بسم الله الرحمٰن الرحيم

(وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ)

Endocrine Anatomy, Histology & Embryology | MID 3

Thyroid Gland

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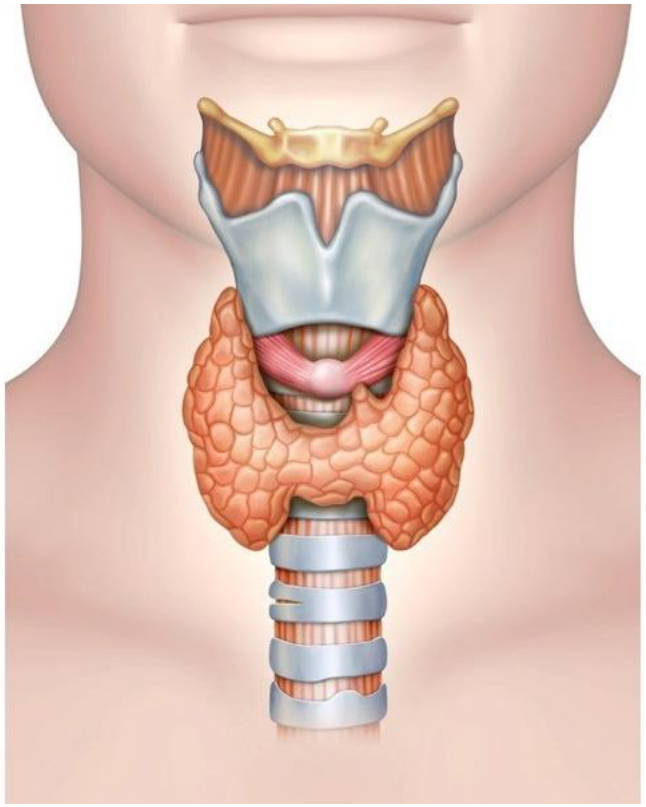
Thyroid Gland

Surgical Accessibility & Difficulty Hierarchy

- The thyroid gland is **located superficially in the neck,** covered primarily by **skin, fascia, and superficial muscles**. This anatomical position **provides direct surgical access,** making operations relatively straightforward compared to deeper, bony-encased endocrine organs.

Easier | Thyroid Gland → Adrenal glands → Pituitary | Harder

- **Thyroid Gland:** Highly accessible due to its superficial position in the anterior neck.
- **Adrenal Glands:** Moderately difficult; located retroperitoneally in the abdominal cavity, requiring laparoscopic or open posterior/anterior approaches.
- **Pituitary Gland:** Most difficult; deeply embedded within the sella turcica of the sphenoid bone, requiring complex transsphenoidal (through the nasal cavity).



Neuroendocrine Regulation (The HPT Pathway)

- Thyroid hormone release is strictly **regulated by the Hypothalamic-Pituitary-Thyroid pathway :**

1. The hypothalamus secretes **thyrotropin-releasing hormone (TRH).**
2. **TRH stimulates the anterior pituitary gland** to synthesize and release **Thyroid-Stimulating Hormone (TSH).**
3. **TSH** binds to receptors on the thyroid gland, triggering the **synthesis and secretion of thyroid hormones (T3 and T4).**

Anatomical Position & Gross Morphology

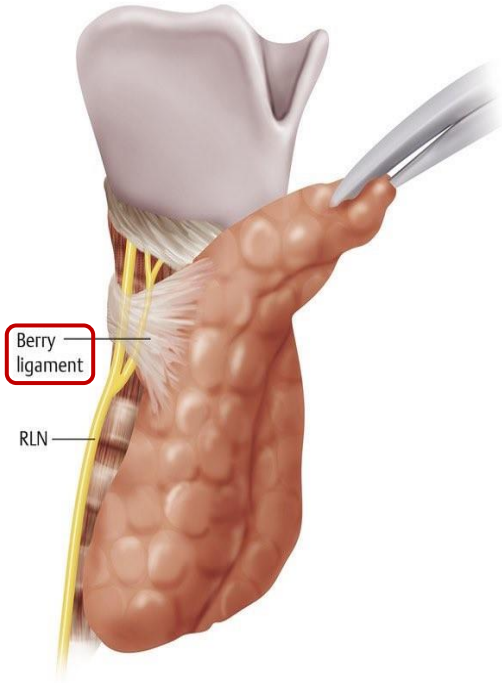
- Vertebral/Anatomical Level: The thyroid spans the **upper portion of the trachea and the lower portion of the larynx.**

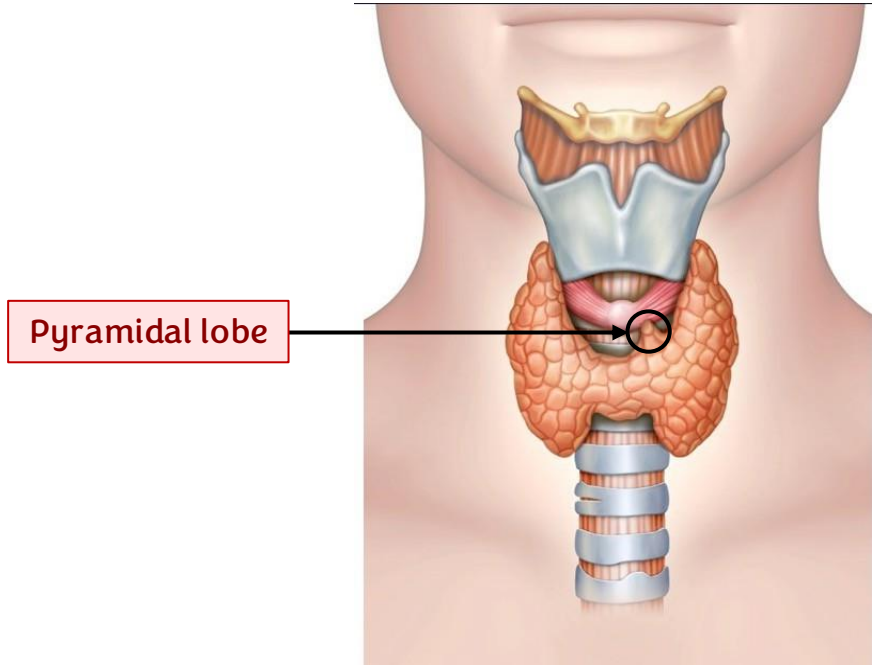
- Shape: It is classically described as **pear-shaped (with a wider base and a tapering apex).** It consists of **two lateral lobes connected by a central isthmus.**

- Anatomical Variation: **A pyramidal lobe may project upward from the isthmus.** its presence or absence has no clinical consequences.

ANATOMY

- **Highly vascular, butterfly-shaped** gland surrounding the **anterior surface of the trachea** just below the larynx.
- located in the **anterior neck and spans C5-T1 vertebrae**
- Consists of **right and left lobes connected by a narrow isthmus.**
- **Surrounded by a sheath** derived from the **visceral pretracheal layer of the deep fascia (attachment to larynx/trachea).**
- Berry ligament!! (Berry's Ligament (Posterior Suspensory Ligament): At the posterior aspect, **the pretracheal fascia condenses to form Berry's ligament,** which **firmly anchors the thyroid lobes to the cricoid cartilage and upper tracheal rings).**

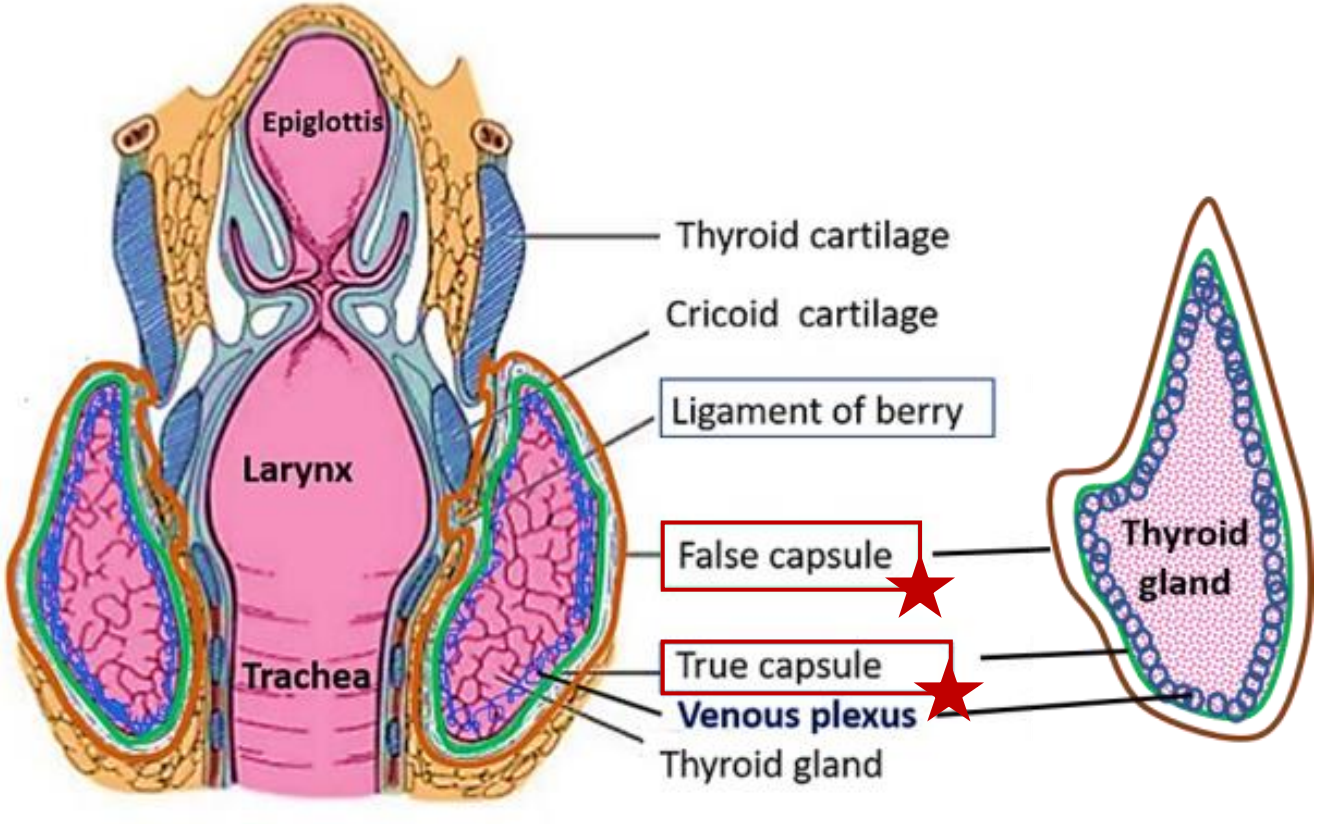




Capsules & Fascial Coverings

- The thyroid is unique because it is invested by **two distinct protective layers:**
  - ***True Capsule ::***
    - **Embryological Origin:** Derived from **condensed embryonic mesenchyme** during development.
    - Note: This process **mirrors adrenal gland development,** where migrating neural crest and mesodermal cells are **encapsulated by surrounding mesenchyme that differentiate to form the capsule**. In the gross anatomy lab, this appears as a tough, fibrous connective tissue (CT) layer directly adherent to the organ.
    - Characteristics: It is **asymmetrical—thicker anteriorly** and **thinner posteriorly**. This structural difference is **clinically significant because a thin posterior capsule offers less resistance, allowing asymmetric thyroid enlargements (goiters) or tumors to expand posteriorly and compress adjacent structures like the trachea or esophagus.**
  - ***False Capsule (Pretracheal Fascia) ::***
    - **The thyroid, trachea, and esophagus** are collectively enclosed by the **visceral pretracheal layer of the deep cervical fascia**. Because it invests the organ outside the true capsule, it is clinically termed the false capsule.

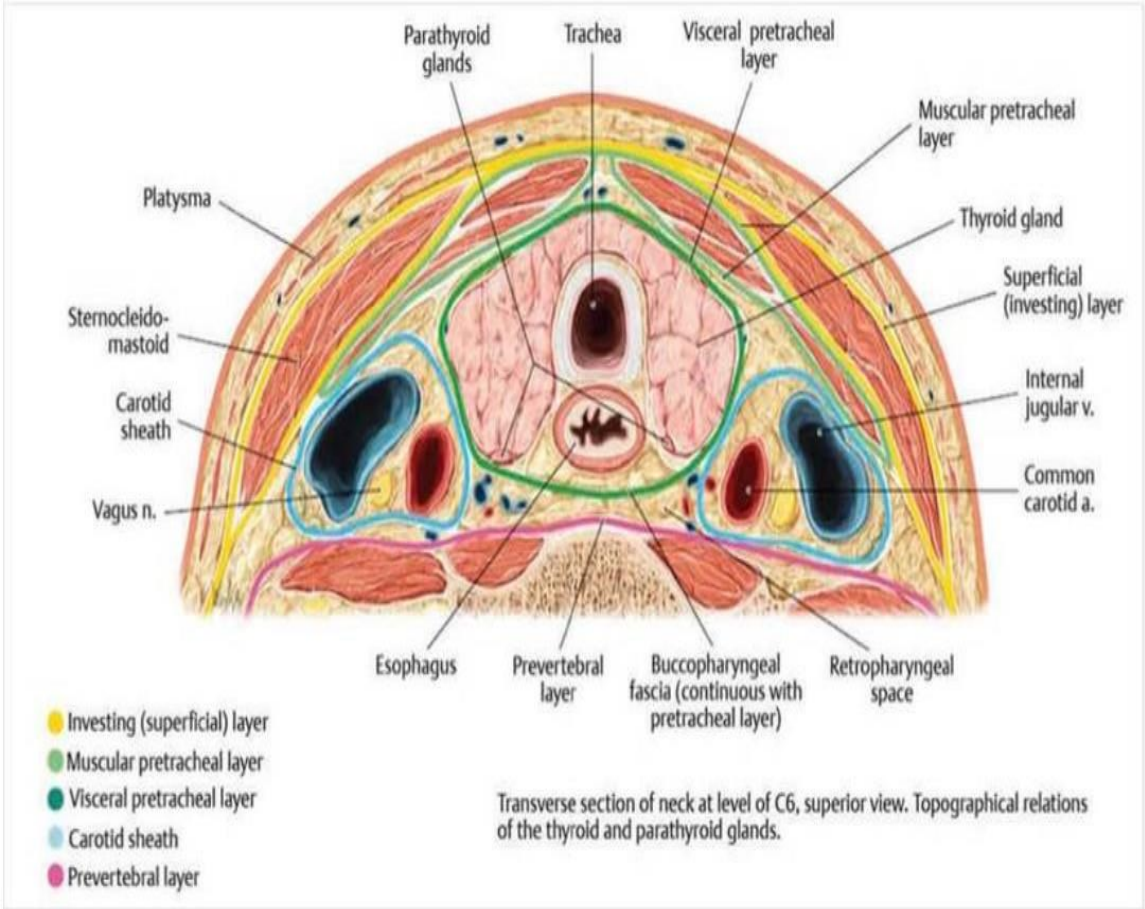
Capsules & Fascial Coverings



Extra image

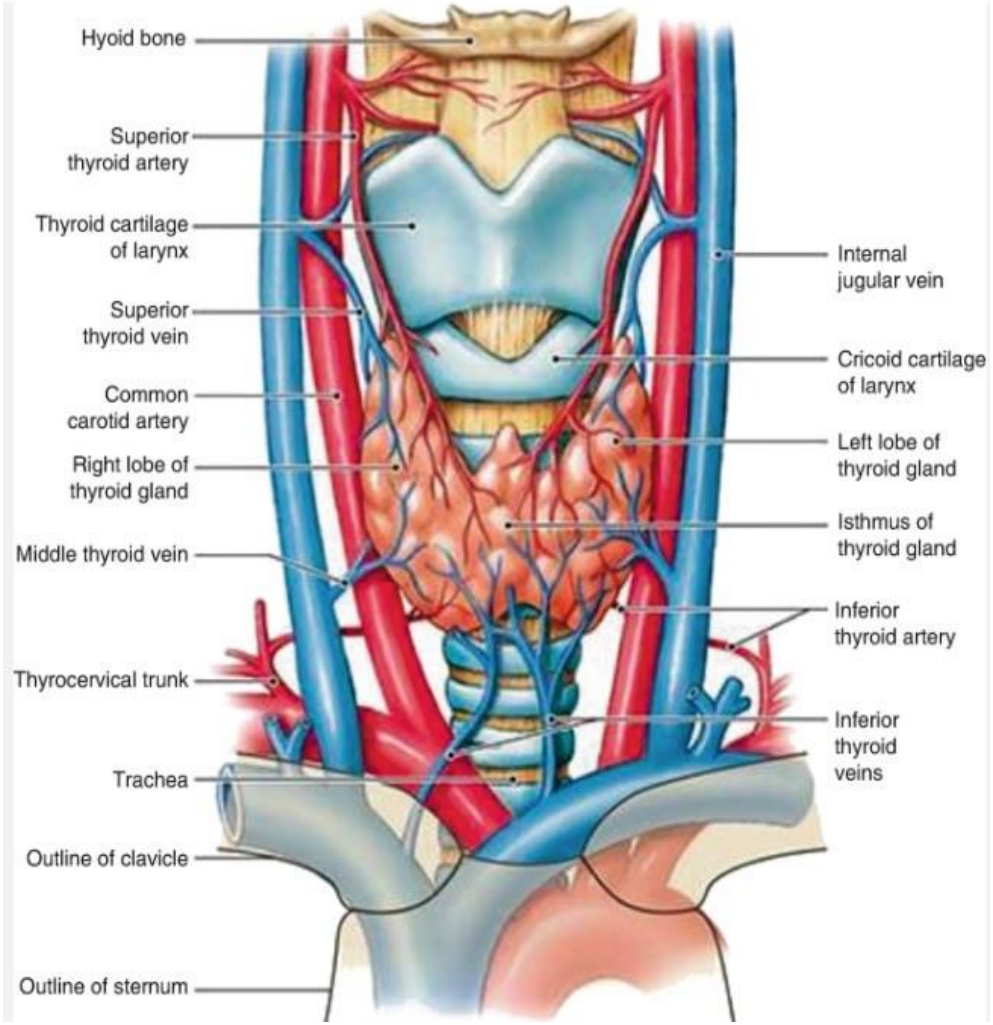
ANATOMY

- Each **lobe** is **pear shaped**-- apex being **directed upward** ----- **oblique line** on the lamina of the thyroid cartilage.
- **Base lies below at the level of the 4th or 5th <u>tracheal ring.</u>**
- The **isthmus** extends across the **midline in front of the 2nd - 4th tracheal rings.**
- A **pyramidal lobe (40%):** Is often present, and it projects upward from the isthmus (band connects it to the HB --- **levator glandulae thyroideae**)

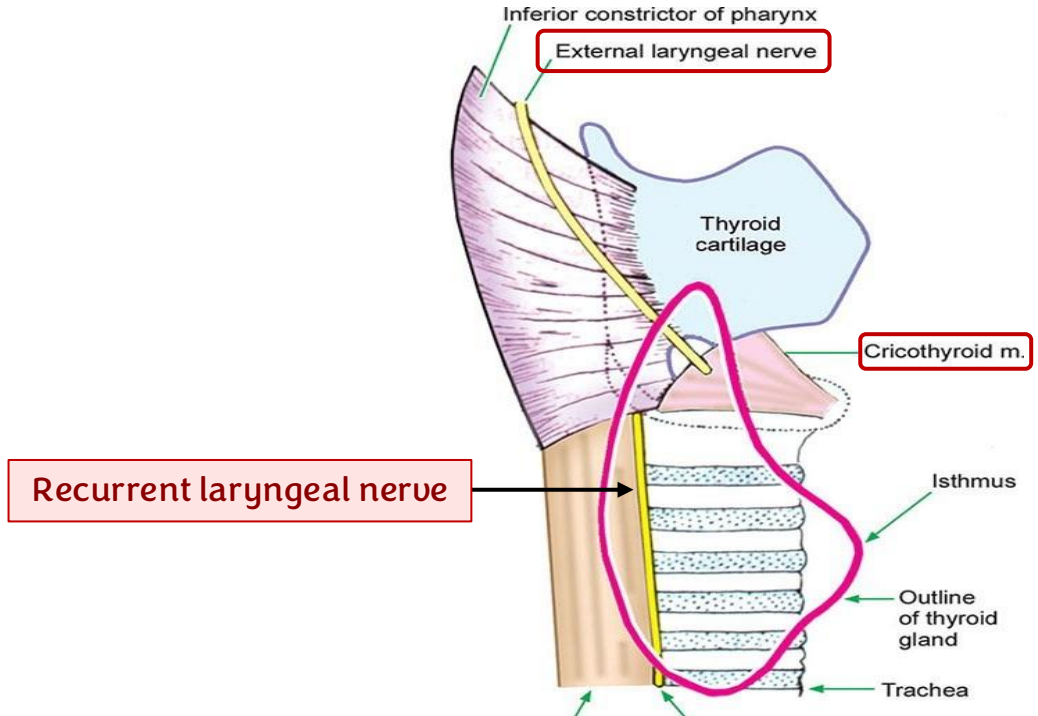


Transverse section of neck at level of C6, superior view. Topographical relations of the thyroid and parathyroid glands.

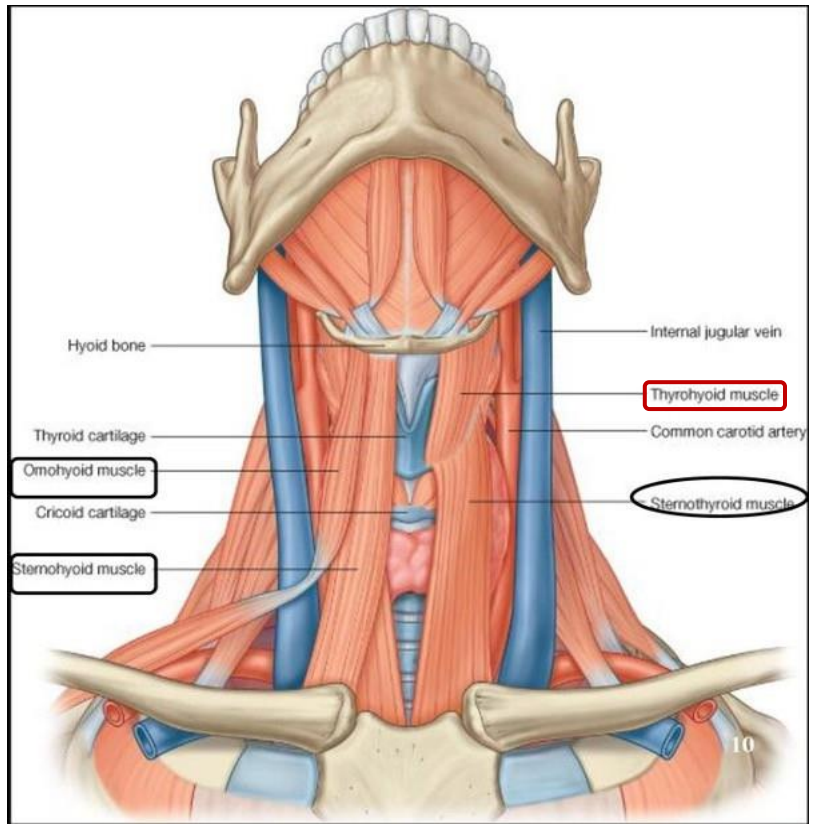
RELATIONS OF LOBES



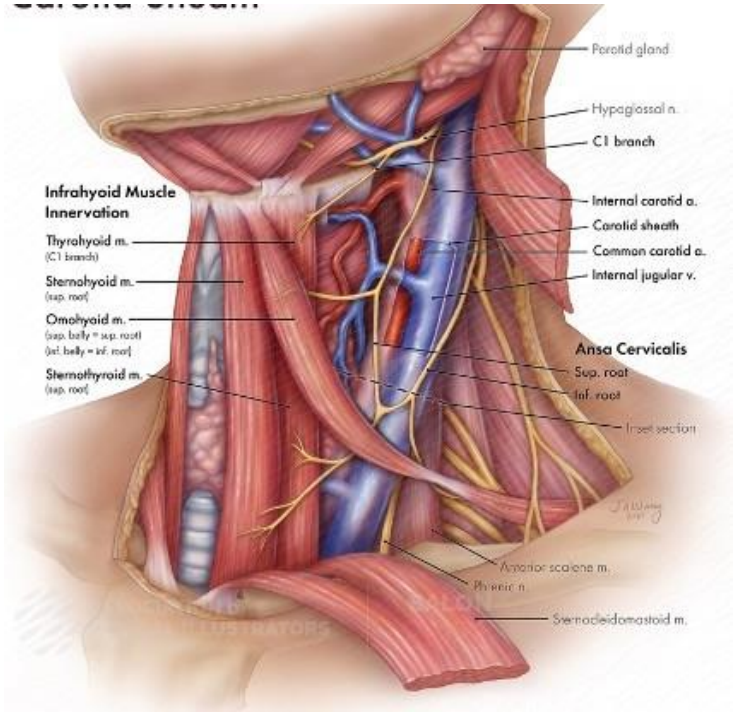
- **Medial**: the **larynx, the trachea, the pharynx,** and **the esophagus** (**cricothyroid muscle** and **its nerve supply, the external laryngeal nerve.** The **recurrent laryngeal nerve** is in the **groove** between the **esophagus and the trachea).**



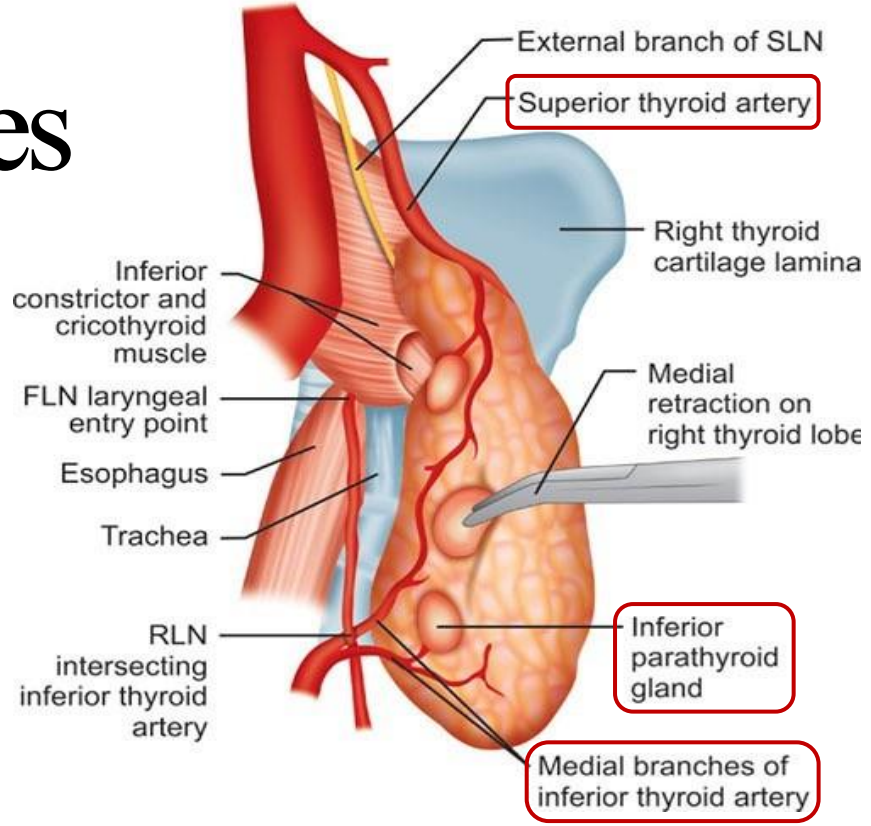
Relations Of Lobes



- **Anterolateral**: **sternothyroid**, **the superior belly of the omohyoid**, the **sternohyoid**, and **the anterior border of the sternocleidomastoid**



- **Posterolateral**: **carotid sheath** with the **common carotid artery, the internal jugular vein, and the Vagus nerve**



- **Posterior**: **superior and inferior parathyroid glands** and **the anastomosis between the superior and inferior thyroid arteries**

Relations Of Lobes

Pay attention to boxes colors…

- **Anterolateral**: **sternothyroid**, **the superior belly of the omohyoid**, the **sternohyoid**, and **the anterior border of the sternocleidomastoid.**

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- **Posterior**: **superior and inferior parathyroid glands** and **the anastomosis between the superior and inferior thyroid arteries**

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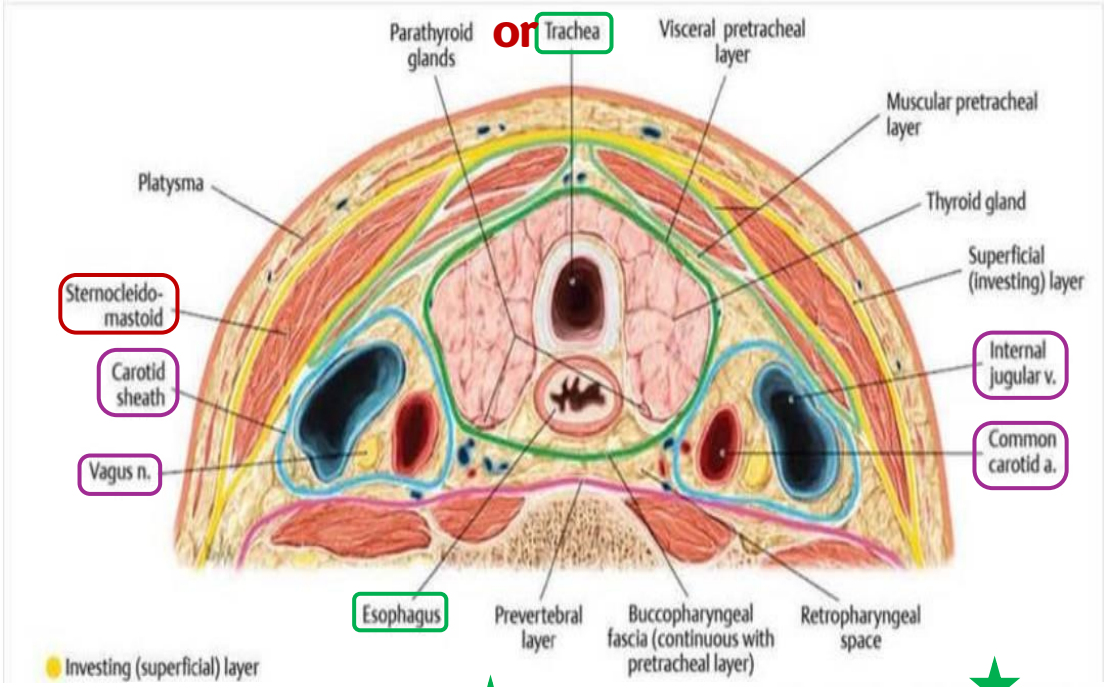
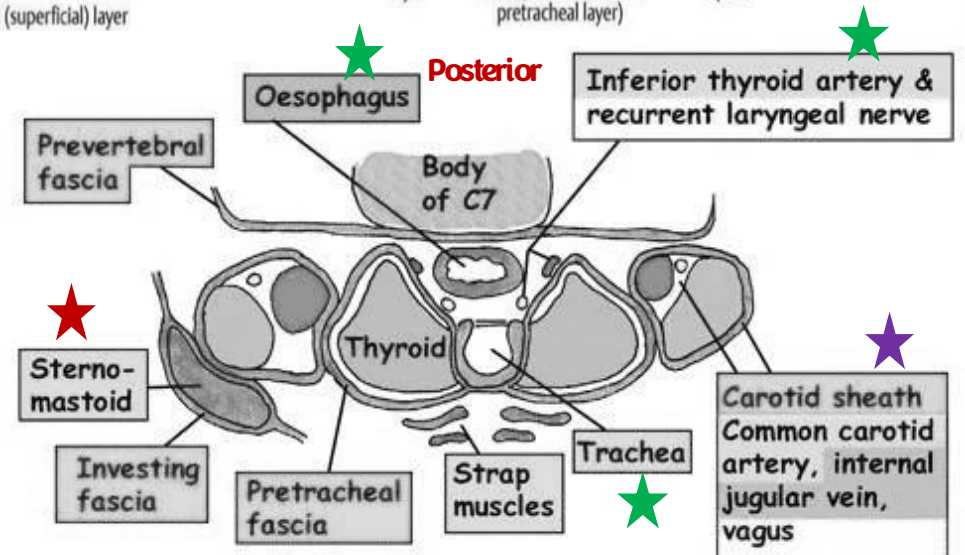
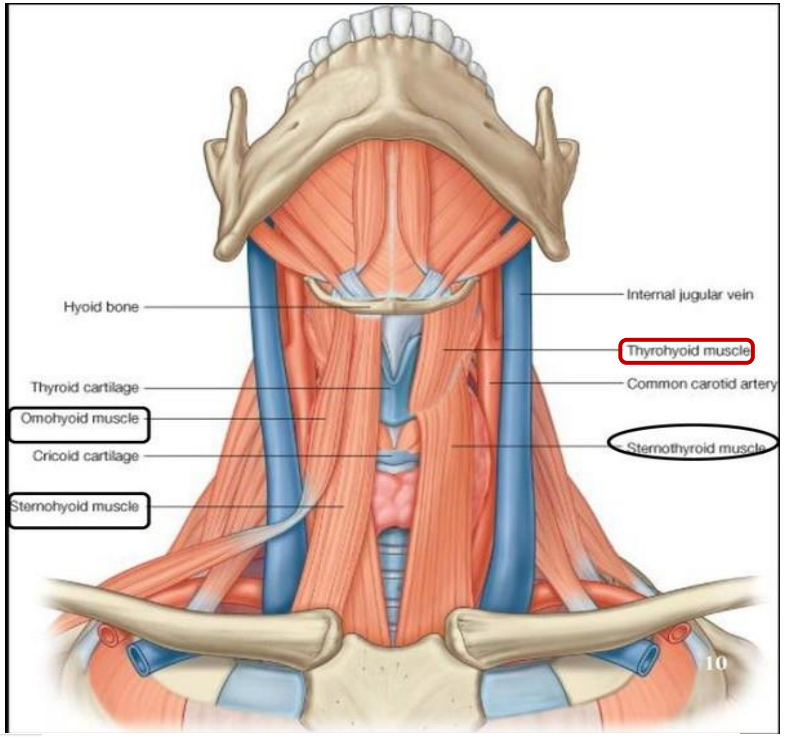
Anteri or





Isthmus Relations

- **Superior**: terminal branches of the superior thyroid arteries (+anastomosis).
- **Posterior**: 2-4 tracheal rings.

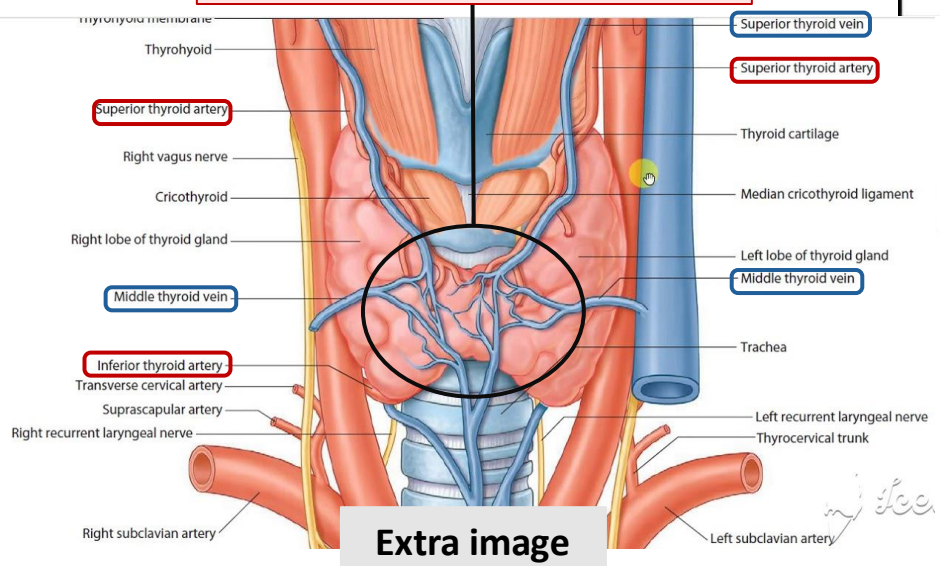


- **Anterior**: sternothyroid, the sternohyoid, anterior jugular veins, fascia, and skin.

- The significant part of the isthmus is exposed anteriorly, meaning it is not covered by muscles from the anterior side; it is only covered by skin and fascia.

- Laterally, the isthmus is related to the strap muscles, mainly the sternohyoid and sternothyroid muscles.

Arteries Anastomosis **at the superior and posterior border of the isthmus**



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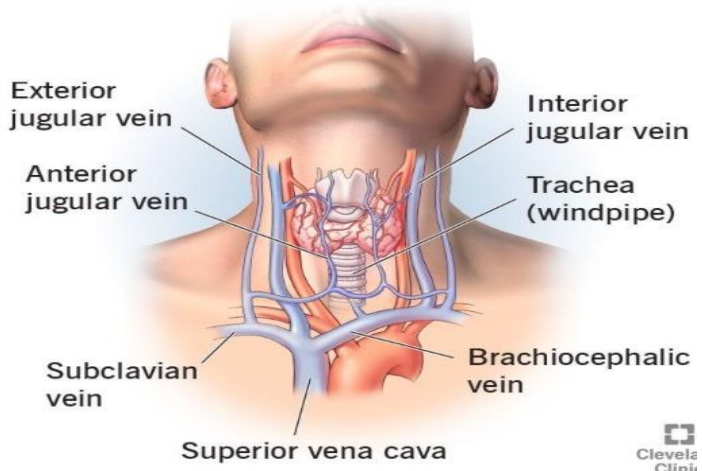
Jugular Veins



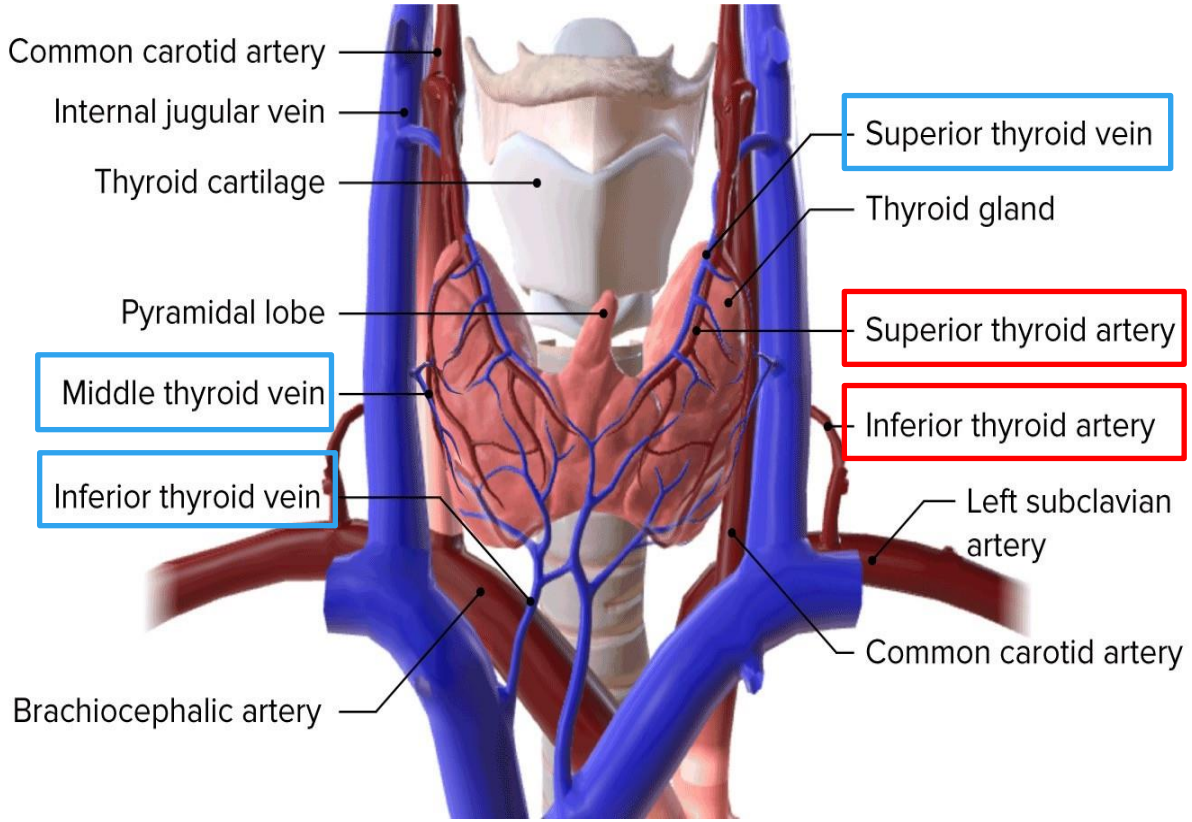
Summary table - Relations

Region	Boundary / Relation	Specific Anatomical Structures Included
The Lobes	Medial (Deep midline)	Trachea, esophagus, larynx, and pharynx
	Posterolateral	Carotid sheath (Internal jugular vein, vagus nerve, common carotid artery)
	Anterolateral (Superficial muscles)	Anterior border of sternocleidomastoid, and infrahyoid "strap" muscles (sternohyoid, sternothyroid, thyrohyoid)
The Isthmus	Medial / Central Zone	Deep fascia and skin only (highly palpable)
	Lateral Zone	Medial edges of the infrahyoid strap muscles (where they diverge)

Blood Supply/Venous D.

1. The **superior thyroid artery (ECA):** divides into ant., post., and lateral branches. Accompanied by the external laryngeal nerve.

Anastomosis



3. The **thyroidea ima (BCA, arch of aorta, rtCCA))**, if present (10%), It ascends in front of the trachea to the isthmus. **Located in midline**

2. The **inferior thyroid artery (TCT; subclavian a.): divides into sup. and inf. branches.** reaches the posterior border of the gland. The recurrent laryngeal nerve crosses either in front of or behind the artery, or it may pass between its branches.

Superior and middle thyroid Vs ------ IJV.
Inferior thyroid —- 1) left—LBCV, rt---- RBCV/SVC
2) trunk (2 Vs)--- LBCV, RBCV, or SVC

Blood Supply/Venous D.

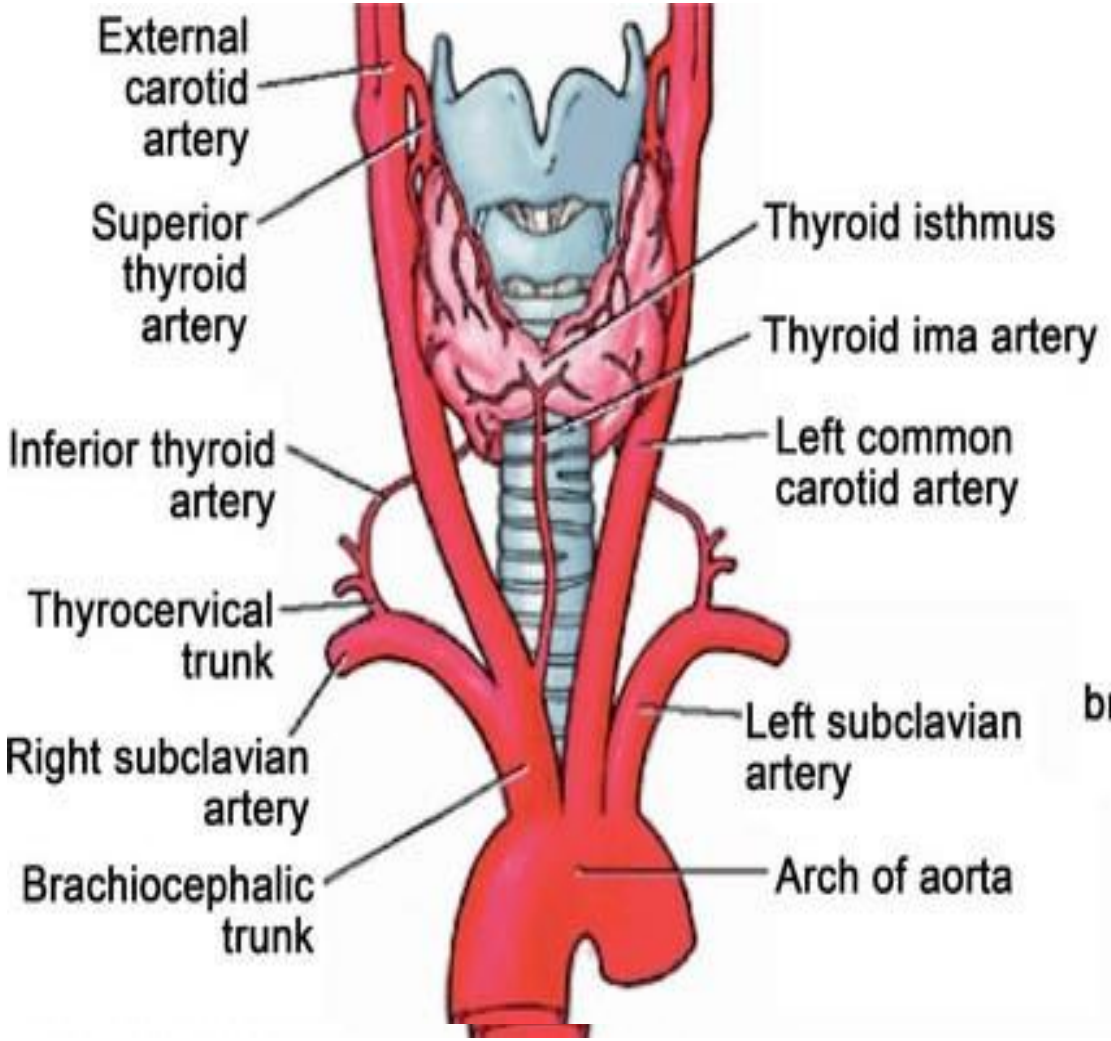
- The superior thyroid artery arises from the external carotid artery , which is a branch of the common carotid artery.

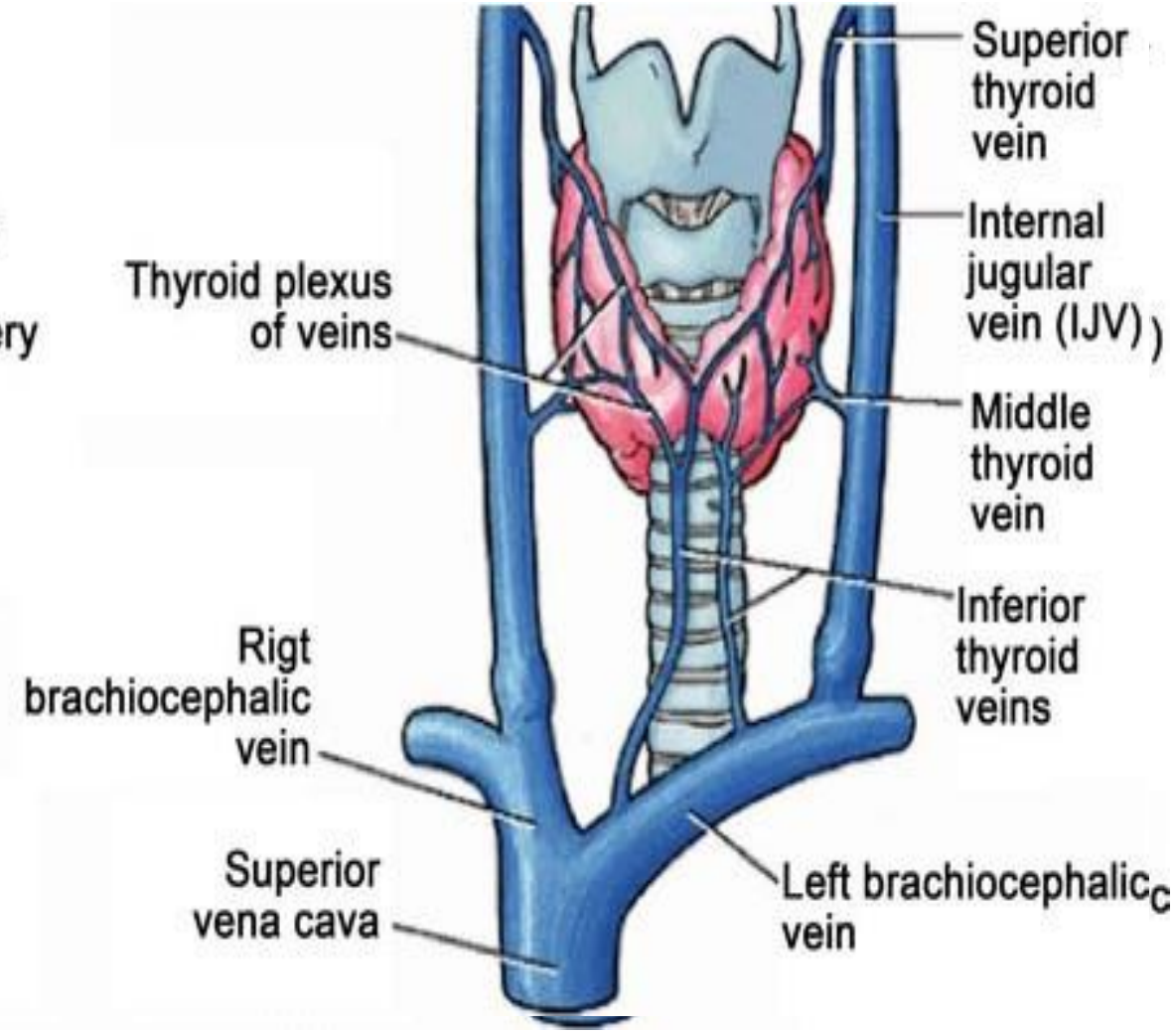
- The STA gives small branches to the thyroid gland. Since the thyroid gland has no distinct hilum, these branches penetrate the gland and supply different parts of the gland.
- The inferior thyroid artery gives small branches that supply the anterior part of the thymus gland.

- It also gives posterior branches that form anastomoses with branches of other thyroid arteries.

- The thyroid ima artery, when present, also contributes to the anastomotic network of the thyroid gland.

Blood Supply/Venous D.





Blood Supply/Venous D.

- The superior thyroid vein and middle thyroid vein drain into the internal jugular vein (IJV).
- The inferior thyroid veins have a variable drainage pattern:
    - The right inferior thyroid vein usually drains into the right brachiocephalic vein (RBCV).
    - The left inferior thyroid vein usually drains into the left brachiocephalic vein (LBCV).
    - Sometimes, the right and left inferior thyroid veins unite to form a common venous trunk, which drains into the right brachiocephalic vein, left brachiocephalic vein, or directly into the superior vena cava (SVC).

Summary table – Arterial Supply/ Venous Drainage

Category	Vascular Structure	Origin / Destination	Branching & Anatomical Course	Key Nerve Relationships & Variations
Arteries	Superior Thyroid Artery	External Carotid Artery (ECA)	Divides into anterior, posterior, and lateral branches.	Accompanied closely by the external laryngeal nerve.
	Inferior Thyroid Artery	Thyrocervical Trunk (TCT) / Subclavian Artery	Reaches the posterior border of the gland and divides into superior and inferior branches.	Recurrent laryngeal nerve relationship: Crosses either in front of or behind the artery, or may pass between its branches.
Veins	Superior & Middle Thyroid Veins	Drains into the Internal Jugular Vein (IJV)	Outflow from the superior and lateral aspects of the lobes.	Direct tributaries to the primary deep venous channel of the neck.
	Inferior Thyroid Veins	Drains into Brachiocephalic Veins (BCV) / Superior Vena Cava (SVC)	Outflow from the lower poles and isthmus, presenting in two main configurations: 1. Separate: Left drains to LBCV; Right drains to RBCV or SVC. 2. Trunk (2 Veins): Common trunks drain into LBCV, RBCV, or SVC.	

Lymph D./ Nerve Supply

We need to focus on the lymphatic drainage of glands because glands are potential sites for malignancy.
Early detection and management are easier before lymph node involvement. However, once the tumor spreads to the lymph nodes and develops metastasis, management becomes more difficult and the prognosis is poorer.

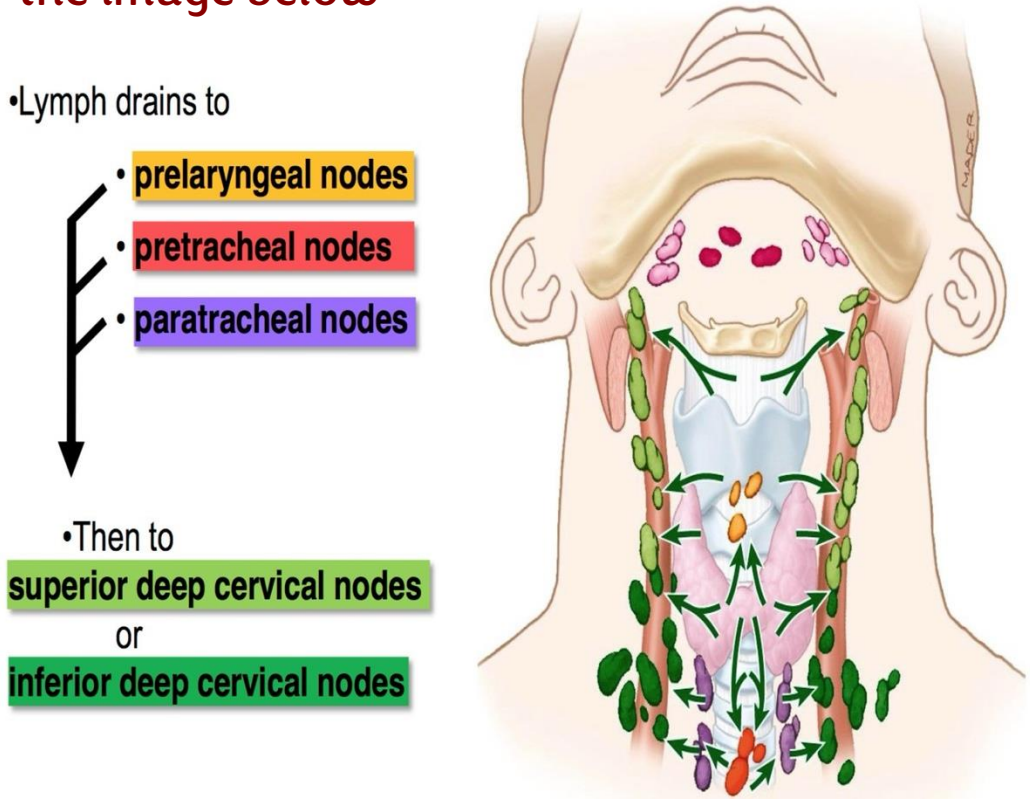
Lymph drainage

- Drains mainly laterally into the **deep cervical lymph nodes**. A few lymph vessels to the paratracheal nodes (prelaryngeal, pretracheal!!).

Nerve supply

- Superior, middle, and inferior cervical sympathetic ganglia. The Vagus nerve provides the main parasympathetic fibers

The explanation is shown in the image below



Thyroid embryological development

- Development of the thyroid gland begins during the 3rd4-th week of development.It is considered the earliest endocrine gland to become fully functional.
- The thyroid originates from endoderm in the midline region of the primitive pharynx, between the first and second pharyngeal pouches, near the future tongue.
- The endodermal cells undergo invagination (inward folding) and form a deeper finger-like projection called the thyroid diverticulum.
- The thyroid diverticulum then descends inferiorly in the midline through the neck until it reaches its final position between C-5T1 vertebral levels.
- During its descent, the developing thyroid remains connected to the tongue by a narrow tube called the thyroglossal duct (TGD), which represents its original connection with the primitive pharynx.

Thyroid embryological development

- Initially, the thyroid diverticulum is a hollow structure, but during migration the cells proliferate and increase in number, causing solidification and formation of the thyroid tissue.
- The thyroid enlarges and expands, forming the right and left lobes. The tissue between the two lobes remains in the midline and forms the isthmus.
- During development, the thyroid tissue undergoes maturation and differentiation to form:

  - Thyrocytes (follicular cells)→ (responsible for production of thyroid hormones T3 and T4.
  - Parafollicular cells (C cells) →responsible for secretion of calcitonin.
  - The parafollicular C cells do not originate from the same endodermal cells as thyrocytes. They arise from the ultimobranchial bodies, which develop from the 4th and 5th pharyngeal pouches and later migrate into the thyroid gland.
  - →That is why we find parafollicular cells beside follicular cells inside the thyroid.

Thyroid Embryological Development

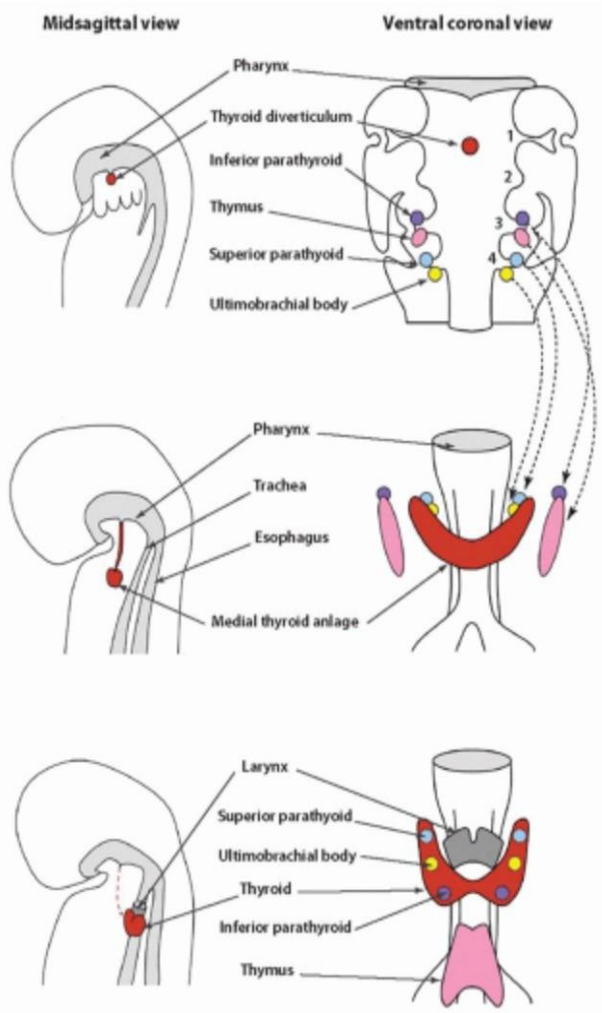
- By the 7th week, the thyroid reaches its final position in the neck, and descent stops.

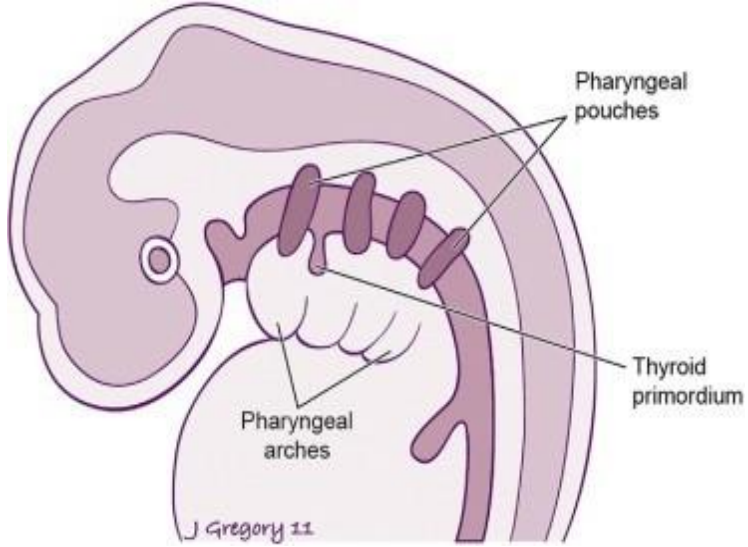
- By the 10th week, the thyroglossal duct normally degenerates and disappears. Failure of complete obliteration can lead to:

  - Thyroglossal duct cys.
  - Pyramidal lob.

- By approximately the 12th week (3 months), the thyroid gland becomes functionally mature and starts functioning.
- Failure of normal descent may result in an ectopic thyroid, most commonly a lingual thyroid.

Embryology





- Development begins as a diverticular outgrowth from the primitive pharynx.
- The diverticulum then descends inferiorly to reach its final destination in the neck.
- During its descent, the thyroid connects to the tongue by the thyroglossal duct

Embryology

- Originates from endoderm between the 1st /2nd pharyngeal pouches near the base of the tongue.
- Around day 20-24, endodermal cells of the primitive pharynx proliferate--- thyroid diverticulum—earliest endocrine gland to develop.

In the fifth week :

- The diverticulum migrates caudally (midline)---- attached to the tongue via thyroglossal duct (TGD)
- In early descent, the thyroid is hollow but then solidifies during migration---- follicular elements of the thyroid.
- Division of the thyroid into right and left lobes.
- Ultimobranchial bodies arise from the 4th/5th pharyngeal pouches ---parafollicular c-cells.

Embryology

By the seventh week:

- TG reach its final destination in the neck

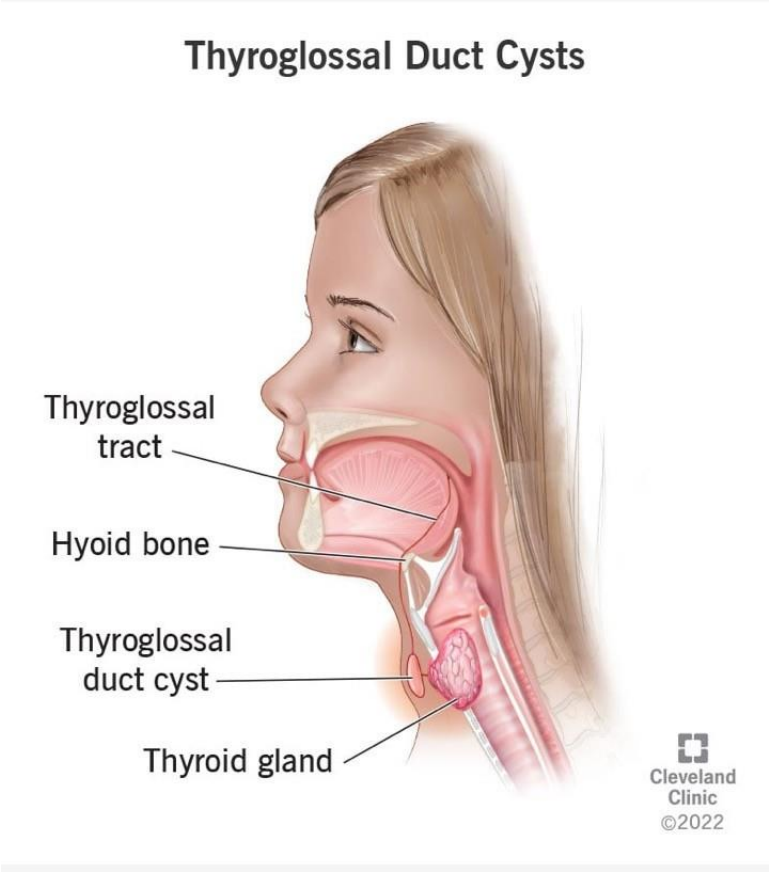
By the tenth week :

- TGD degenerates ---**incomplete** obliteration of the duct can lead to abnormalities, including thyroglossal duct cysts, or a pyramidal lobe.

By the twelfth week

- Functionally mature
- Incomplete descent of the thyroid could lead to **lingual thyroid**.

Incomplete Degenration Of Thyroglossal Duct



Incomplete descent of thyroid

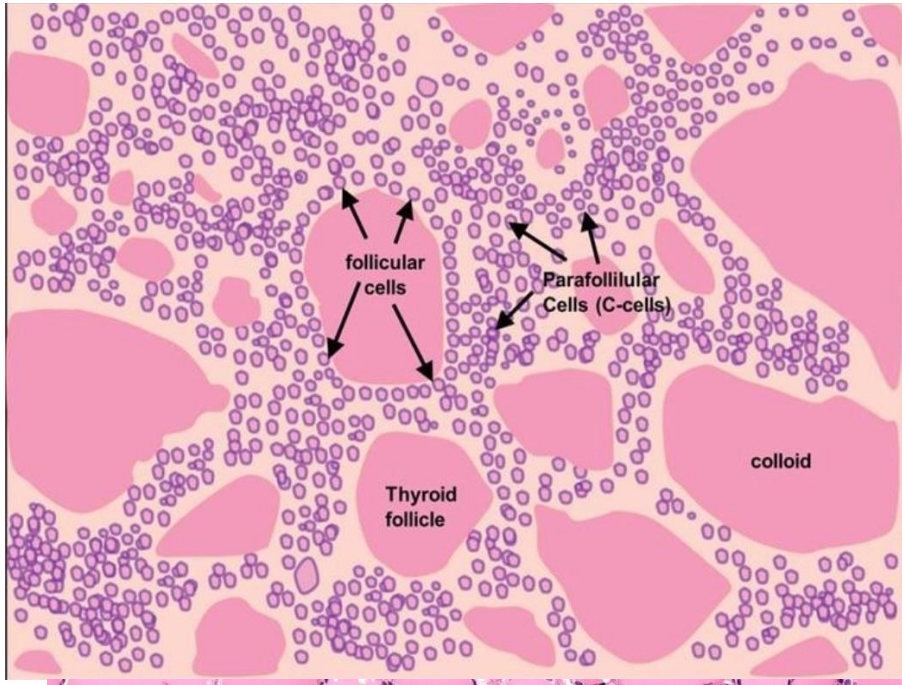
- LINGUAL THYROID

HISTOLOGY

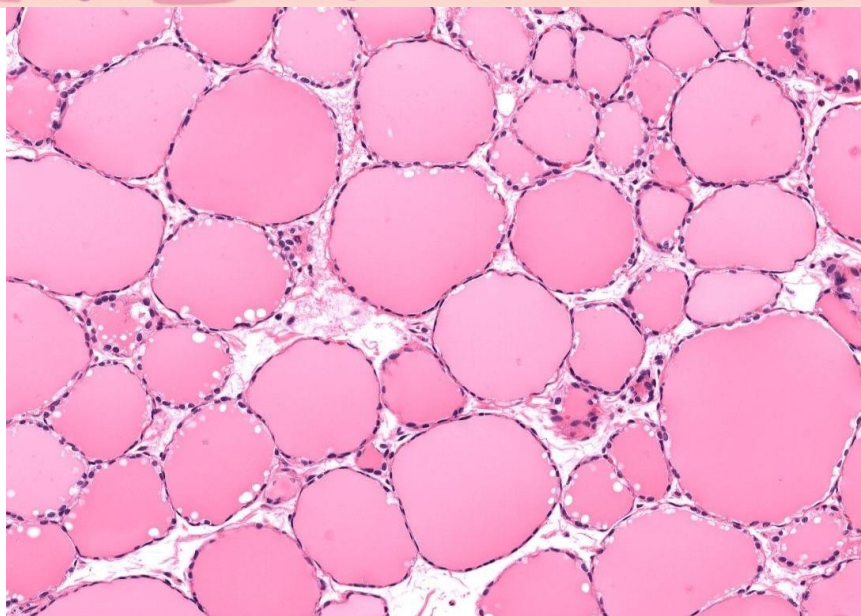
The thyroid as a gland typically as any other glands has supporting cells(stromal cells): fibroblasts and its subtypes like reticular cells and its products which is fibers.
We also have parenchymal cells(secretory, functioning cells) that make up the gland itself

The **parenchyma** is composed of millions of rounded epithelial thyroid **follicles** (follicular cells line the round cells ur seeing and pour their products into colloids of variable diameter, each with simple **epithelium** and a central lumen densely filled with gelatinous acidophilic **colloid.**

Follicular cells are the cells associated with anterior pituitary, which release TSH that follicular cells have receptors for TSH and TSH only get released if TRH is release from hypothalamus, also they are basophils



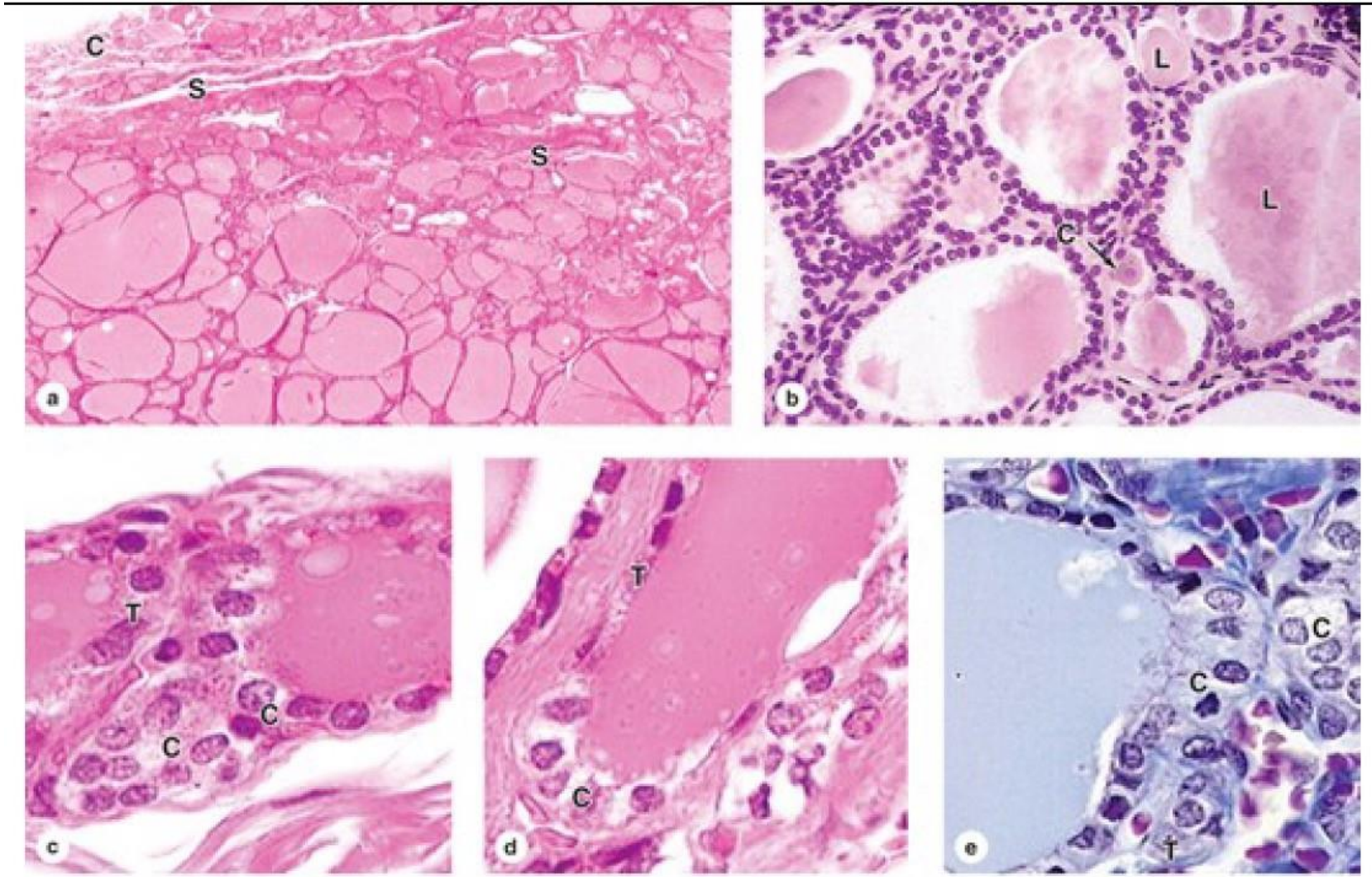
- Only endocrine gland in which a large quantity of secretory product is stored.
- Storage is outside the cells--- in the colloid of the follicle lumen.
- There is sufficient hormone in follicles to supply the body for up to 3 months.
- Thyroid colloid contains the large glycoprotein **thyroglobulin** (raw hormone)**---**the precursor for the active thyroid hormones.



Strongly rec u watch the histology parts of this lecture to help u understand more!

Thyroid Histology

- If u see them flat(squamous)
- A bit tall(columnar)
- If flat(inactive gland)
- Cuboidal(active)
- MOST OF THE CELLS SHOULD BE CUBOIDAL TO SAY ITS ACTIVE!(look at image in general, most wins)



Cells are more cuboidal

(a) thin capsule (C), septa (S).
(b) The lumen (L), present are large pale-staining parafollicular or C cells (C).
(c-e) Thyrocytes (T) from parafollicular C cells (C) by their smaller size and darker staining properties

Thyroid Histology

- As mentioned before, the thyroid gland is surrounded by a **capsule**, and there are **two capsules**:
  - **True capsule**
  - **False capsule**

- **How is the capsule formed?**
  - Endodermal cells descend and invaginate into the surrounding **mesenchyme**.
  - The mesenchyme acts like a supportive environment in which the gland develops.
  - The **endodermal cells** differentiate to form the **parenchyma** (functional tissue of the thyroid).
  - Meanwhile, the surrounding **mesenchymal cells** differentiate into the **stroma** (supporting connective tissue) and begin producing **reticular fibers (type III collagen)**.

- The **outermost part** of the capsule is made of **connective tissue rich in type I collagen**, providing strength and protection.

- Inside the gland, **type I collagen is not suitable** because a more delicate supporting framework is needed. Instead, the gland contains **reticular fibers (type III collagen)**.

- These reticular fibers are produced by **mesenchymal stem cells** that differentiate into specialized **fibroblasts**, commonly called **reticular cells**. They are fibroblasts whose main function is the secretion of **reticular fibers**.

- The capsule also sends **connective tissue septa** into the gland, dividing it into smaller compartments (lobules).

Thyroid Histology

- The **thyroid primordium** develops from **endoderm** located between the **first and second pharyngeal pouches**. It descends caudally to its final position in the neck (approximately **C5–T1**).

- During its descent, it meets the **ultimobranchial body** (also derived from endoderm). Cells from the ultimobranchial body become the **parafollicular (C) cells**, which are completely different from follicular cells.

- **Parafollicular (C) cells:**
  - Do **not** respond to **TSH**.
  - Secrete **calcitonin**.
  - Release calcitonin **directly into the bloodstream through capillaries**.
  - Their hormone is **not stored in the colloid**.

- In contrast, **follicular cells** produce **thyroglobulin**, which is stored in the **colloid**. T3 and T4 are synthesized from thyroglobulin and are later released into the bloodstream.

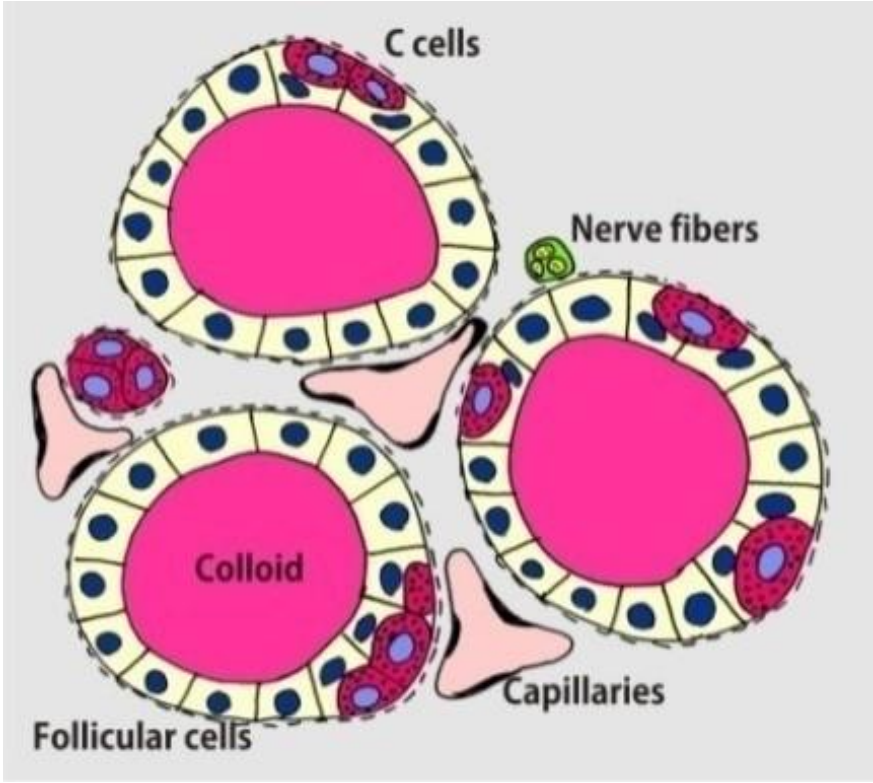
Thyroid Follicular Cells And Parafollicular Cells.

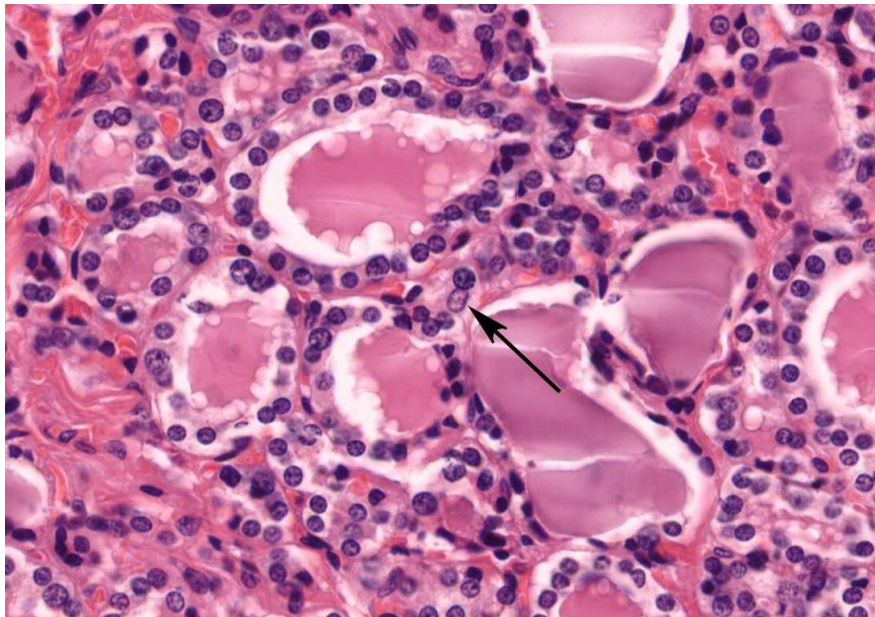
- Is covered by a fibrous capsule **sends**--- septa. **To further create small compartments inside**
- Follicles are densely packed together--- sparse reticular connective tissue **can find lost of capillaries between follicles** .
- Stroma is very well vascularized with fenestrated capillaries.
- The follicular cells, or thyrocytes (**in pituitary we say thryotrophs)**, range in shape from squamous to low columnar(most active, cell enlarge as it becomes more active cause more organelles) (activity related **to** TSH(less TRH=less TSH=less activity).
- The cells exhibit organelles indicating active protein synthesis
- The nucleus is generally round and central.
- rER are basally. **Cause we got proteins!**
- Apically: Golgi, granules, and other organles.

Parafollicular Cells.

From endoderm of 4th -5th pharyngeal pouches (OBVIOUSLY the one from 1st – 2nd starts first in development, 4th -5th follow them after 2-3 weeks to join the descent

- Parafollicular cell (C cell), is also found inside the basal lamina of the follicular cells or as isolated clusters between follicles
- Derived from the neural crest or endoderm!!!!! (Stick to endoderm)
- Somewhat larger than follicular cells and stain less intense (cytoplasm is a bit clear/less stained).
- Not in contact with colloid!
- Smaller amount of rER(less organelles, not working 24/7(unlike thyroid)), large Golgi complexes, numerous small granules containing **calcitonin**.
- Secretion of calcitonin is triggered by **elevated blood Ca^{+2}** levels, and it inhibits osteoclast activity (we inc absorption and dec secretion, as a last resort we go take from bones). Low calcium is more dangerous than elevated.





Production of thyroid hormone & its control

Read, brief intro to biochem

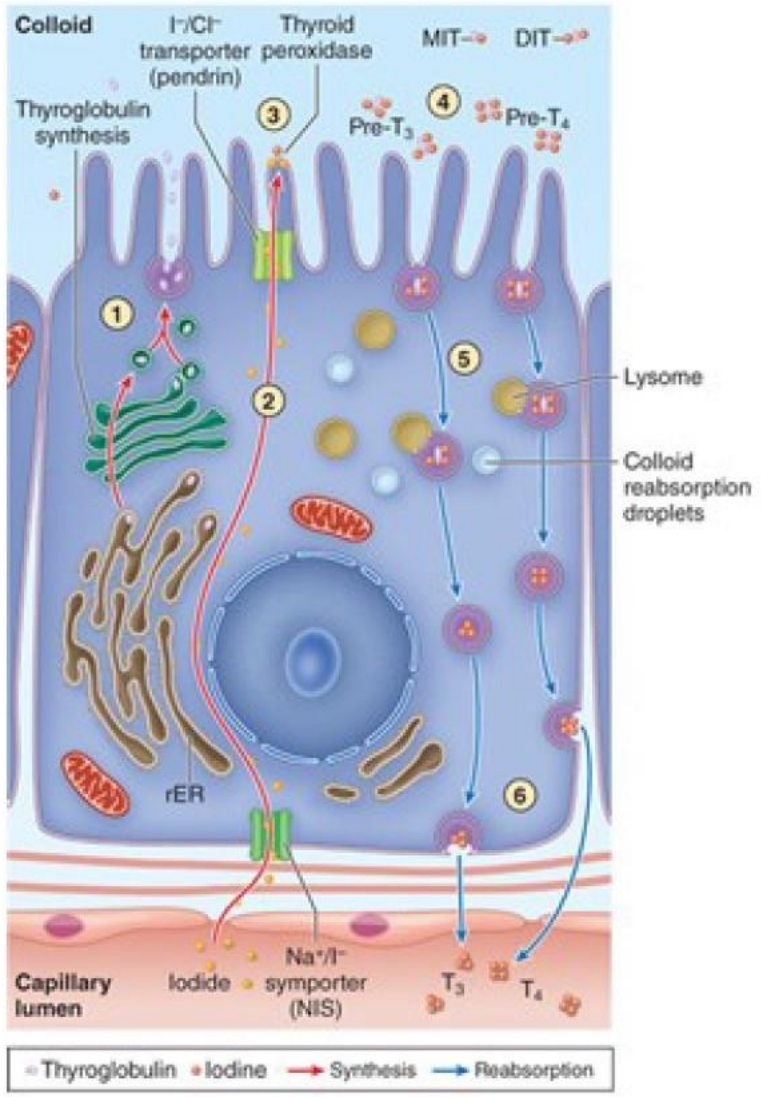
The major activities of this process

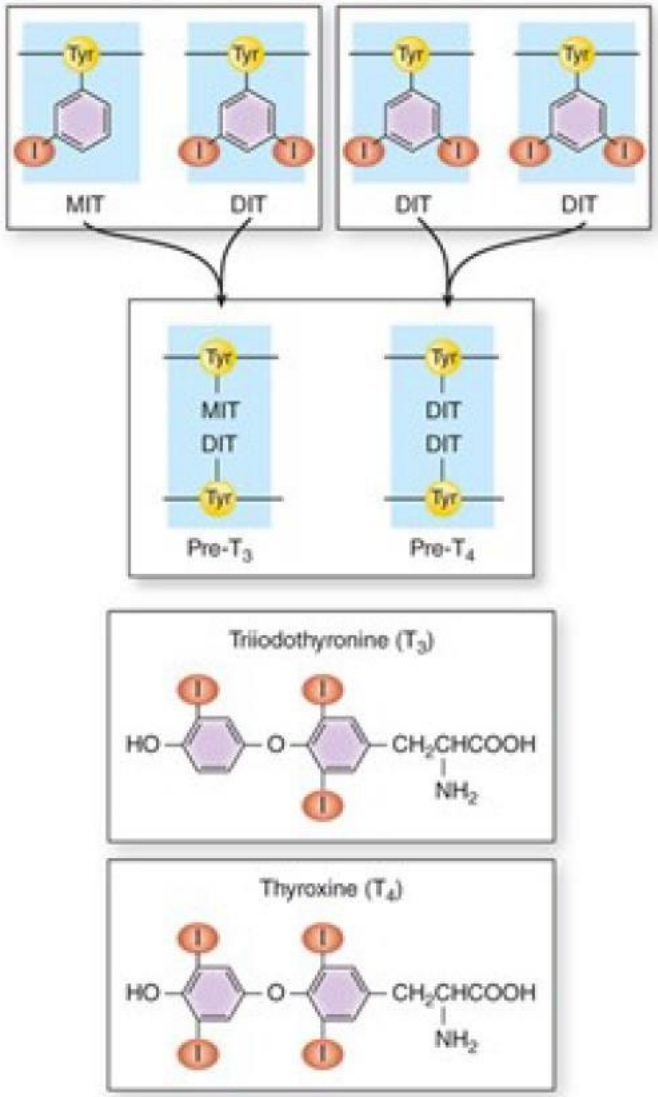
- The production of **thyroglobulin** (140 tyrosyl residues)
- The uptake of iodide (30-fold concentration)
- Iodination of tyrosyl residues (oxidation of iodide)
- Formation of T3 and T4
- Endocytosis of iodinated thyroglobulin (lysosomal proteases)
- Secretion of T4 and T3

Production Of Thyroid Hormones

Read, brief intro to biochem

Involve an unusual,
multistage process in the thyrocytes---with both an exocrine/ endocrine phases
promoted by TSH. and occur in the same cell.





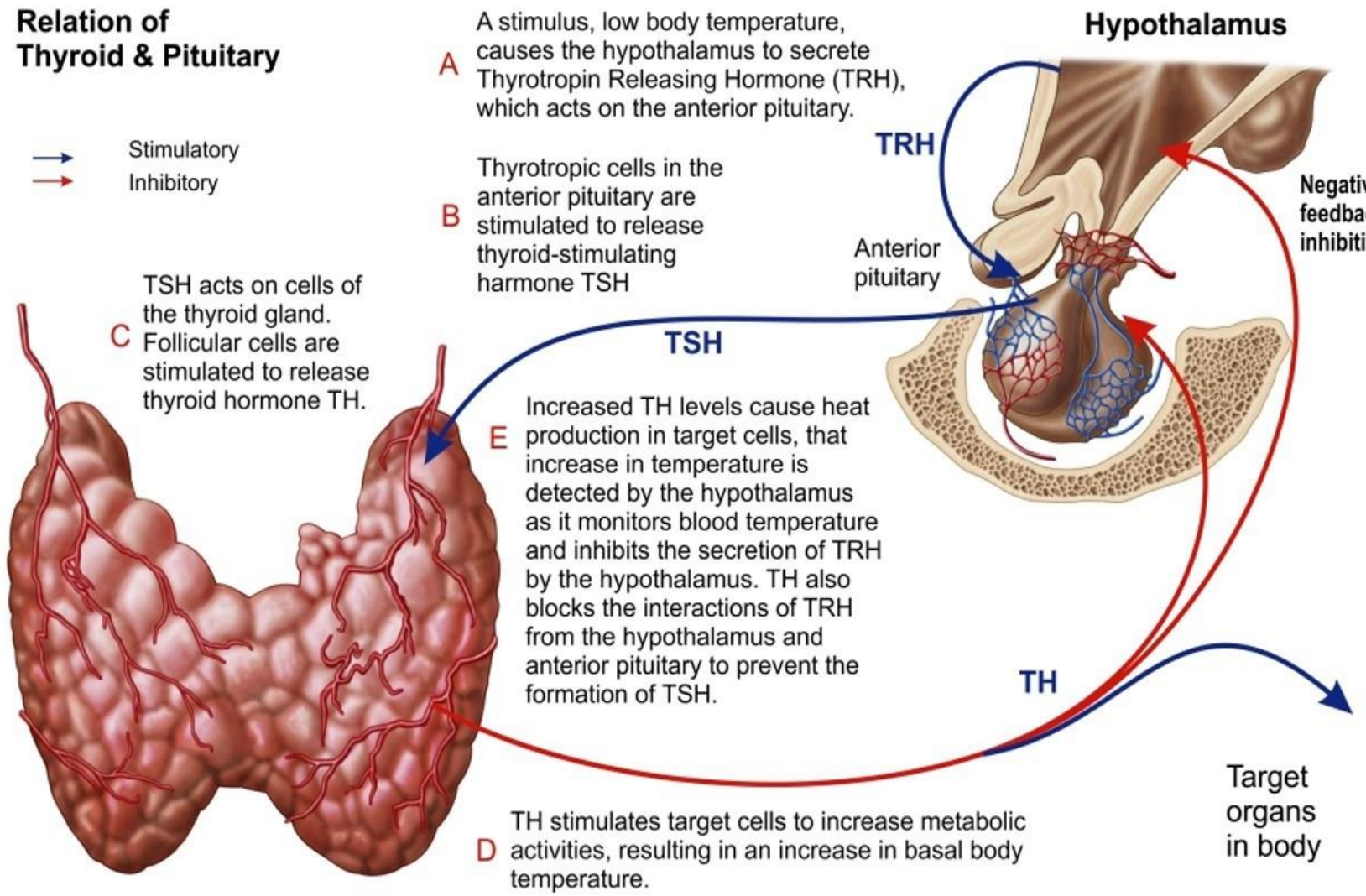
- The diagram shows the multistep process by which thyroid hormones are produced via the stored thyroglobulin intermediate. In an exocrine phase of
- The process, (1) the glycoprotein thyroglobulin is made and secreted into the follicular lumen and (2) iodide is pumped across the cells into the lumen.
- In the lumen (3) iodide is converted to iodine by membrane-bound thyroid peroxidase and added to tyrosine residues of thyroglobulin (4) to form monoiodotyrosine (MIT) or diiodotyrosine (DIT), which are then covalently coupled to form t3 and t4 still within the glycoprotein. The iodinated
- Thyroglobulin is then (5) endocytosed by the thyrocytes and degraded by lysosomes, (6) releasing free active T3 and T4 to the adjacent capillaries in
- An endocrine manner. Detailed steps are given in the text. Both phases are promoted by TSH and may occur simultaneously in the same cell.

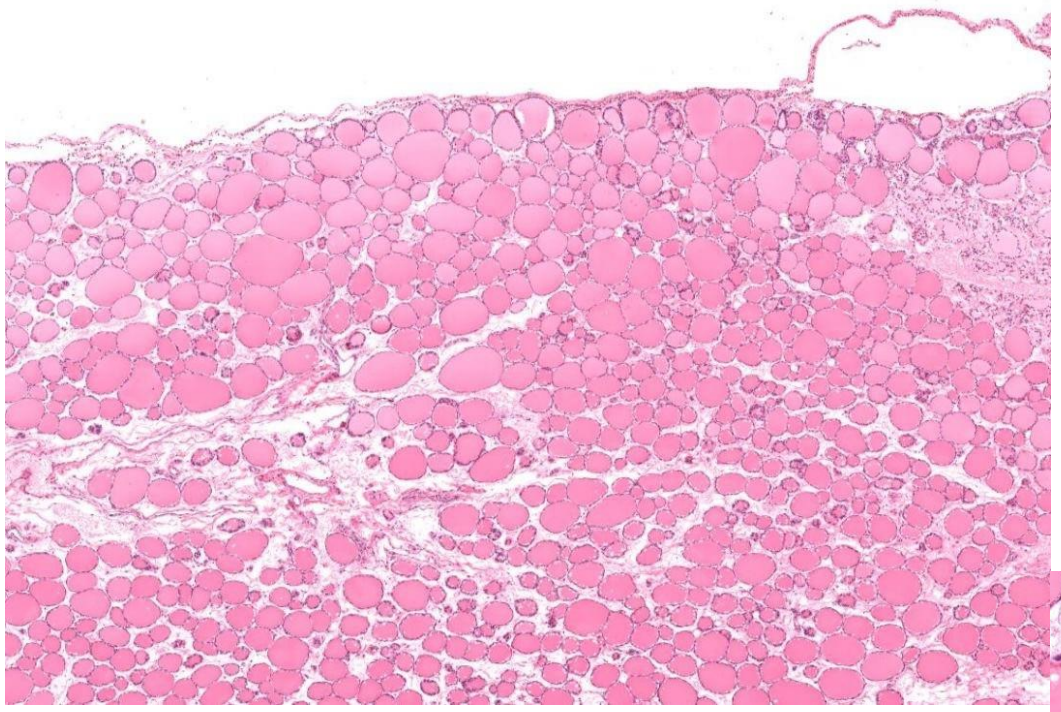
Negative Feedback Loops Affecting Anterior Pituitary Secretion

- Alrdy know, TRH goes to pituitary giving us TSH which goes to thyrocytes (TRH goes to thyrotrophes) and releases T3 AND T4 (from storage) slice and add iodine then bloodstream
- This whole thing is initiated by basal body temperature (metabolism);

1. Low temperature—> excitatory signal/activation signal to hypothalamus.

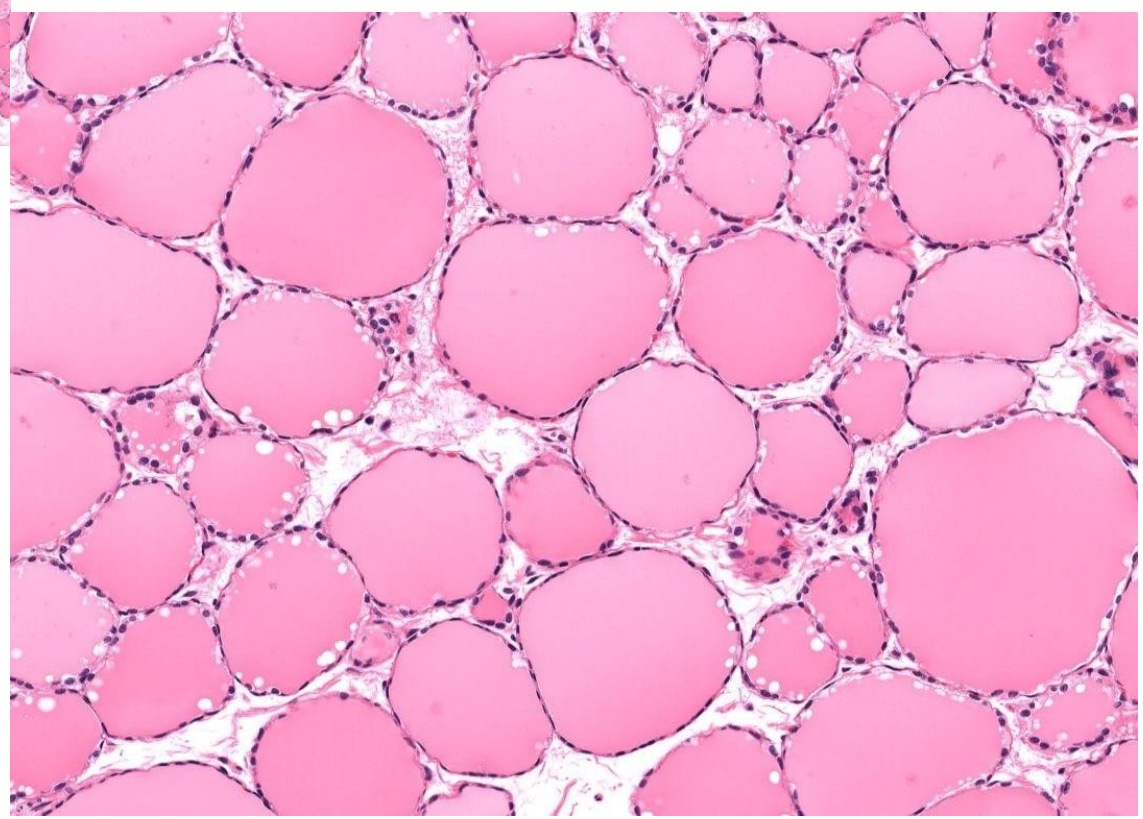
Ongoing cycle (nonstop) to maintain basal body temperature

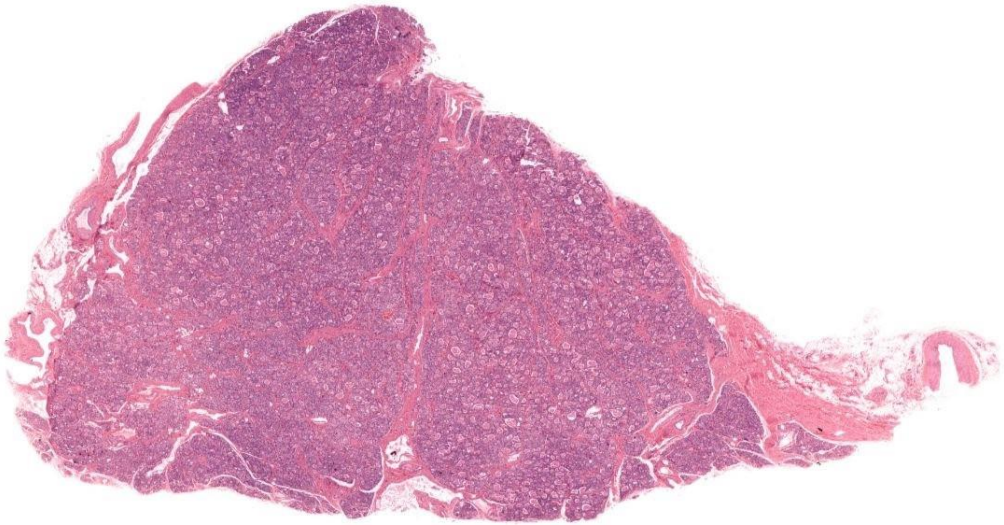


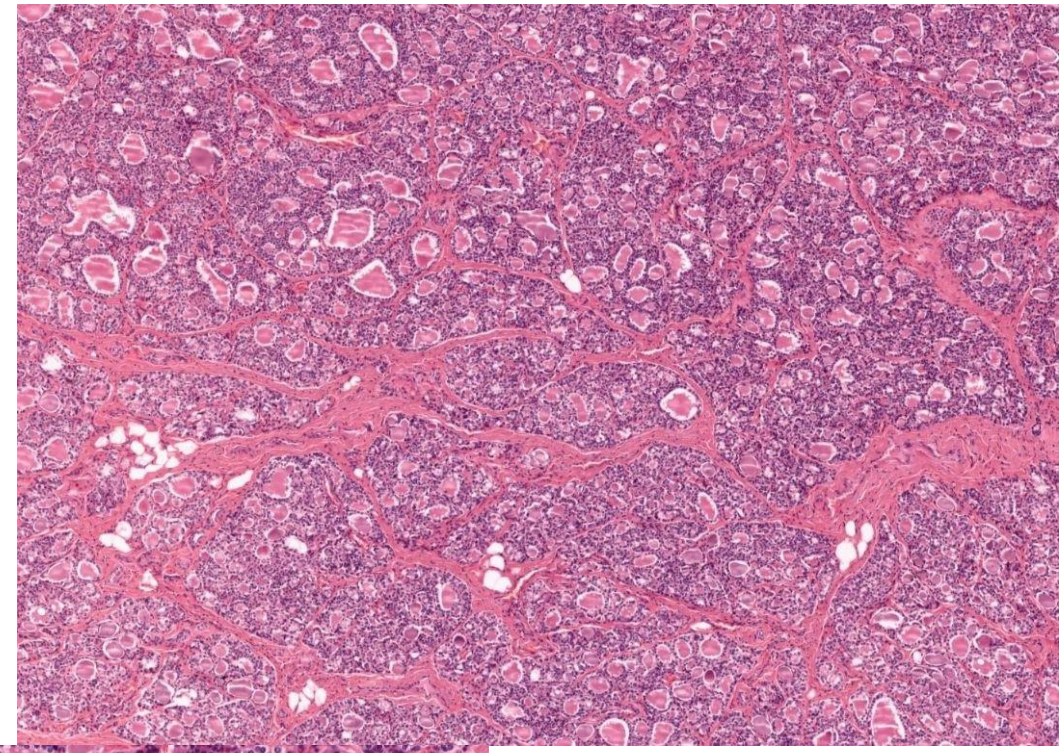


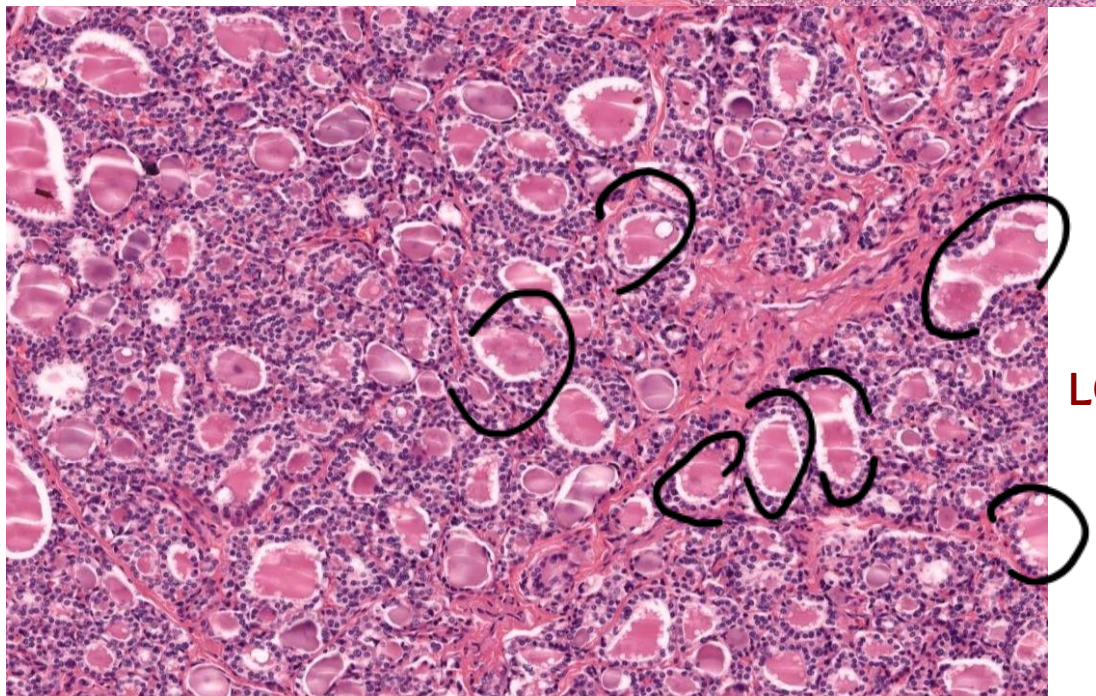
THYROID: ACTIVE OR INACTIVE?

INACTIVE, NUCLEI MAINLY FLAT

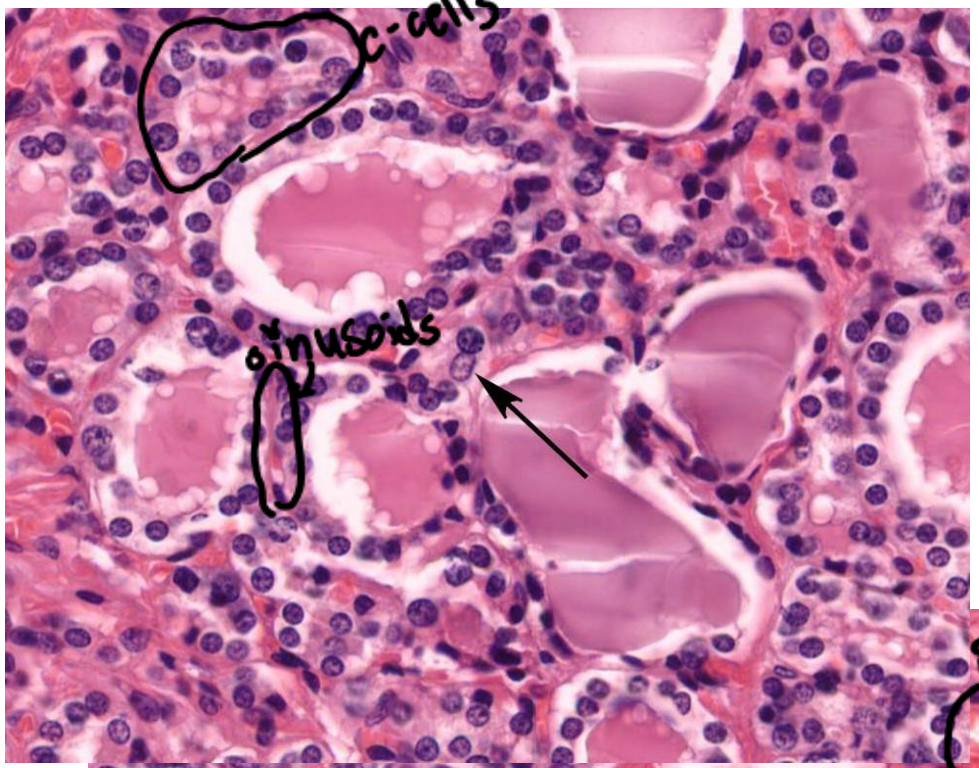


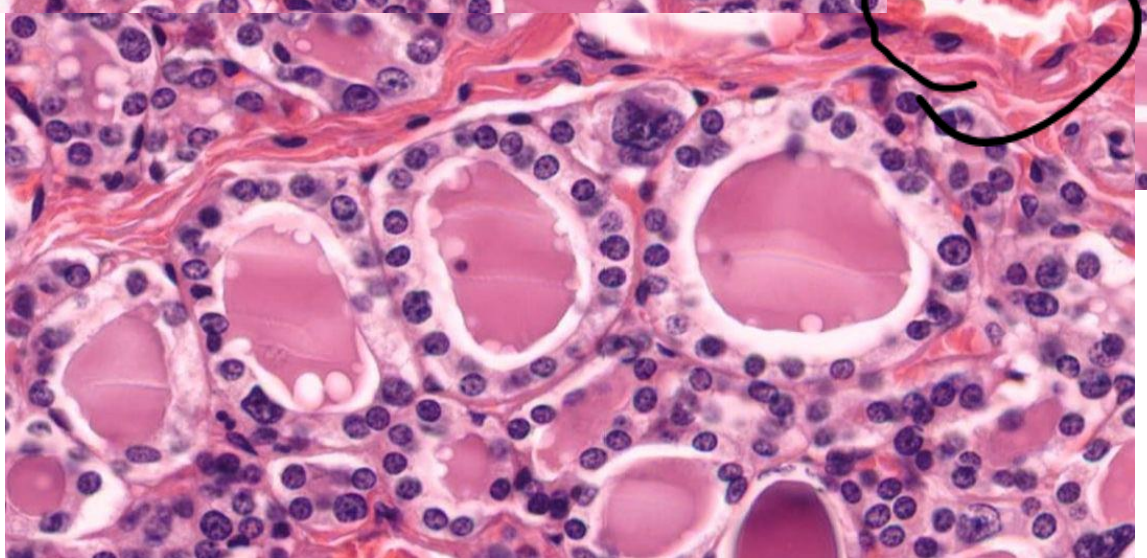


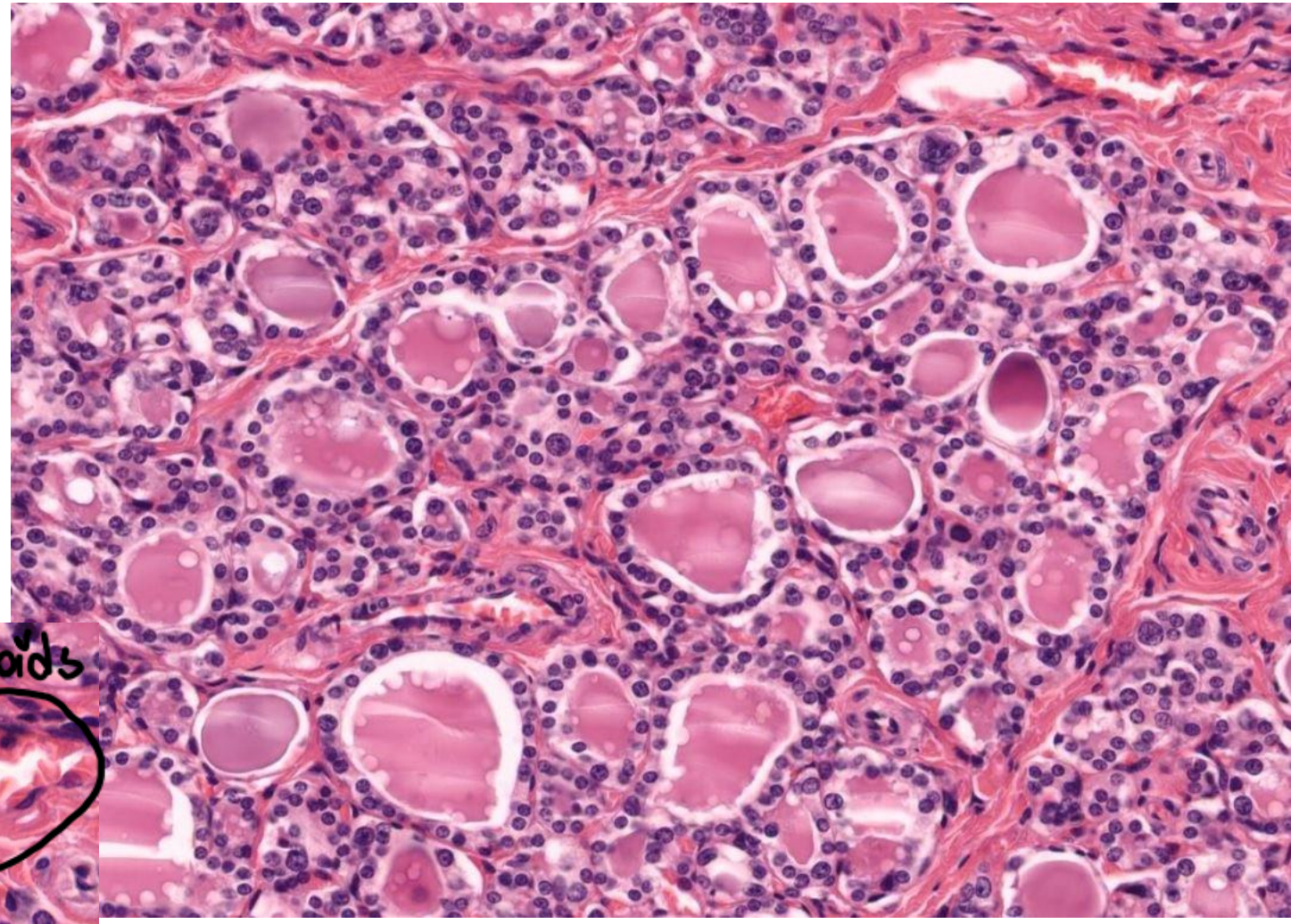




LOTS OF COLLOID, LOTS OF CELLS!!

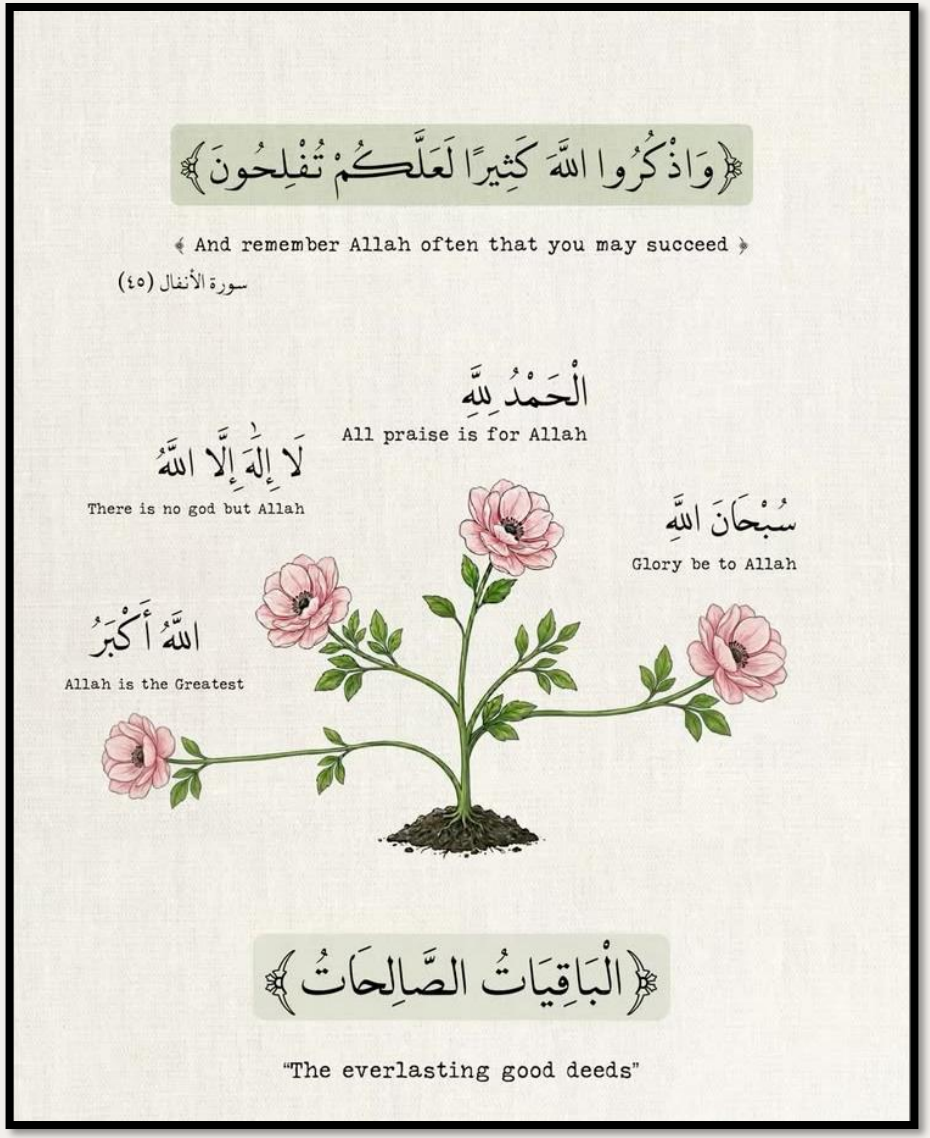






ACTIVE!!!!!!!!!

رسالة من الفريق العلمي:



For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			