENAL (ADRENAL) GLAND

Suprarenal(Adrenal) Glands: Two small yellowish glands situated anterosuperior to each superior renal pole

Characteristics of Adrenal glands –from slides-

1)Retroperitoneal and located at the level of T12

2)Surrounded connective tissue that contains perinephric fat



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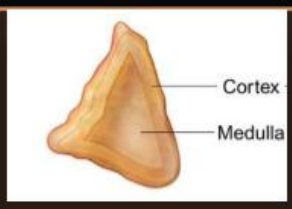
3) Enclosed by renal fascia but separated from the kidneys by fibrous tissue

4) Each one is divided into: Cortex and Medulla

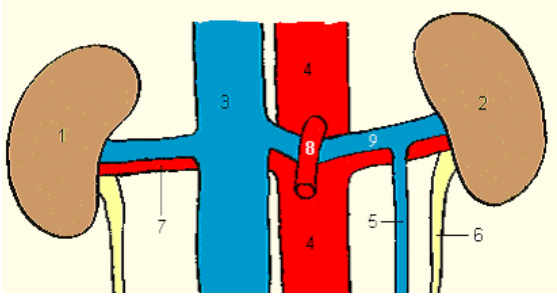
5) Each gland is: ~50X30X10mm. Its weight is ~ 5gm (90% cortex and 10% medulla)

- there are differences between the left and the right suprarenal glands, these differences are shown in the table below.

Right Suprarenal	Left Suprarenal
	
Triangular (pyramidal)	Crescentic (semilunar)
Does NOT reach the hilum of the right kidney	Reaches the hilum of the left kidney
The hilum is directed upwards	The hilum is directed downwards
Its vein is short and drains to the IVC	Its vein is long and drains to the left renal vein.

Regarding the venous drainage of these glands, You must already know that it's identical for the both glands embryological wise. During development of the embryo, there were once two Inferior Vena Cavas, a right and a left one.

With time, The right Inferior Vena Cava persisted and the left one transformed to become the left renal vein. So you'd notice that the left testicular vein in men and the left ovarian vein drain into the Left Renal Vein



whereas the right testicular vein in men and the right ovarian vein in women drain into the inferior Vena Cava. Keep in mind that both sides are equivalent to each other(Right venous drainage= Left venous Drainage)

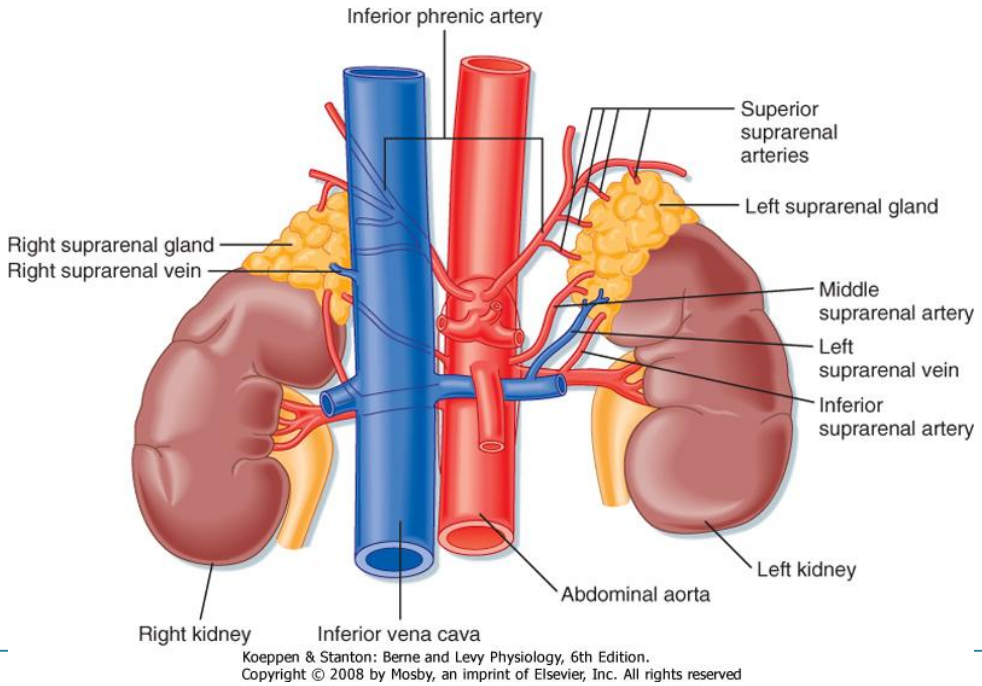
In Jordan, 5 in every 1000 people have a persistent left vena cava, this also results in a short left renal vein.

-Anatomical relations of both glands

	Anatomical relations of right Adrenal gland	Anatomical relations of the left Adrenal Gland
Anterior relations	Inferior vena cava (medially) / Right hepatic lobe (laterally)	Stomach, behind the stomach the lesser sac of peritoneium, the inferior area is in touch with the pancreas and the splenic vein
Posterior relations (same for both)	Right crus of Diaphragm/ Superior pole of the right kidney	Left crus of diaphragm/ Superior pole of the left Kidney.

. Blood supply of Adrenal glands: (important)

Each gland receives 3 arteries: (1) Superior Suprarenal artery coming from the inferior phrenic artery (2) Middle suprarenal artery coming from the abdominal aorta (3) Inferior suprarenal artery coming from the renal artery.



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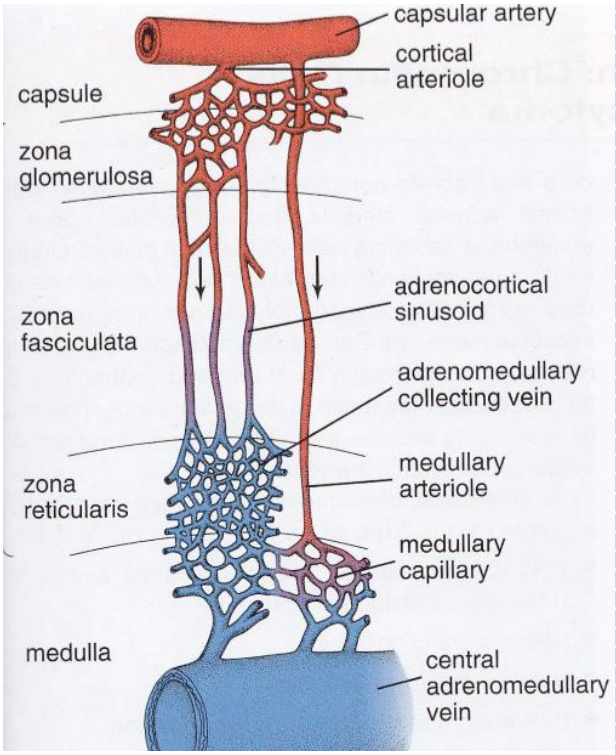
Note: The suprarenal gland receives the highest blood supply in the body/gm of tissue and all its arteries are from major blood sources. EXTRA INFO: This may be one of the reasons that lung cancer commonly metastasizes to the adrenals.

⟶ All 3 arteries head towards the Adrenal gland and they either anastamose before entering the capsule of the gland OR they cross the capsule and anastamose forming the capsular network of blood vessels. Since there's an anastamose between the 3 arteries supplying the adrenal gland then that means that the blood going to the gland is going to be a mixture of blood of all 3 arteries.

60 arterioles would arise from this anastamose. These 60 arterioles are divided unequally into 2 sets:

the first Set is called Medullary arterioles: The arteriole here passes directly from the plexus of arterioles in the capsule down to the medulla of the adrenal gland forming eventually a medullary capillary WITHOUT supplying the cortex of the gland at all.

#The second set contains Fenestrated cortical sinusoidal capillaries draining into fenestrated medullary capillaries; Here the arteriole reaches the upper part of the cortex of the gland, then It divides into a set of capillaries of the fenestrated type. This division in a rounded pattern would push the cells of the cortex to arrange themselves in a glomerus circular pattern around the capillaries. Therefore, this upper part of the cortex was called Zona Glomerulosa.



Cells of this region are responsible for the synthesis and secretion of mineralocorticoid (Aldoesterone) which plays a role in increasing sodium & H2O reabsorption from the urine. These cells appear rounded, acidophilic, collected in groups and their vacuoles are very small.

Arteries would complete their way downwards from the Zona Glomerulosa region in a straight-like fashion, that would push the cells of the next region to be organized in elongated straight lines around the capillaries. Therefore, this area was called Zona Fasiculata, found below the first layer. Cells of this region are responsible for the synthesis and secretion of Glucocorticoids(Cortisol). The zona fasiculata is the largest layer.

After that, arteries continue to descend to the next region in a network fashion forming a reti (a net). Thus, the next region was called Zona Reticularis. Arteries in this region expand over the upper part of the medulla providing an additional blood supply to the upper part of the medulla of the gland. Also, cells of this region secrets Gonadocorticoids (weak androgens).

As was mentioned above, the cortex of the adrenal gland is divided into 3 regions (Zona Glomerulosa/ Zona fasiculata/ Zona Reticularis). Keep in mind that there isn't a sharp separation between these regions which might causes some cells of the Zona Fasiculata to go upwards to the region of Zona Glomerulosa and stay there and get remarked as ectopic cells (Cells aren't in their right place). Thus, a confusion might occur that the cells of the region of Zona glomerulosa are responsible for the secretion of the secretion of Aldoesterone and Cortisol whereas in the reality, the region would have 2 kinds of cells; each secrets a hormone.

Clinical note:

Cortex of the adrenal gland is essential for the living. However, you can live without the medulla of the gland. A condition regarding the medulla of the adrenal gland is called Pheochromocytoma (A neuroendocrine tumor of the medulla where the adrenal gland would secret excess Adrenaline and noradrenaline). Of course, Surgical resection of the tumor from the medulla is the treatment of first choice.

That been said, you should know that you cannot live without the cortex because the cortisol and the aldoesterone cannot be compensated nor secreted from any other place in the body leading to water and electrolyte disturbances as well as other problems.

-Cortisol is a stress hormone and it is multifunctional, therefore abusing it by excessively taking it from external sources would lead to many negative impacts. How come? Well, the Zona fasiculata is under the control of the pituitary gland and taking excessive amounts of cortisol would neglect the control of the Pituitary gland and that would lead to negative impacts on the pituitary gland itself to the extent where it might stop secreting its essential hormones and the pituatry gland would then be inhibited.

Clinical note:

If you're taking a high dose of Cortisol medication and you want to stop taking it, then you should start tapering your dose gradually to give the pituitary gland a chance to refunction and secret The Adrenocorticotropic hormone (ACTH) which is responsible for stimulating the Adrenal gland to synthesize and secret Cortisol. Stopping taking the medication immediately would never give the pituitary gland the chance to function again

o bt9fe zy el 7zen mjbour tebl3 Cortisol lal 8abr. :p

End of the sheet.

Shout out to Momen Rbeihat, Nijmeh Alsaadi, Jamil Sahouri :") , Heifa wahbe, Mohamad Nawayseh, Alia-Khamis, Hadeel Samy. ☺

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