

CHRONIC LEUKEMIA

BY:

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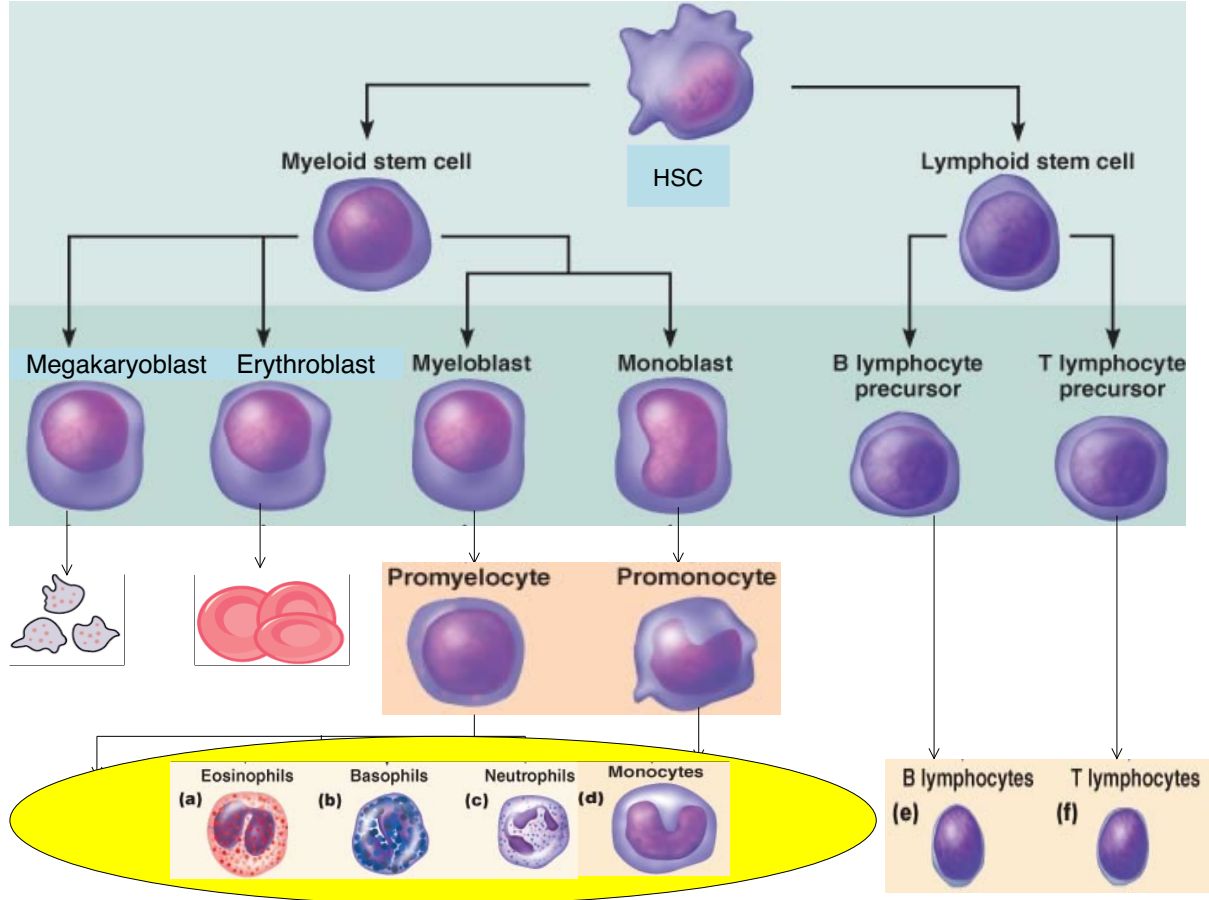
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DEPARTMENT OF PATHOLOGY

Chronic Leukaemias

- Heterogeneous group of hematopoietic neoplasms
- Uncontrolled proliferation and decreased apoptotic activity with variable degrees of differentiation
- Composed of relatively mature cells
- Indolent. (If untreated, the course is in months or years)
- Occurs mainly in adults



Main Types of Leukemia

Chronic	Acute	
LPN(CLL)	ALL	Lymphoid
MPN/MDS (CML)	AML	Myeloid
	Acute Biphentotypic	Mixed
	Acute	Non

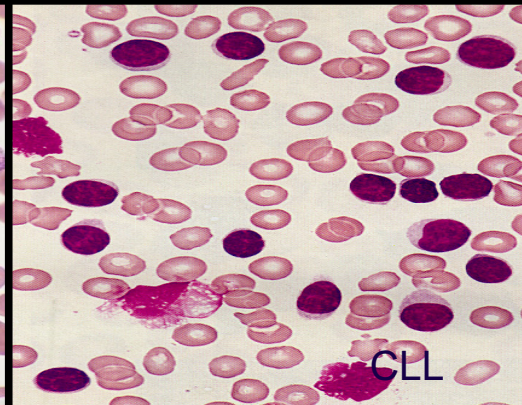
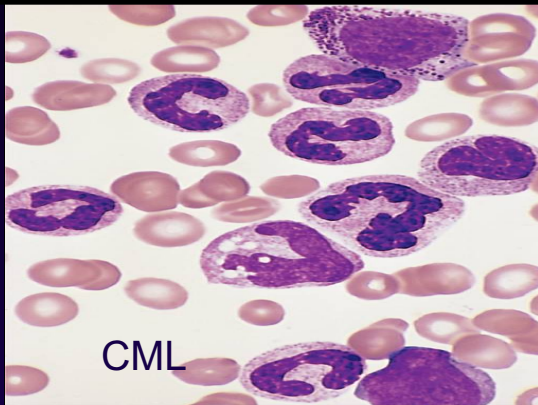
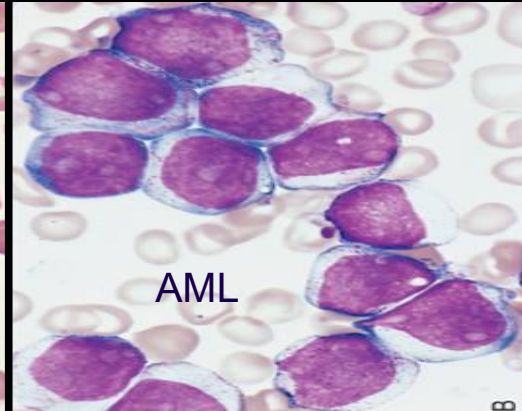
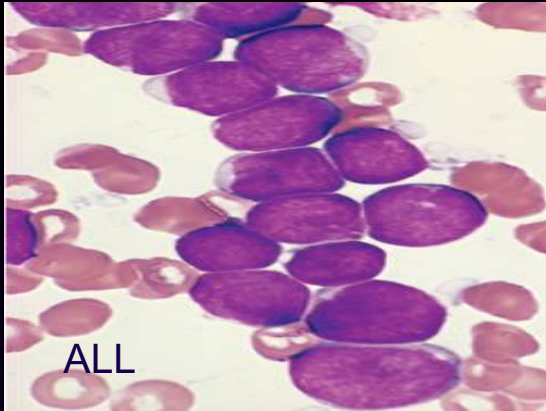


Table 1. Classification of Myeloid Neoplasms According to the 2008 World Health Organization Classification Scheme

1. Myeloproliferative neoplasms (MPN)

- 1.1. Chronic myelogenous leukemia, *BCR-ABL1*-positive (CML)
- 1.2. Polycythemia vera (PV)
- 1.3. Essential thrombocythemia (ET)
- 1.4. Primary myelofibrosis (PMF)
- 1.5. Chronic neutrophilic leukemia (CNL)
- 1.6. Chronic eosinophilic leukemia, not otherwise specified (CEL-NOS)
- 1.7. Mast cell disease (MCD)
- 1.8. MPN, unclassifiable

2. Myeloid and lymphoid neoplasms with eosinophilia and abnormalities of *PDGFRA*, *PDGFRB*, and *FGFR1*

3. MDS/MPN

- 3.1. Chronic myelomonocytic leukemia (CMML)
- 3.2. Juvenile myelomonocytic leukemia (JMML)
- 3.3. Atypical chronic myeloid leukemia, *BCR-ABL*-negative (aCML)
- 3.4. MDS/MPN, unclassifiable

4. Myelodysplastic syndromes (MDS)

5. Acute myeloid leukemia (AML)

Myeloproliferative Neoplasms

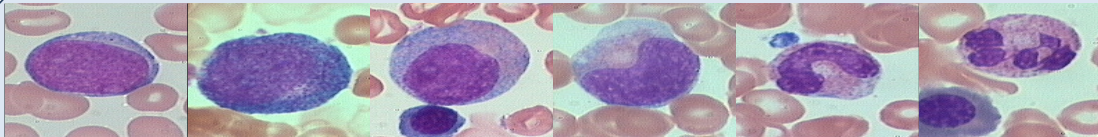
- Malignant proliferation of myeloid cells (maturing cells) which are mainly granulocytes, in blood and bone marrow.
- Occur mainly in adults
- Slow onset and long course

MPN features

- Cytosis
- Organomegaly (mainly splenomegaly)
- High uric acid
- Hypercellular bone marrow
- Progression to acute leukaemia (mainly AML)

Chronic Myeloid Leukemia (CML)

- Stem cell MPN.
- Predominant proliferation of granulocytic cells.
- Consistently associated with the BCR-ABL1 fusion gene located in the Philadelphia (Ph) chromosome which results from t(9;22) .



myeloblast

promyelocyte

myelocyte

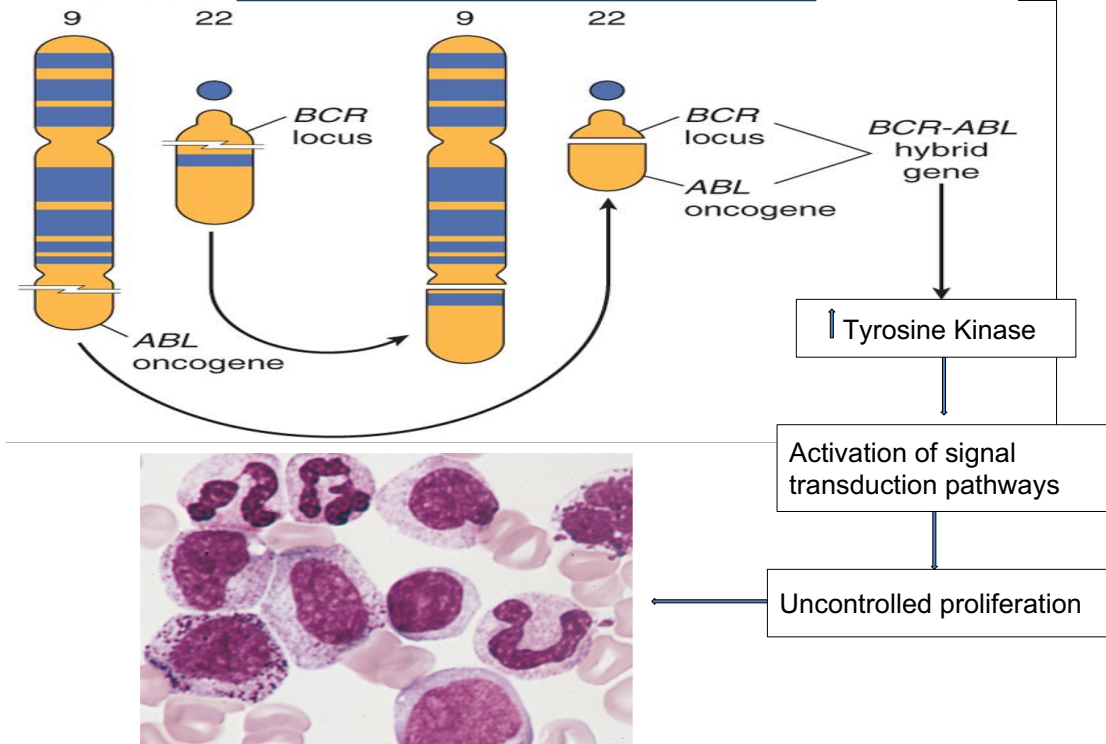
metamyelocyte

band

neutrophil

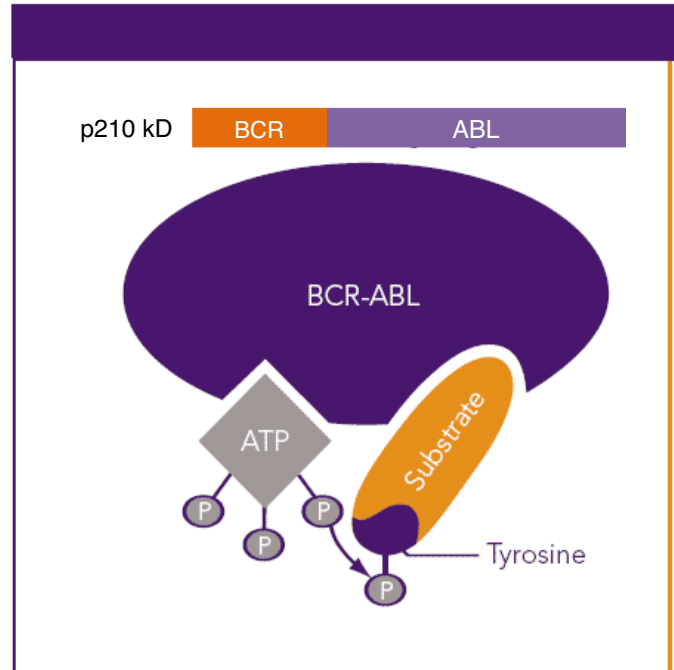
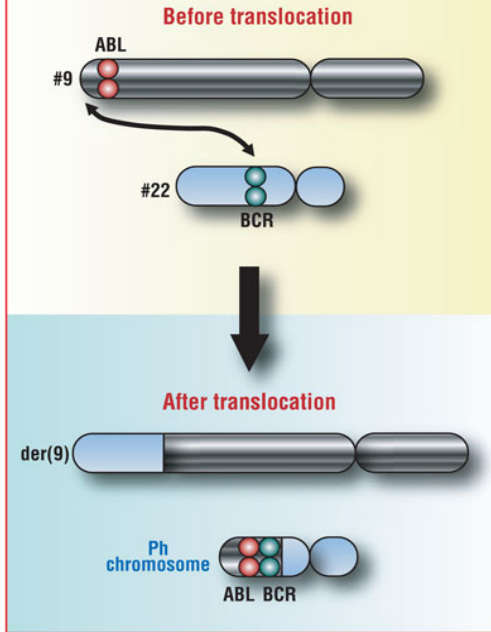
MATURATION

Pathogenesis of CML



Pathogenesis of CML

Figure 1: The Philadelphia (Ph) Chromosome



Clinical Presentation

- ❑ Asymptomatic presentation(20-40%):
- ❑ Routine CBC : marked leukocytosis
- ❑ Common symptoms : Fatigue ,weight loss or night sweating
- ❑ Abdominal discomfort due to splenomegaly
- ❑ Splenomegaly (Massive)



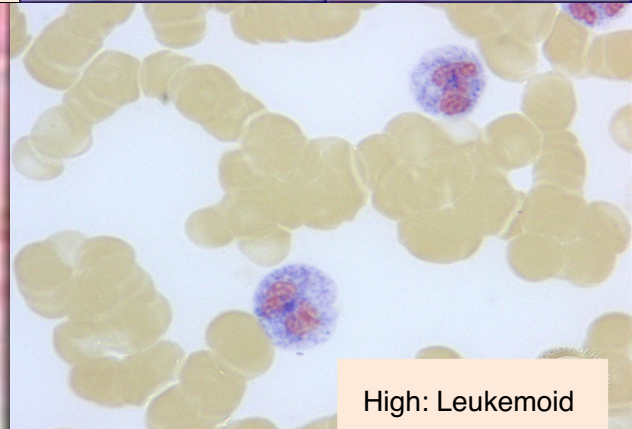
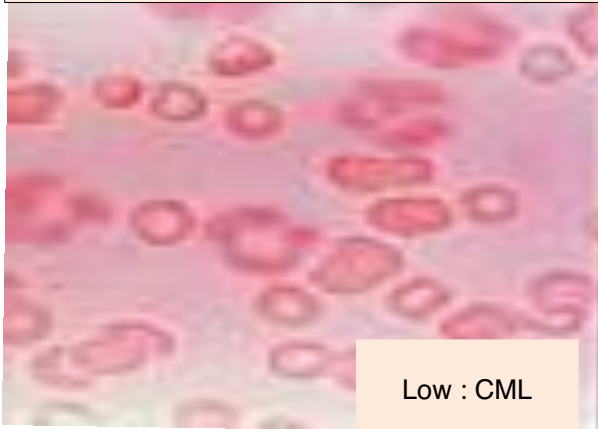
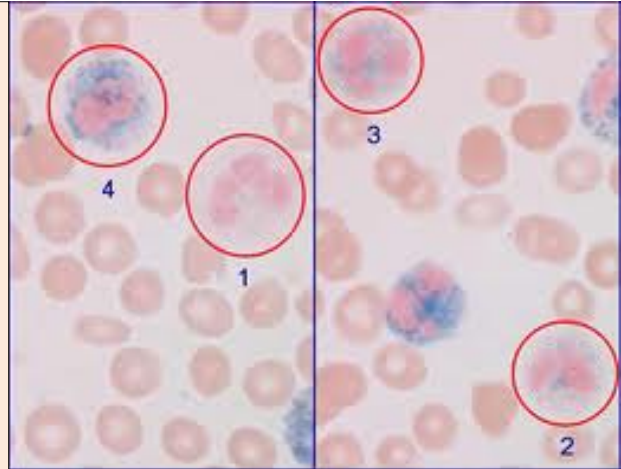
Main Differential Diagnosis

- 1- Chronic myelomonocytic leukemia (monocytosis ,BCR-ABL –ve) .
- 2-Leukemoid reaction: Leukocytosis due to physiological response to stress or infection

Leukaemoid	CML	
Any age	Adult	Age
High but <100,000	High	WBC count
Mainly Bands	Mainly myelocytes and segmented	Differential
Toxic	Hypogranular	Morphology
-/+	+	Splenomegaly
High	Low	NAP score
-ve	+ve	BCR/ABL
Acute	Chronic	Onset

Neutrophil Alkaline Phosphatase (NAP) score :

- Cytochemical stain that estimate the amount of alkaline phosphatase enzyme in neutrophils .



CML Phases

Chronic phase

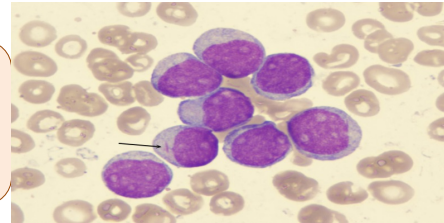
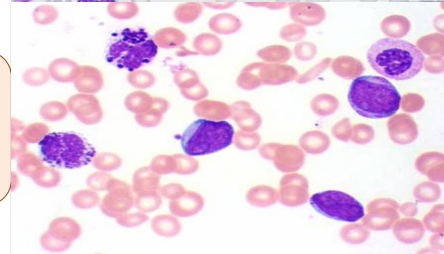
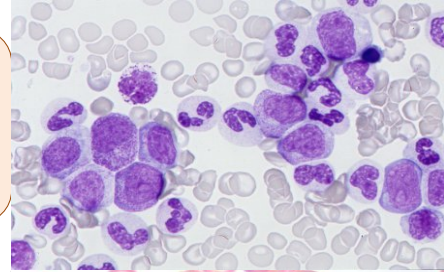
- Leukocytosis ($12-1000 \times 10^9/L$)
- Mainly neutrophils & myelocytes
- Blasts $\leq 10\%$, Basophils $\leq 20\%$
- Stable course (years)

Accelerated phase

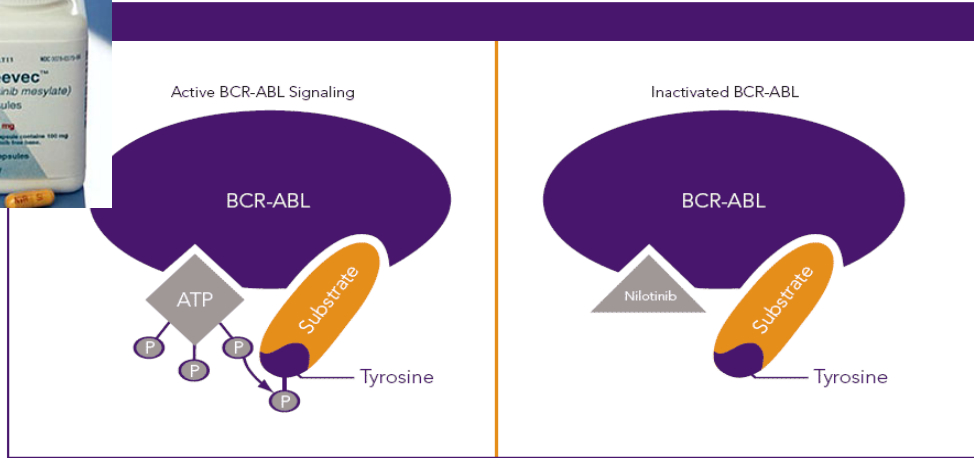
- Increasing counts
- 10-19% blasts (basophils $\geq 20\%$)
- Unstable course (months)

Blastic phase

- $\geq 20\%$ blasts = Acute Leukemia
- 80% AML & 20% ALL
- (course: Weeks)



CML Treatment

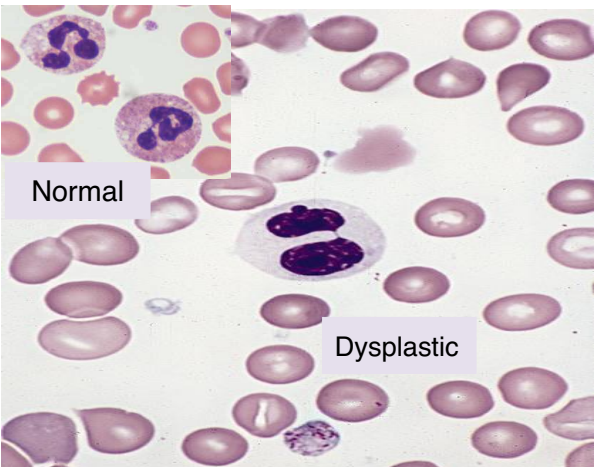


- Targeted therapy (tyrosine kinase inhibitors like Imatinib)
- Excellent response (5y overall survival $\geq 90\%$)
- If no response ; stem cell transplantation

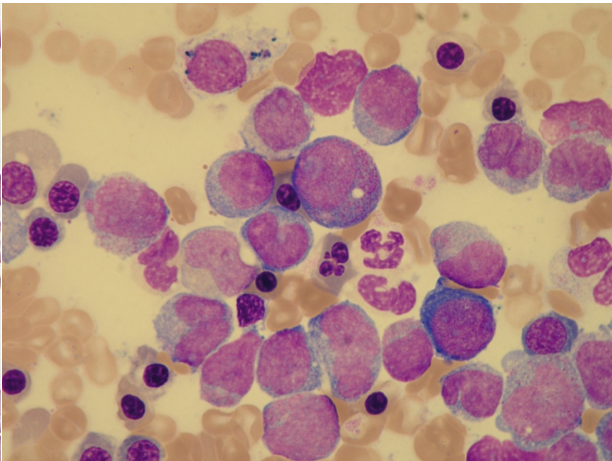
Myelodysplastic Syndromes MDS

- Group of myeloid neoplasms characterized by:
 - 1-Peripheral cytopenia (Low HB \pm Low WBC & Low PLT)
 - 2- Dysplasia (abnormal morphology)
 - 3- Ineffective hematopoiesis (hypercellular marrow)
 - 4-Progression to AML (preleukaemic disease)
 - 5-Enhanced apoptosis

Myelodysplastic Syndromes MDS



Blood: Pancytopenia with dysplasia



BM: Hypercellular with dysplasia

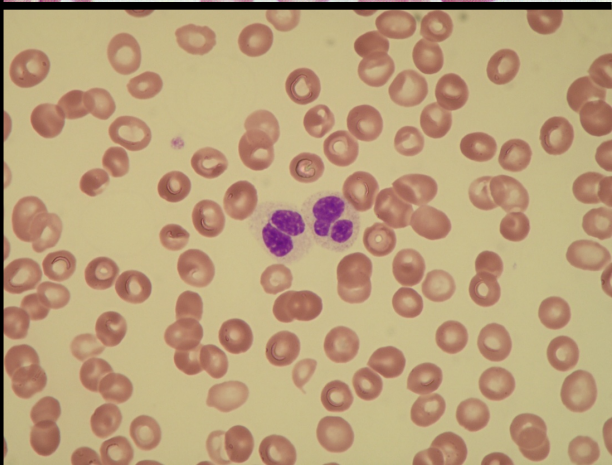
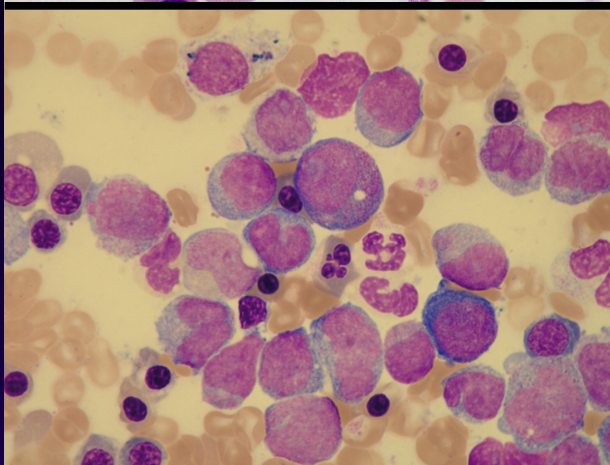
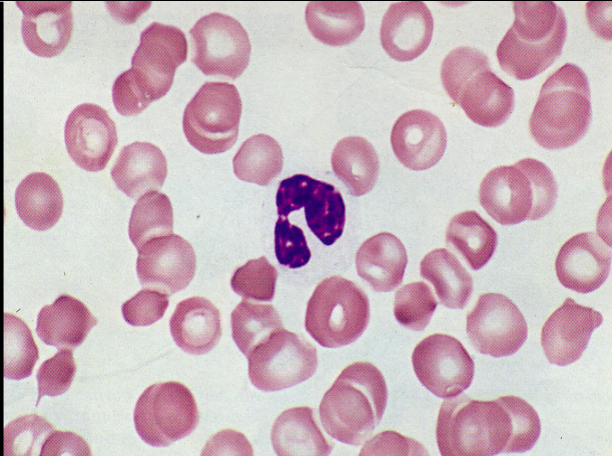
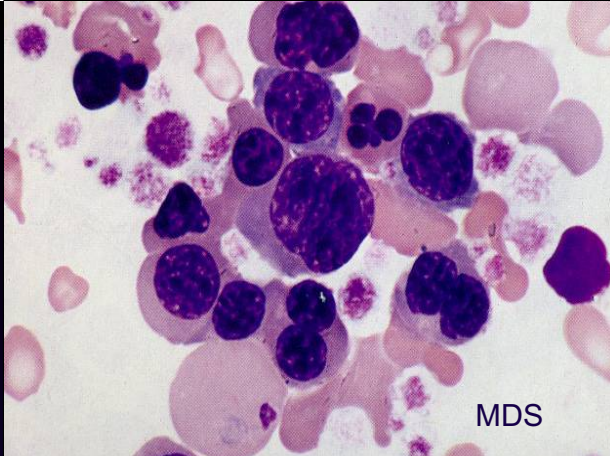
↑ Proliferation



↑ Apoptosis



Ineffective
Hematopoiesis



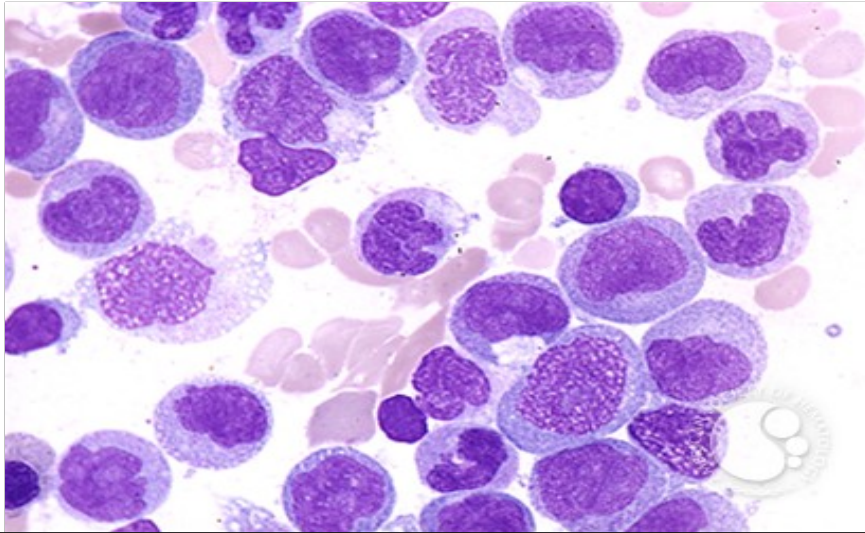
Myelodysplastic Syndromes MDS

- Many subtypes according to:
 - 1-Blast count
 - 2-Degree of dysplasia
 - 3-Genetics
- Variable genetic abnormalities mainly -5, -7
- Treatment : supportive +/- chemotherapy

Chronic Myelomonocytic Leukemia (CMML)

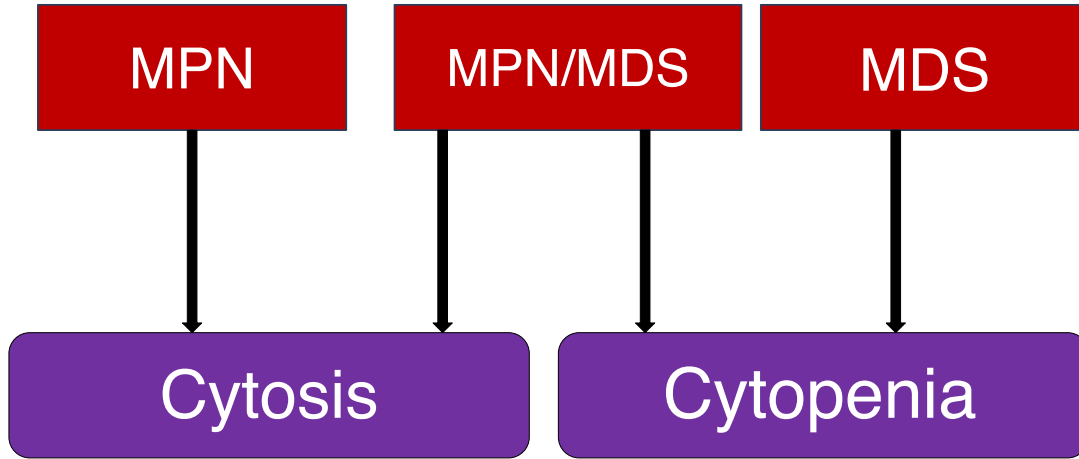
- Clonal Hematopoietic malignancy characterized by proliferation of both monocytes and neutrophils.
- MDS/MPN disease:
 - * Features of MDS (dysplasia & enhanced apoptosis)
 - * Features of MPN (marked proliferation)
- Philadelphia chromosome must be negative
- Blast must be less than 20%.

CMML



- Aggressive course (survival rate around 2.5 y)
- Treatment : Chemotherapy \pm SCT

MPN vs. MDS vs. MPN/MDS



A tropical beach scene at sunset. The sky is a mix of deep blue, purple, and orange, with scattered clouds. Several palm trees are silhouetted against the sky. The ocean is visible in the background, and a small island or reef is visible in the distance. The foreground is a sandy beach.

Thank you !!!