

DISEASES OF THE MEDIASTINUM II

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MEDISTINUM

- Mediastinum is the central space within the thoracic cavity bounded by:
 - Sternum anteriorly
 - Lungs and parietal pleura laterally
 - The vertebral column posteriorly
 - The thoracic inlet superiorly
 - The diaphragm inferiorly
- Mediastinum is divided into: superior and inferior compartments.
- The later is divided into anterior, middle and posterior compartments.

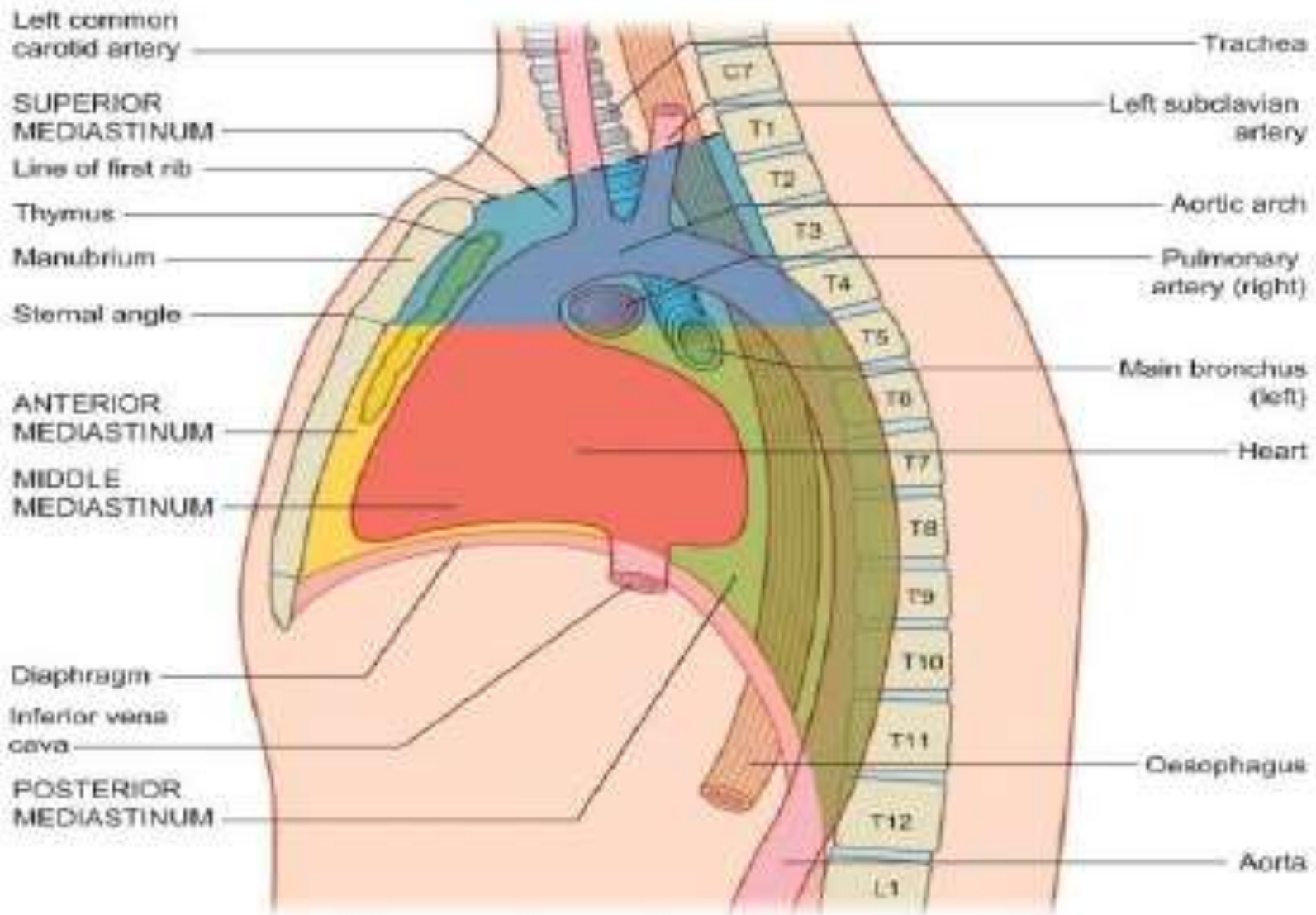
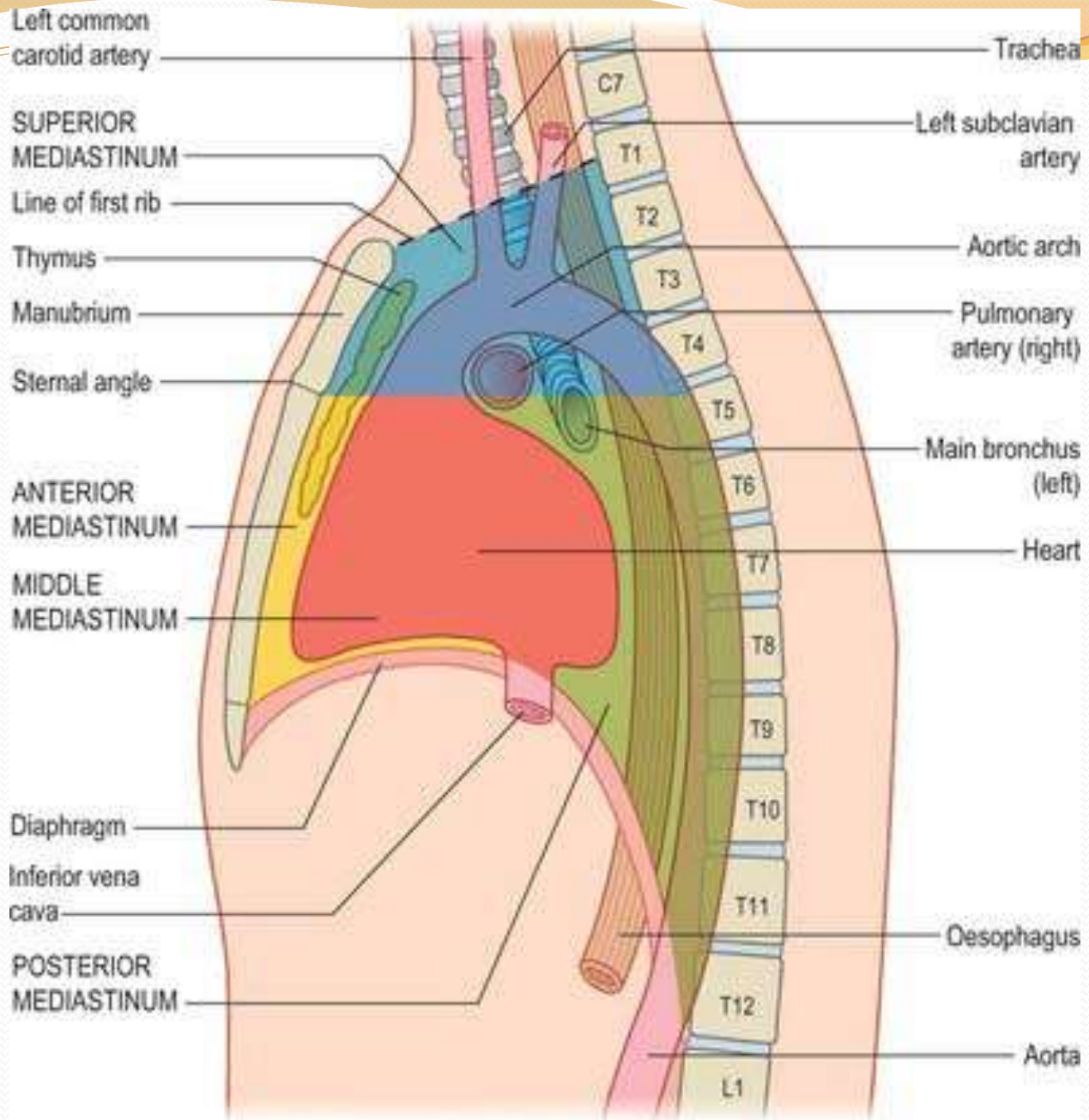


Fig. 55.1 The major divisions of the mediastinum (see text for further details). Note that not all mediastinal contents are depicted.





THYMUS

Anatomy of Thymus Gland

- The thymus is a *lobulated* organ covered by capsule and divided into *cortical* and *medullary* portions.
- The cortex is sub-divided into *subcapsular* (outer) and *deep region*.

- **The cortex** stains more deeply basophilic due to higher proportion of lymphocytes compared to cortical epithelial cells, while **the medulla** is more pale as a result of fewer lymphocytes compared to medullary epithelial cells including *Hassall corpuscles*.
- *The two major cell types* are endodermally derived **epithelial cells**, with minor ectodermal contribution, and bone marrow-derived *lymphocytes*.

1. **Epithelial cells** are divided on the basis of their location, appearance, and phenotypic properties into *cortical (dendritic), subcapsular, medullary, and Hassall corpuscle related.*
- Epithelial cells are *keratin positive and express HLA-DR antigens.*
- The keratin profile shows differences related to the *anatomic compartment and the functional status* (growth phase or involution) of the gland.

- One or more of these cells are ***responsible for the differentiation of T lymphocytes.***
- 2. **Thymic lymphocytes** (traditionally known as ***thymocytes***) have a ***T-cell phenotype.***
- *A whole range of differentiation exists among them; subcapsular thymocyte, cortical thymocyte, medullary thymocyte, and mature (peripheral type) T lymphocyte.*

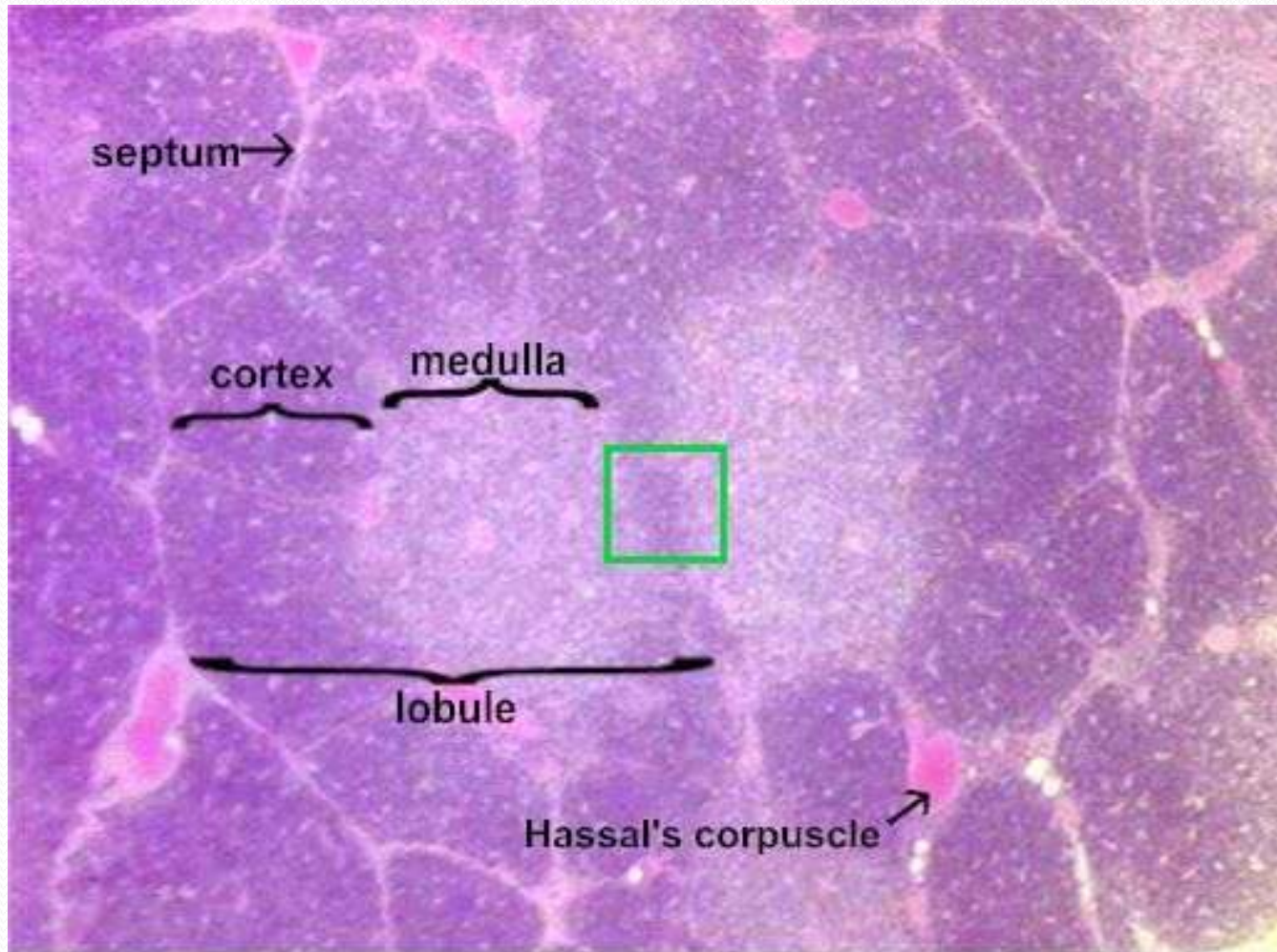
3. Other cells normally present in the thymus include **B cells** present in the thymic medulla and in the perivascular compartment, **interdigitating reticulum cells**, **Langerhans cells**, **mast cells**, **eosinophils** (particularly in neonates), and **nonspecific stromal cell**.
4. Aggregates of **benign nevus cells** is also found within the substance of the thymus.

- 5. Another subtype of stromal cell found in the thymic medulla and possibly playing role in the pathogenesis of myasthenia gravis is **skeletal muscle cell** known as **myoid cell**.
- The embryologic origin and functional significance of these enigmatic cells remain controversial.
- *The thymus undergoes normal involution after puberty, although it never disappears completely.*

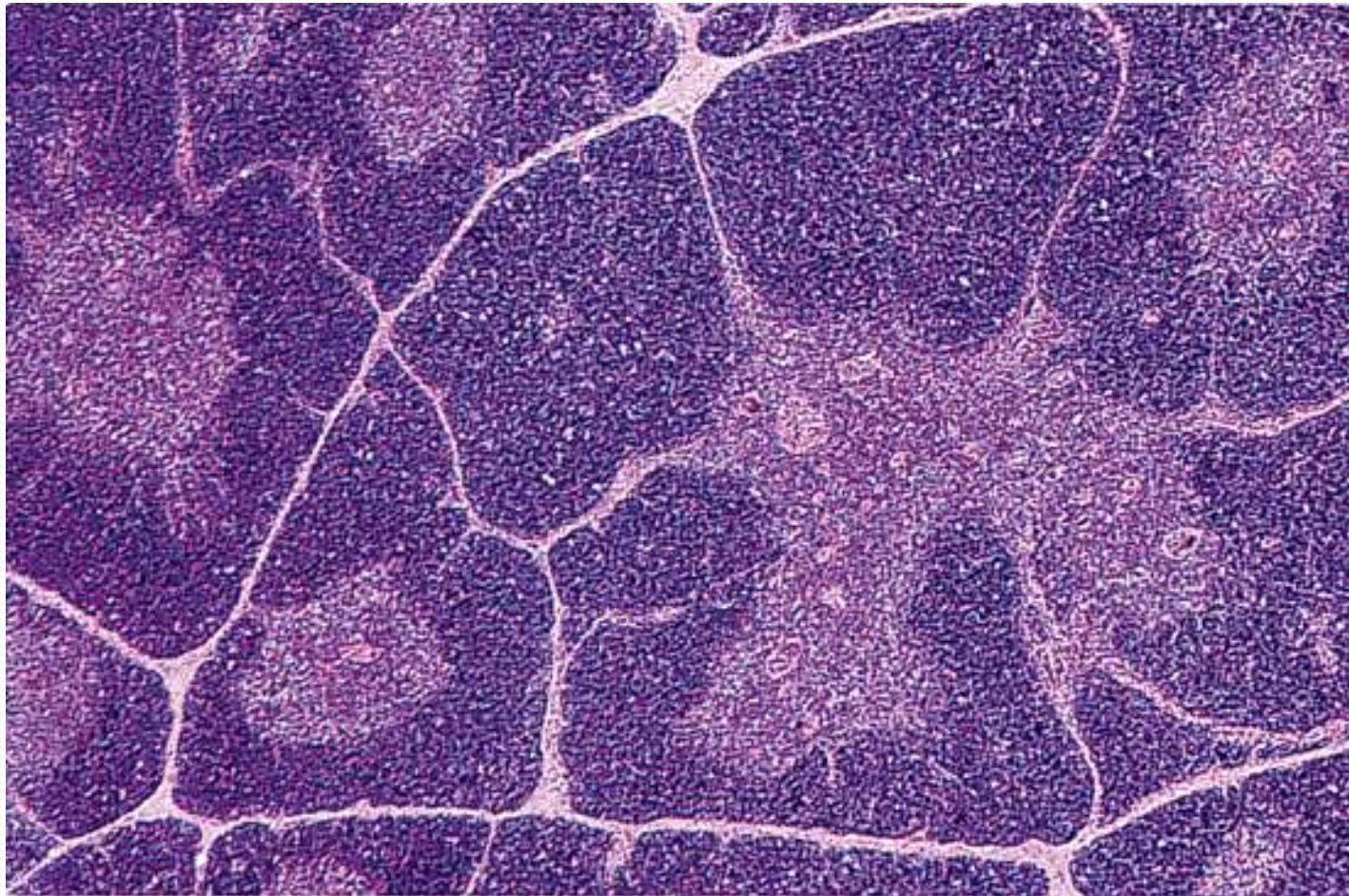
- Islands of thymic tissue are microscopically found on *prepericardial fat* and sometimes in the *retrocarinal fat*.
- The islands predominantly composed of *lymphocytes* may be confused with lymph nodes, whereas those mainly made up of *epithelial cells* show *trabecular* or *rosette-like formations* and may be *misinterpreted as carcinomatous or neuroendocrine*.

- Occasionally *epithelial component acquires nodular character*.
- This change can also be seen in **ectopic thymus**, and probably represents *nodular hyperplasia (or a thymic tumorlet)* and should be distinguished from a bona fide *small thymoma (“microthymoma”)*.

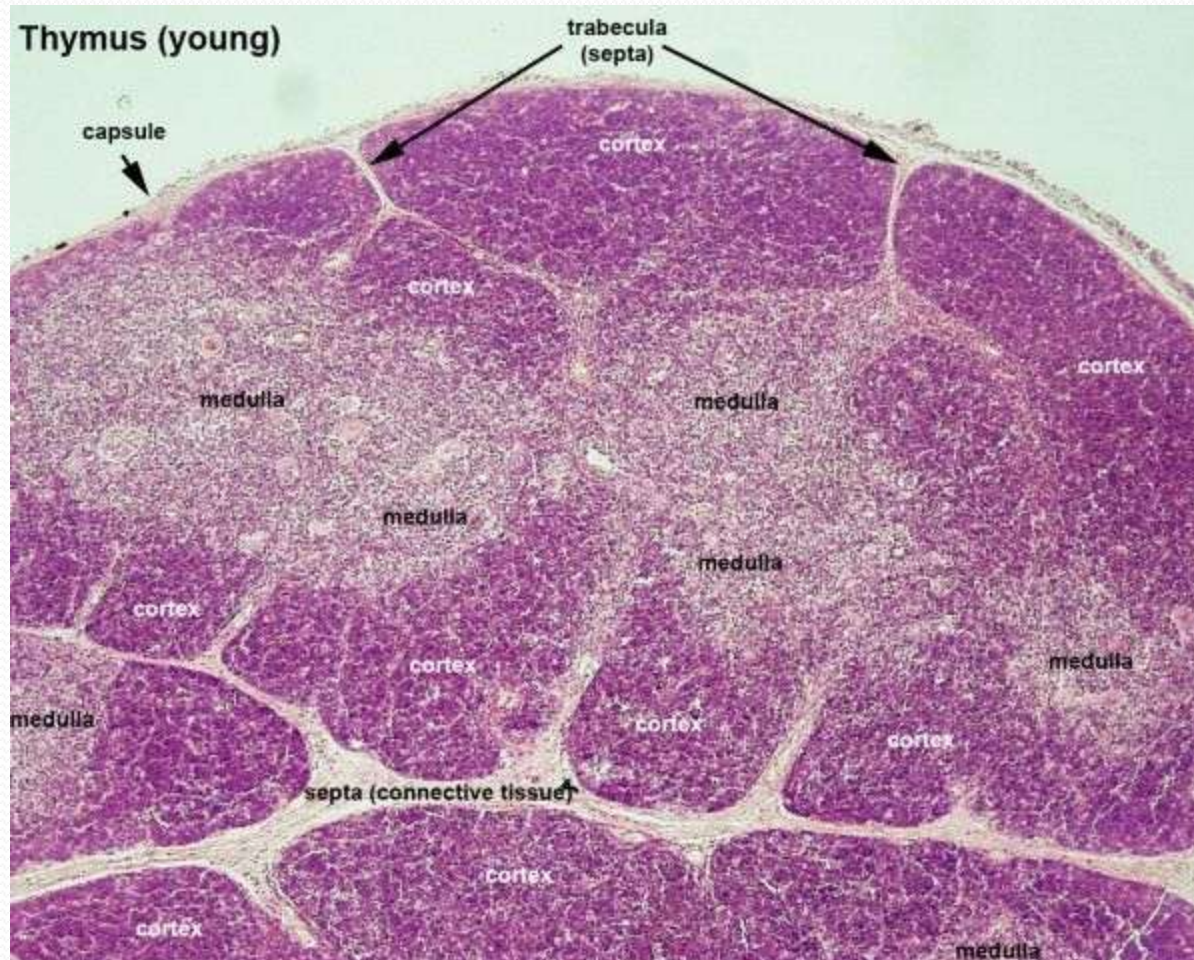
Thymus Gland



Thymus Gland



Thymus Gland



Thymic Cysts

- **Thymic cysts is divided into two distinct types.**
 1. **Unilocular thymic cysts** are of developmental origin, thought to arise from remnants of the third branchial pouch-derived thymo-pharyngeal duct.
- They are generally *small and located in the neck more often than in the mediastinum.*

- The cervical cysts tend to be *elongated* and can be found anywhere along a line extending from the angle of the mandible to the manubrium sternum.
- The wall is thin and translucent, and inflammation is usually lacking.
- The epithelial lining is flattened, cuboidal, columnar, or rarely squamous.
- *Thymic tissue is present in the wall*, some of it connecting with the lining epithelium.

2. **Multilocular thymic cyst** an acquired cyst of reactive nature.
- It is multilocular by definition and always accompanied by inflammation and fibrosis.
 - It can be *an incidental microscopic finding or result in a large tumor-like mass adherent to other mediastinal structures, simulating malignant process.*
 - The lining of the individual cysts may be *flat, cuboidal, ciliated columnar, or often squamous, either single or stratified.*

- The lining may be absent, have highly reactive appearance, or occasionally acquiring features of *pseudo-epitheliomatous hyperplasia*.
- *Cholesterol granulomas* are common.
- In some instances the inflammatory infiltrate is very prominent, with formation of *numerous lymphoid follicles*.

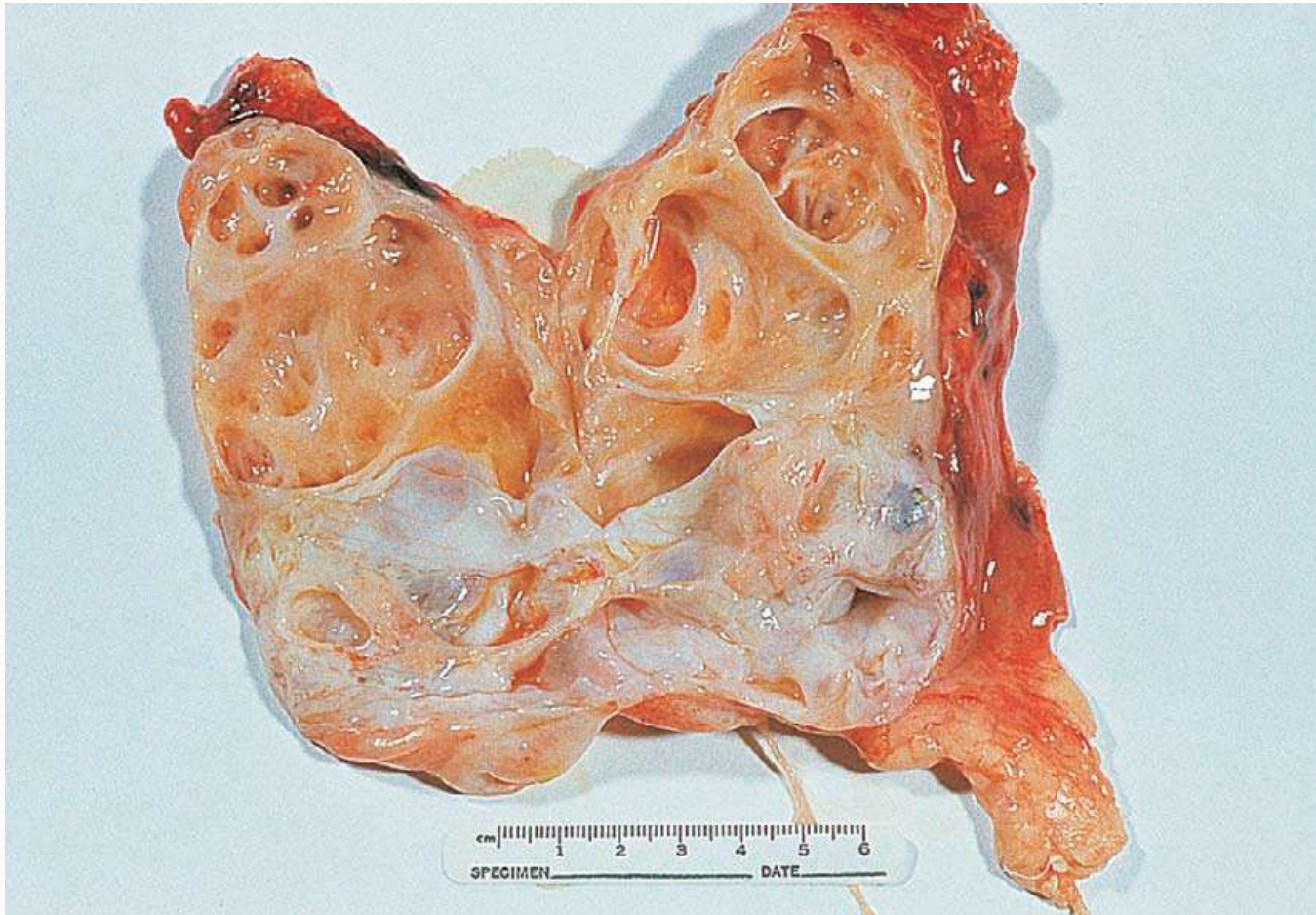
- Multilocular thymic cyst may result from *acquired cystic dilation of medullary duct, induced by inflammatory reaction of the thymic parenchyma.*
- **Inflammation** is usually *idiopathic*, or due to *HIV infection or autoimmune.*
- The so-called **Dubois abscesses** described in the thymuses of neonates with congenital syphilis probably also belong to this category.

- Morphologically similar change can be seen in about half of the thymuses having ***nodular sclerosis Hodgkin Lymphoma or germinoma.***
- It can also be seen, with much lesser frequency, *in association with thymoma, large cell lymphoma, yolk sac tumor, and mature teratoma.*

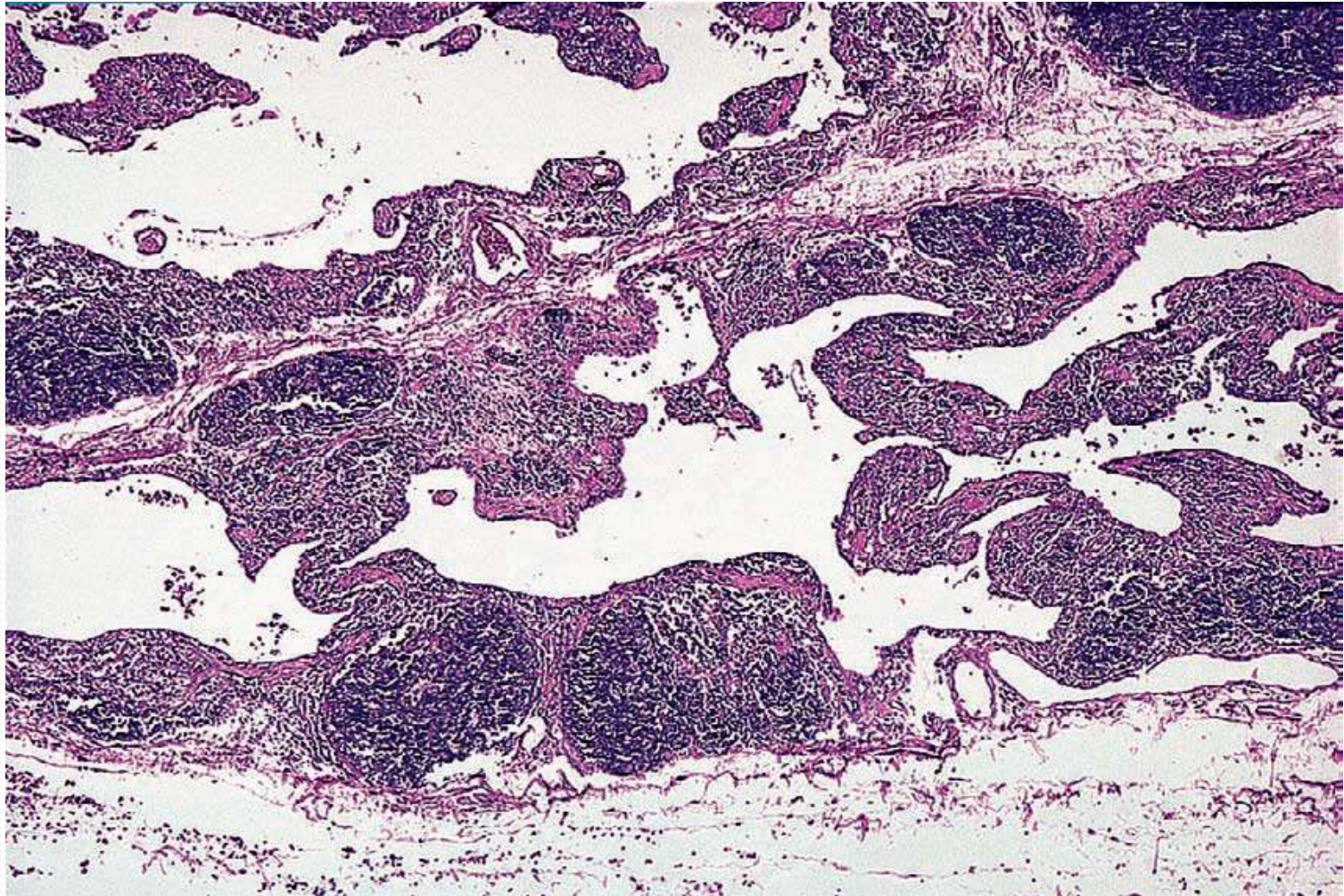
- *In the presence of these cystic changes it is important to determine whether the changes are purely inflammatory or an underlying neoplastic process is present.*
- **In the two malignant tumors** most commonly associated with it (Hodgkin lymphoma and seminoma), *the non-neoplastic lymphocytic component is particularly prominent.*

- *Lymphocyte-induced cystic ductular dilation resulting in multilocular thymic cyst is also responsible for the development of branchial cleft cyst, branchial cleft-like cysts in Hashimoto thyroiditis, lymphoepithelial cysts in parotid glands with HIV infection, and possibly Warthin tumor of parotid.*
- ***Multilocular thymic cysts must be distinguished from thymomas undergoing cystic degeneration and from cystic lymphangioma.***

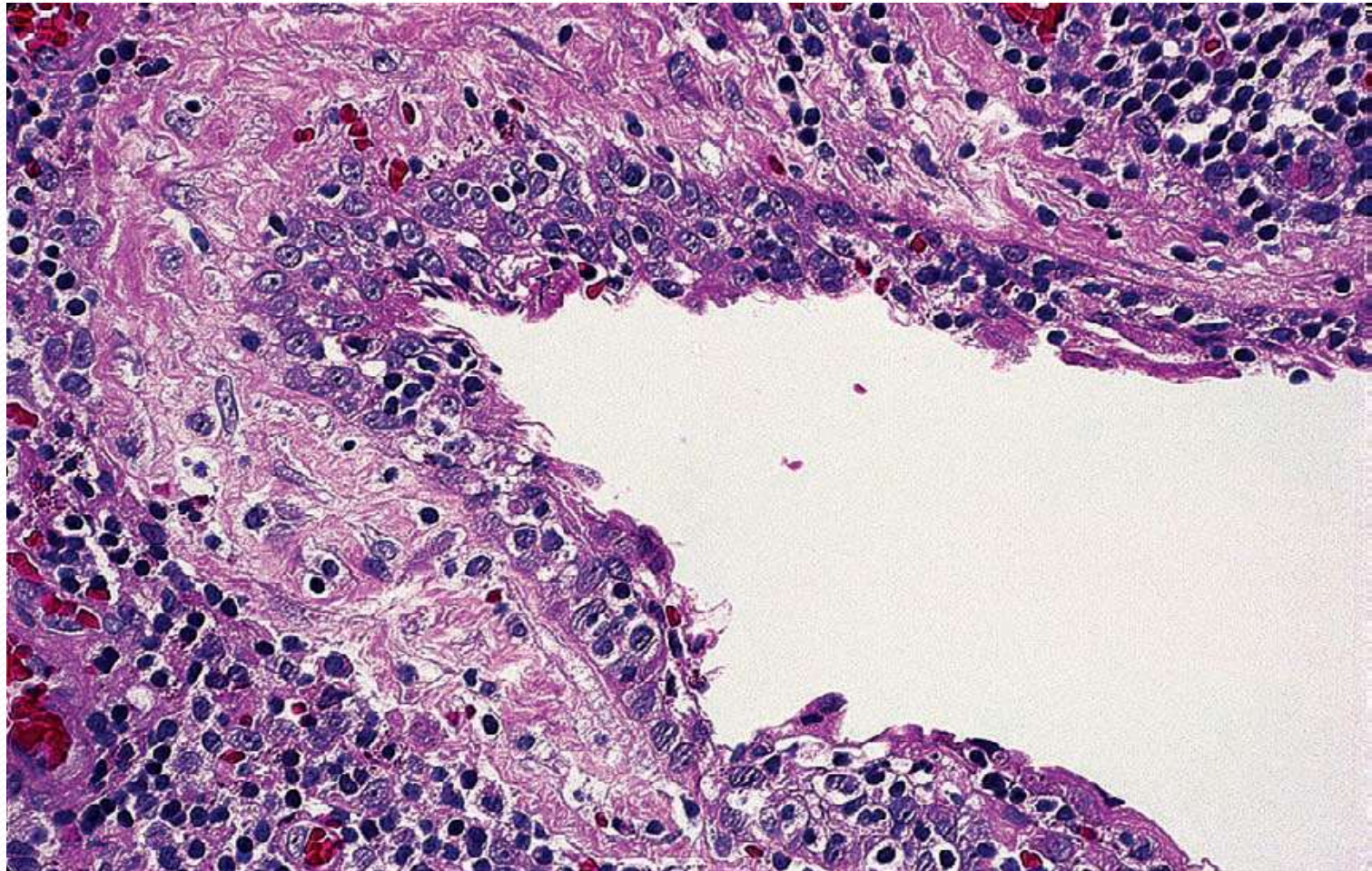
Multilocular Thymic Cyst



Multilocular Thymic Cyst



Multilocular Thymic Cyst





Other Non-Neoplastic Diseases

Ectopic thymus

- **Ectopic thymus** with an entirely normal microscopic appearance can *present as a mass in the neck or pleural surface.*
- The maldescended thymic tissue in the neck can be *unilateral or bilateral.*
- It is often located *adjacent to the thyroid gland* and usually *associated with parathyroid gland.*

- *Ectopic thymic tissue in the skin of the neck can be a clue to the branchio-oculo-facial syndrome.*
- *Ectopic tissues sometimes found in a normally located thymus include parathyroid gland (they have common embryogenesis) and sebaceous glands.*

Acute Thymic Involution

- **Acute thymic involution** is a constant feature of *chronic, debilitating diseases*.
- These changes are of *secondary nature* and should not be misinterpreted as evidence of primary immune defect.

- In *HIV infection*, thymic involution is pronounced and is accompanied by effacement of cortico-medullary junction, marked lymphocytic depletion, variable degrees of plasma cell infiltration and fibrosis, and inconspicuous Hassall corpuscles.
- These late changes are preceded by *thymic follicular hyperplasia*.

Diffuse Thymic Fibrosis

- *Diffuse thymic fibrosis is seen in absence of another primary thymic lesion.*
- *It is not clear whether it is a non-specific injury or a distinct entity, but the former seems more likely.*

True Thymic Hyperplasia

- *It is defined as thymic enlargement beyond the upper limits of normal for the age but accompanied by a microscopic normal gland.*
- It is most often described *in infants and children* but is also found *in adults*, sometimes *after successful chemotherapy for malignant disease.*

- It may represent a failure of involution, but in others it is clearly an acquired phenomenon secondary to some therapeutic manipulation.

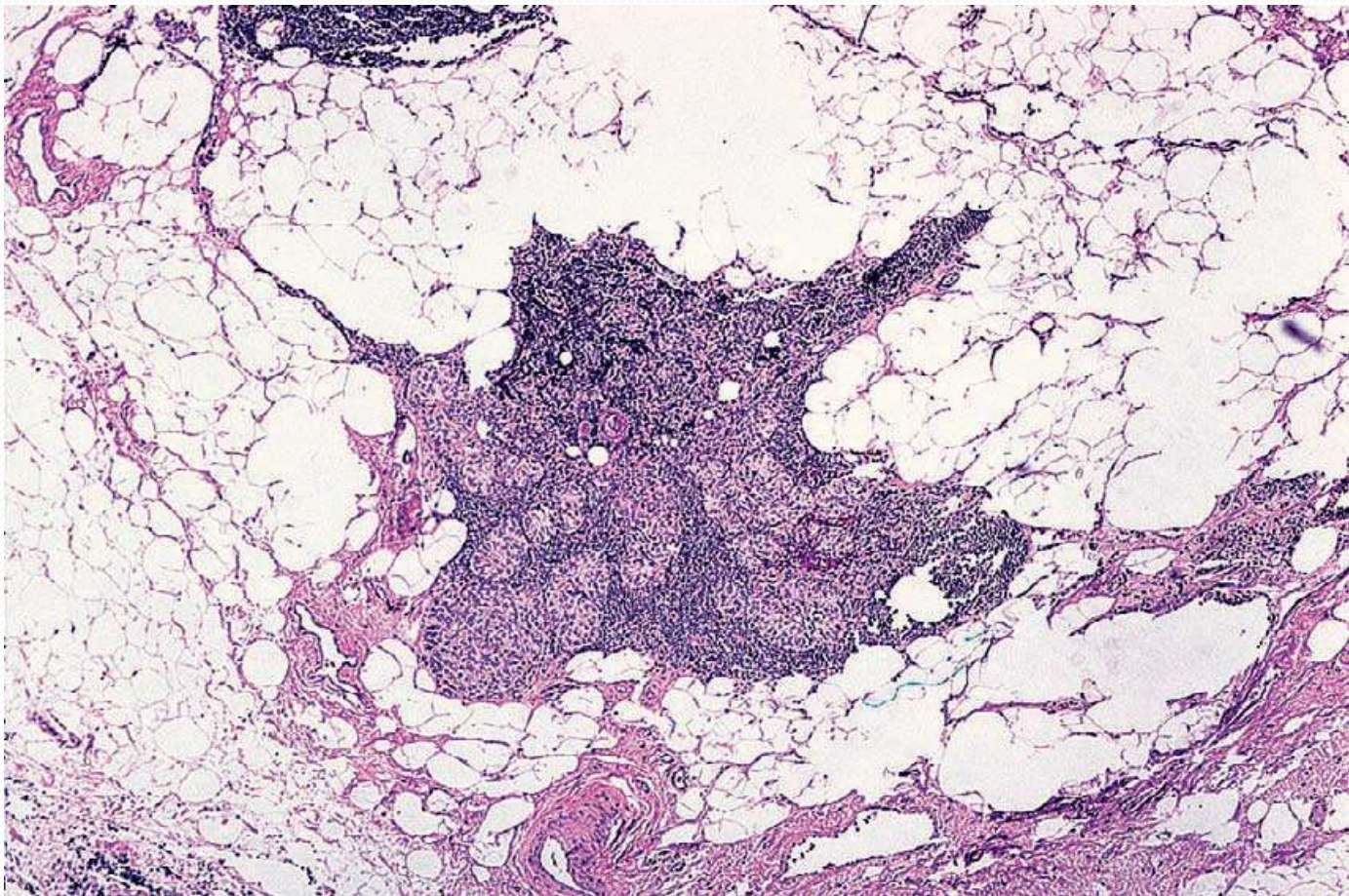
Thymic Follicular Hyperplasia

- **Thymic follicular hyperplasia** (often called simply “*thymic hyperplasia*”, a misleading term) is defined as *the presence of more than an occasional lymphoid follicle in the thymus independent of the size of the gland.*
- *The weight of most of the thymuses with lymphoid hyperplasia is within normal limits.*

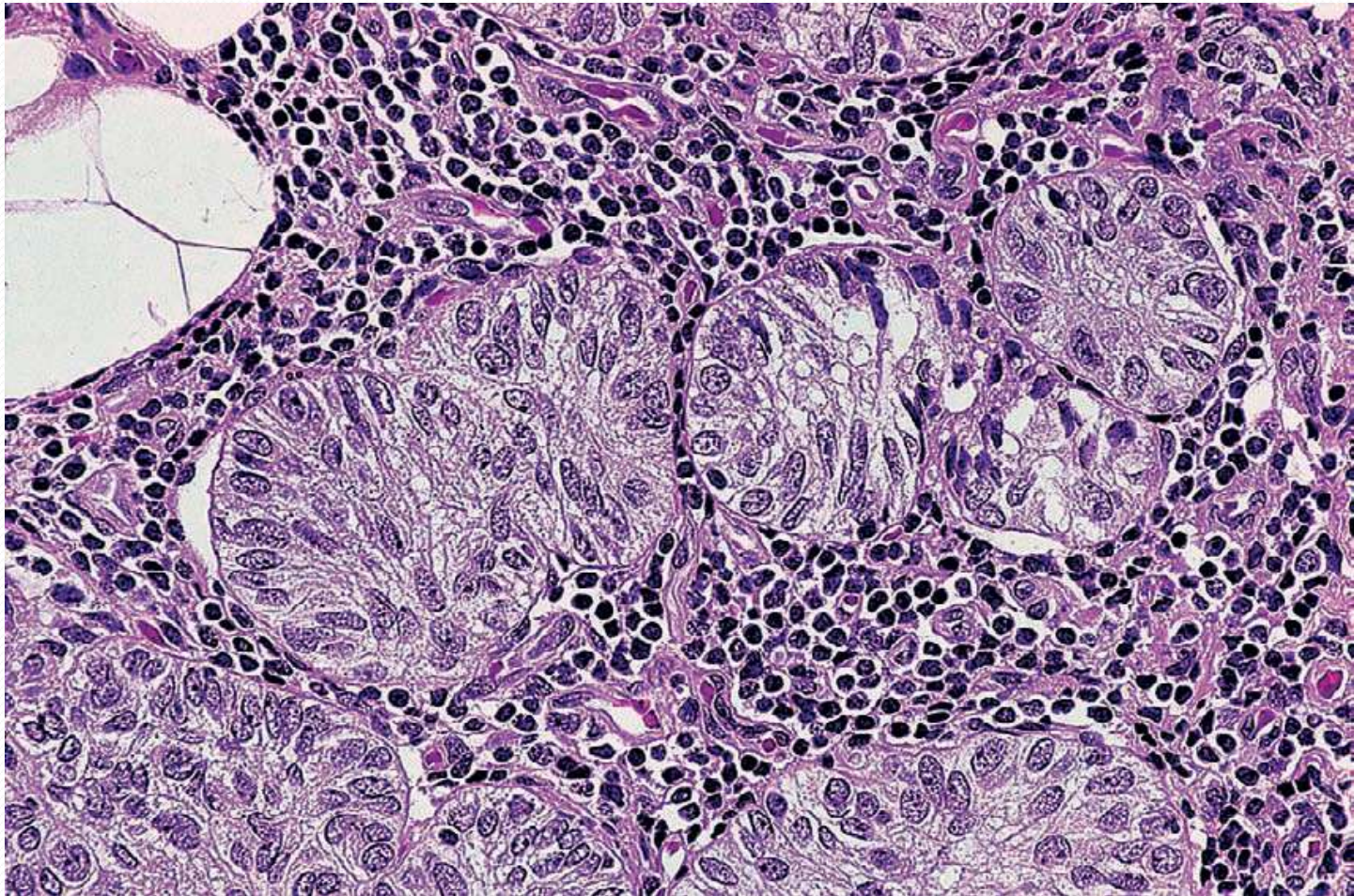
- *These follicles are of secondary type, with germinal center formation, and are largely composed of B lymphocytes.*
- *Their presence is accompanied by a disorder arrangement and hypertrophy of medullary epithelial cells.*
- Follicular hyperplasia is seen in most patients with ***myasthenia gravis***.
- It is also common in patients with ***Addison disease, hyperthyroidism, SLE***, and other immune-mediated diseases.

- It is described in *early stage of HIV infection*, associated with multilocular cystic formation.
- Few germinal centers also may be found in the apparently normal thymus, *especially during infancy and childhood*.
- *Only their presence in a substantial number in adult patients can be viewed as a distinctly abnormal finding.*

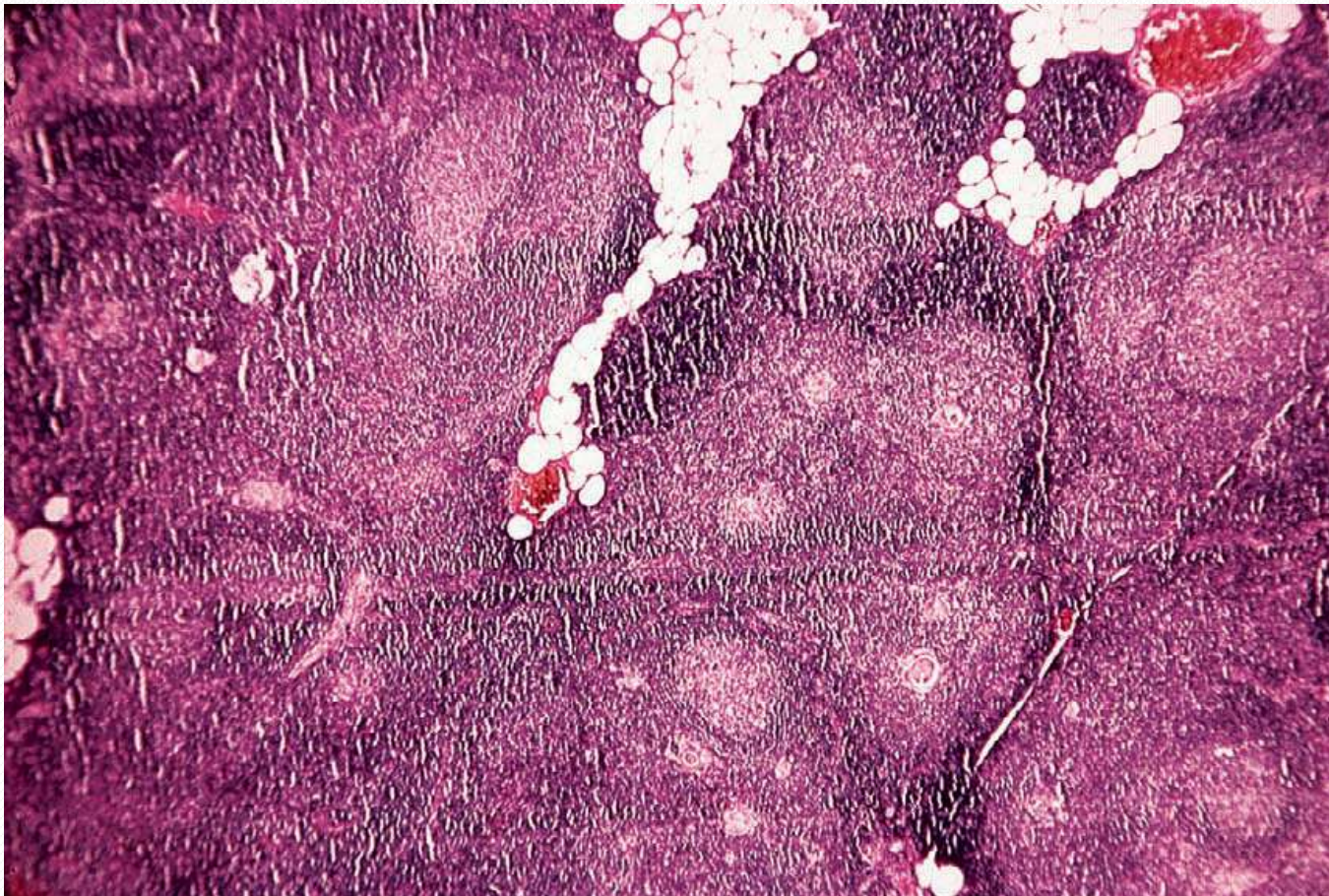
Thymic Nodular Hyperplasia



Thymic Nodular Hyperplasia



Thymic Follicular Hyperplasia



Langerhans Cell Histiocytosis

- It can present as a thymic mass, either alone or with involvement of other sites.
- **Microscopic appearance** is characteristic, and the overall prognosis is excellent.
- Exceptionally, it is seen *in association with myasthenia gravis*.
- It may also *coexist with multilocular thymic cyst*.

- *Granulomas containing numerous eosinophils and simulating Langerhans cell histiocytosis* develop in the thymic capsule result in *pneumomediastinum*, that is equivalent to *reactive eosinophilic pleuritis* seen in patients with pneumothorax.
- Other inflammatory diseases that can involve the thymus are *eosinophilic granulomatosis with polyangiitis (Churg–Strauss disease)* and *Castleman disease (giant lymph node hyperplasia)*.



Thank you