2.
Neoplastic Proliferations of White Cells

~ Histiocytic Neoplasms

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Langerhans Cell Histiocytoses

- Histiocytosis is an “umbrella” designation for a variety of proliferative disorders of **dendritic cells or macrophages**.
- Some are highly malignant neoplasms (very rare histiocytic sarcomas), others are completely benign & reactive such as most histiocytic proliferations in lymph nodes
- Between these two extremes lie a group of uncommon tumors comprised of Langerhans cells**, the Langerhans cell histiocytoses.**

in skin

Dendritic cells

Cxs: 43(GJCs, HCs), 45

Panxs: 1 (HCs?)

Follicular dendritic cells

Cxs: 43 (GJCs)

Panxs: 1 (HCs?)

Monocyte/macrophages

Cxs: 37 (HCs), 43 (GJC, HCs)

Panxs: 1 (HCs)

Kupffer cells

Cxs: 43 (GJCs)

Panxs: 1

Osteoclast

: 43 (HCs and GJCs)

Panxs: 1? 3?

Microglia

Cxs: 32 (HCs), 36, 43 (GJCs, HCs), 45

Panxs: 1 (HCs)

Neutrophils

Cxs: 37 (HCs), 40, 43 (GJCs?, HCs)

Panxs: 1 (HCs)

B cells

Cxs: 40, 43 (GJCs)

Panxs: 1 (HCs?)

What are histiocytes?

Histiocytes are a type of **tissue-resident macrophage** derived from **monocytes**. They include:

- **Macrophages**
- **Dendritic cells**
- **Langerhans cells**
- **Kupffer cells (liver)**
- **Microglia (CNS)**
- **Osteoclasts (bone)**

(إضافي للتوضيح)

(APCs, Ag presenting cells)

Langerhans Cell Histiocytoses

- Langerhans cells are a special type of immature dendritic cell that are found in the epidermis; similar cells are found in many other organs.
- Function → to capture antigens and display them to T cells.

Langerhans Cell Histiocytoses

a group of diseases

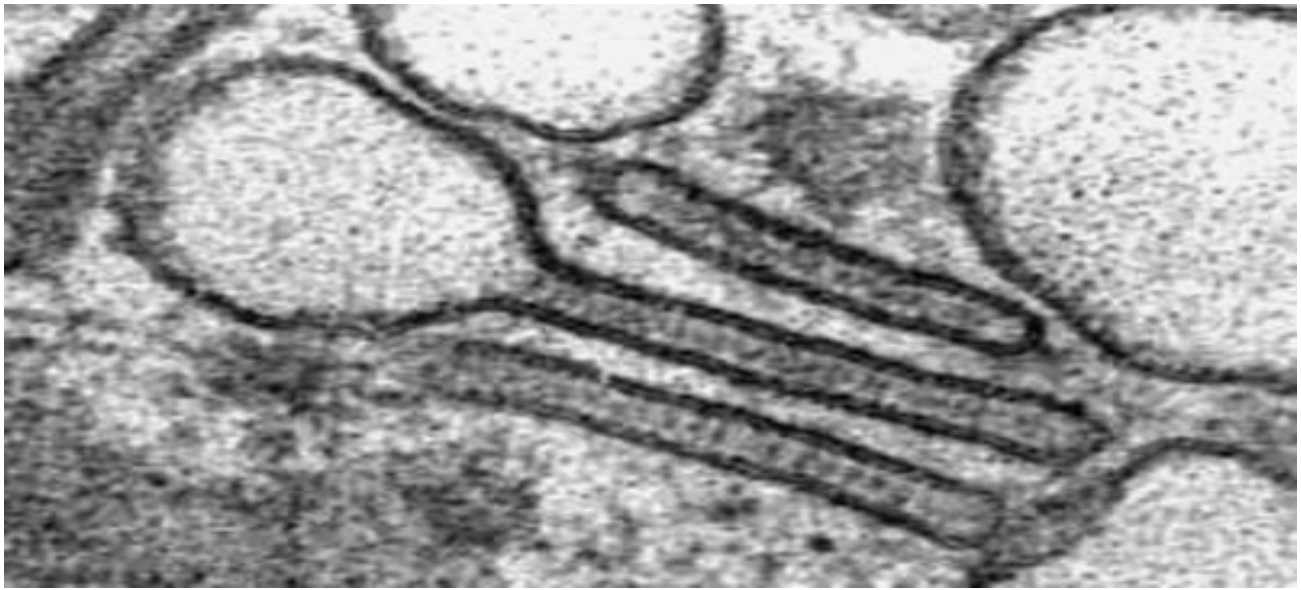
- Langerhans cell proliferations take on different clinical forms, but all are believed to be variations of the same basic disorder.
- The proliferating Langerhans cells express **MHC class II** antigens, **CD1a, and langerin.**

on Ag presenting cells

specific

- **Langerin**: is a transmembrane protein found in Birbeck granules.
- **Birbeck granules:** cytoplasmic rodlike tubular structures, they have a characteristic electron micrographs tennis racket appearance.

Langerhans Cell Histiocytoses – Birbeck granules

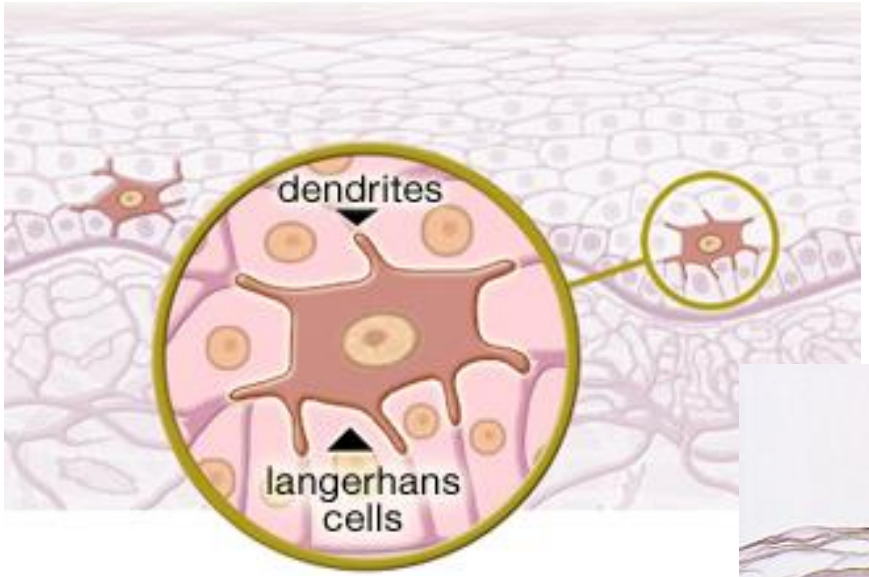


Electron microscope

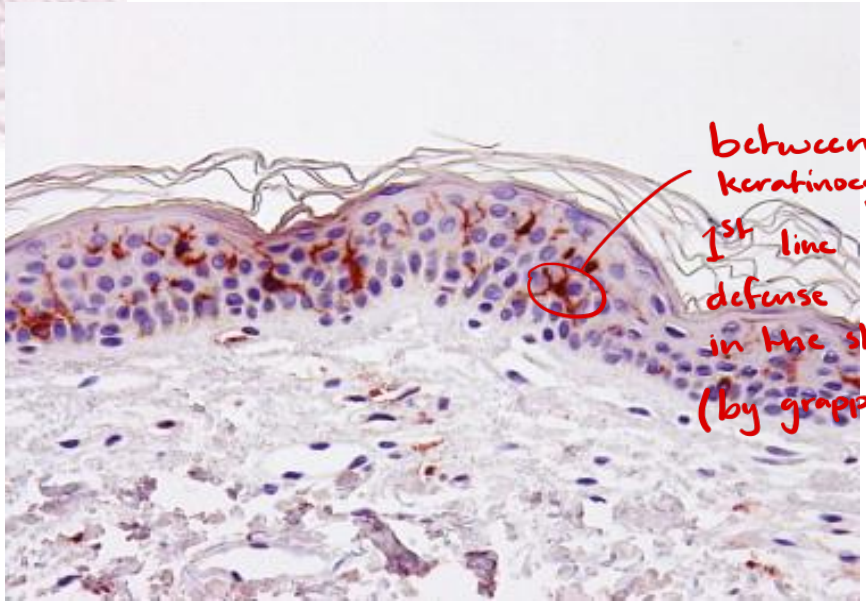
- inside the cytoplasm of histiocytes
- tennis racket appearance
- Contain langerin
- Specific to langerhans cells

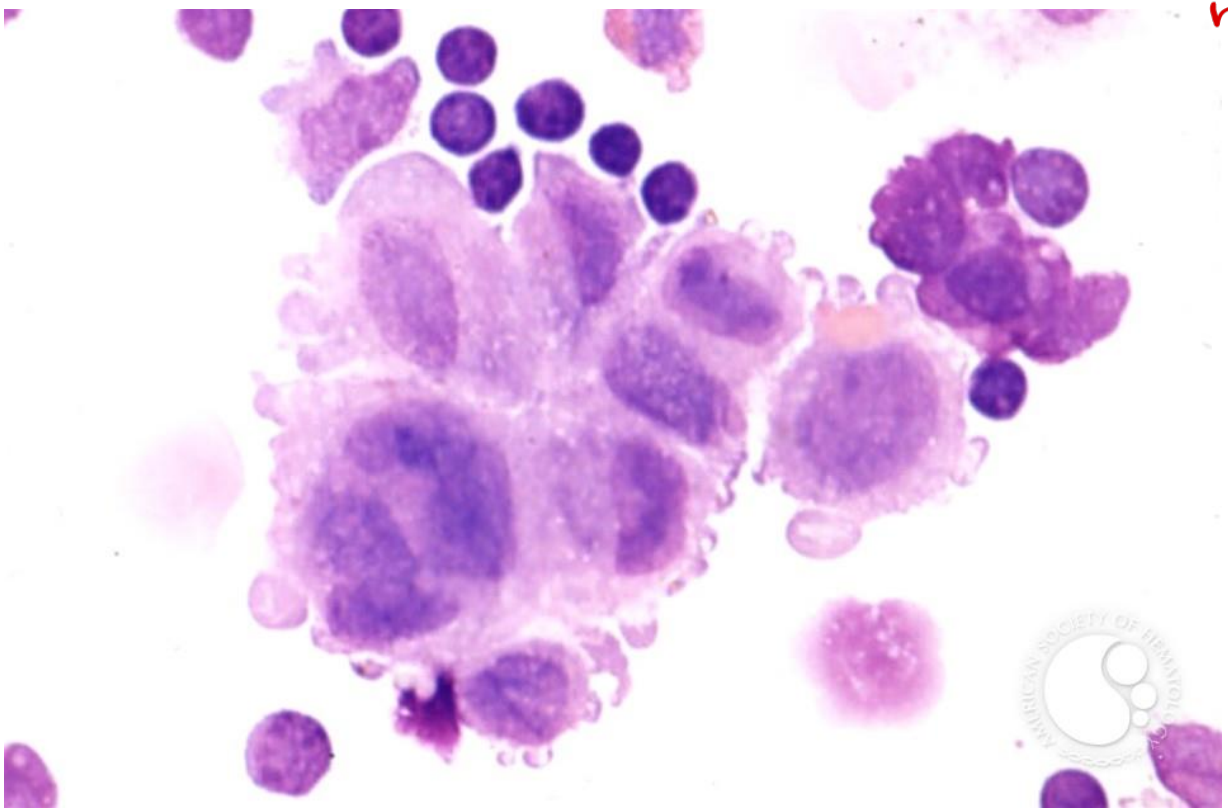
Langerhans Cell Histiocytoses

- Under the light microscope, the proliferating Langerhans cells do not resemble their normal dendritic counterparts.
- They have larger, abundant, often vacuolated cytoplasm and vesicular nuclei, an appearance more akin to that of tissue macrophages (histiocytes)— hence the term Langerhans cell histiocytosis.



immune stain, not H&E





microglial cells

Langerhans Cell Histiocytoses – Pathogenesis

- The different clinical forms (benign & malignant) are frequently associated with an acquired mutation in the kinase BRAF → ↑↑ proliferation hyperactivity of the kinase.
- This same mutation is found in a variety of other tumors, including; benign nevi, malignant melanoma, papillary thyroid carcinoma, and some colon cancers. → not specific

Langerhans Cell Histiocytoses

- Langerhans cell histiocytoses can be grouped into two major relatively distinctive clinicopathologic entities:

Multisystem Langerhans cell histiocytosis (Letterer-Siwe disease)

- أسرأواحدفيهم -

Very rare

- Children younger than 2 years of age.
- Manifests with multifocal cutaneous lesions that grossly resemble seborrheic skin eruptions.

Scaly lesions
بتشبه قشرة الشعر

- Most affected patients have hepatosplenomegaly, lymphadenopathy, pulmonary lesions, and (later in the course) destructive osteolytic bone lesions.

Multisystem Langerhans cell histiocytosis (Letterer-Siwe disease)

- Extensive marrow infiltration often leads to pancytopenia.
- The disease is **rapidly fatal** if untreated.
- With intensive chemotherapy, 50% of patients survive 5 years.

Unisystem Langerhans cell histiocytosis (eosinophilic granuloma)

- Unifocal or multifocal.
- Characterized by expanding accumulations of Langerhans cells, usually within either the medullary cavities of bones or less commonly in the skin, lungs, or stomach.
- The Langerhans cells are admixed with variable numbers of lymphocytes, plasma cells, neutrophils, & **eosinophils (prominent).**
- Virtually any bone may be involved; the calvaria, ribs, and **femur are most commonly affected.**

non-neoplastic cells recruitment (as Hodgkin)

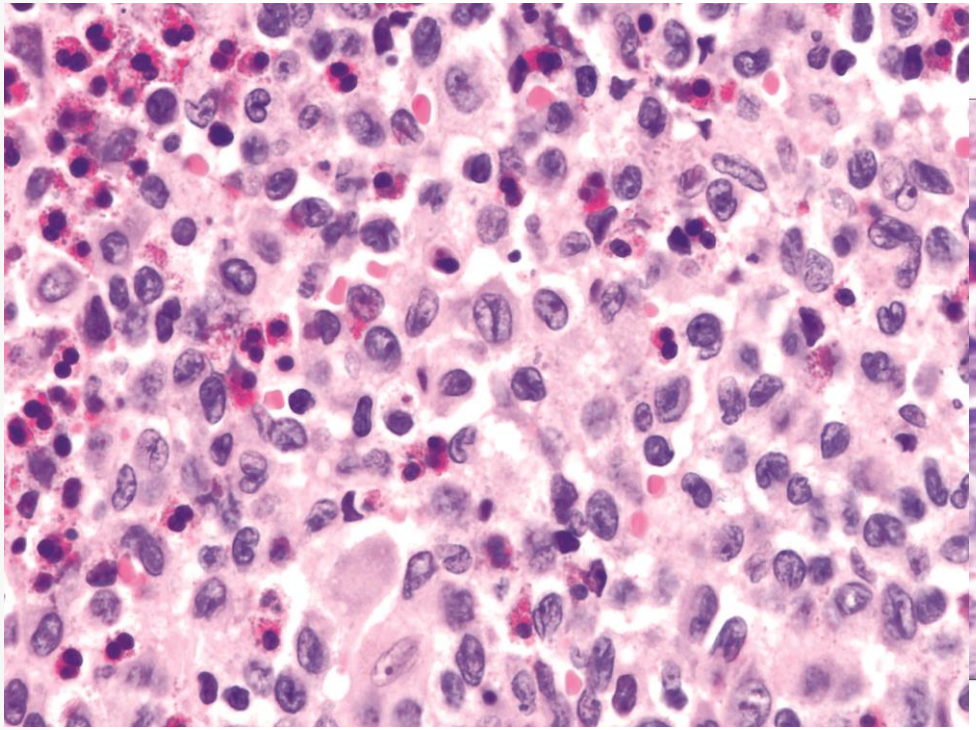
bones of skull

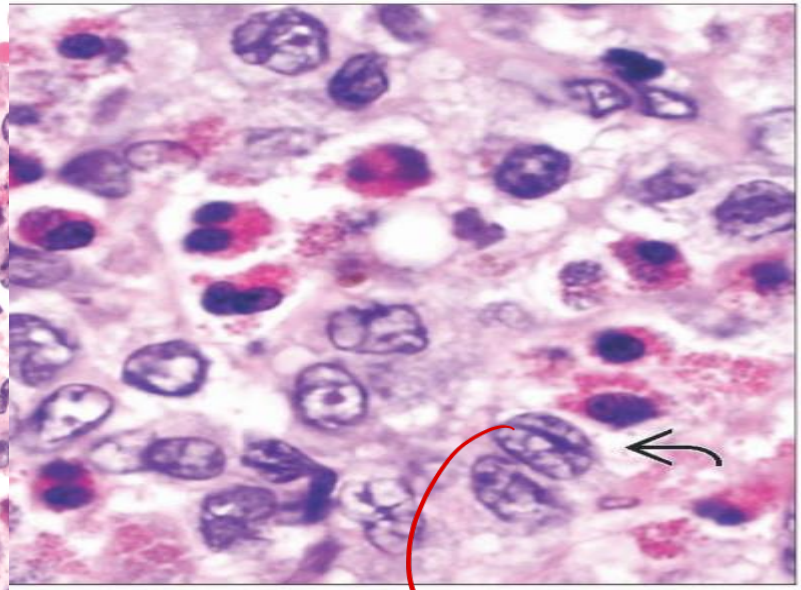
MC in osteosarcoma too

Unisystem Langerhans cell histiocytosis (eosinophilic granuloma) – morphology of both {multisystem, unisystem}

most prominant

histiocytes accumulation





coffee bean appearence of nucleus (بین شکلی)

Unisystem Langerhans cell histiocytosis (eosinophilic granuloma) – **Unifocal**

- **Unifocal** disease most often involves a single bone.
- Asymptomatic or cause pain (mass effect), tenderness, and pathologic fracture.
- It is an indolent disorder that may heal spontaneously or be cured by local excision or irradiation.

Unisystem Langerhans cell histiocytosis (eosinophilic granuloma) – Multifocal

معظمهم بينشوفهم بالأطفال

- **Multifocal** unisystem disease usually affects children
- Typically manifests with multiple erosive bony masses that sometimes extend into soft tissues.
- In about 50% of cases, involvement of the posterior pituitary stalk of the hypothalamus leads to diabetes insipidus.

Secrete

close to sella turcica (bone)

- Many patients experience spontaneous regressions; others are treated effectively with chemotherapy.

3.
Disorders of the Spleen and Thymus

Spleen – SPLENOMEGALY

- The spleen is frequently involved in a wide variety of systemic diseases.
- In virtually all instances the spleen responds by enlarging (**splenomegaly**) e.g. (150-250)g → 1 kg
- **Symptoms**; dragging sensation in the left upper quadrant & discomfort after eating.
- **Hypersplenism**; chronically enlarged spleen removes excessive numbers of one or more of the formed elements of blood, resulting in anemia, leukopenia, or thrombocytopenia. → MC
- **Platelets** are particularly susceptible to sequestration in the of the red pulp→thrombocytopenia is more prevalent and severe in persons with splenomegaly than is anemia or neutropenia

SPLENOMEGALY – Disorders

- According to the degree of splenomegaly they are grouped:

1. Massive splenomegaly (weight > 1000 g)

Myeloproliferative neoplasms (CML, primary myelofibrosis); indolent leukemias (CLL and hairy cell leukemia); lymphomas; infectious diseases(e.g., malaria); Gaucher disease

SPLENOMEGALY - Disorders

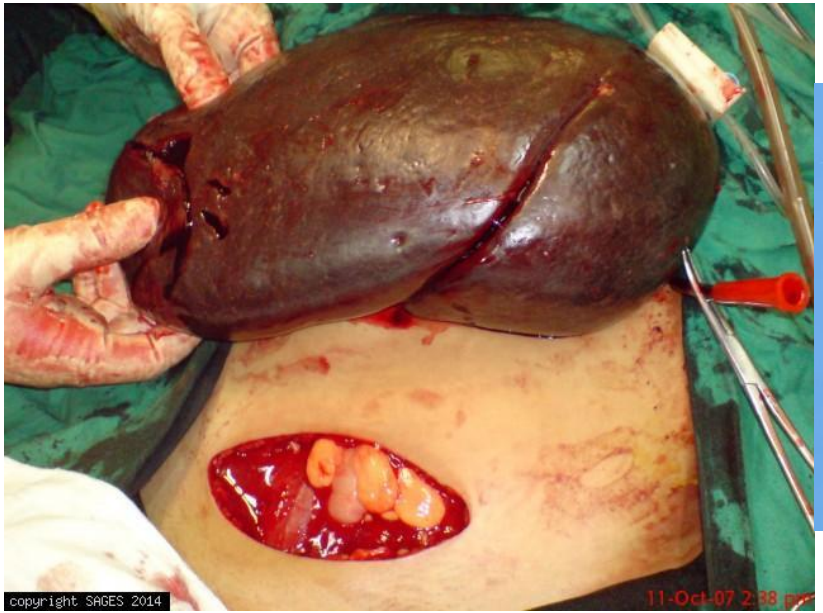
2. Moderate splenomegaly (500–1000 g) Chronic congestive splenomegaly (portal hypertension or splenic vein obstruction); acute leukemias; extravascular hemolysis (hereditary spherocytosis, thalassemia major, autoimmune hemolytic anemia; many infections, including infective endocarditis, tuberculosis, & typhoid; metastatic disease.
3. Mild splenomegaly (< 500 g): Acute splenitis; acute splenic congestion; infectious mononucleosis; septicemia, and intraabdominal infections

reversible

SPLENOMEGALY - Disorders

* بعد splenectomy بتحسن ITP
↓
immune thrombocytopenic purpura

* في كمان ممكن نعمل splenectomy؟
in accidents when spleen is injured & lacerated
↓
to prevent intra-abdominal bleeding



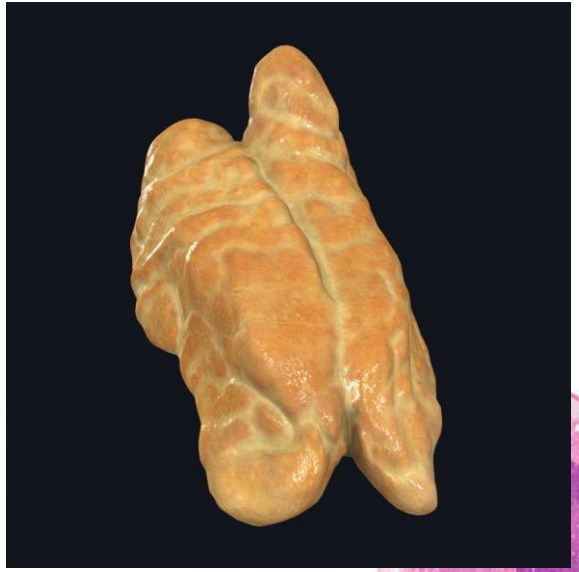
Normal

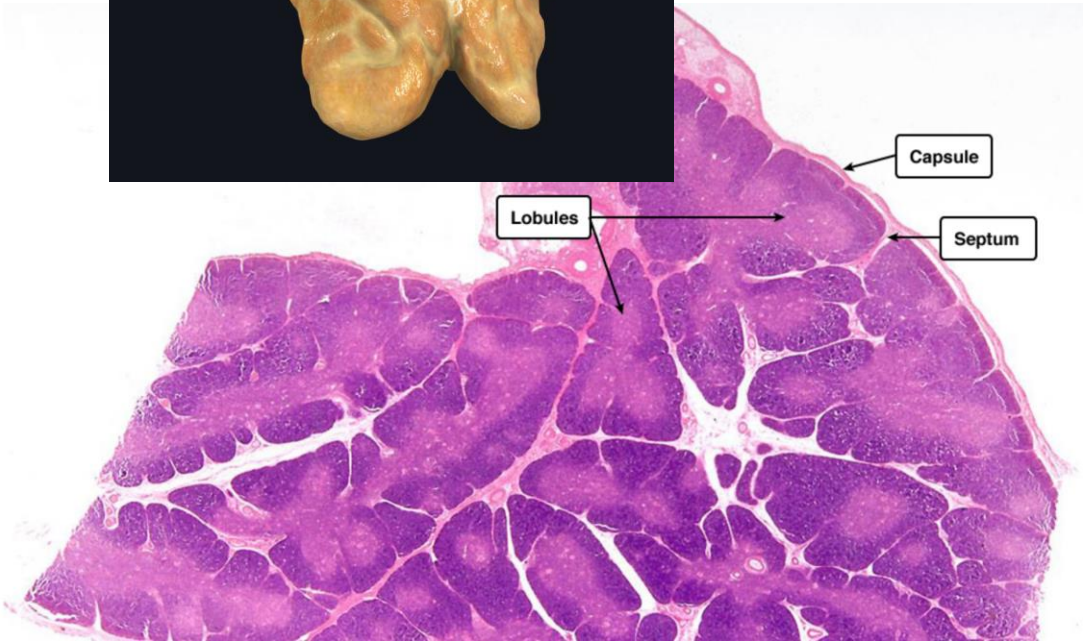
* After splenectomy, patients must receive extra vaccines, espicially against encapsulated bacteria.

THYMUS

- Thymus has a crucial role in T-cell maturation.
- Can be involved by lymphomas,particularly those of T-cell lineage.

▷ Prevents autoimmunity





THYMUS – Thymic hyperplasia

- Thymic enlargement often is ass/w the presence of lymphoid follicles, or germinal centers, in the medulla.
- These germinal centers contain reactive B cells, which are only present in small numbers in normal thymuses.
- Thymic follicular hyperplasia is found in most patients with myasthenia gravis and sometimes in other autoimmune diseases, such as systemic lupus erythematosus & rheumatoid arthritis.
- Removal of the hyperplastic thymus is often beneficial early in the disease.

20% of them have hyperpl. (MC) or Thymoma

THYMUS – Thymomas

- Thymomas are rare, most occur in middle-aged adults.
- 30% asymptomatic; 30-40% produced local manifestations (cough, dyspnea, and superior vena cava syndrome).
- The remainder were associated with a systemic disease, most commonly **myasthenia gravis (MG).**
- Thymoma is discovered in 15-20% of patients with MG, & removal of the tumor **often leads to improvement**.
- Thymomas may be associated with several other paraneoplastic syndromes; include (in rough order of frequency) pure red cell aplasia, hypogammaglobulinemia, and multiorgan autoimmunity.

THYMUS – Thymomas

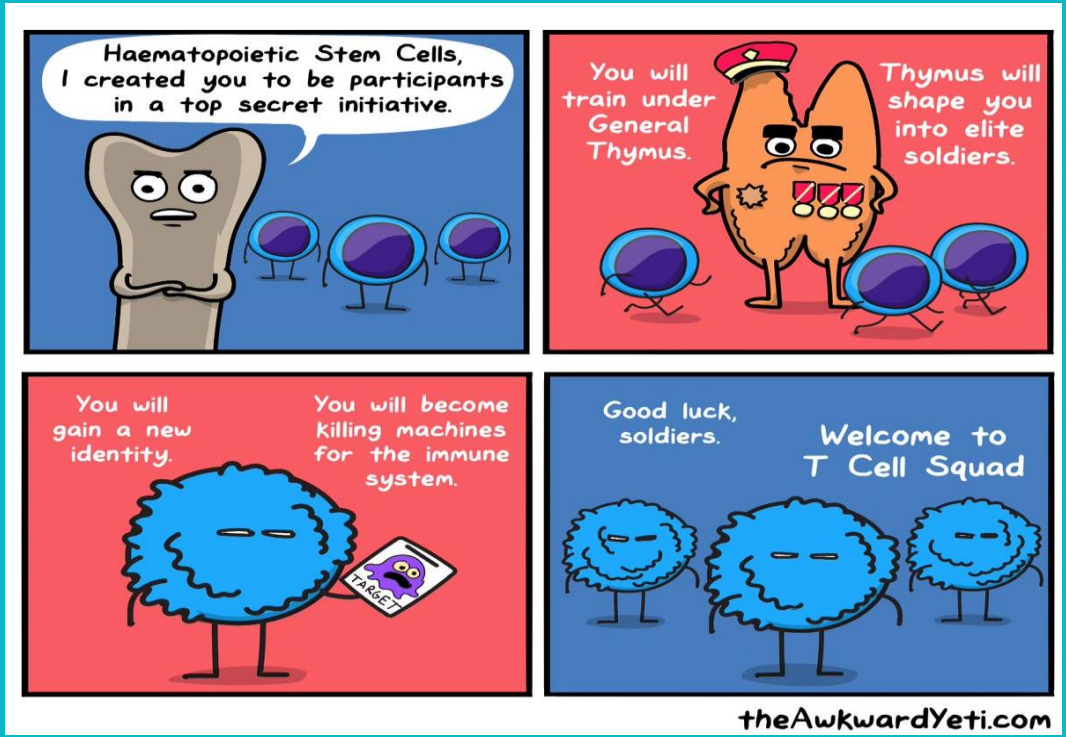
- Tumors of thymic epithelial cells.
- Several classification systems for thymoma based on cytologic & biologic. One simple & clinically Classification:

1. Benign or encapsulated thymoma: cytologically & biologically benign → resection if autoimmune
2. Malignant thymoma → infiltration حاملة benign حتى لو بتشبه الـ

Type I: cytologically benign but infiltrative & locally aggressive

Type II: (thymic carcinoma): cytologically & biologically malignant

thymic carcinoma → in thymic epithelial cells


Haematopoietic Stem Cells, I created you to be participants in a top secret initiative.
You will train under General Thymus.
Thymus will shape you into elite soldiers.
You will gain a new identity.
You will become killing machines for the immune system.
TARGET
Good luck, soldiers.
Welcome to T Cell Squad
theAwkwardYeti.com

”

Thank You