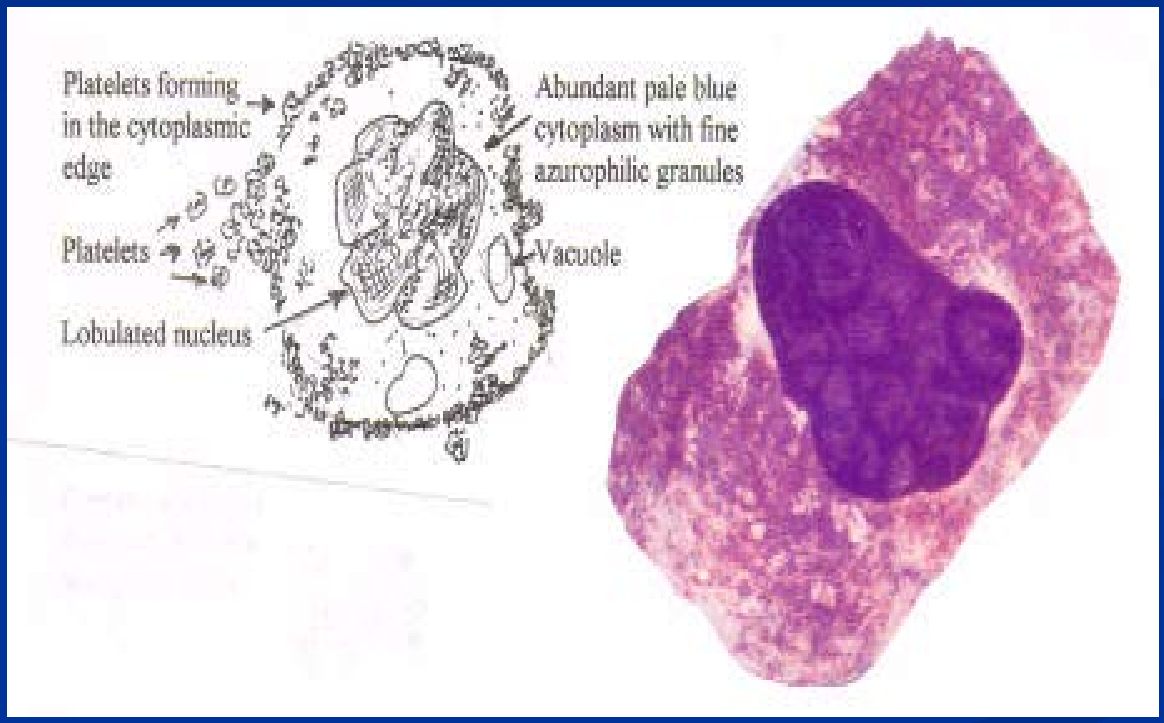
Hematologic Malignancies



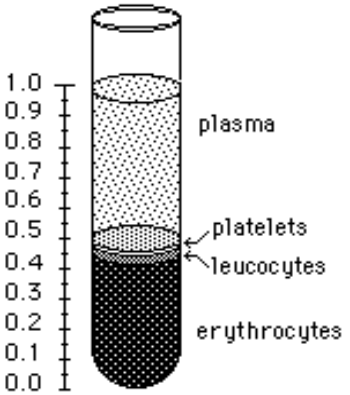
White Cell Basics

You are now at the beginning of the WBC Basics study section.

Leukocytes or WBCs are found in a thin gray layer known as the buffy coat in centrifuged blood. Above the leukocytes lie the platlets.

Leukocytes are primarily defensive, but also have important sanitation and recycling duties.

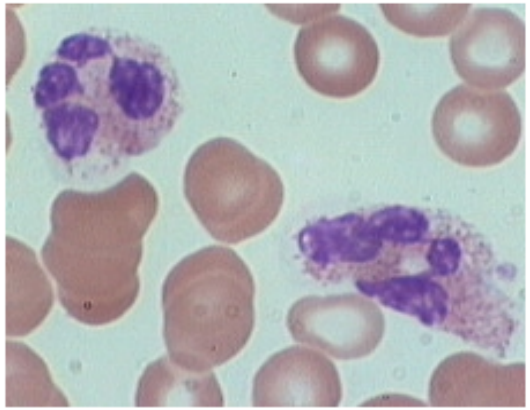
Before reviewing the origin and development of WBCs let us first look at the mature WBC population normally found in the peripheral blood (buffy coat), including neutrophils, eosinophils, basophils, monocytes, and lymphocytes.



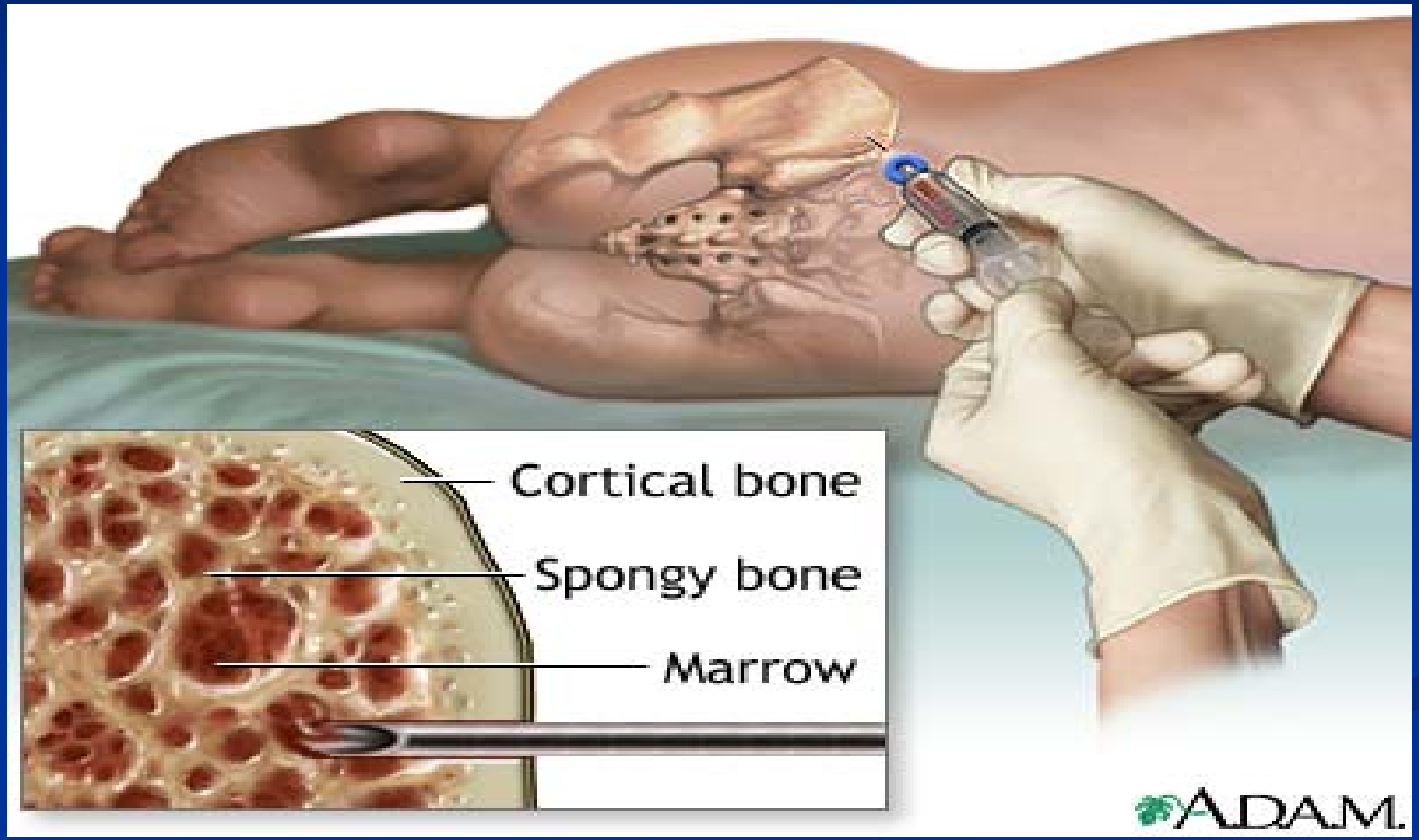
Neutrophils The mature neutrophil (12-15u dia) is characterized by segmentation into 2-5 lobes. The chromatin is dense and clumped with distinct lighter areas of parachromatin.

The cytoplasm is lightly eosinophilic with variable numbers of light staining "neutral" granules and a few and a few azurophilic 1 granules, persistent from earlier stages.

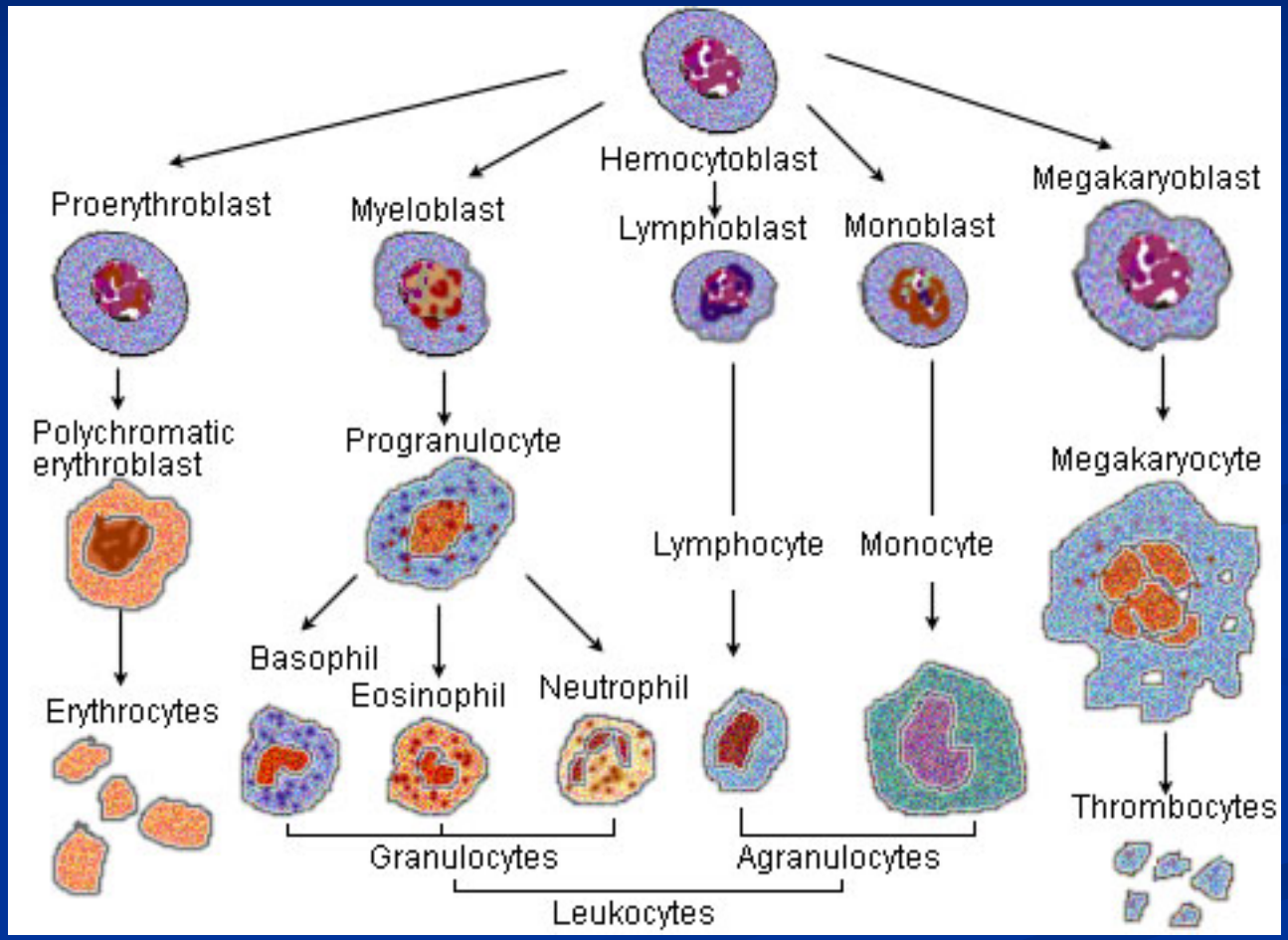
Neutrophils are important in the inflammatory process (as phagocytes and mediators of inflammatory reactions).



Bone Marrow



Hemopoiesis: The Blood Cell Lineage



“Blast” Forms

- “Blast” forms – immature cells, undifferentiated
- Blasts – CD34 Ag
- Percentage of “blasts” often determines label

Pluripotential Stem Cell

- Red Blood Cells (transport hemoglobin)
- Granular Cells (derive from myelocytes)
- Megakaryocytes - platelets
- Lymphocytes, Monocytes

Leukocytes - Granulocytes

Leukocytes – engulf and kill bacteria & viruses

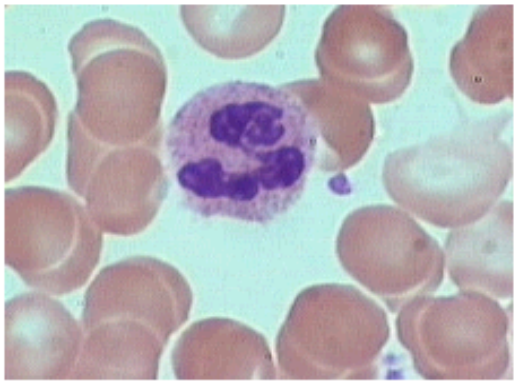
- a.k.a. WBCs – 5 types
- Granulocytes & Agranulocytes
- Granulocytes
  - neutrophils
  - eosinophils
  - Basophils

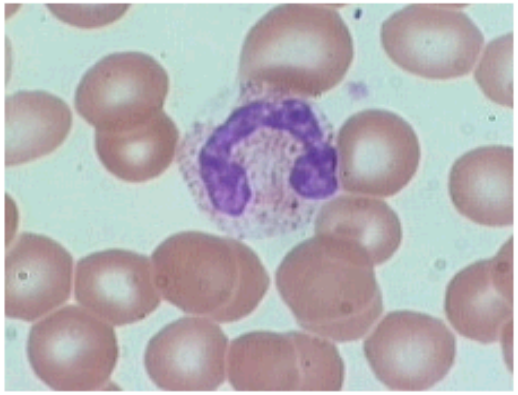
Leukocytes - Agranulocytes

Lymphocytes - in blood, also spleen, lymph nodes

- “B” – plasma cell – multiple myeloma, macroglobinemia
- “T” – thymus

Monocytes

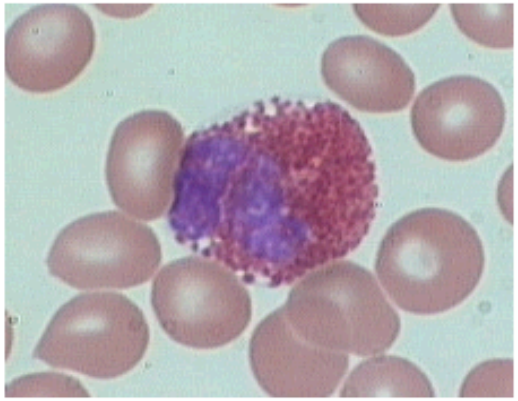




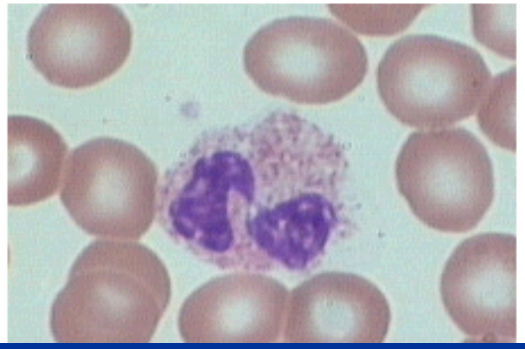
Eosinophils The large orange granules of the eosinophil make the eosinophil the most readily recognizable cell in the blood. The eosinophil (12-15u diameter has chromatin similar to that of a neutrophil, but usually fewer (2-3) lobes.

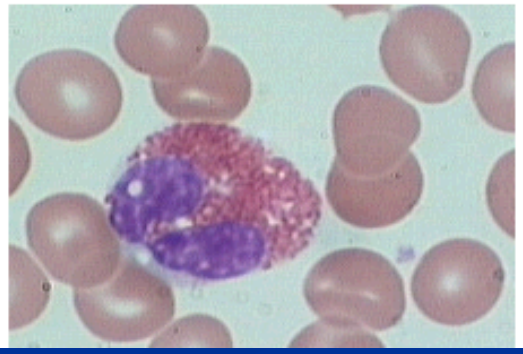
Normally 0-6% eosinophils are found in the peripheral blood.

The eosinophil specific granules contain rhomboid crystals by EM. This core contains Major Basic Protein (MBP), known to be toxic to several parasites (helminths, microfilariae; schistomiasis), and some mammalian cells.

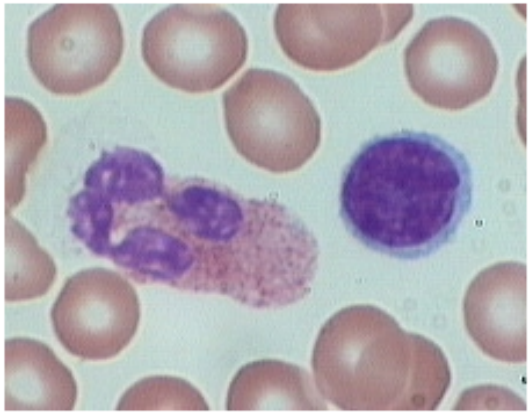


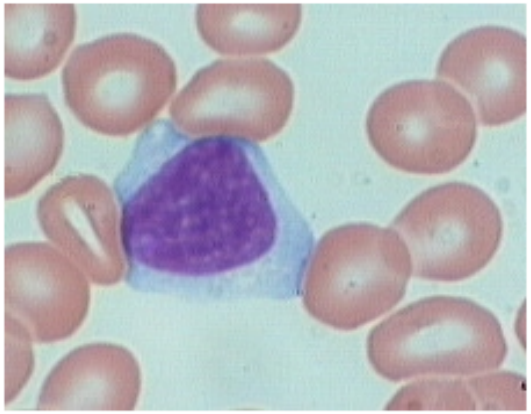
Compare the granules of the neutrophil (at left) with those of the eosinophil (at right).





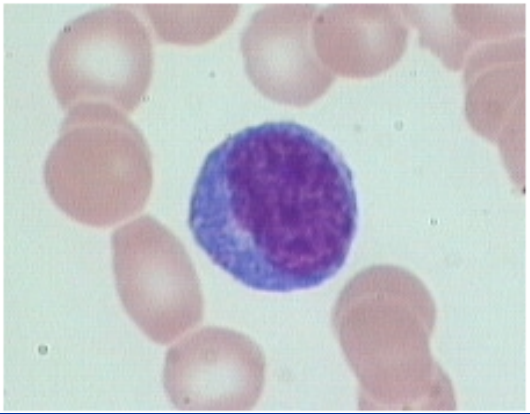
Lymphocytes vary greatly in size (7-20m dia) and in nuclear and cytoplasmic character. The small lymphocyte (7-12m dia) has a round-oval nucleus with dense clumped "smudgy" chromatin; no visible nucleolus. Scanty light blue cytoplasm, while usually agranular, may contain a few small red granules. Contrast the chromatin of the lymphocyte and neutrophil. The lymphocyte at right is 15-18m dia.

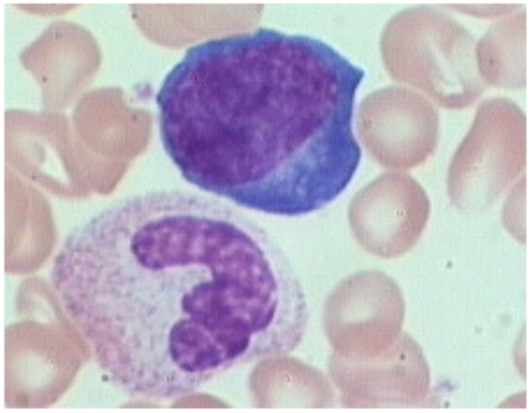




Normal peripheral blood lymphocyte percentages vary from I5-60%.

Lymphocytes with peripherially clumped chromatin and often deep blue cytplasm similar to plasma cells are termed plasmacytoid lymphocytes.





Leukemia

Definition:

"An uncontrolled production of white blood cells, which is caused by cancerous mutation of myelogenous or lymphogenous cells"

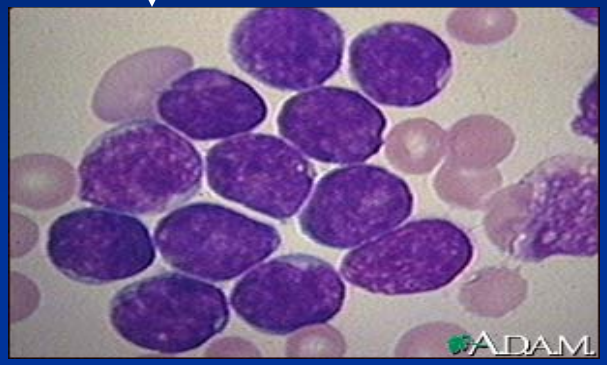
Guyton, Arthur C. Textbook of Medical Physiology 10th Edition. 2000.

Leukemias: Classification

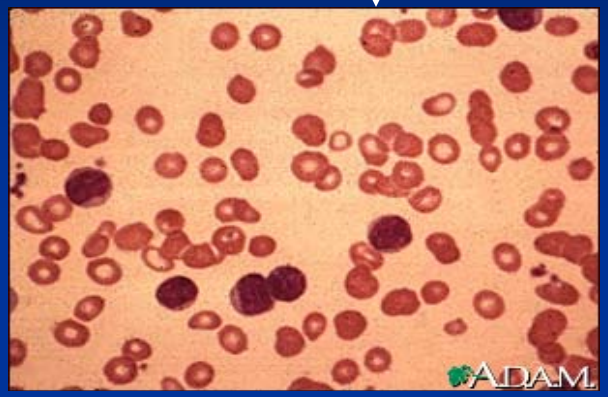
Leukemias

Acutes

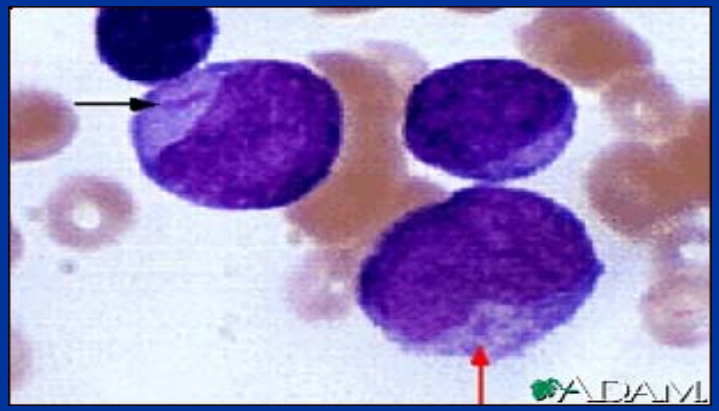
Chronics



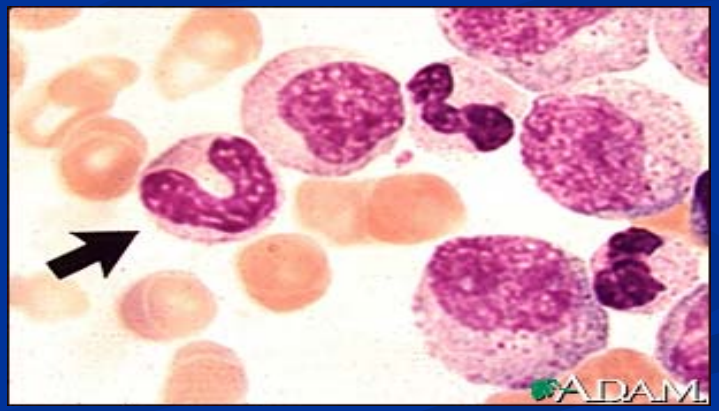
Lymphocytic (ALL)



Lymphocytic (CLL)



Myelocytic (AML)



Myelocytic (CML)

Features of Major Leukemias

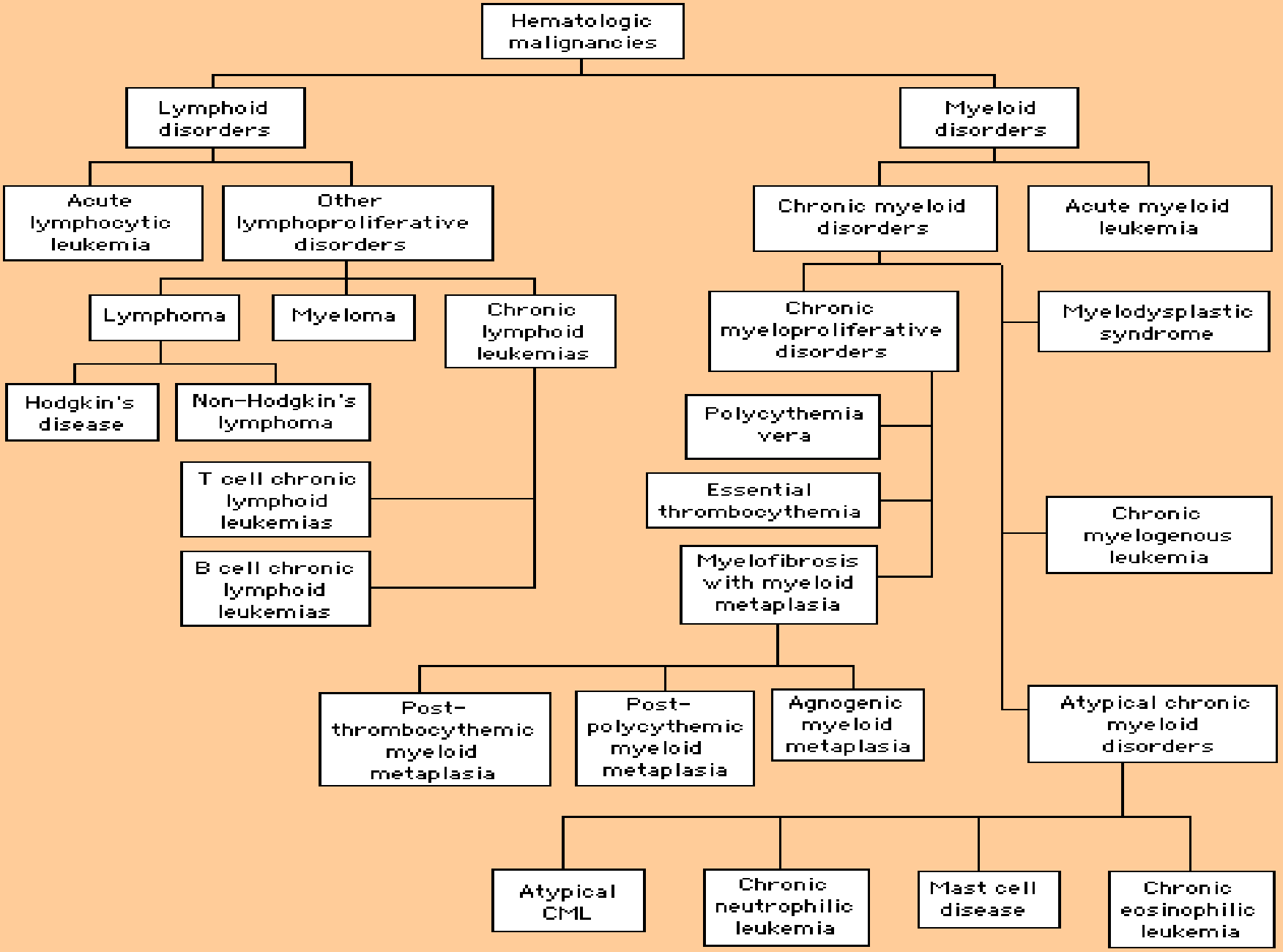
Feature	Acute Lymphoblastic	Acute Myelogenous	Chronic Lymphocytic	Chronic Myelocytic
Peak age of incidence	Childhood	Any age	Middle and old age	Young adulthood
WBC concentration	H in 50% N or L in 50%	H in 60% N or L in 40%	H in 98% N or L in 2%	H in 100%
Differential WBC count	Many lymphoblasts	Many myeloblasts	Small lymphocytes	Entire myeloid series
Anemia	In > 90%, severe	In > 90%, severe	In about 50%, mild	In 80%, but mild
Platelets	L in > 80%	L in > 90%	L in 20–30%	H in 60%; L in 10%
Lymphadenopathy	Commonly seen	Occasionally seen	Commonly seen	Infrequently seen
Splenomegaly	60%	50%	Usual and moderate	Usual and severe
Other features	50% CNS occurrence after 1 yr	Rare CNS occurrence; Auer rods may be seen in myeloblasts	Occasional hemolytic anemia and hypogammaglobulinemia	Leukocyte alkaline phosphatase low; Philadelphia chromosome positive in 85%

L = low; N = normal; H = high.

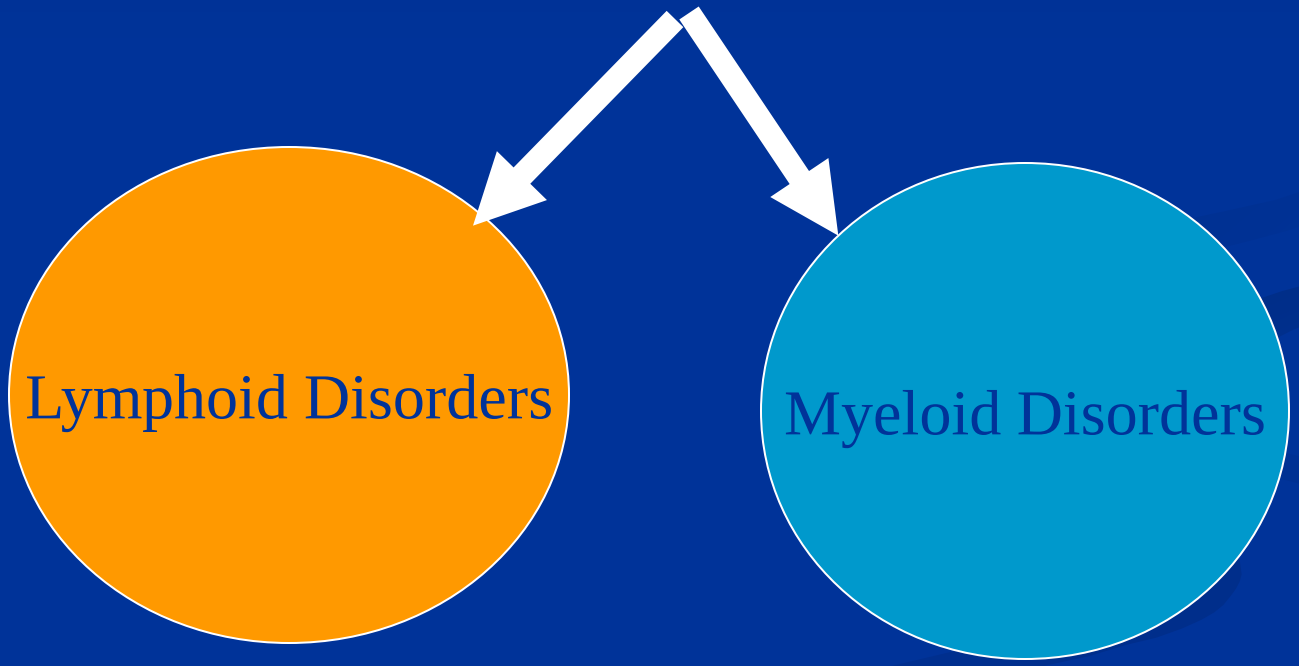
Further Classified by:

- Cell types
- Chromosomal abnormalities
- Molecular & Immunologic Markers

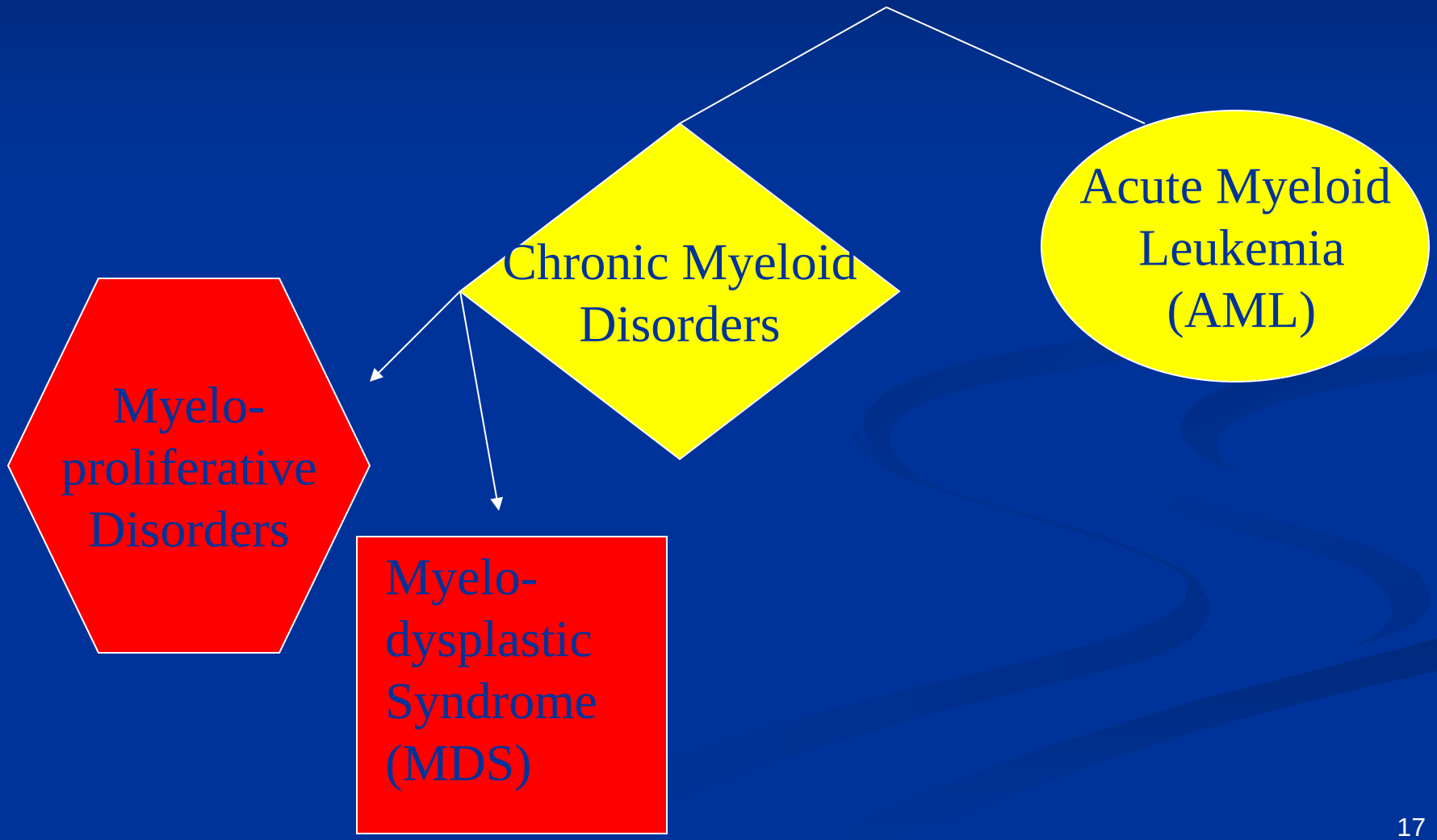
Conceptual Organization of Hematologic Malignancies



Hematopoietic Disease



Myeloid Disorders



Myelodysplastic Syndromes (MDS)

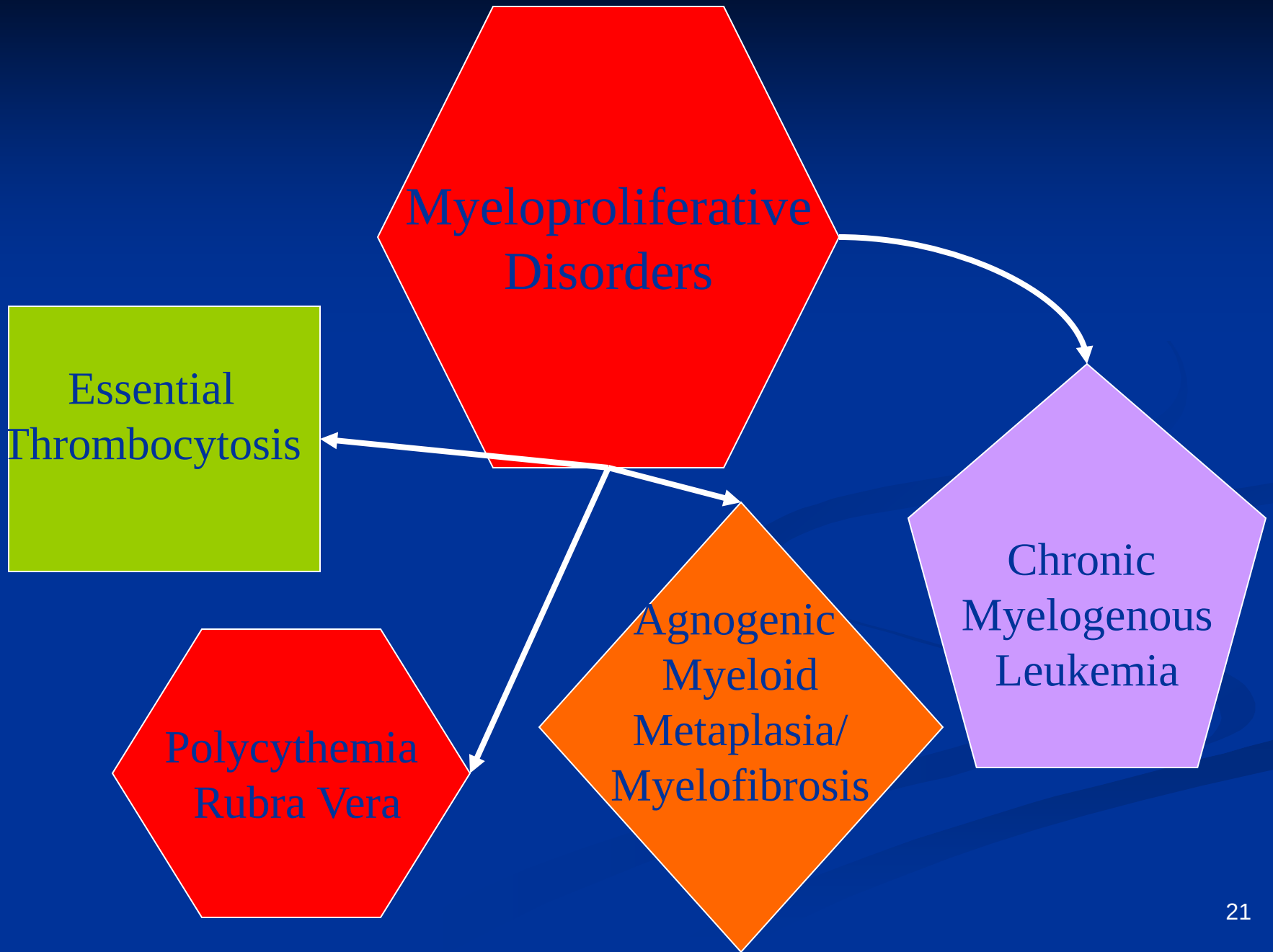
- Bone Marrow Dysfunction
- Impaired production and maturation
- a.k.a. pre-leukemia, sub-acute leukemia, smoldering leukemia, refractory anemia

MDS

- Neoplastic clonal stem cell disorder
- Results in ineffective hematopoiesis; Cells destroyed before leave BM: cytopenia
  - Refractory anemia, neutropenia, thrombocytopenia
  - May precede acute leukemia (AML) or BM failure
  - Often follows chemo/radiation therapy
  - Dx often made in retrospect

MDS

Some are
“unclassifiable”
or “atypical”


Myeloproliferative Disorders
Essential Thrombocytosis
Chronic Myelogenous Leukemia
Agnogenic Myeloid Metaplasia/ Myelofibrosis
Polycythemia Rubra Vera

MyeloProliferative Disorders

- **Abnormal proliferation of one or more cell lines.**
- CML - granulocytosis
- Polycythemia vera - RBC
- Essential thrombocythemia - thrombocytosis
- Myelofibrosis –aka myeloid metaplasia
- Mastocytosis
- **See Bulletins 3-11, 3-32**

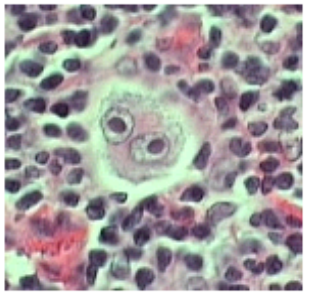
Lymphomas

- **Diverse group of tumors arising from immune cells (solid, lymphoid lineage)**
  - Neoplastic proliferation of lymphoid cells that disseminate thru body
  - “lymphoproliferative disorder”
  - aka reticulosarcoma (old term)

Hodgkin's vs. Non-Hodgkin's Lymphoma (NHL)

Hodgkin's	Non-Hodgkin's Lymphoma (NHL)
Reed Sternberg cell	Disseminated
Localized to specific nodes	
Spreads orderly and contiguous	Rapid spread, non-contiguous
Diagnoses – usually early stage	Usually later stage

Lymphoma: Hodgkin Lymphoma (Part 1)

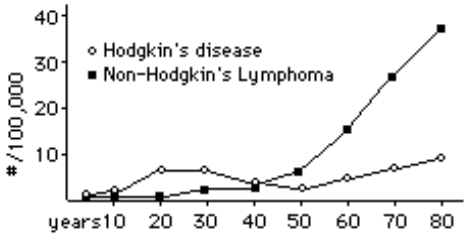


Hodgkin lymphoma is a neoplastic proliferation of lymphoid cells predominantly involving lymphoid tissues. The malignant cell is the Reed-Sternberg cell. Reed-Sternberg (R-S) cells are essential to the diagnosis of Hodgkin lymphoma. The presence of R-S cells is necessary, but as R-S cells are not unique to HD, R-S cells alone are not sufficient for the diagnosis.

The Reed-Sternberg cell is a lymphoid cell and in most cases, is a B cell, and clonal. R-S cells are very large with abundant pale cytoplasm and two or more oval lobulated nuclei containing large nucleoli (red on H & E).

Hodgkin lymphoma was first described by Thomas Hodgkin in an 1832 series of tumors of the absorbent (lymph) glands. The characteristic Reed-Sternberg cell was decribed by Carl Sternberg (I898) and Dorothy Reed (I902).

Hodgkin lymphoma repesents about 30% of all lymphoma or almost 10,000 cases per year (2-3 /100,000/year) in the United States.



Hodgkin lymphoma is separated from non-Hodgkin lymphoma not only by a unique histologic appearance, but also because the systemic manifestations (such as fever) and the clinical presentation are distinctive.

Hodgkin lymphoma generally presents as regional enlargement of a single group of peripheral lymph nodes, as opposed to non-Hodgkin lymphoma in which nodal involvement is more widely disseminated.

Bulletin 3-11

Define the following as primary cancers of the bone

- Myelofibrosis w/myeloid metaplasia
- Polycythemia vera (p vera)
- P vera with leukocytosis and thrombocytosis
- Myelodysplastic Syndrome
- Carcinoid tumors (except of appendix)

Bulletins 3-32

- Brain cancer: cerebrum, cerebellum, brain stem and diencephalon (thalamus, pituitary, pineal)
- Cancer of pleura is distinct from lung cancer
- Urethral – consider as bladder
- P vera and variants – consider bone cancer
- Essential thrombocytosis or thrombocythemia – consider as bone cancer

DMC Referral

- These are often very complicated conditions to classify with over-lapping clinical and pathologic features (NCI lists 52 types).
- If the diagnosis is not clear: request an opinion from DMC who is a hematologist/oncologist

What we have learned

- Blood Cell Lineage
- Types of granulocytes and agranulocytes
- 4 basic types of leukemias
- Current conceptual classification of hematologic malignancies

What we have learned

- Distinction between myelodysplastic syndrome and myeloproliferative disorders
- Some distinctions between Hodgkins and non-Hodgkins lymphomas
- Need for a hematologist/oncologist DMC opinion if the diagnosis is unclear

Questions