Chronic leukemia

GNT Block

COLOR INDEX:

- Main text
- Dr. Notes
- Male's text
- Femal's text
- Important
- Extra

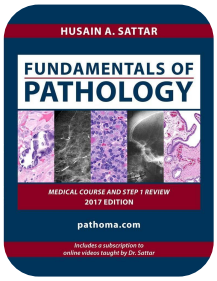
Editing file:

Objectives

*No objectives were found in both male and female slides

Click HERE for summarised Podcast & written TEXT!

Click on PATHOMA for a revision and more info!



Our YouTube's playlist for this lecture!

This lecture was given by: Dr. Mansour Aljabry and Prof. Fatma Al Qahtani

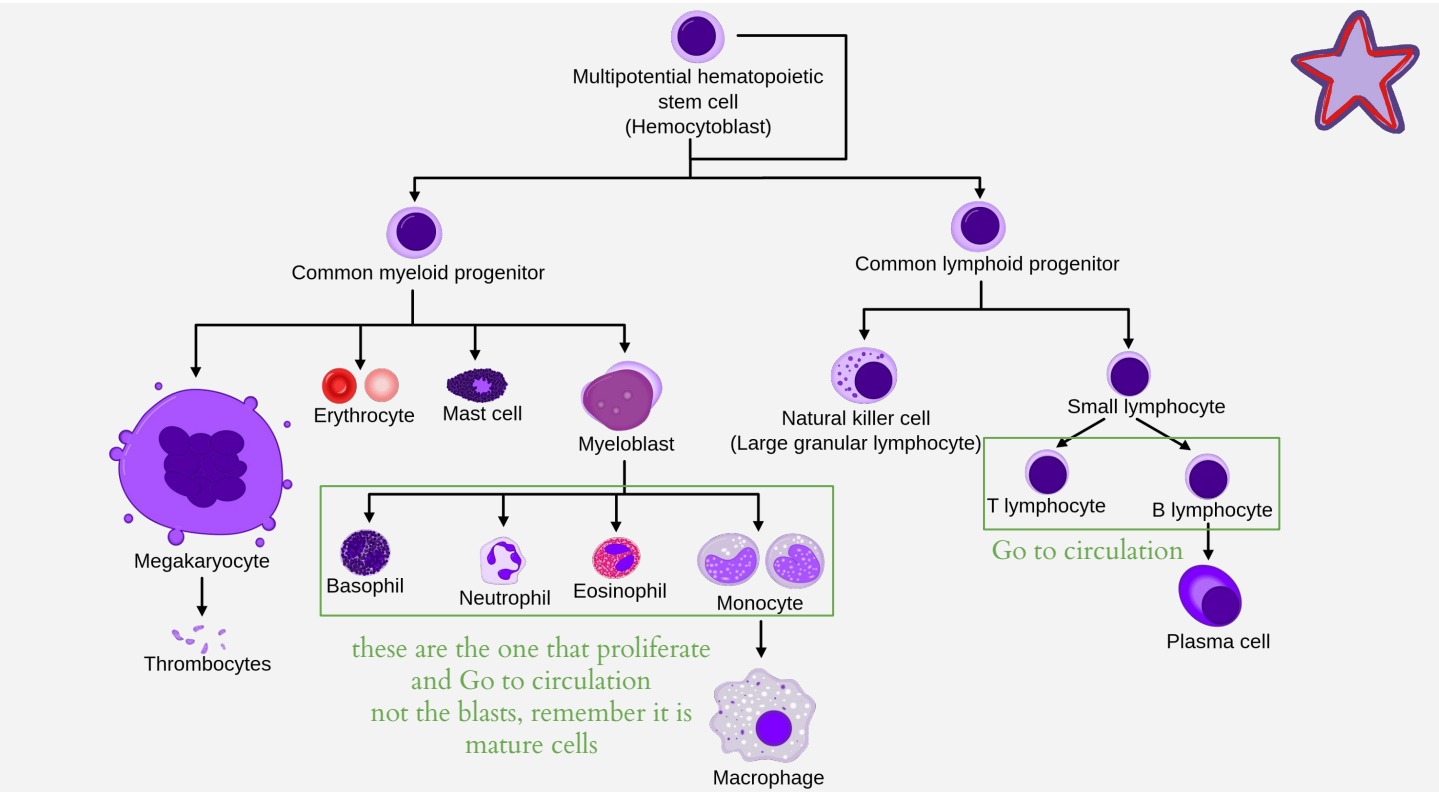
Chronic Leukaemias

Heterogeneous group of hematopoietic neoplasms.

Uncontrolled proliferation and decreased apoptotic activity with variable degrees of differentiation.

Composed of relatively mature cells.

Indolent(خامل). (If untreated, the course is in months or years). Occurs mainly in adults.



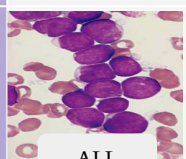
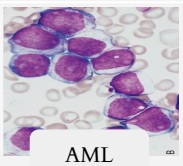
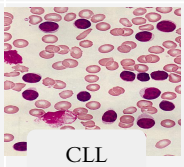
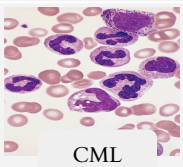
Main types of Leukaemia		
	Acute	Chronic
Lymphoid	ALL	LPN[1](CLL) Lymphoproliferative Neoplasm
Myeloid	AML	MPN/MDS (CML)
Mixed	Acute Biphenotypic	-
None	Acute Undifferentiated (Still in early detection)	-
Microscopy	 ALL	 AML
	 CLL	 CML

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)**

↳ Last level that happen in almost all types of Chronic usually

MPN

Myeloproliferative Neoplasms

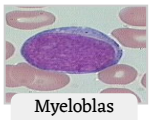
- Malignant proliferation of myeloid cells (maturing cells) which are mainly granulocytes, in blood and bone marrow.
- Occur mainly in adults
- Slow onset and long course

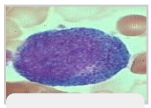
MPN features

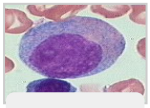
- Cytoses (increase number of mature cells)
- Organomegaly (mainly splenomegaly) (remember even in AML "Acute phase" spleen was affected, but in ALL, spleen changes were rare)
- High uric acid (MPNs lead to the overproduction of blood cells, including white blood cells. As these cells break down and are replaced rapidly, they release purines, which are substances that, when broken down, form uric acid.)
- **Hypercellular bone marrow**
- Progression to acute leukaemia (mainly AML) (Last level that happen in almost all types of Chronic usually)

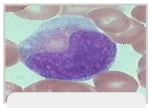
Chronic Myeloid Leukemia (CML)

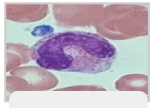
- Stem cell MPN. (specific subtype of myeloproliferative neoplasm (MPN))
- Predominant proliferation of granulocytic cells. Neutrophils
- Consistently associated with the **BCR-ABL1** fusion gene located in the **Philadelphia** (Ph) chromosome which results from **t(9;22)** (translocation of genetic material between chromosomes 9 and 22.)

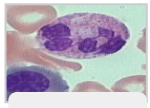

Myeloblast


Promyelocyte


Myelocyte

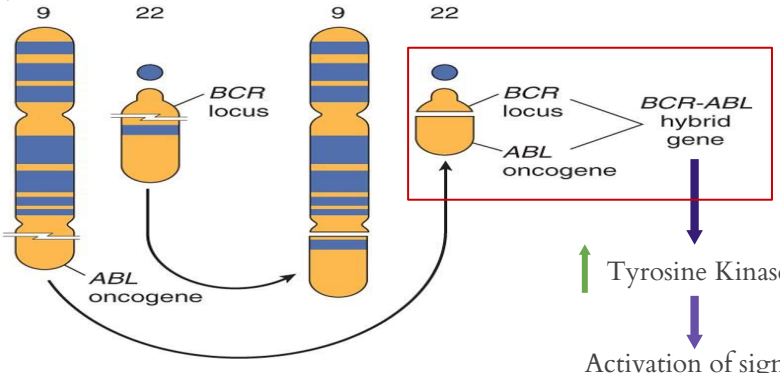

Metamyelocyte

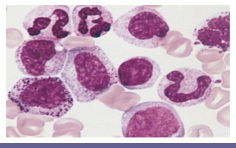

Band

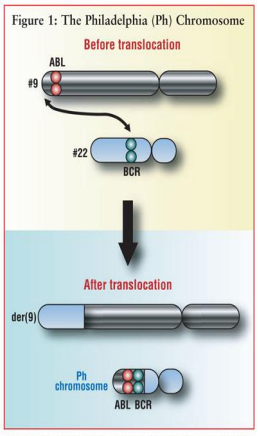

Neutrophil

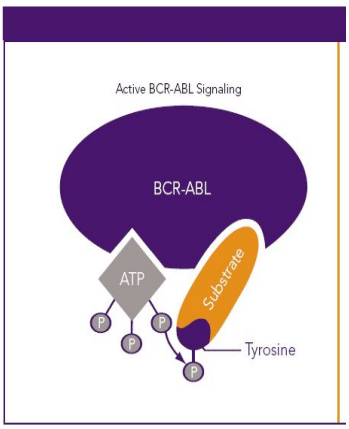
Mutations

Pathogenesis of CML



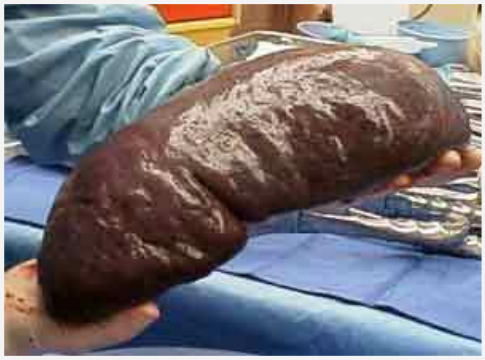






CML

Clinical Presentation

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

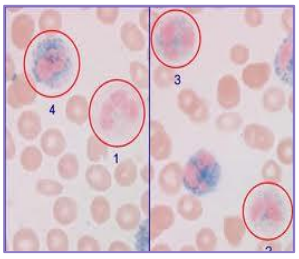
Main Differential Diagnosis

Chronic myelomonocytic leukemia "CMML" (monocytosis, BCR-ABL –ve) .

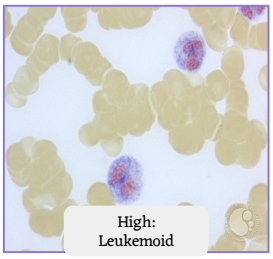
Leukemoid reaction: Leukocytosis due to physiological response to stress or infection

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

Neutrophil Alkaline Phosphatase (NAP)score :
Cytochemical stain that estimate the amount of alkaline phosphatase enzyme in neutrophils .
If low -> CML
If high -> leukemoid reaction

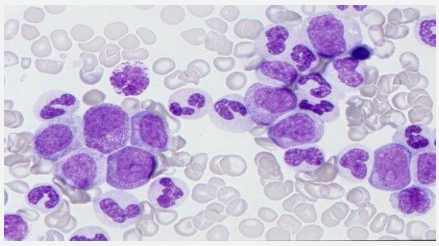
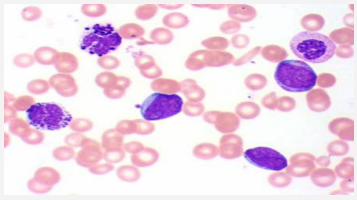
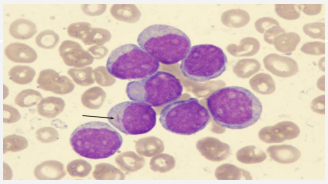



Low: CML


High: Leukemoid

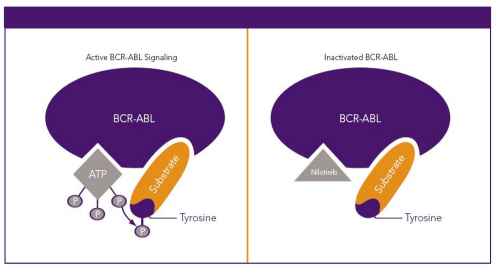
CML

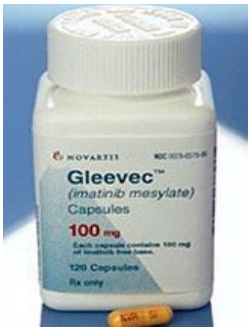
CML phases

Chronic phase Silent	• Leukocytosis (12-1000×10⁹/L) • Mainly neutrophils & myelocytes • Blasts ≤10% ,Basophils≤ 20% • Stable course (years)	
Accelerated phase	• Increasing counts • 10-19% blasts(increased)(basophils ≥20%) • Unstable course (months)	 
Blastic phase When blasts are more than 20%, this is an indication of transforming from chronic into acute	• ≥20% blasts = Acute Leukemia • 80% AML & 20% ALL • (coarse: Weeks)	

CML treatment

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

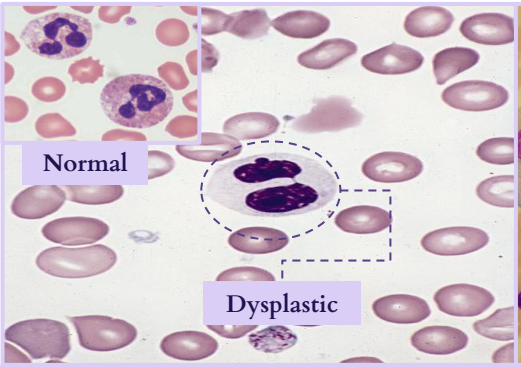


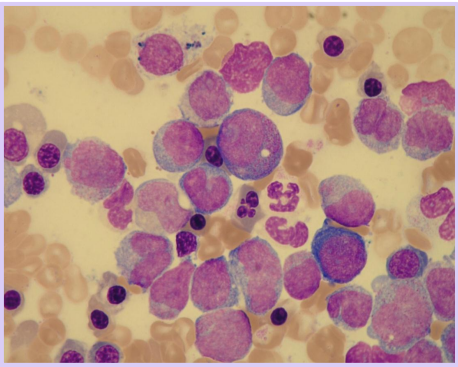


Myelodysplastic Syndromes MDS

MDS are group of myeloid neoplasms **characterized by:**

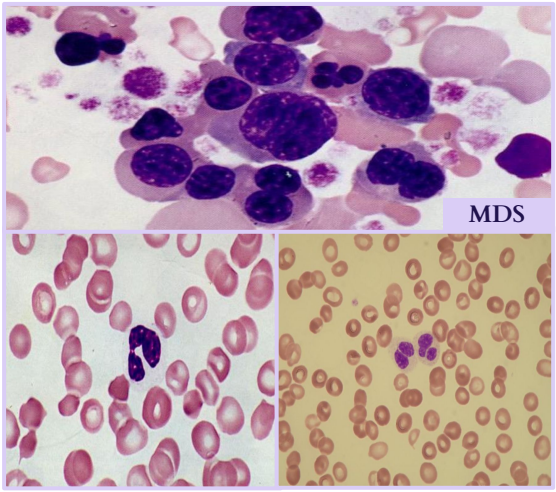
- Peripheral **cytopenia** (Low HB ± Low WBC & Low PLT)
- **Dysplasia** (abnormal morphology)
- **Ineffective hematopoiesis** (**hypercellular marrow**)
- **Progression to AML** (preleukaemic disease)
- Enhanced **apoptosis**





Blood: Pancytopenia with dysplasia

BM: Hypercellular with dysplasia



i when cells comes out from bone marrow, it encounter apoptosis

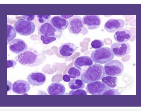
Proliferation − **Apoptosis** = **Ineffective Hematopoiesis**

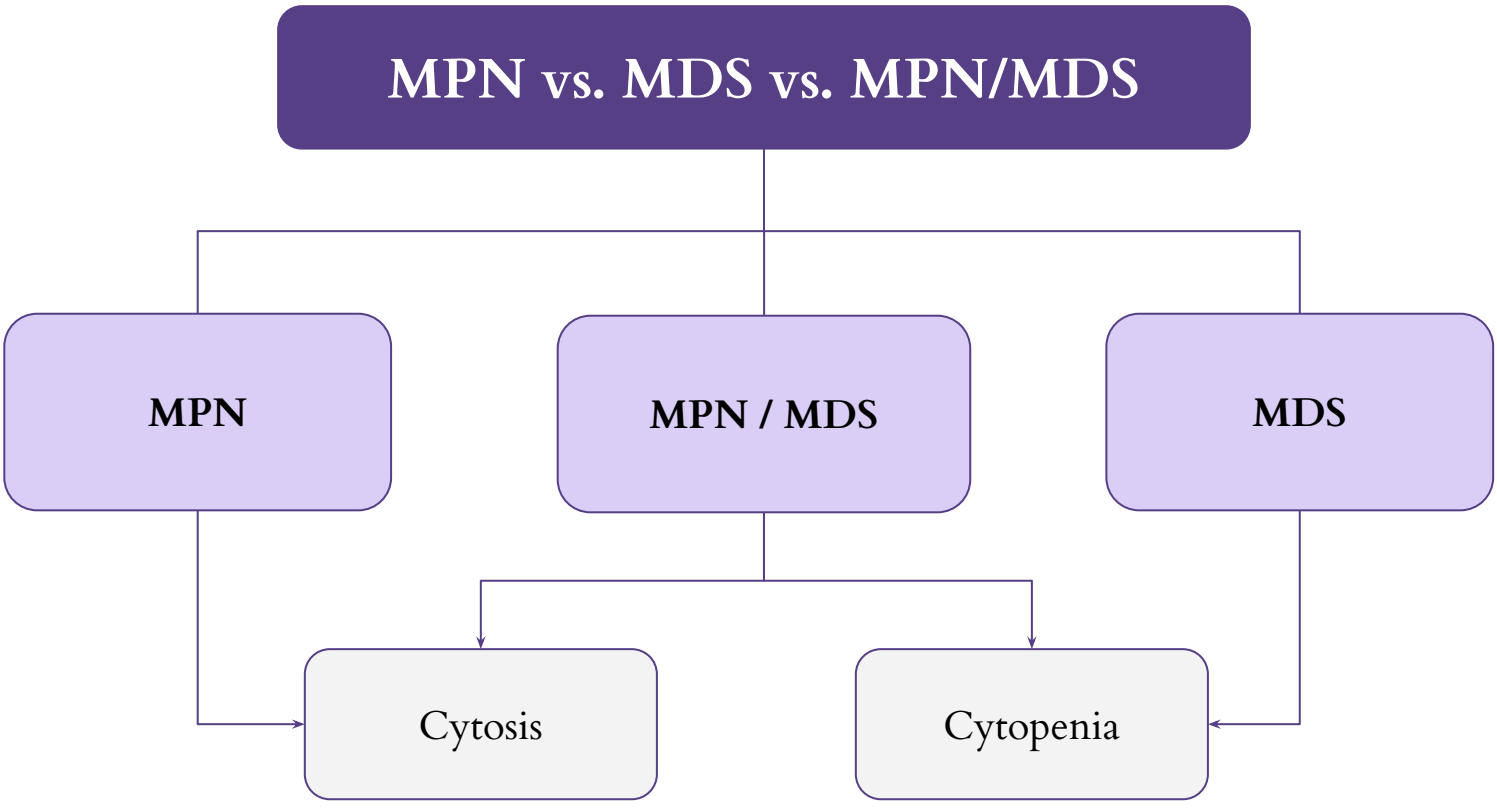
-Many subtypes according to:
1-Blast count
2-Degree of dysplasia
3-Genetics

Variable genetic abnormalities **mainly -5, -7**

Treatment : **supportive +/- chemotherapy**

CMML

Chronic Myelomonocytic Leukemia (CMML) 	
Definition	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%.	
Aggressive course (survival rate around 2.5 y)	
Treatment	Chemotherapy ±SCT
BCR/ABL	**-VE**



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