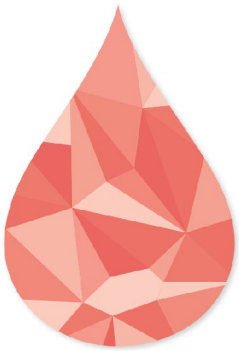


= Haematology 435 =

➢ **Color Codes:**

- Pink: Girls' notes. Blue: Boys' notes. Red: Important Notes. Gray: Extra notes.
- Purple: Lecture notes & Pathoma notes.

➢ **Done by:** **Abdulaziz Alshalan** , Khalid Alzhrani , Sami Aljuhani , Naif Alhadi

➢ **Revised by:** **Raghda Alqassim , Samar Alotaibi**

➢ **References:**

- Girls&Boys Doctors Slides and Notes.
- Team 434 & 433.

➢ **Correction file:** (HERE)

➢ **Check Your Understanding!** (HERE)

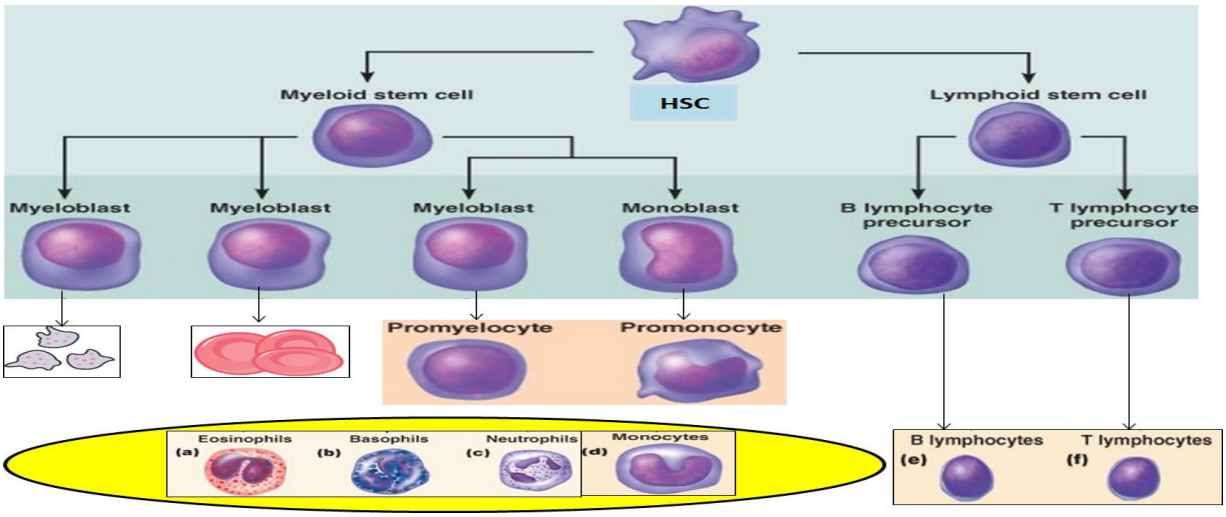
Revised by
خولة العماري & هشام الغفيلي

: Outline

MPN	MPN/MDS	MDN
Cytosis	Cytopenia	

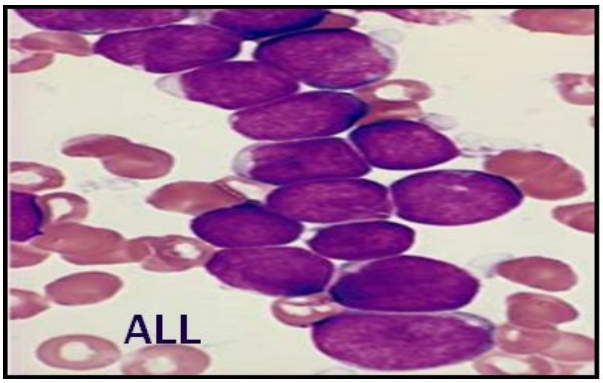
❖ Chronic leukemia

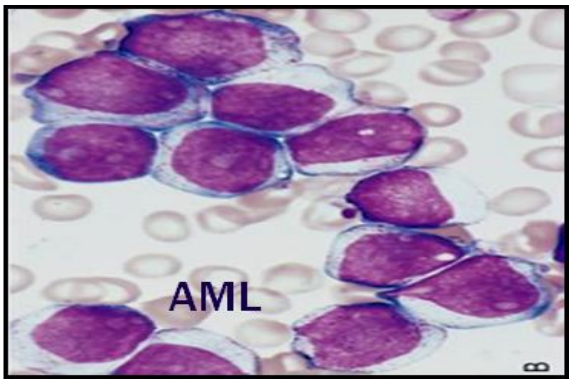
- Heterogeneous group of hematopoietic neoplasms
- Uncontrolled proliferation and decreased apoptotic activity with variable degrees of differentiationزيادة غير منظمة في الخلايا وما تموت هذي الخلايا
- Composed of relatively **mature cells**
- Indolent (progress slowly) (If untreated, the course is in months or years) (pts might be asymptomatic for years)
- Occurs mainly in adults



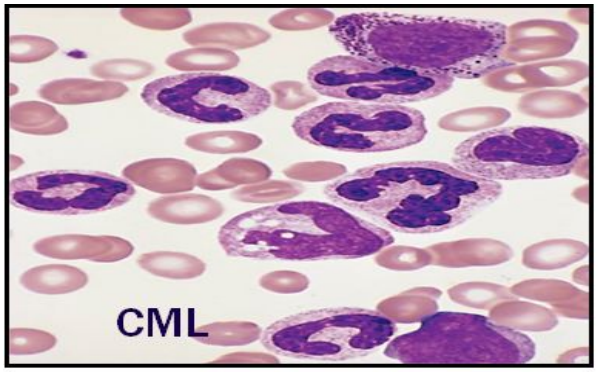
❖ Main types of leukemia

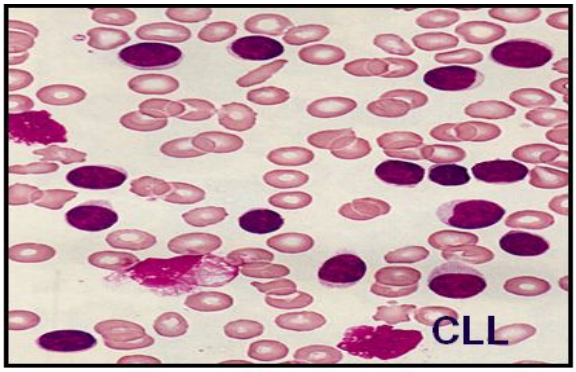
	Acute	Chronic
Lymphoid	Acute Lymphocytic Leukemia (ALL)	lymphoproliferative neoplasm (chronic lymphocytic leukemia)
Myeloid	Acute Myeloid Leukemia (AML)	**myeloproliferative neoplasm /myelodysplastic syndrome (chronic myeloid leukemia)**
Mixed	Acute biphenotypic (it has both markers)	
Non	Acute undifferentiated (very early blast)	





- **Mainly immature blast cells**





- **Mature Granulocytes** **mature lymphocytes**

❖ Myeloproliferative Neoplasms:

- proliferation of mature cells myeloid cells **mainly Granulocytes** in bone marrow or in blood
- Occur mainly in adults
- Slow onset and long course

➢ MPN (myeloproliferatice neoplasm) features:

- Cytoses (cytosis is single)
- Organomegaly (mainly splenomegaly)
- High uric acid (increase destruction of cells) (might lead to gout)
- Hypercellular bone marrow (normally <50% is cells and the remainder is fat)

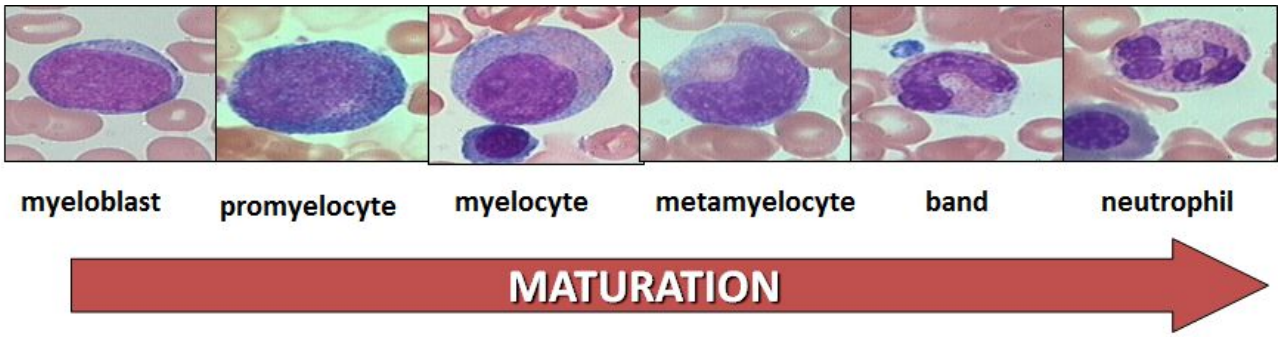
this feature must be present, if not present go see something else.

- Progression to acute leukaemia (mainly **AML**) + marrow fibrosis.

➢ Chronic Myeloid Leukemia (CML):

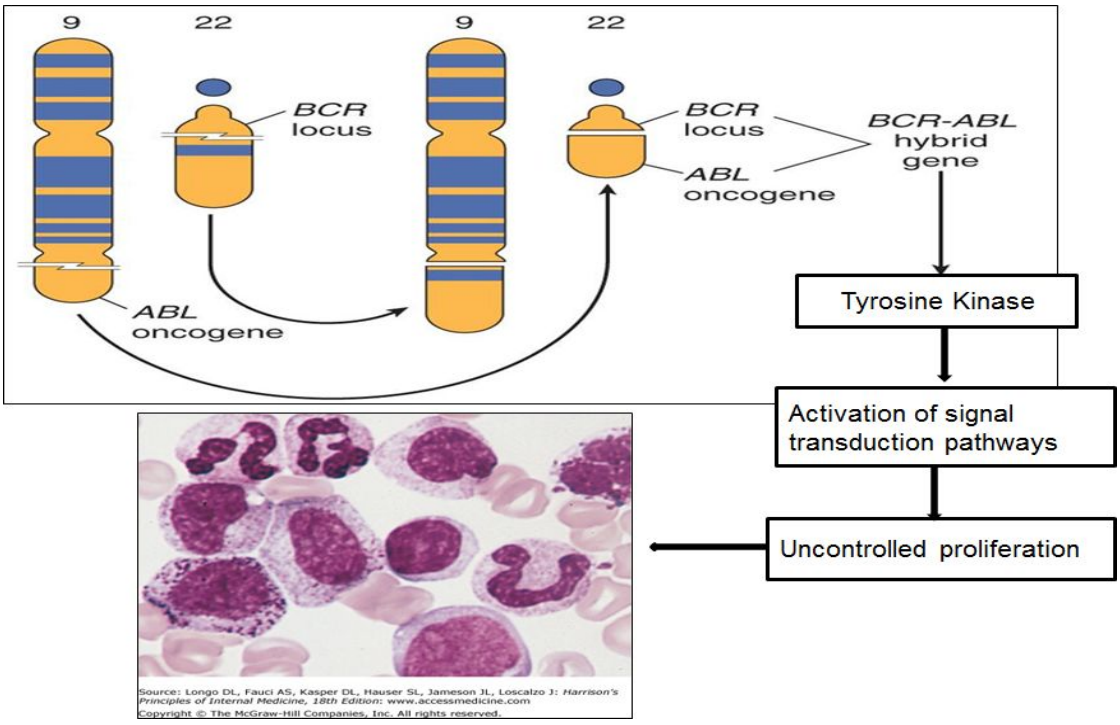
- Stem cell MPN. (mature myeloid cells)
- Predominant proliferation of **granulocytic cells**. (very important)
- Consistently associated with the BCR-ABL1 fusion gene located in the Philadelphia (Ph) chromosome (abnormal chromosome) which results from t(9;22) protein weight P210KD.

t(9;22) also occur in ALL (B-Lymphoid) BUT the difference is in protein weight P190KD.



Note: The predominant cells are myelocyte and neutrophils .

➢ Pathogenesis of Chronic myeloid leukemia:

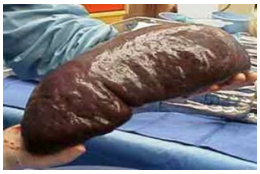


Note: The main two consequences in pathogenesis are increase proliferation & decrease apoptosis.

➢ Clinical Presentation:

- Asymptomatic presentation (20-40%)
- Routine CBC : marked leukocytosis
- Common symptoms : Fatigue ,weight loss or night sweating
- Abdominal discomfort due to splenomegaly (not normal, its massive)

- Splenomegaly (Massive) Also in leishmeniae spleen called in Arabic الدمام



➢ Main Differential Diagnosis:

1- **Chronic myelomonocytic leukemia (CMML)** (**monocytosis** ,**BCR-ABL –ve**) .
2-**Leukemoid reaction**: Leukocytosis due to physiological response to stress or infection(not malignancy)

	CML	Leukemoid reaction
Age	Adult	Any age
WBC count	High	High but <100,000
Differential	Mainly myelocytes and segmented	Mainly Bands
Morphology	**Hypogranular** (non-functioning)	Toxic
Splenomegaly	+	-/+
NAP score هذا يفرق بينهم بسرعة	Low	High
BCR/ABL هذا يبغاله وقت عشان يطلع	+ve	-ve
Onset	Chronic	Acute

➢ Neutrophil Alkaline Phosphatase (NAP)score: (Old method)

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

High: Leukemoid	Low : CML

➢ Chronic Myeloid Leukemia (Tri phasic disease) Phases

➢ Chronic phase (Target therapy)

- Leukocytosis (12-1000×10^9/L)
- Mainly neutrophils and myelocytes
- Blasts ≤10% اقل من,Basophils≤ 20% اقل من
- Stable course (years)

➢ Accelerated phase

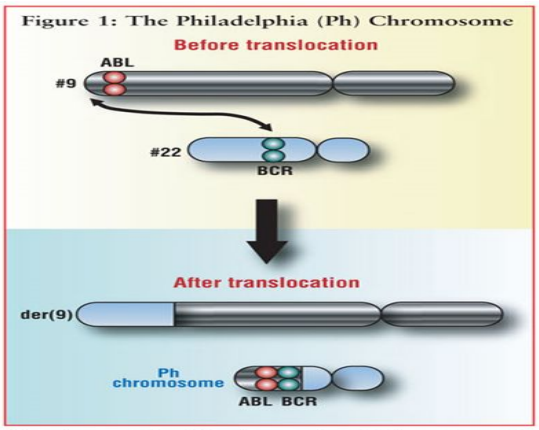
- Increasing counts
- 10-19% blasts (Why 19% ? because if it is 20 it will be AML) (basophils ≥20%) اكثر من
- Unstable course (months)

➢ Blastic phase (Die)

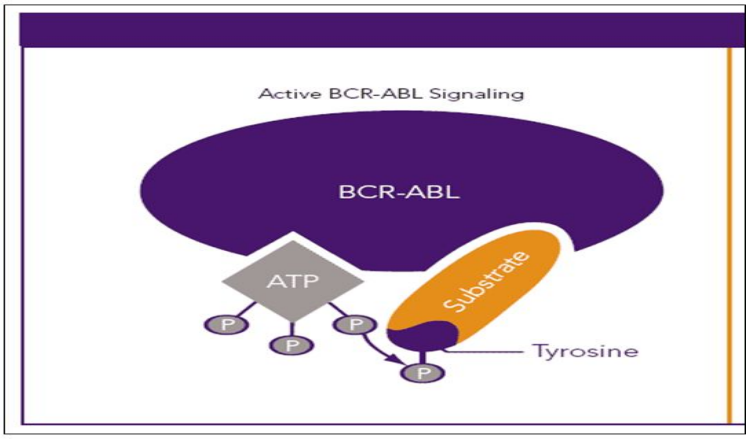
- (≥20% اكثر من blasts = Acute Leukemia)
- (80% AML & 20% ALL)
- Coarse (Weeks)

➢ Treatment: فِي تيم 433و434 ذاكرين انه مو مهم))

- 1st line therapy (tyrosine kinase inhibitors like Imatinib)
  -Excellent response (5 years survival ≥ 90%) it prevent the fusion of BCR-ABL
- 2nd line therapy If **no response** : stem cell transplantation.

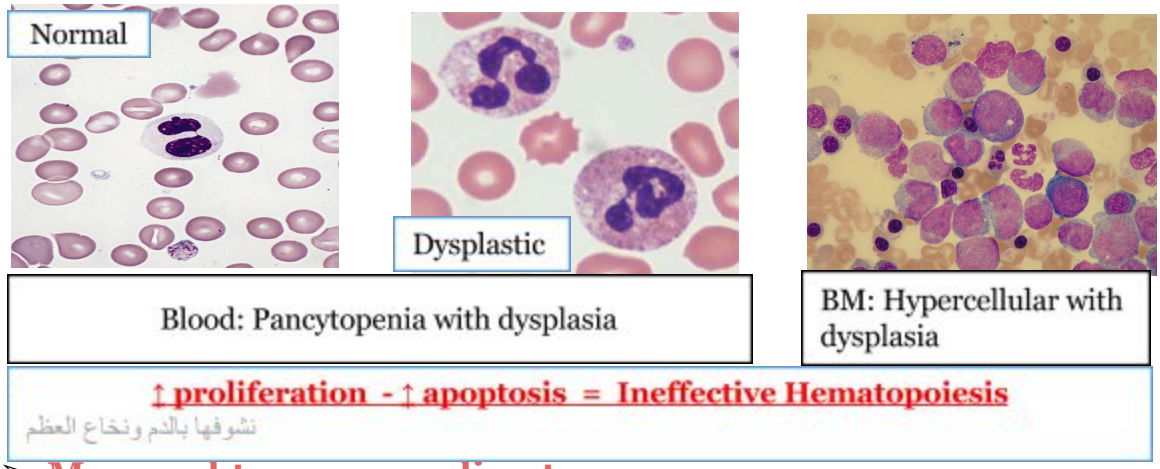


When chromosomes 9 and 22 exchange portions of their genetic material, this translocation results in the formation of der(9), an elongated chromosome 9, and the Ph chromosome, which contains the hybrid BCR-ABL gene.



Myelodysplastic Syndromes (MDS)

Group of myeloid neoplasm's characterized by:
1- Peripheral cytopenia (low Hemoglobin ± low WBC & low PLT).
2- Dysplasia (abnormal morphology).
3- Ineffective hematopoiesis (hypercellular bone marrow). Ineffective means ما منه فايدة
4- Progression to AML (preleukaemic disease).
5- Enhanced apoptosis. in the perepheral blood cause cytopenia



➢ **Many subtypes according to:**

1- Blast count. (لازم نسويه)
2- Degree of dysplasia.
3- Genetics :Variable genetic abnormalities mainly (-5 good prognosis , -7 bad prognosis)

➢ **Treatment:** (في تيم 433و434 ذاكرين انه مو مهم)

supportive +/- chemotherapy

Chronic Myelomonocytic Leukemia (CMML)

Clonal Hematopoietic malignancy characterized by **proliferation of both monocytes and neutrophils**

MDS/MPN disease: MIXED

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