Lymphoma

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LEARNING OBJECTIVES

- Definition
- Concepts
- Classification
- Epidemiology
- Clinical presentation
- Diagnosis
- Staging
- Types of lymphoma

How Lymphoma Develops

- Normal cells are programmed to multiply, die when they're old
- Signals to multiply and die are controlled by specific genes
- Mutations can occur in these genes
- If enough mutations occur in genes controlling growth or cell death a cell begins to **multiply uncontrollably**
- The cell has then become cancerous or "malignant"

Features common to cancer cells

- Growth in the absence of “go” signals
- Growth despite “stop” signals
- Locally invasive growth and metastases to distant sites

Hematopoietic Malignancies

- ***Lymphoma*** *is used for* proliferations that arise as discrete tissue masses.

- ***Leukemia*** *is used for neoplasms that present with widespread* involvement of the bone marrow and (usually, but not always) the peripheral blood.

What is the Lymphatic System?

- Made up of organs, such as the tonsils, spleen, liver, bone marrow and a network of lymphatic vessels that connect glands, called lymph nodes
- Lymph nodes located throughout the body
- Lymph nodes filter foreign particles out of the lymphatic fluid
- Contain B and T lymphocytes

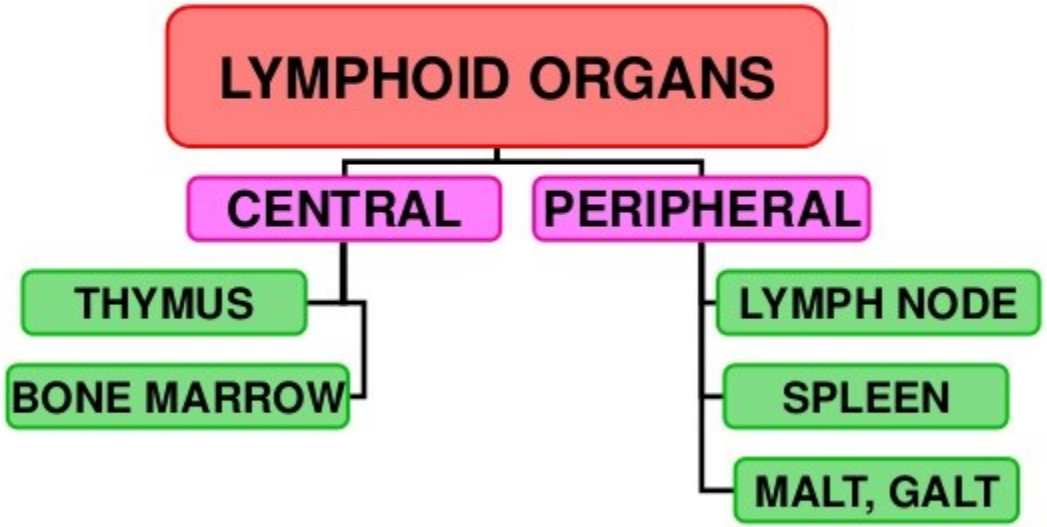
Lymphatic System

- Lymph nodes act as a filter to remove bacteria, viruses, and foreign particles

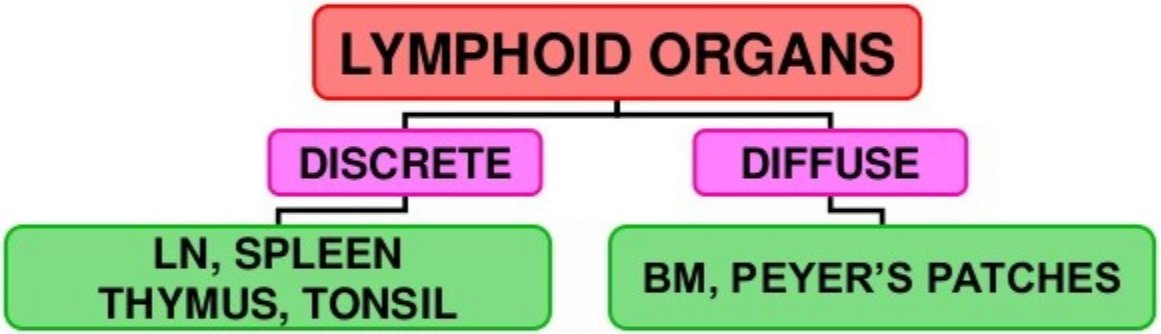
- Most people will have had “swollen glands” at some time as a response to infection

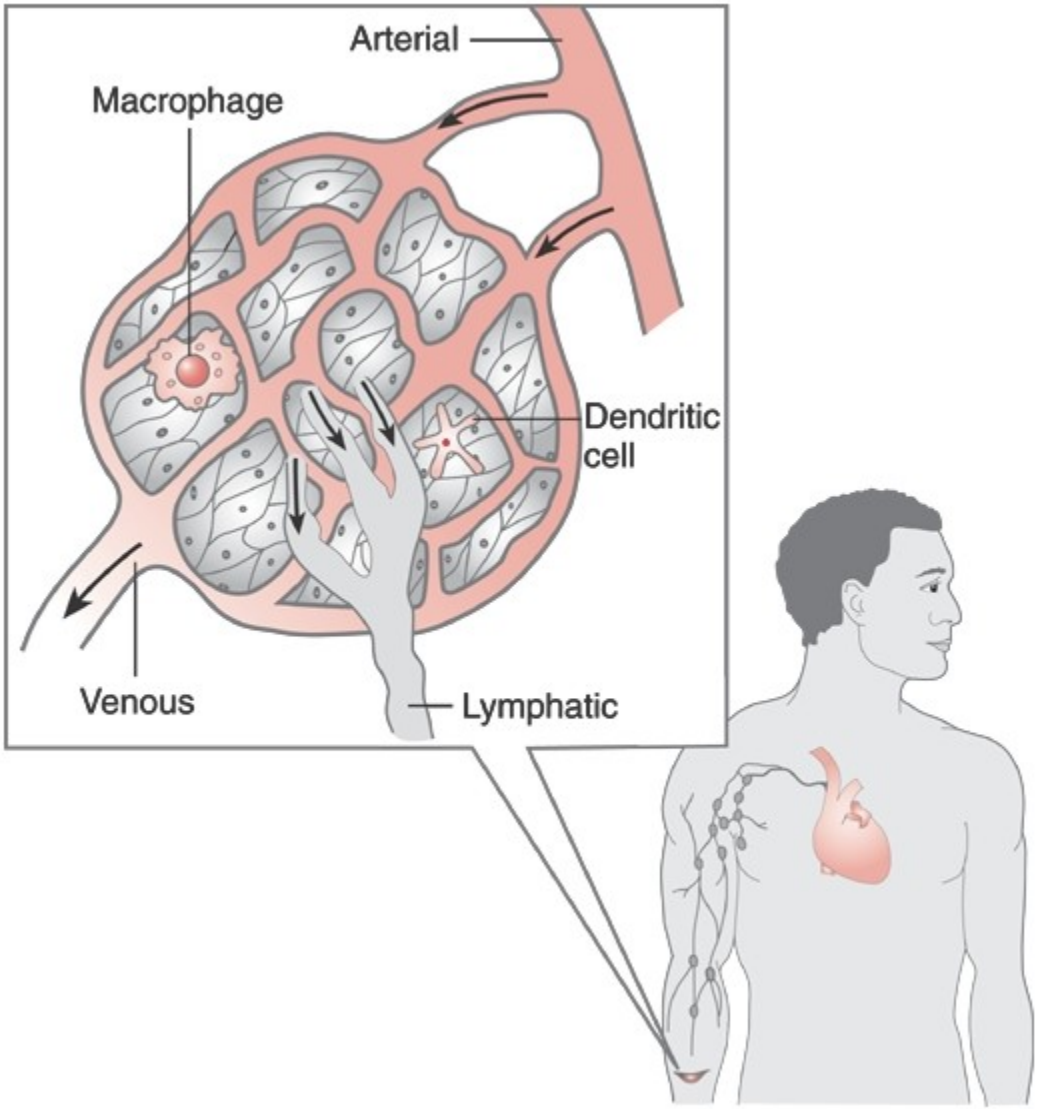
CLASSIFICATION

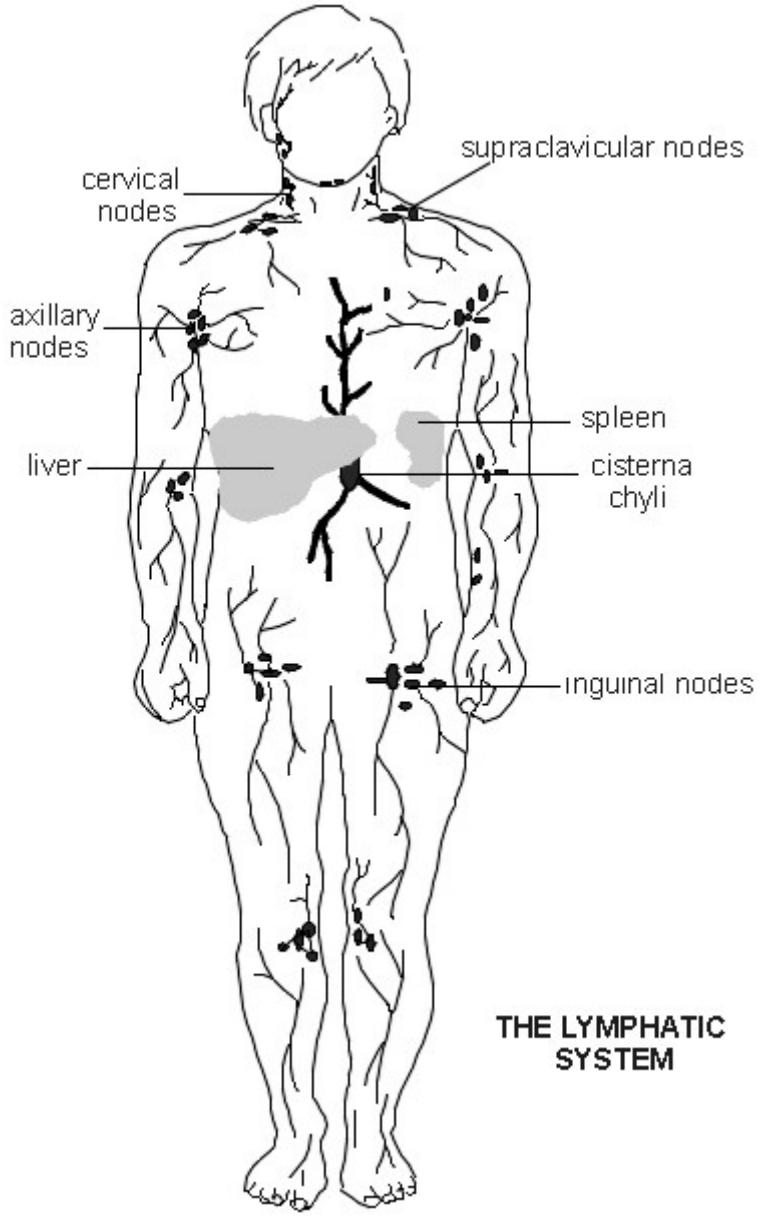
I. FUNCTIONAL



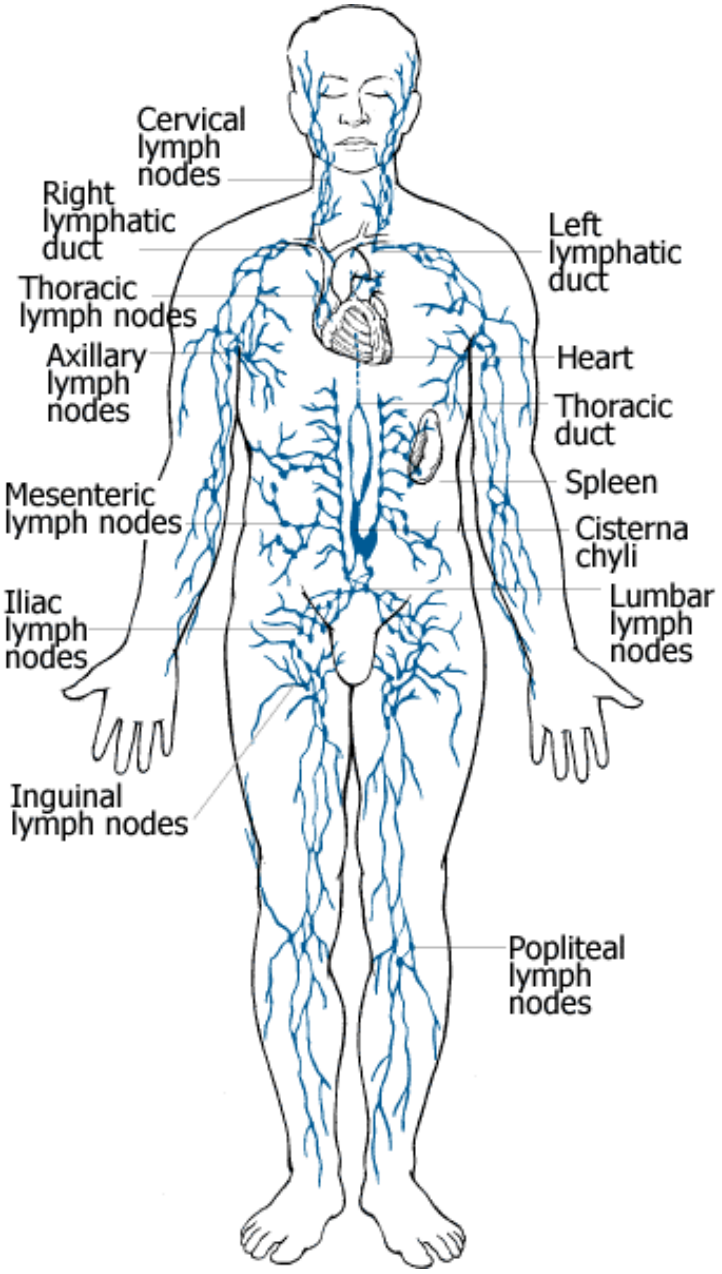
II. MORPHOLOGICAL



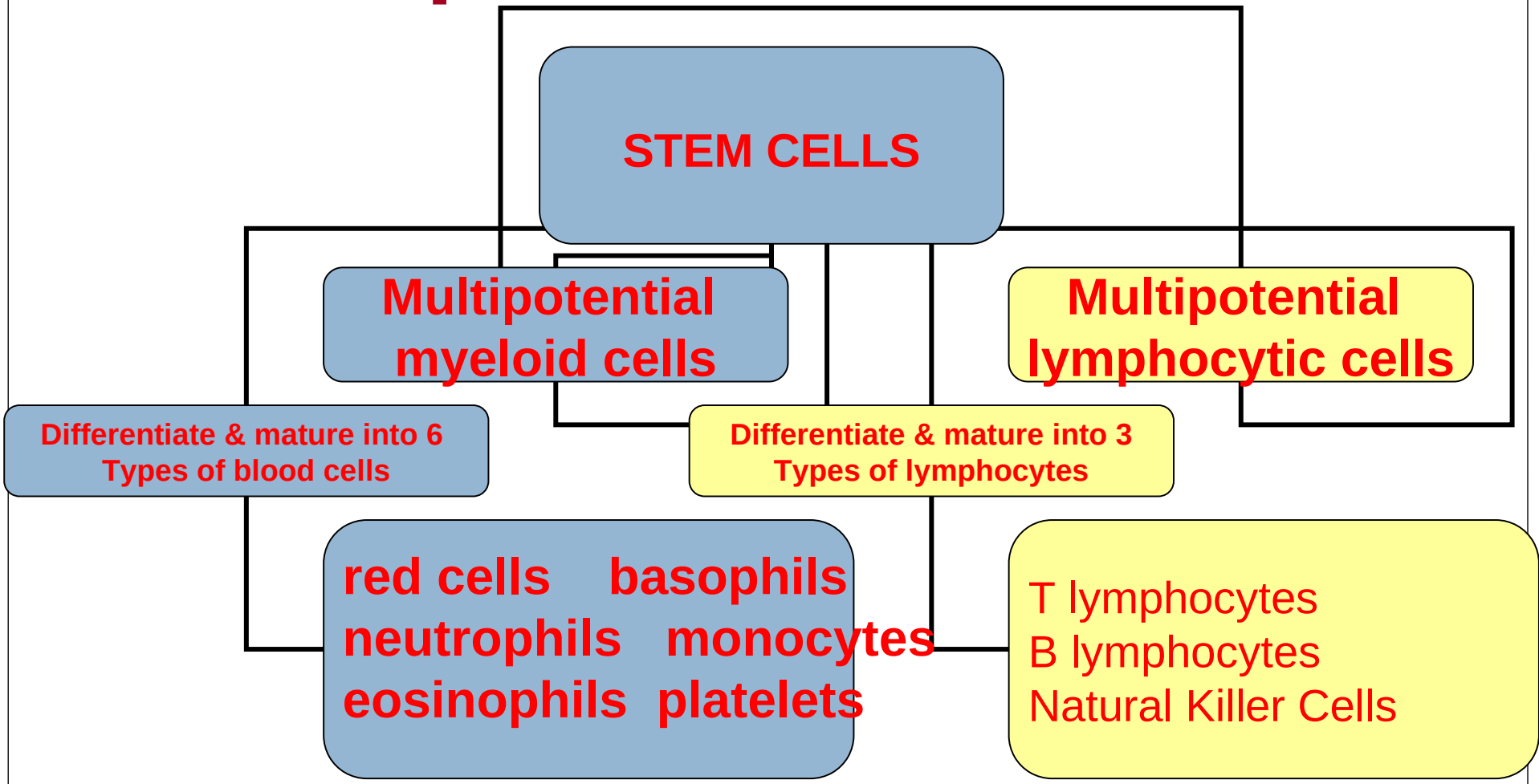




THE LYMPHATIC SYSTEM



Blood Cell and Lymphocyte Development



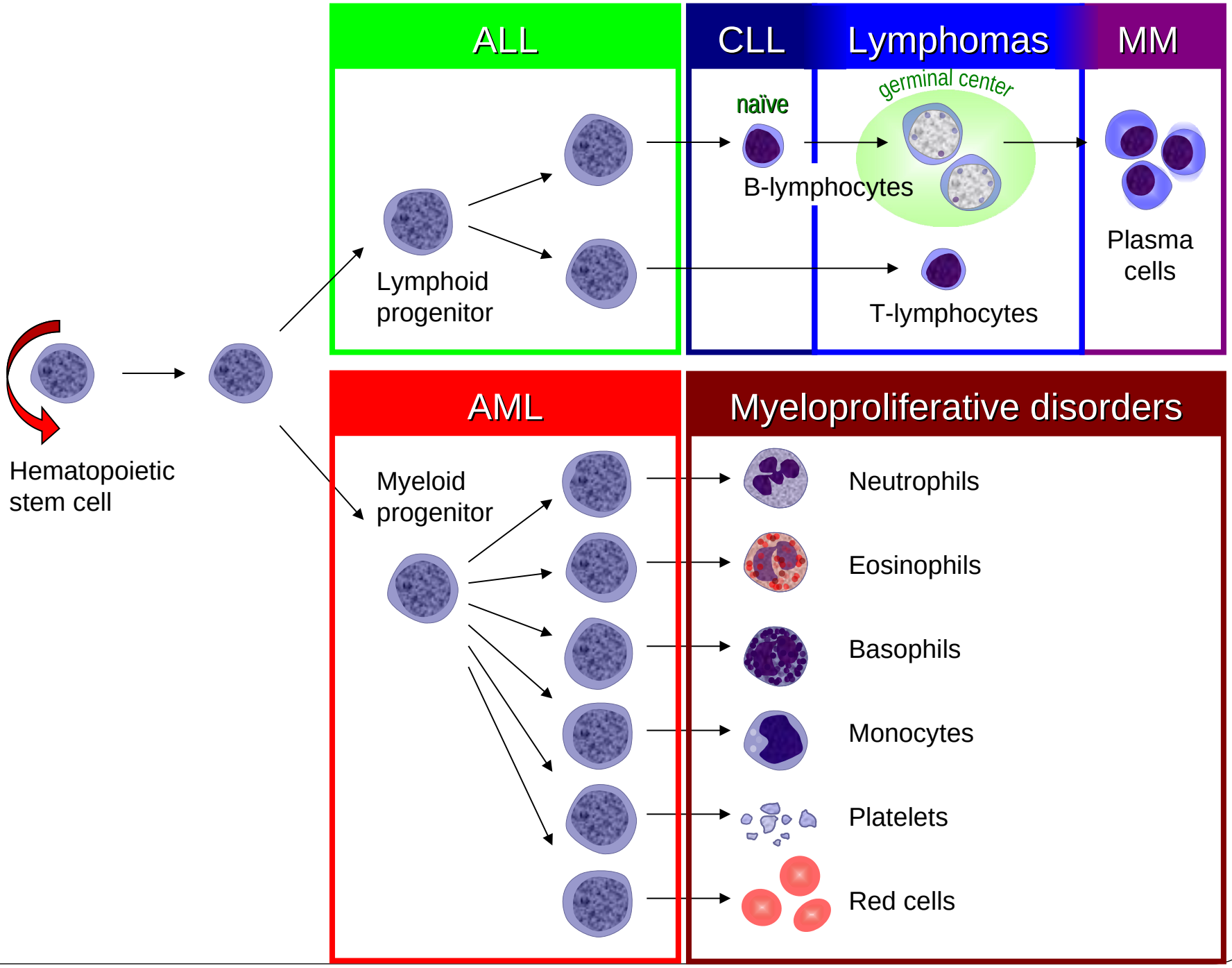
Lymphocytes

- Most lymphocytes are in lymph nodes, spleen, bone marrow and lymphatic vessels
- 20% of white blood cells in blood are lymphocytes
- T cells, B cells, natural killer cells
- B cells produce antibodies that help fight infectious agents
- T cells help B cells produce antibodies and they fight viruses

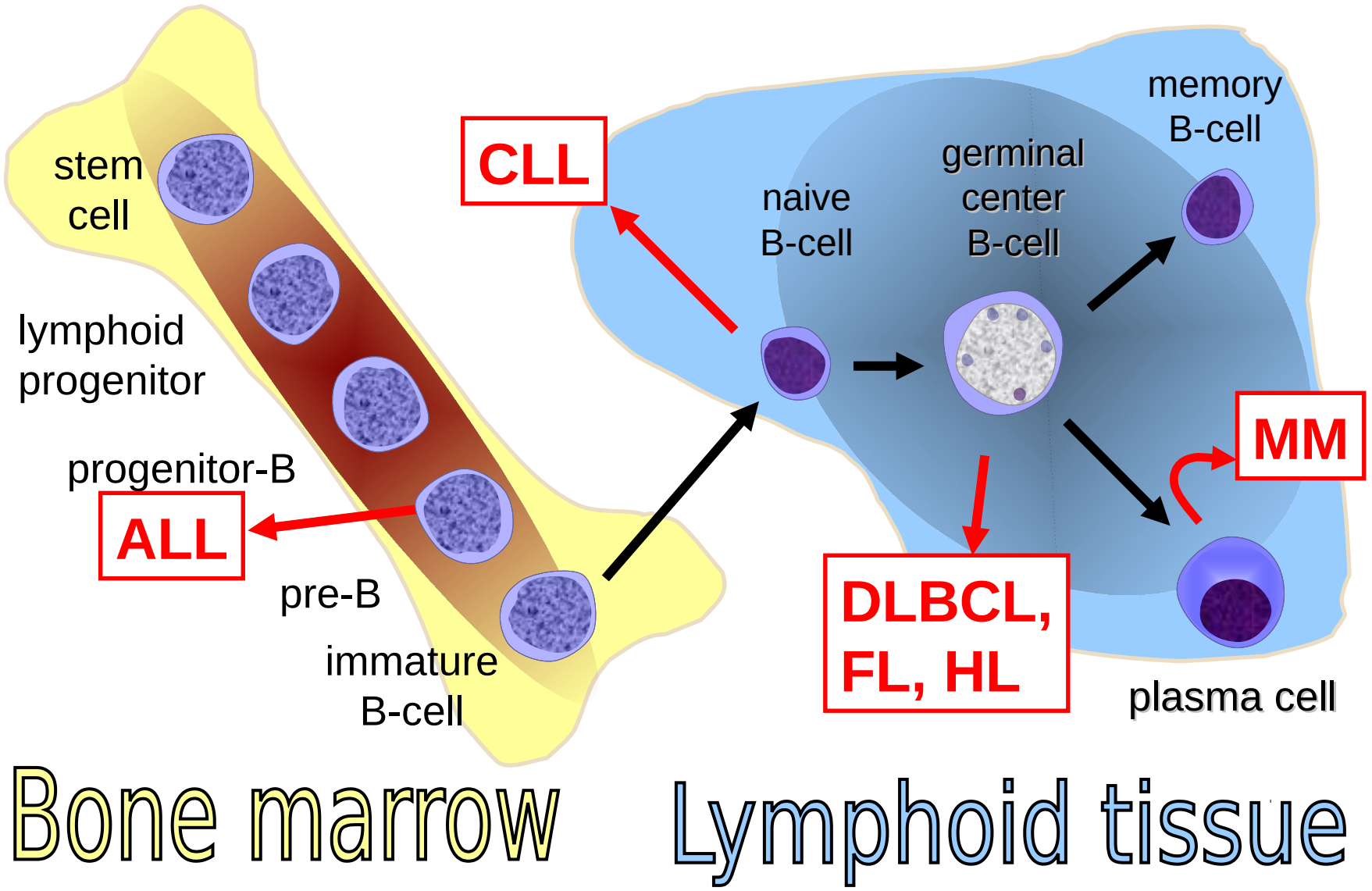
T-Cells and B-Cells

- **Immature lymphocytes that travel to the thymus differentiate into T-Cells**
  - **“T” is for thymus**

- **Immature lymphocytes that travel to the spleen or lymph nodes differentiate into B cells**
  - **"B" stands for the bursa of Fabricius, which is an organ unique to birds, where B cells mature.**


ALL
CLL
Lymphomas
MM
naïve
germinal center
B-lymphocytes
Plasma cells
Lymphoid progenitor
T-lymphocytes
Hematopoietic stem cell
AML
Myeloproliferative disorders
Myeloid progenitor
Neutrophils
Eosinophils
Basophils
Monocytes
Platelets
Red cells

B-cell development



What is Lymphoma

- Lymphomas are cancers that begin by the “malignant transformation” of a lymphocyte in the lymphatic system
- Many lymphomas are known to be due to specific genetic mutations
- Follicular lymphoma due to over expression of BCL-2 (gene that blocks programmed cell death)

Classification

- Usually classified by how the cells look under a microscope and how quickly they grow and spread
  - Aggressive lymphomas (high-grade lymphomas)
  - Indolent Lymphomas (low-grade lymphomas)

Lymphoma classification

- B-cell neoplasms
  - precursor
  - mature
- T-cell & NK-cell neoplasms
  - precursor
  - mature
- Hodgkin lymphoma

Non-Hodgkin Lymphomas

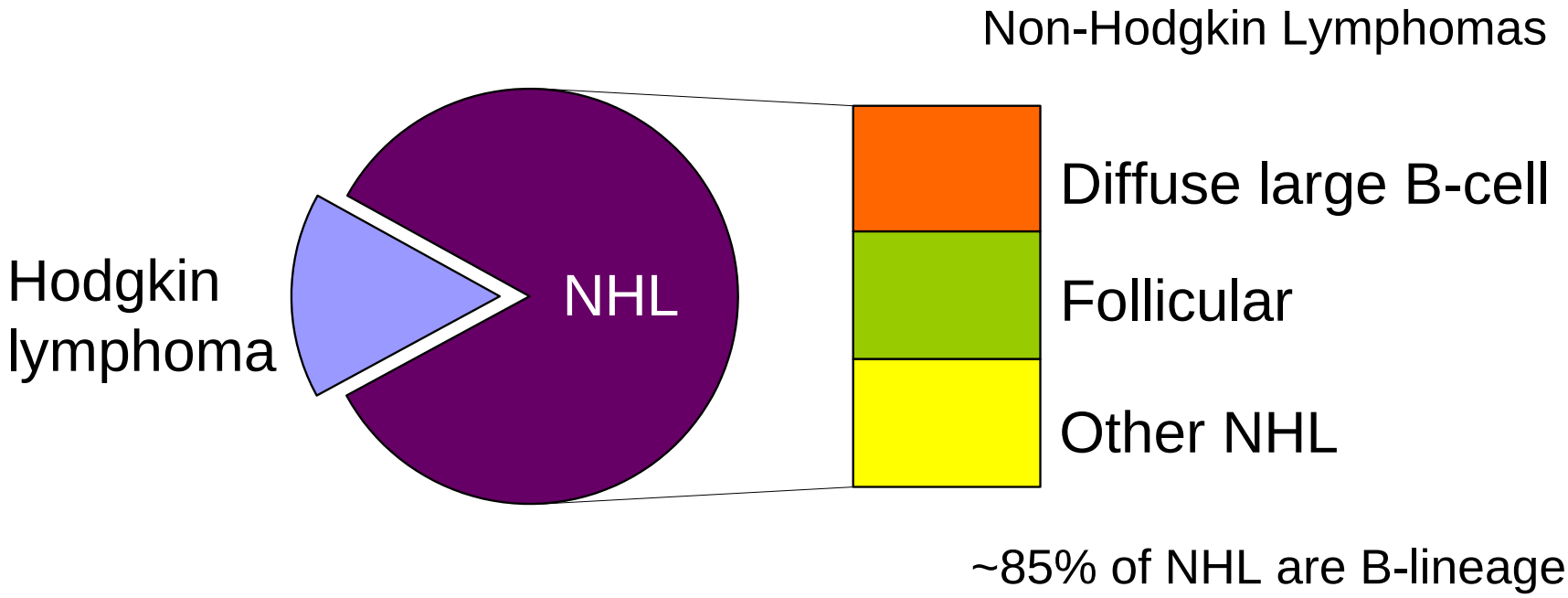
World Health Organization Classification of Lymphoid Neoplasms

I. Precursor B-Cell Neoplasms
B-cell acute lymphoblastic leukemia/lymphoma (B-ALL)
II. Peripheral B-Cell Neoplasms
Chronic lymphocytic leukemia/small lymphocytic lymphoma
B-cell prolymphocytic leukemia
Lymphoplasmacytic lymphoma
Splenic and nodal marginal zone lymphomas
Extranodal marginal zone lymphoma
Mantle cell lymphoma
Follicular lymphoma
Marginal zone lymphoma
Hairy cell leukemia
Plasmacytoma/plasma cell myeloma
Diffuse large B-cell lymphoma
Burkitt lymphoma
III. Precursor T-Cell Neoplasms
T-cell acute lymphoblastic leukemia/lymphoma (T-ALL)
IV. Peripheral T-Cell and NK-Cell Neoplasms
T-cell prolymphocytic leukemia
Large granular lymphocytic leukemia
Mycosis fungoides/Sézary syndrome
Peripheral T-cell lymphoma, unspecified
Anaplastic large-cell lymphoma
Angioimmunoblastic T-cell lymphoma
Enteropathy-associated T-cell lymphoma
Panniculitis-like T-cell lymphoma
Hepatosplenic γδT-cell lymphoma
Adult T-cell leukemia/lymphoma
Extranodal NK/T-cell lymphoma
NK-cell leukemia
V. Hodgkin Lymphoma
Classical subtypes
Nodular sclerosis
Mixed cellularity
Lymphocyte-rich
Lymphocyte depletion
Lymphocyte predominance

Common lymphomas

- Follicular lymphoma
- Diffuse large B-cell lymphoma
- Mantle cell lymphoma
- Burkitt lymphoma
- Splenic marginal zone lymphoma

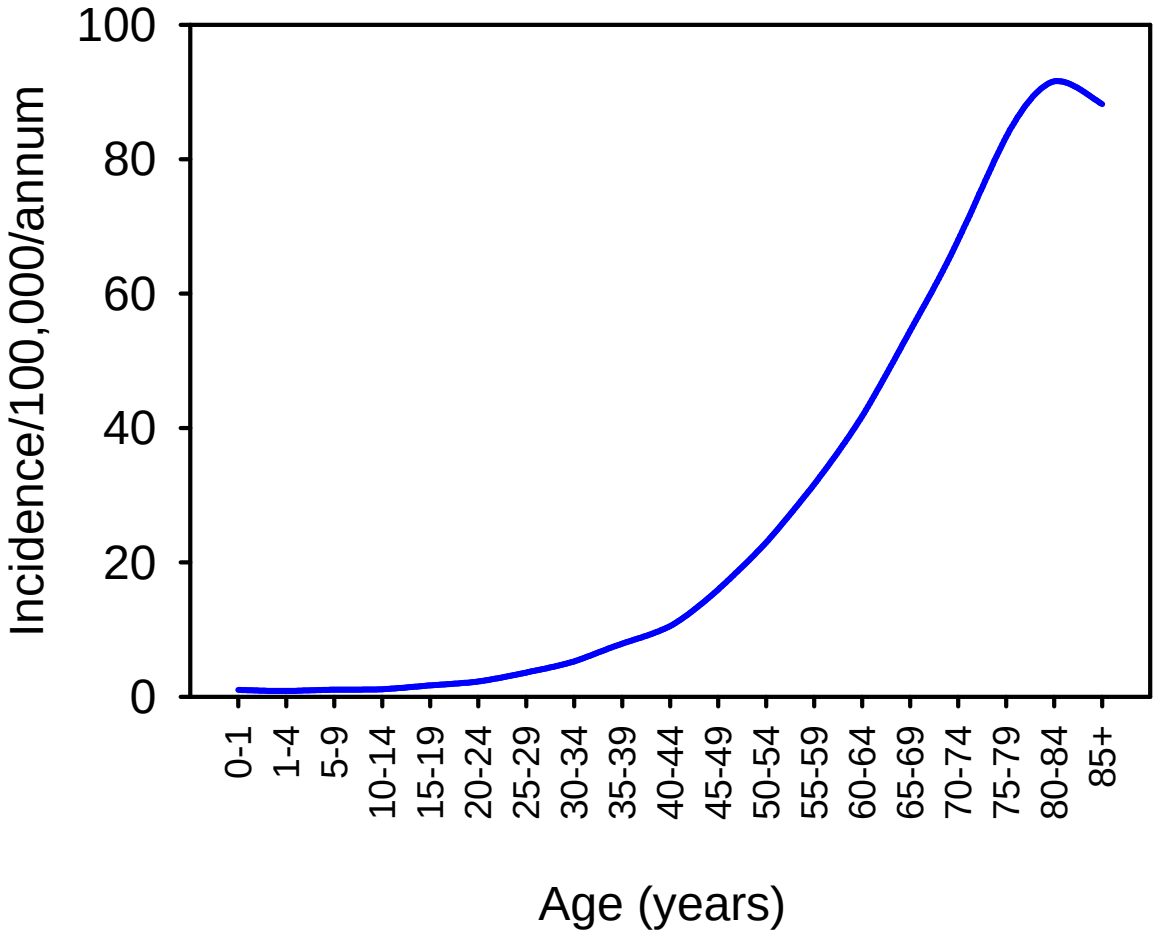
Relative frequencies of different lymphomas



Epidemiology of lymphomas

- males > females
- incidence
  - NHL increasing
  - Hodgkin lymphoma stable
- in NHL: 3rd most frequently diagnosed cancer in males and 4th in females
- in HL: 5th most frequently diagnosed cancer in males and 10th in females

Age distribution of new NHL



Risk factors for NHL

- Immuno-suppression or immunodeficiency– HIV
- Connective tissue disease
- Family history of lymphoma
- Infectious agents– Epstein Barr Virus
- Ionizing radiation and chemical agents

Clinical manifestations

- Variable
  - severity: asymptomatic to extremely ill
  - time course: evolution over weeks, months, or years
- Systemic manifestations
  - fever, night sweats, weight loss, anorexia, pruritis
- Local manifestations
  - lymphadenopathy, splenomegaly most common
  - any tissue potentially can be infiltrated

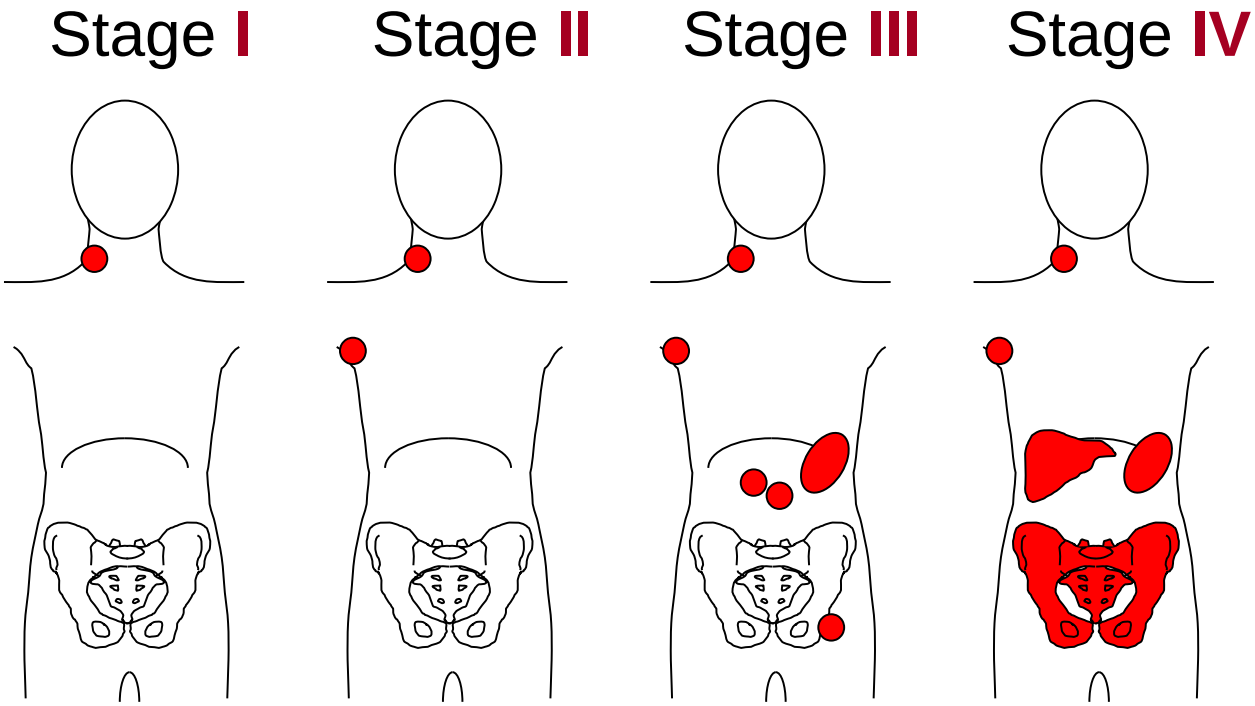
Non-Hodgkin's Lymphoma Staging

- Stage is the term used to describe the extent of tumor that has spread through the body (**I** and **II** are localized where as **III** and **IV** are advanced.

- Each stage is then divided into categories **A**, **B**, and **E**

  - **A**: No systemic symptoms
  - **B**: Systemic Symptoms such as fever, night sweats and weight loss
  - **E**: Spreading of disease from lymph node to another organ

Staging of lymphoma



A: absence of B symptoms
B: fever, night sweats, weight loss