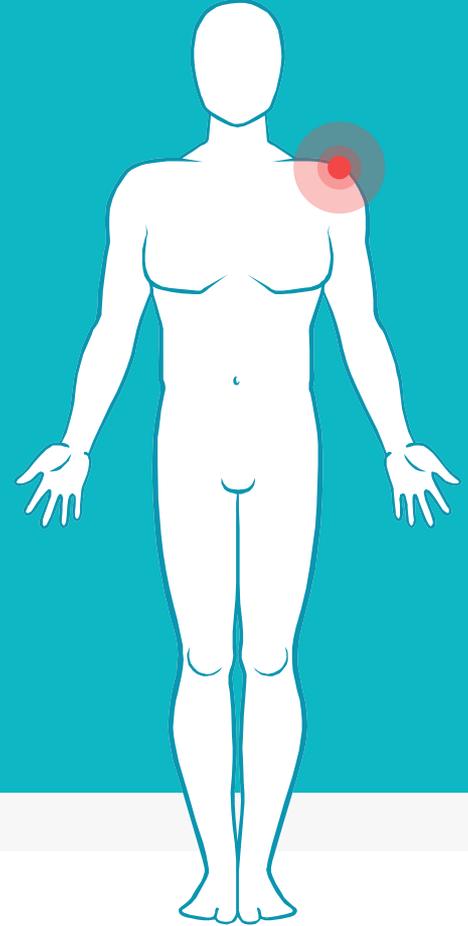
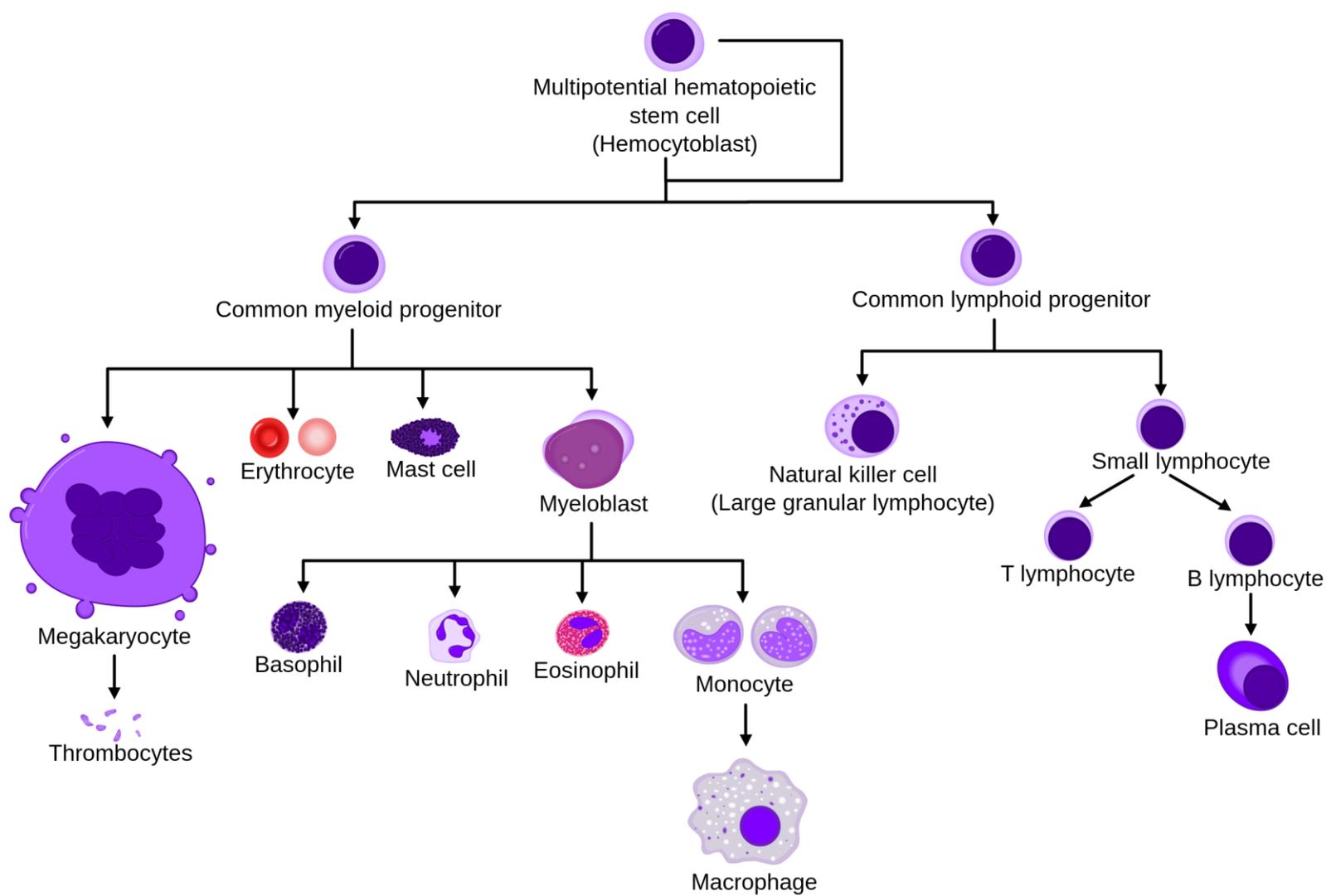


Hematopoietic & Lymphoid System

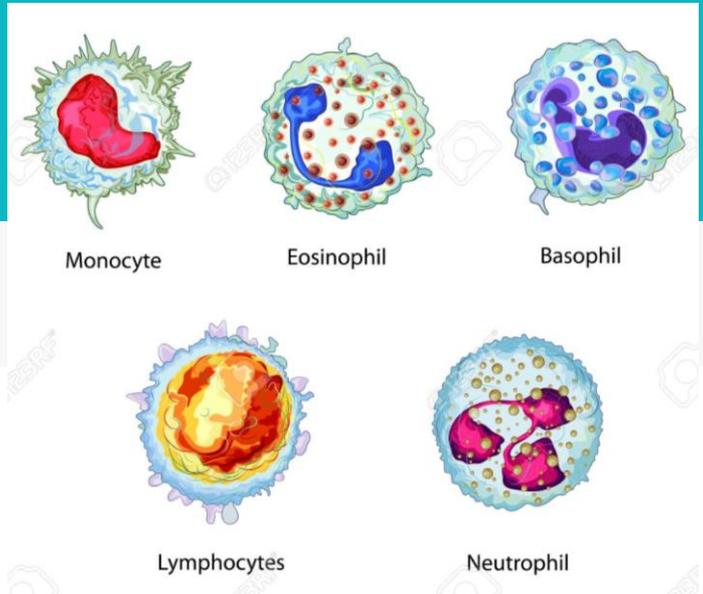
White Cell disorders



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1. Nonneoplastic disorders of white cells



- ▶ Disorders include **deficiencies** (abnormally low count → leukopenias) and **proliferations** (leukocytosis), which may be reactive or neoplastic.

Cell Type	
White cells ($\times 10^3/\mu\text{L}$)	4.8-10.8
Granulocytes (%)	40-70
Neutrophils ($\times 10^3/\mu\text{L}$)	1.4-6.5
Lymphocytes ($\times 10^3/\mu\text{L}$)	1.2-3.4
Monocytes ($\times 10^3/\mu\text{L}$)	0.1-0.6
Eosinophils ($\times 10^3/\mu\text{L}$)	0-0.5
Basophils ($\times 10^3/\mu\text{L}$)	0-0.2
Red cells ($\times 10^3/\mu\text{L}$)	4.3-5, men; 3.5-5, women
Platelets ($\times 10^3/\mu\text{L}$)	150-450

5 major types of WBCs

- ▶ Neutrophils
- ▶ Lymphocytes
- ▶ Monocytes
- ▶ Eosinophils
- ▶ Basophils

Neutropenia/Agranulocytosis

- ▶ Neutropenia: a reduction in the number of granulocytes in blood, when severe, agranulocytosis. (<500)
- ▶ Most common Leukopenia.
- ▶ Neutropenic persons are susceptible to severe, potentially fatal bacterial and fungal infections.
- ▶ Two major mechanisms:
 - ❖ Decrease production
 - ❖ Increase peripheral destruction of neutrophils

Neutropenia/Agranulocytosis

Decrease production

- ▶ Marrow hypoplasia in patients who receive chemotherapy or radiation therapy
- ▶ Leukemia or other tumors replacing the marrow
- ▶ Medications
- ▶ Certain types of neoplastic lymphocytic proliferations involving marrow.

Neutropenia/Agranulocytosis

Increased peripheral destruction/consumption:

- ▶ Autoimmune destruction
- ▶ Overwhelming bacterial, fungal or rickettsial infection (peripheral use)
- ▶ Splenomegaly (sequestration & accelerated removal of neutrophils.)

Neutropenia/Agranulocytosis

Clinical features:

- ▶ **Infections**
- ▶ Fever, chills, malaise.
- ▶ Mucocutaneous necrotizing ulcers
- ▶ High risk of sepsis

Tx: broadspectrum antibiotics (bacterial and fungal), granulocyte colony-stimulating factor (G-CSF).

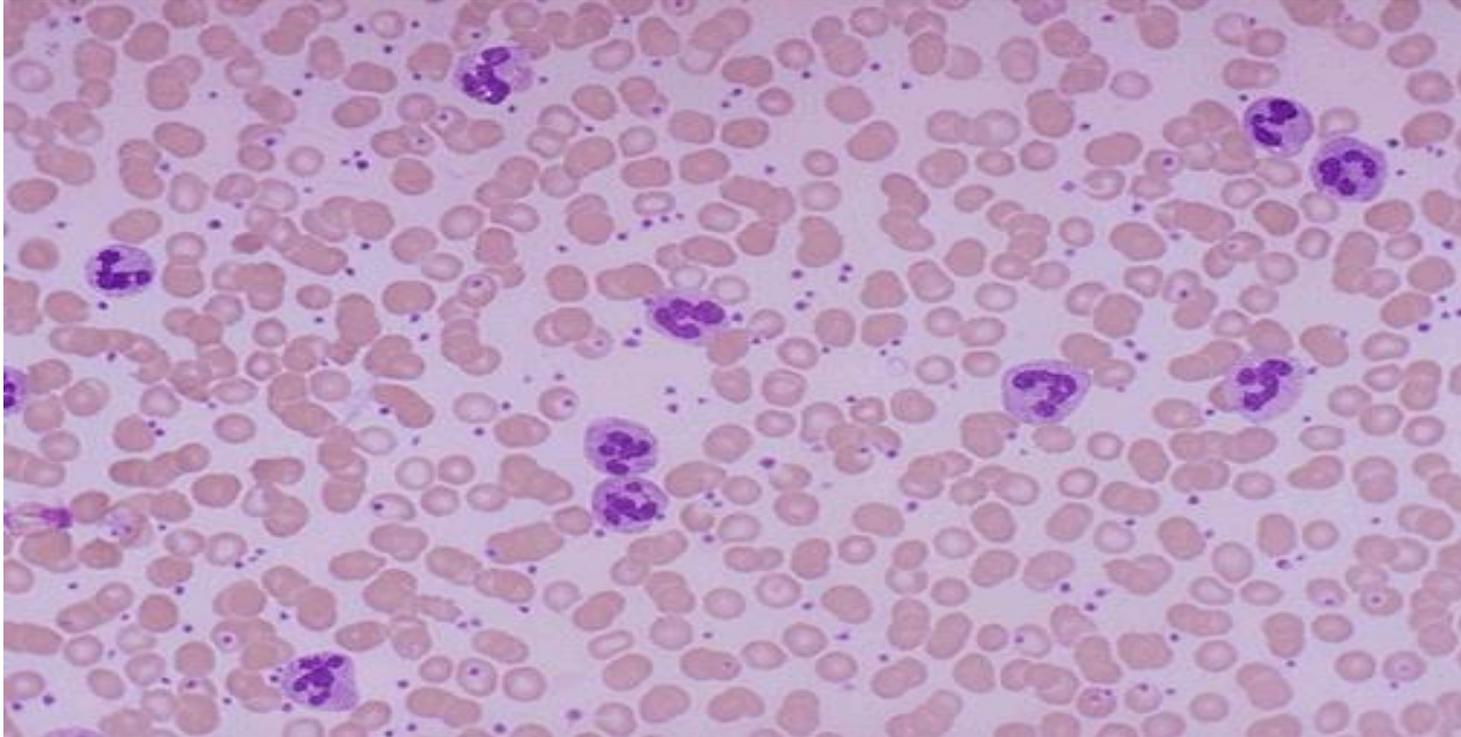
Lymphopenia

- ▶ Much less common.
- ▶ Associated with rare congenital immunodeficiency diseases, advanced human immunodeficiency virus (HIV) infection, & high doses of corticosteroids Tx.
- ▶ Certain acute viral infections → stems from lymphocyte redistribution (to lymph nodes & increased adherence to endothelial cells) rather than a decrease in the number.

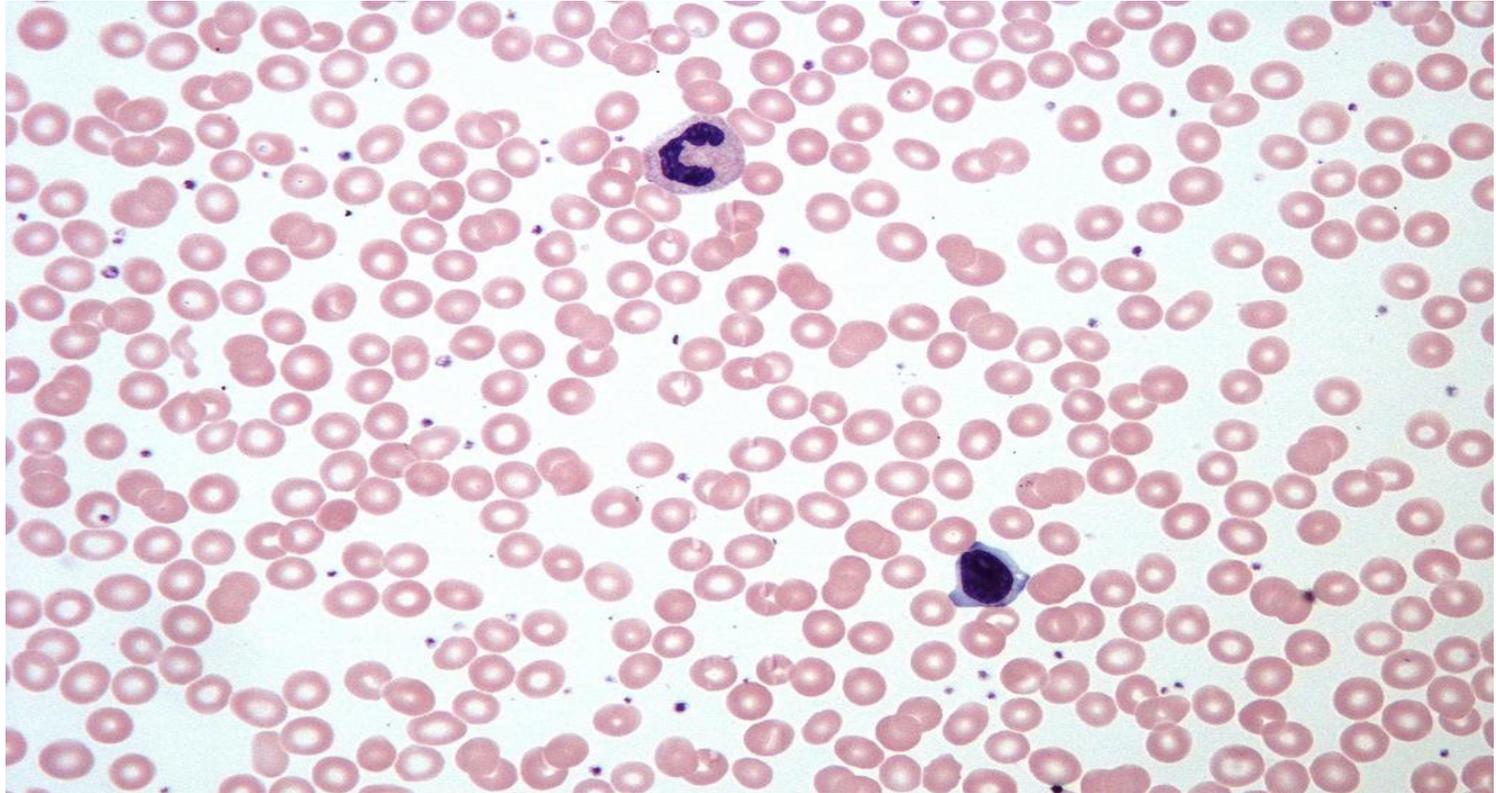
Leukocytosis

- ▶ Increase in the number of white cells in the blood.
- ▶ A common reaction to a variety of inflammatory states.
- ▶ Leukocytoses are relatively nonspecific and are classified according to the particular white cell series that is affected:
 - 1) **Neutrophilic**: Acute bacterial infections, sterile inflammation caused by tissue necrosis or burn.

Leukocytosis - neutrophilia



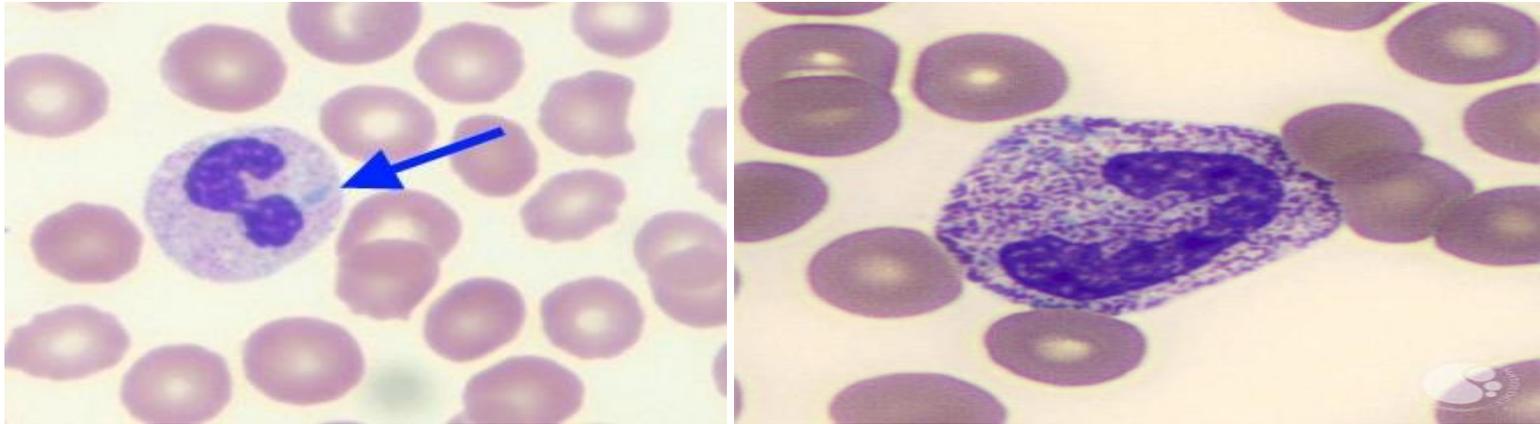
Normal Blood film



Leukocytosis - neutrophilia

In sepsis or severe inflammation neutrophilia is accompanied by morphologic changes:

- + cytoplasmic vacuoles
- + Toxic granules, coarser & darker than normal granules
- + **Döhle bodies**: patches of dilated ER (appear → sky-blue cytoplasmic “puddles.”)



Leukocytosis

- ▶ **Eosinophilic:** (eosinophilia) Allergic disorders (e.g., asthma), parasitic infestations or drugs.
- ▶ **Basophilic:** (basophilia) Rare, often indicative of a myeloproliferative disease.
- ▶ **Monocytosis** Chronic infections (e.g., tuberculosis), autoimmune disorders; inflammatory bowel diseases.
- ▶ **Lymphocytosis;** chronic immunologic stimulation (e.g., tuberculosis, brucellosis); viral infections (e.g., HAV, CMV, EBV).

Leukemoid reaction

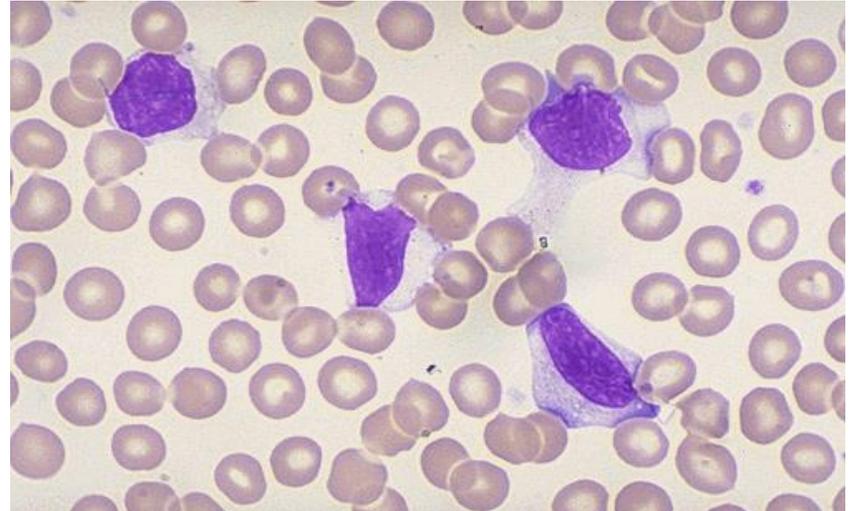
- ▶ Happens in severe infections, many immature granulocytes appear in the blood, mimicking a myeloid leukemia
- ▶ must be differentiated from true white cell malignancies. (e.g., CML);
 - +Younger age,
 - +No BCR/ABL fusion gene
 - +Subsides with treatment of underlying infection

Infectious mononucleosis

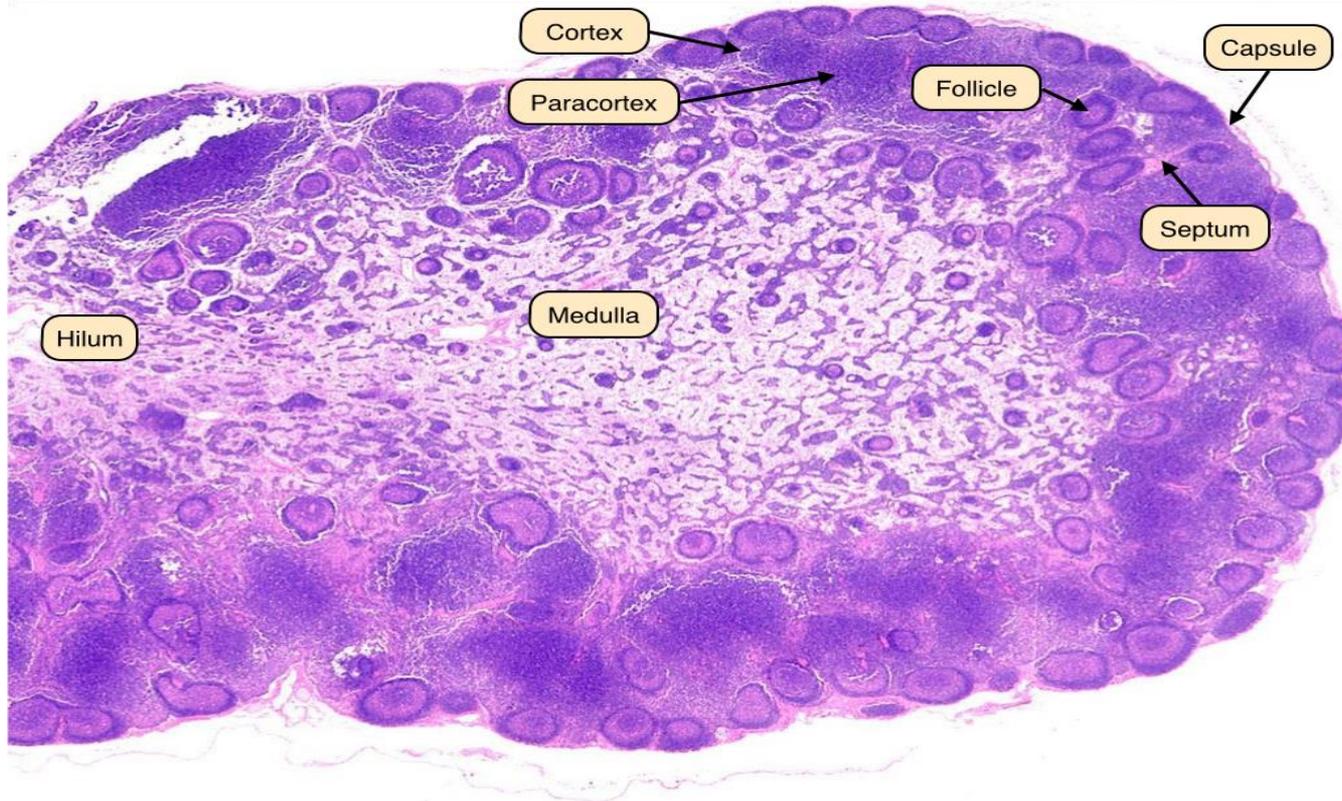
- ▶ Acute, self-limited disease of adolescents & young adults.
- ▶ Caused by Epstein-Barr virus (EBV), herpesvirus family.
- ▶ EBV invades B-cells & cause them to proliferate, cytotoxic (CD8+ T-cells) respond against B-cells.
- ▶ Usually present with:
 1. Fever, sore throat, generalized lymphadenitis
 2. Lymphocytosis of activated CD8+ T cells. (up to 18,000)

Infectious mononucleosis

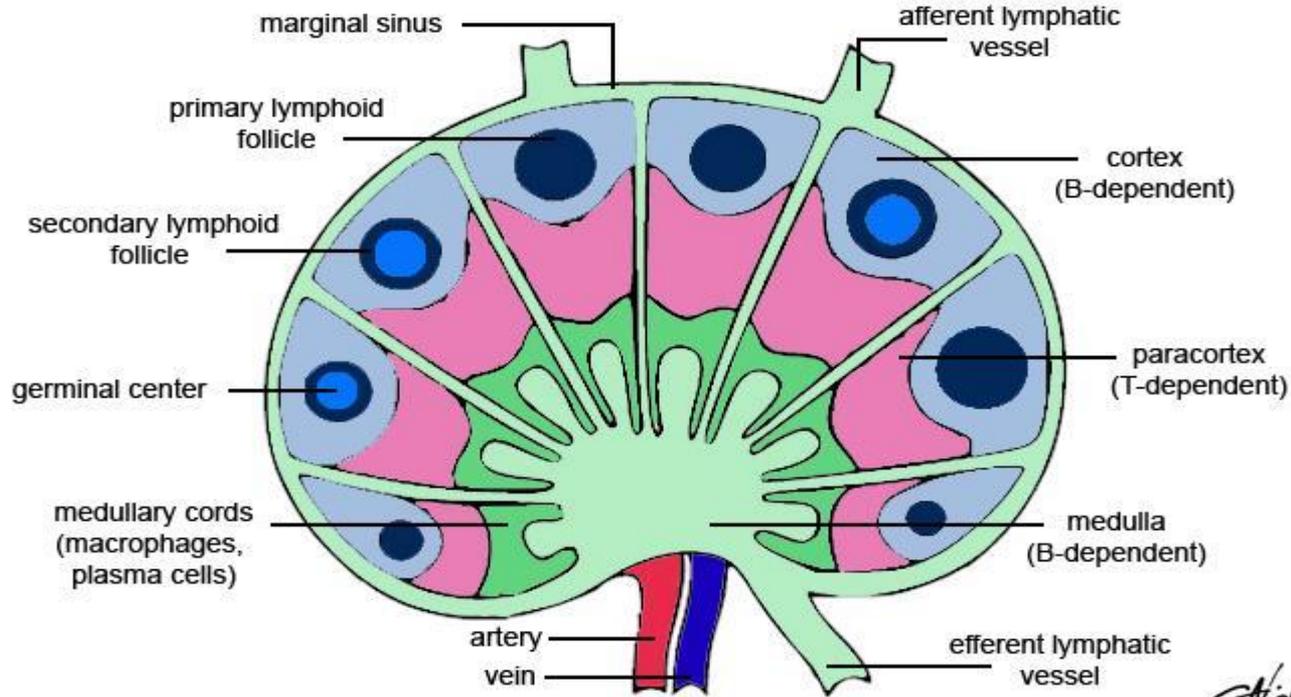
- ▶ More than half of these cells are large atypical lymphocytes; with an oval, indented, or folded nucleus & abundant cytoplasm with a few azurophilic granules



Reactive Lymphadenitis



Reactive Lymphadenitis



Reactive Lymphadenitis

Acute Nonspecific Lymphadenitis

- Can be:
 - Localized → draining a local infection.
 - Generalized → systemic infectious & inflammatory conditions
- Inflamed nodes are swollen & tender.
- With infection control lymph nodes may revert to a normal appearance or, if damaged, undergo scarring.

Reactive Lymphadenitis

Histologic morphology:

- ▶ Large follicles with germinal center formation
- ▶ Frequent GC mitoses & macrophages
- ▶ Sinus enlargement with histiocytes
- ▶ Parafollicular neutrophils, necrosis and possible pus formation (If pyogenic microbes)

Reactive Lymphadenitis

Chronic Nonspecific Lymphadenitis

- ▶ Depending on the causative agent, chronic nonspecific lymphadenitis can assume one of three patterns:
 - 1) Follicular hyperplasia. B-cells
 - 2) Paracortical hyperplasia. T-cells
 - 3) Sinus histiocytosis. Macrophages

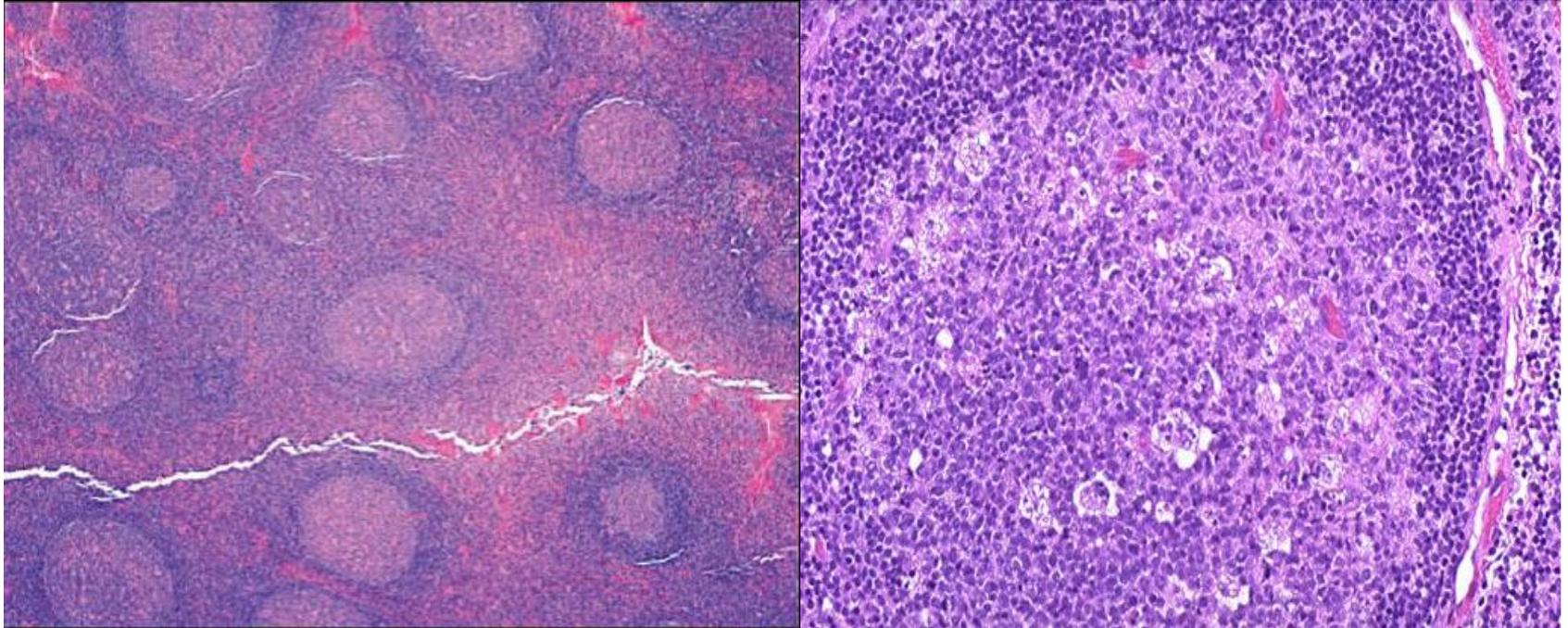
Reactive Lymphadenitis

Chronic Nonspecific Lymphadenitis - Follicular hyperplasia.

- ▶ Stimuli that activate humoral immune responses.
- ▶ defined by the presence of large germinal centers (secondary follicles), With tingible-body macrophages
- ▶ Causes include rheumatoid arthritis, toxoplasmosis, & early stages of infection with HIV

Reactive Lymphadenitis

Chronic Nonspecific Lymphadenitis - Follicular hyperplasia.



Reactive Lymphadenitis

Chronic Nonspecific Lymphadenitis - Follicular hyperplasia.

This form of hyperplasia is morphologically similar to follicular lymphoma, Features **favoring** a reactive (nonneoplastic) hyperplasia include:

- (1) preservation of the lymph node architecture.
- (2) Variation in the shape and size of the follicles.
- (3) Frequent GC mitotic figures & phagocytic macrophages, & recognizable light and dark zones. (absent in neoplastic follicles)

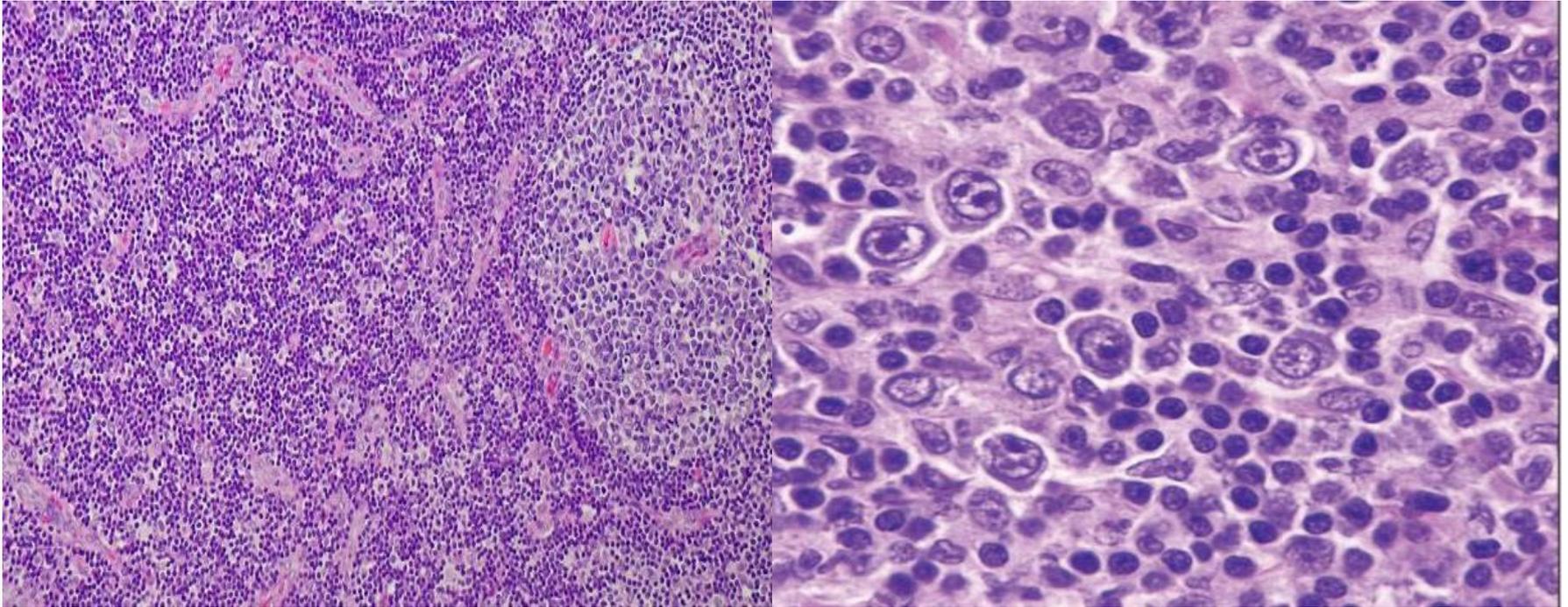
Reactive Lymphadenitis

Chronic Nonspecific Lymphadenitis - Paracortical hyperplasia

- ▶ Caused by immune reactions involving the T cell regions.
- ▶ Activated parafollicular T cells transform into large proliferating immunoblasts → that efface B cell follicles.
- ▶ Encountered in:
 - 1) viral infections
 - 2) vaccinations (e.g., smallpox).
 - 3) Drugs induced immune reactions (phenytoin)

Reactive Lymphadenitis

Chronic Nonspecific Lymphadenitis - Paracortical hyperplasia



Reactive Lymphadenitis

Chronic Nonspecific Lymphadenitis - Sinus Histiocytosis

- ▶ Distention and prominence of the lymphatic sinusoids,
due to:
 - 1) Marked hypertrophy of lining endothelial cells.
 - 2) An infiltrate of macrophages (histiocytes).
- ▶ In lymph nodes draining cancers.
- ▶ Represent an immune response to the tumor or its products.

Reactive Lymphadenitis

Chronic Nonspecific Lymphadenitis - Sinus Histiocytosis

