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.**

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

Cxs: 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?)

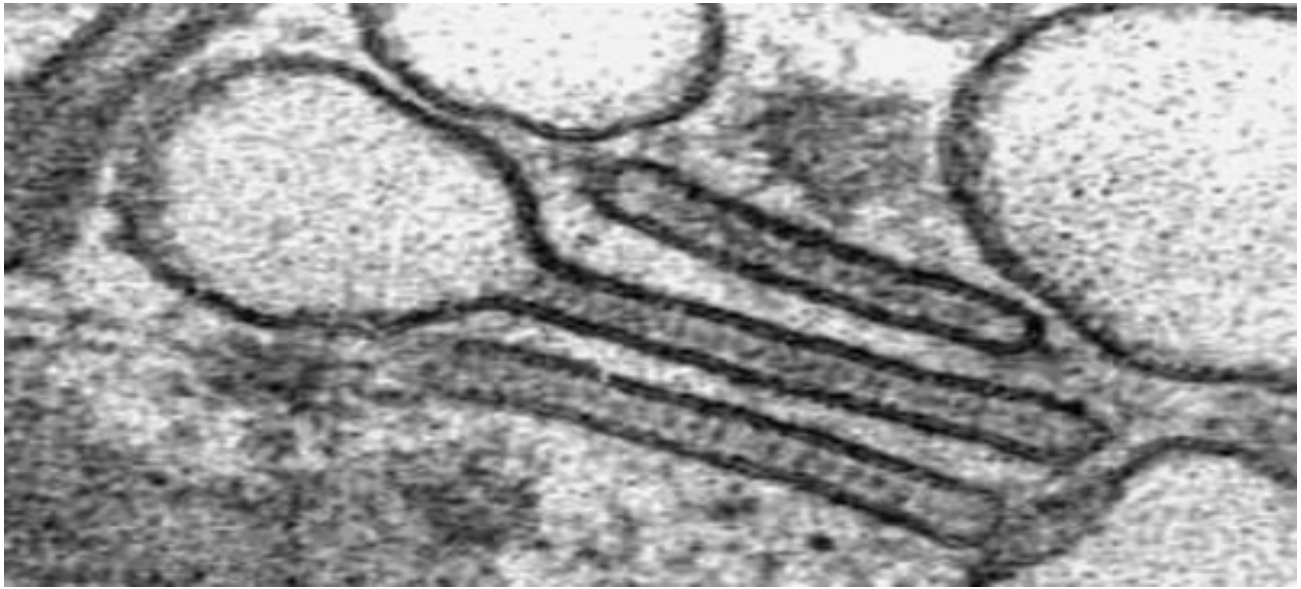
Langerhans Cell Histiocytoses

- 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

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

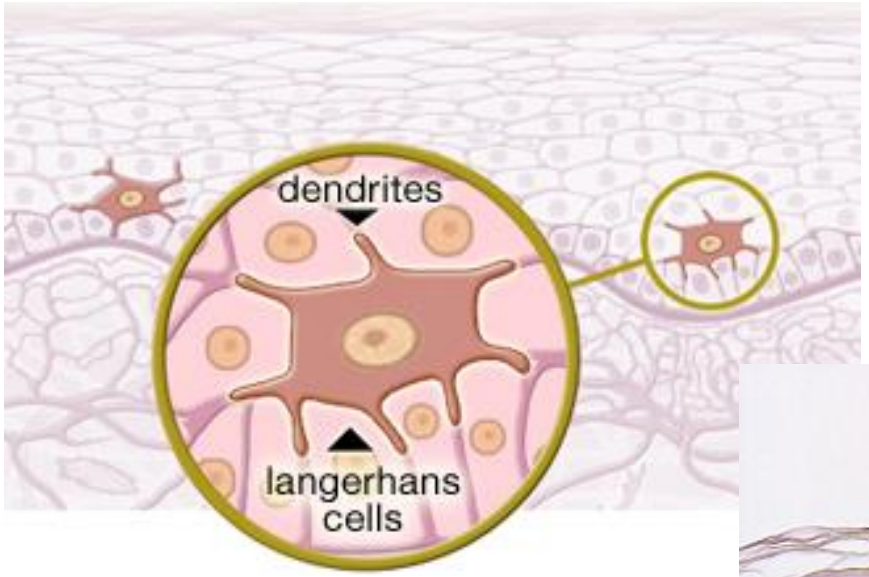
Langerhans Cell Histiocytoses – Birbeck granules

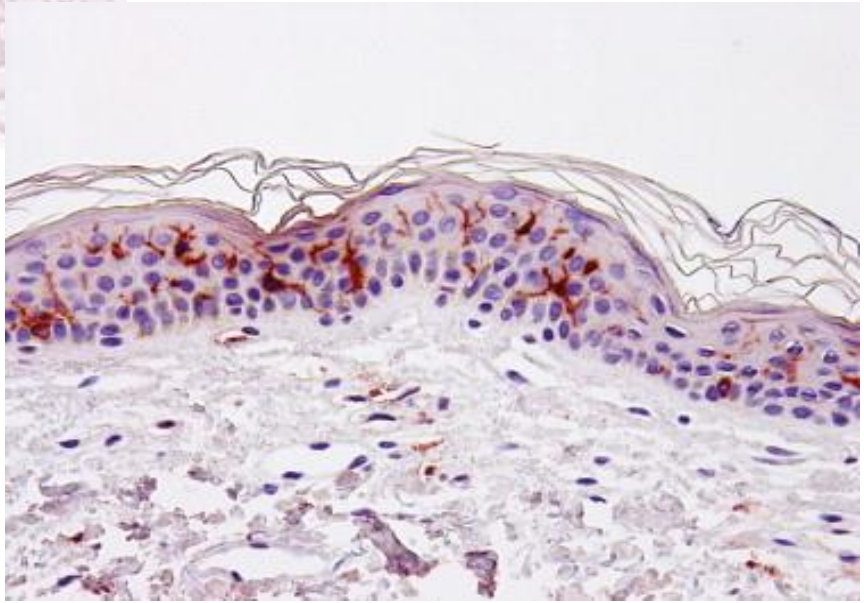


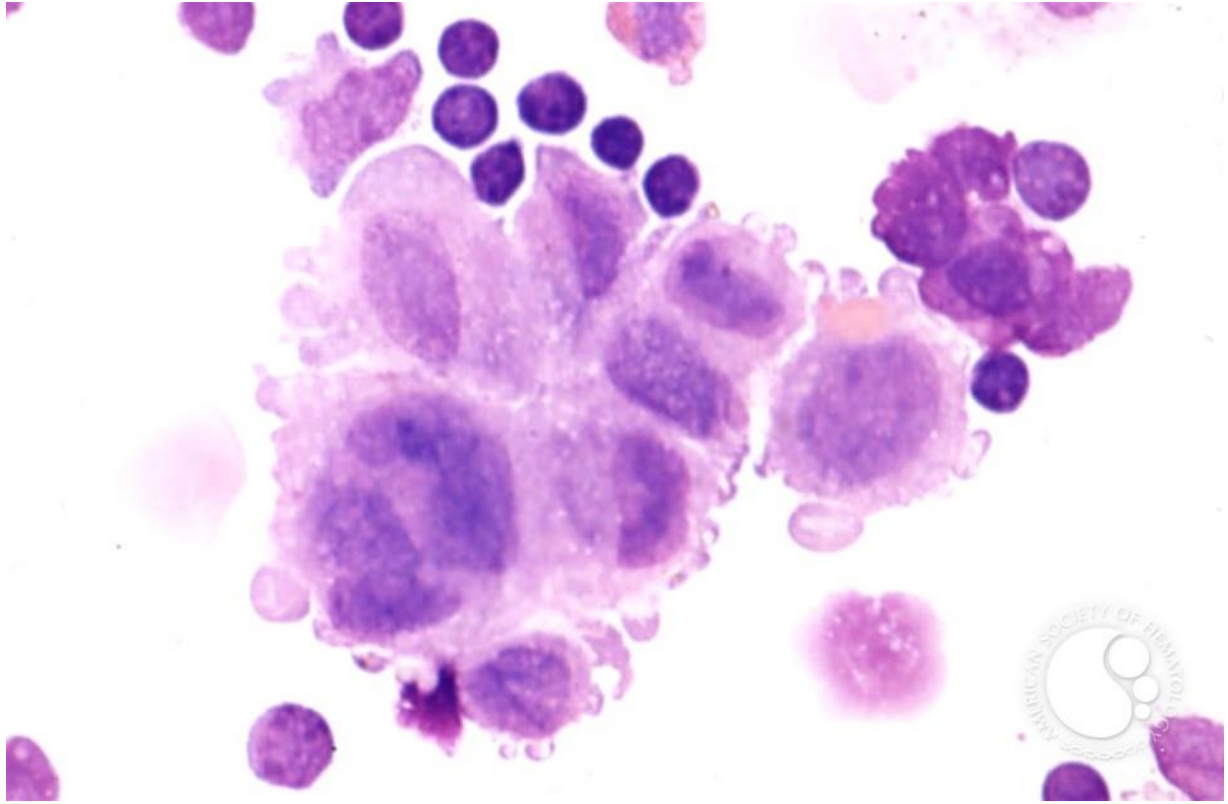
Electron microscope

Langerhans Cell Histiocytoses

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


dendrites
langerhans
cells





Langerhans Cell Histiocytoses – Pathogenesis

- The different clinical forms are frequently associated with an acquired mutation in the kinase BRAF → 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.

Langerhans Cell Histiocytoses

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

Multisystem Langerhans cell histiocytosis (Letterer-Siwe disease)

- Children younger than 2 years of age.
- Manifests with multifocal cutaneous lesions that grossly resemble seborrheic skin eruptions.
- Most affected patients have hepatosplenomegaly, lymphadenopathy, pulmonary lesions, and (later in the course) destructive osteolytic bone lesions.

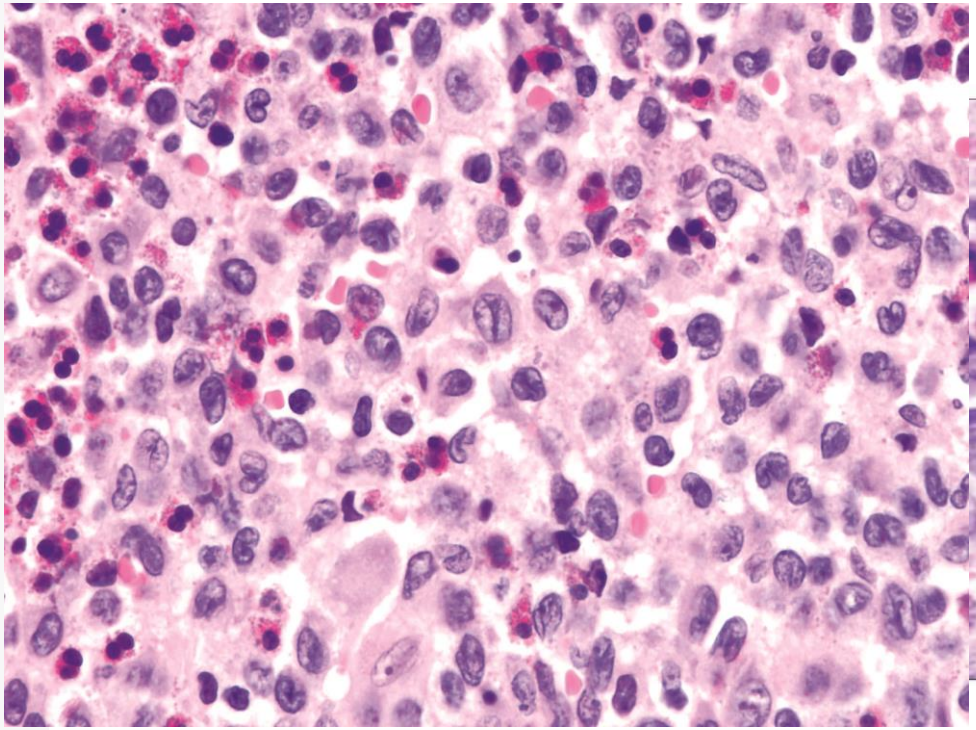
Multisystem Langerhans cell histiocytosis (Letterer-Siwe disease)

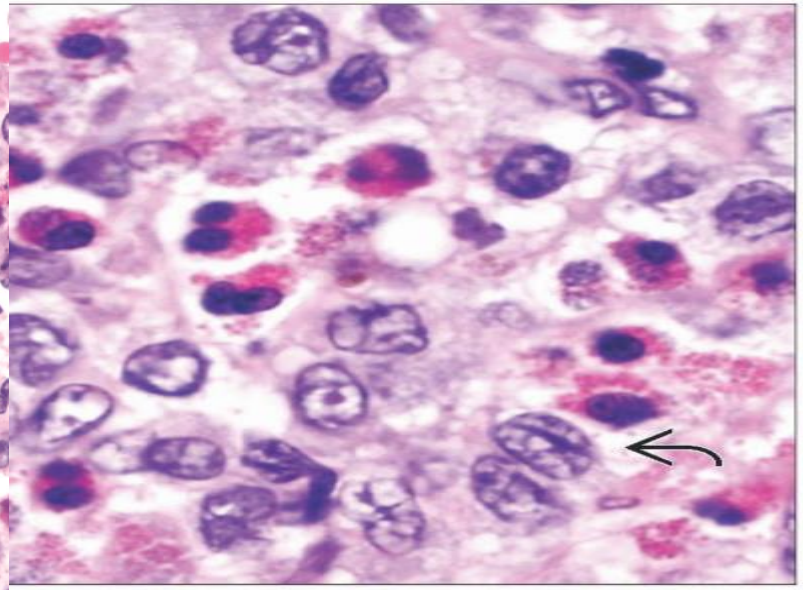
- Extensive marrow infiltration often leads to pancytopenia.
- The disease is **rapidly fatal** if untreated.
- With intensive chemotherapy, 50% of patients survive 5 years.

Unisystem Langerhans cell histiocytosis (eosinophilic granuloma)

- Unifocal or multifocal.
- Characterized by expanding accumulations of Langerhans cells, usually within 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.**

Unisystem Langerhans cell histiocytosis (eosinophilic granuloma) – morphology





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

- **Unifocal** disease most often involves a single bone.
- Asymptomatic or cause pain, 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**

- **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.
- 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**)
- **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.
- **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:

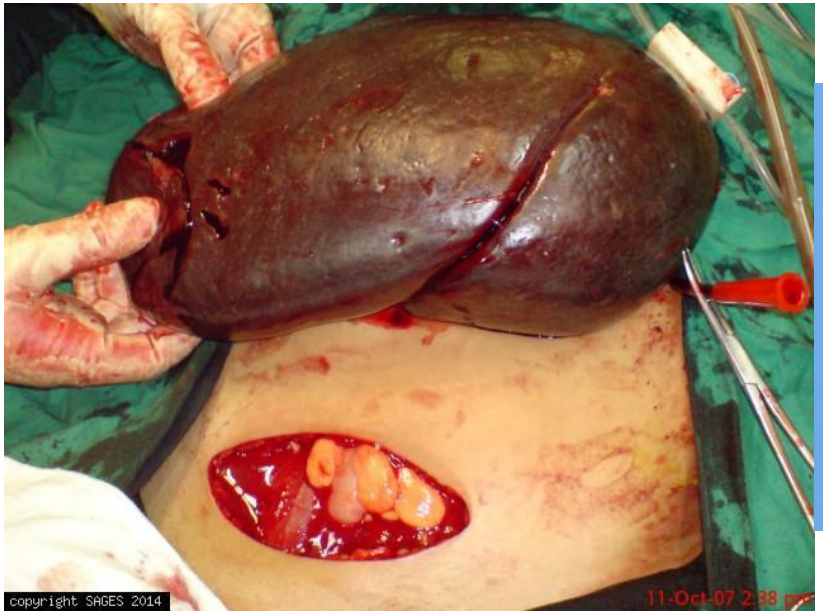
1. Massive splenomegaly (weight > 1000 g)

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

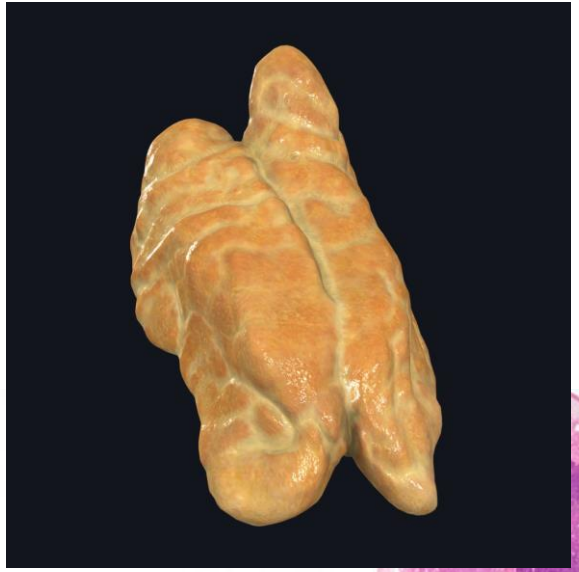
SPLENOMEGALY - Disorders

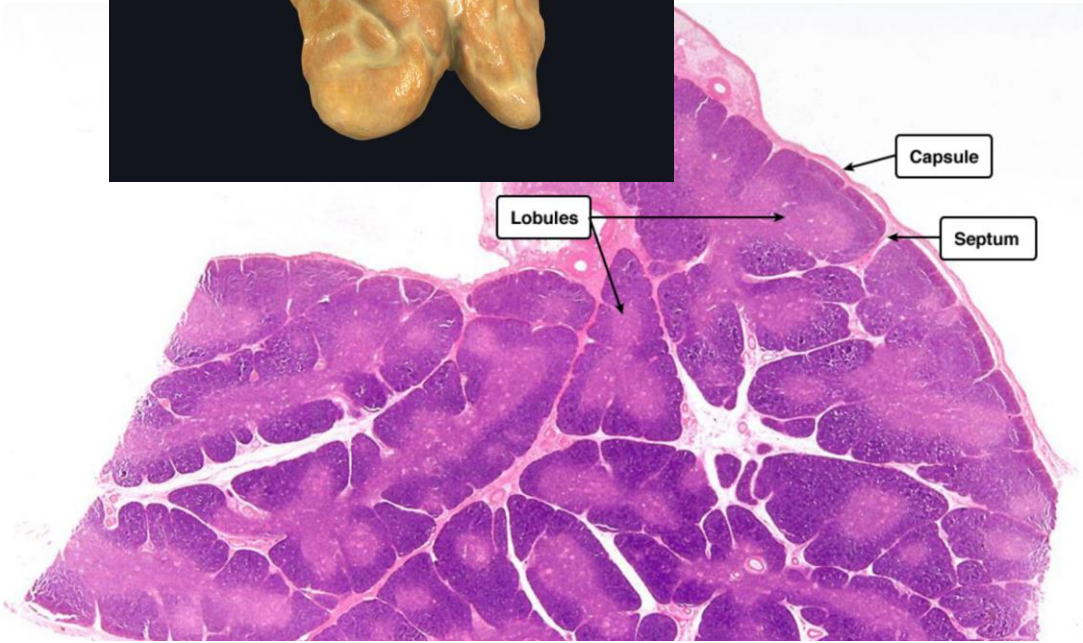


Normal

THYMUS

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





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.

THYMUS – Thymomas

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

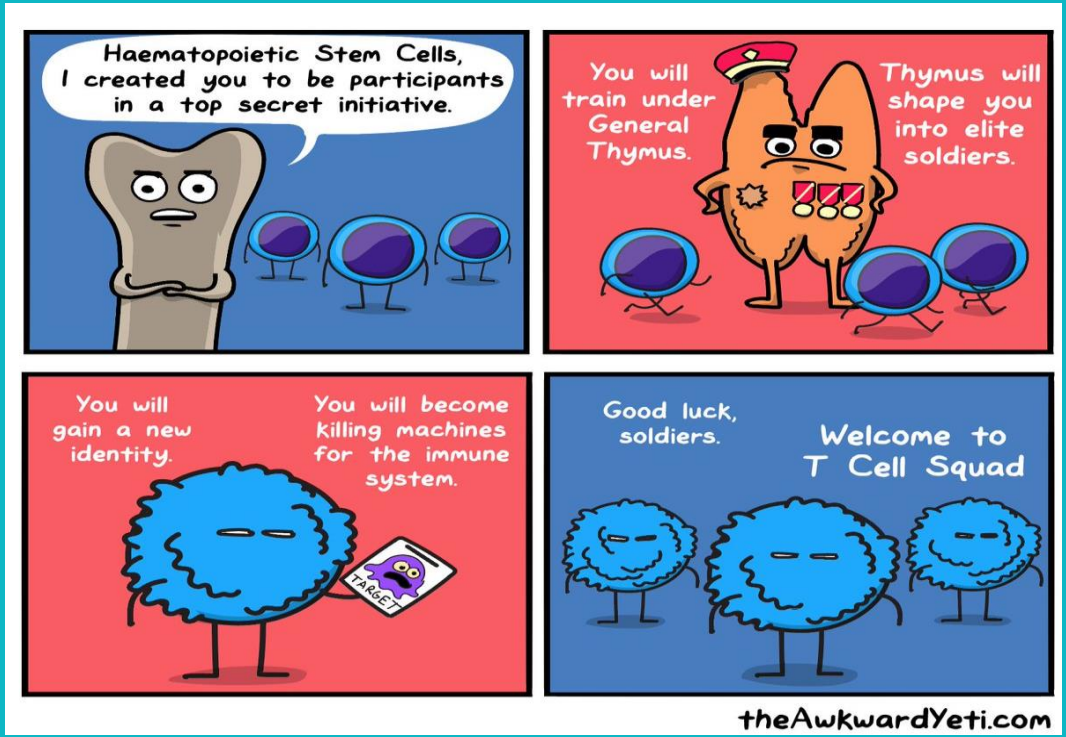
1. Benign or encapsulated thymoma: cytologically & biologically benign
2. Malignant thymoma

Type I: cytologically benign but infiltrative & locally aggressive

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

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.


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

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Thank You