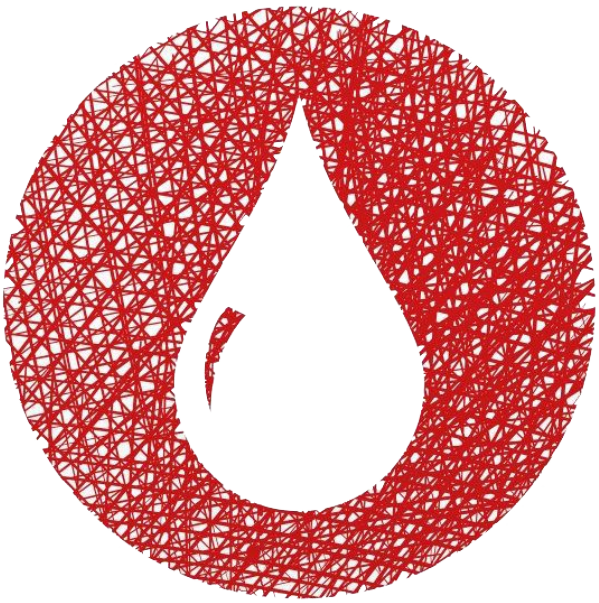


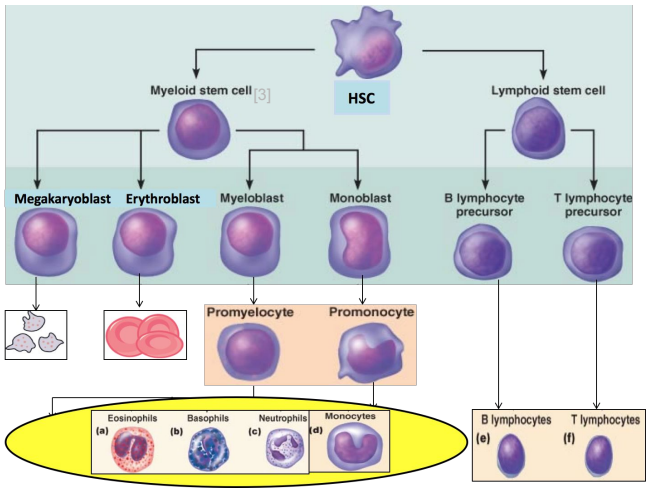
Chronic Leukemia's

Team leaders : Abdulrahman Alageel, Ebtesam Almutairi.
Done by :Khalid aldosari, Saif ALMeshari,
sultan al nasser.

Impotent
Notes
Doctor's slides

Chronic Leukemia's

- Heterogeneous group of hematopoietic neoplasms
- Uncontrolled proliferation and decreased apoptotic activity with variable degrees of differentiation[1]
- Composed of relatively **mature**[2] cells
- Indolent. (If untreated, the course is in months or years)
- Occurs mainly in adults.



	Acute	Chronic [4]
Lymphoid	ALL	LPN(CLL)
Myeloid	AML	MPN/MDS (CML)
Mixed	Acute Biphenotypic	
Non	Acute Undifferentiated	

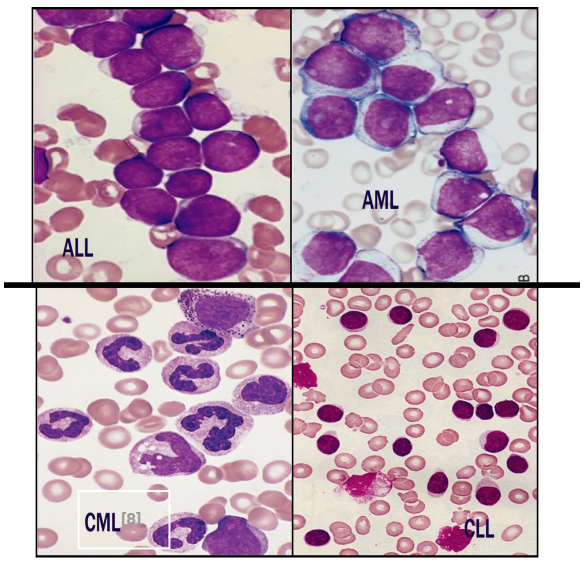


Table 1. Classification of Myeloid Neoplasms According to the 2008 World Health Organization Classification Scheme

1. **Myeloproliferative neoplasms (MPN)**
   - 1.1. Chronic myelogenous leukemia, *BCR-ABL1*–positive (CML)
   - 1.2. Polycythemia vera (PV)[5]
   - 1.3. Essential thrombocythemia (ET) [6]
   - 1.4. Primary myelofibrosis (PMF)
   - 1.5. Chronic neutrophilic leukemia (CNL)
   - 1.6. Chronic eosinophilic leukemia, not otherwise specified (CEL-NOS) Chronic **Basophilic** leukemia will release histamine
   - 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** [7]
   - 3.1. Chronic myelomonocytic leukemia (CMML) In adults
   - 3.2. Juvenile myelomonocytic leukemia (JMML) In children
   - 3.3. Atypical chronic myeloid leukemia, *BCR-ABL*–negative (aCML) Same feature of CML but (-) genetics.
   - 3.4. MDS/MPN, unclassifiable
4. **Myelodysplastic syndromes (MDS)** تشوه في morphology(dysplastic)
5. **Acute myeloid leukemia (AML)**

[1] you will see mature cells: neutrophils, basophils, RBC, platelets.
[1] chronic -> mature cells and take months or years to appear [silent] , acute -> immature and take hours.
[3] No block of differentiation + mutation here will affect stem cell but it will be mature unlike in acute.
[4] Unlike acute there is no ambiguous.
[5]malignancy affecting erythroid precursor will lead to increase number of RBCs, will present with high CBC espiacially **RBCS,HB → differentiation.**
[6]high platelet count mutation in megakaryocyte→ it may increase up to 2 million platelet
Sometime the patient may come with bleeding because of the platelet not functioning and sometime they may come with DVT
[7] MPN: monocytosis or leukositosis or neutrophilia , MDS: Cytopenia , anemia , thrombocytopenia.
[8]In NTs if you see myeloperoxidase absent this is part of malignancy.

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.
-

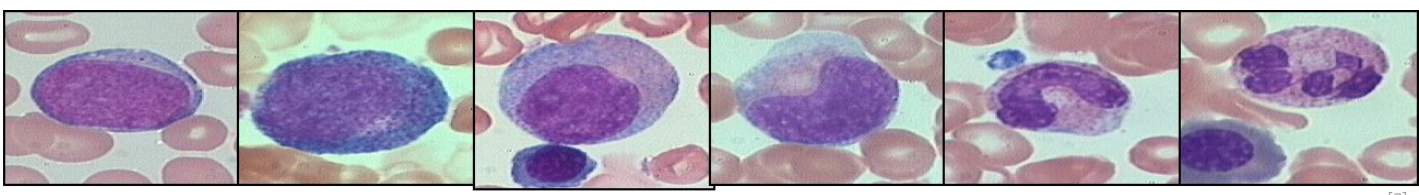
CML and MPN are almost the same
But MPN اشمل it is include CML and polycythemia
All one categorise

Myeloproliferative Neoplasms features :

- **Cytoses** [1]
- **Organomegaly (mainly splenomegaly)** [2]
- **High uric acid**[3]
- **Hypercellular**(mature cell not blast) **bone marrow**
- **Progression to acute leukaemia (mainly AML)**

Chronic Myeloid Leukemia (CML)[4]

- Stem cell MPN.[5]
- Predominant proliferation of **granulocytic** cells.
- Consistently associated with the **BCR-ABL1**(protein) fusion gene located in the Philadelphia (Ph) chromosome which results from t(9;22) . [6]



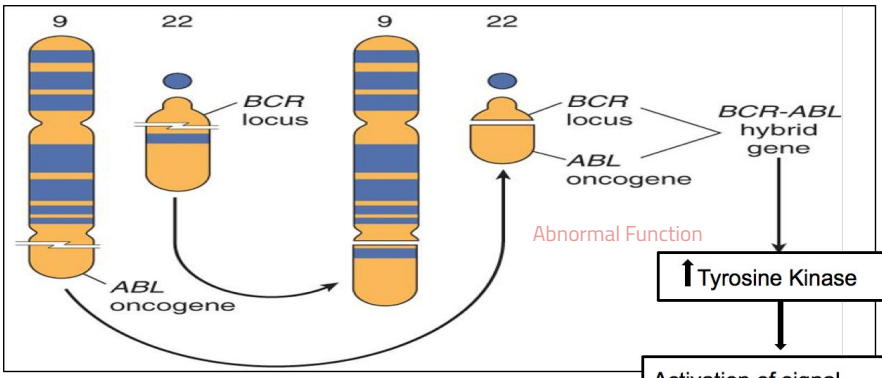
[7]

myeloblast promyelocyte myelocyte metamyelocyte band neutrophil

MATURATION

[1] (leukocytosis, thrombocytosis, erythrocytosis)At least one of them.
[2] It will try to take all cells to decrease the viscosity of the blood to prevent DVT. Sometime it will start to synthesis of cell.
[3] (because of increase destruction of cells)
[4]Before the diagnosis is based on morphology, leukocytosis and splenomegaly. Now it's based on Genetic.
The patient come with leukocytosis and the prognosis 95% death , now it is 95% cure after we know the gene and the drug.
[5]you will have many NTs, myelocytes
[6]No CML without BCR-ABL1
[7] if you see CBC you find myelocyte and neutrophil increase most likely he has CML

Pathogenesis of CML



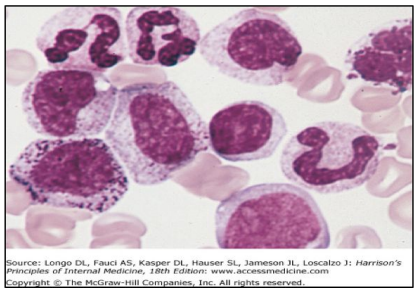
Abnormal Function

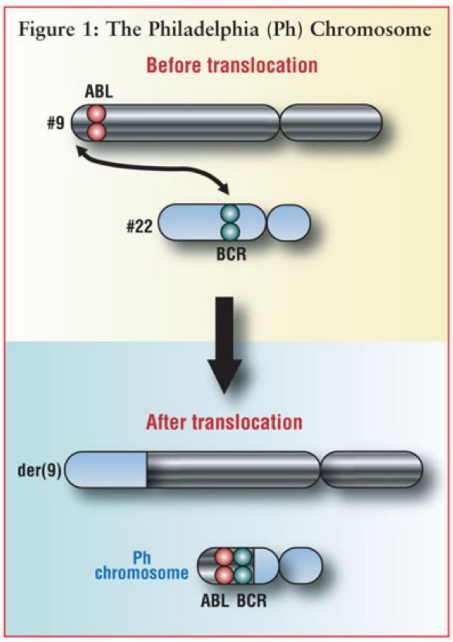
↑ Tyrosine Kinase

Activation of signal transduction pathways

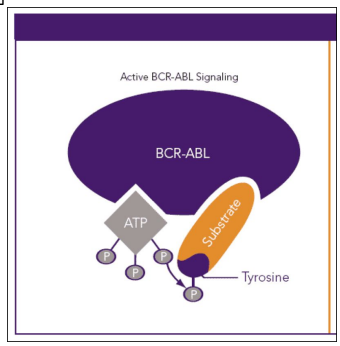
Uncontrolled proliferation

Autonomous proliferation





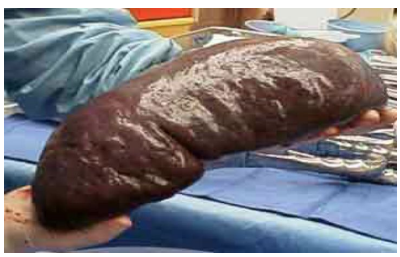
When chromosomes 9 and 22 exchange portions of their genetic material, this translocation results in the formation of der(9), an elongated chromosome 9, and the Ph chromosome, which contains the hybrid BCR-ABL gene.



Will go to nucleus and cause proliferation

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)[1]



[1] massive exceeding the umbilicus
3 causes: 1- CML
2-lieshmenia
3-primary myelofibrosis

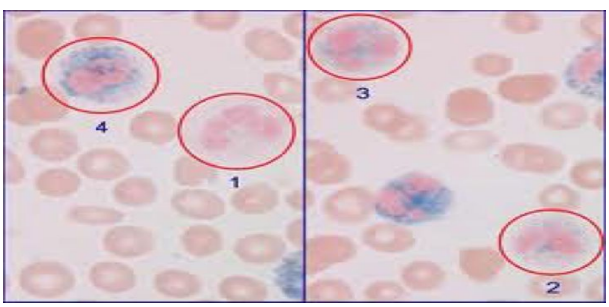
Main Differential Diagnosis

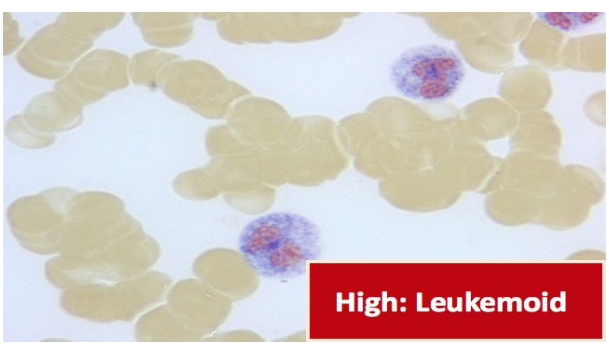
1- Chronic myelomonocytic leukemia (monocytosis ,BCR-ABL –ve) .

2-Leukemoid reaction: Leukocytosis due to physiological response to stress or infection or autoimmune disease.

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

Neutrophil Alkaline Phosphatase (NAP)score :
Cytochemical stain that estimate the amount of alkaline phosphatase enzyme in neutrophilis .

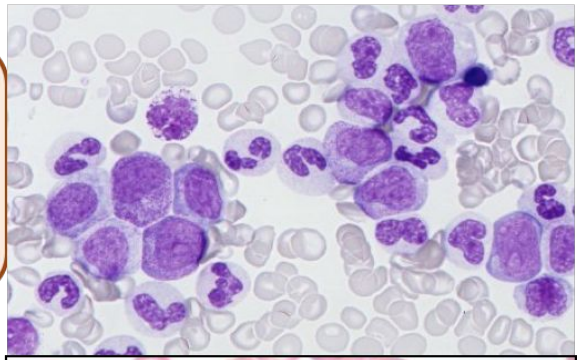




CML Phases

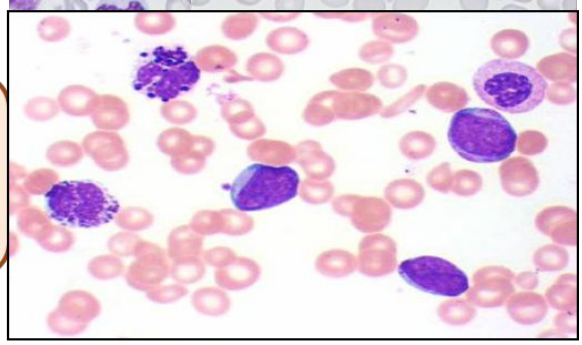
Chronic phase

- Leukocytosis (12-1000×10⁹/L)
- Mainly neutrophils & myelocytes
- Blasts ≤10% ,Basophils≤ 20%
- Stable course (years)



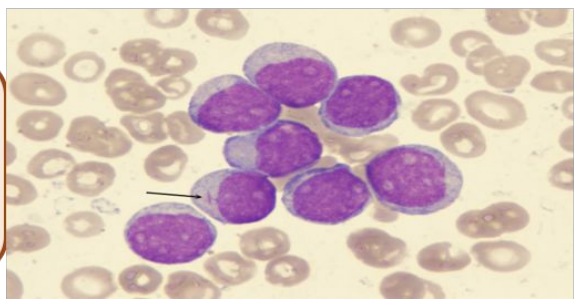
Accelerated phase[1]

- Increasing counts
- 10-19% blasts (basophils ≥20%)
- Unstable course (months)



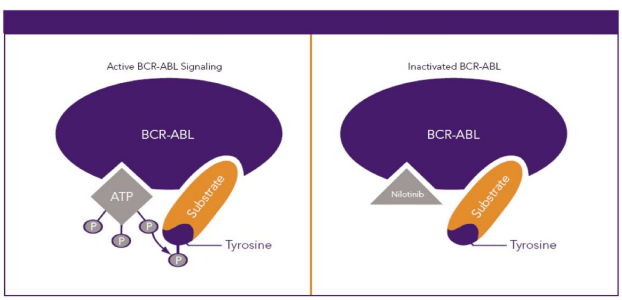
Blastic phase

- ≥20% blasts = Acute Leukemia[2]
- 80% AML & 20% ALL
- (coarse: Weeks)



CML Treatment

- Targeted therapy (tyrosine kinase inhibitors like Imatinib)[3]
- Excellent response (5y overall survival≥ 90%)[4]
- If no response ; stem cell transplantation

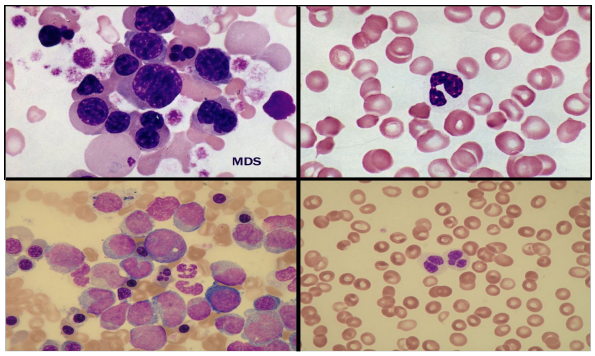


[1] you have to give them chemotherapy لـ عشان مايروحون phase3
[2] AL you should give them chemotherapy
[3] It's expensive and it has little side effect bitter than paracetamol.
[4]10% have mutation in BCR-ABL.

Myelodysplastic Syndromes MDS[1]

Group of myeloid neoplasms characterized by:

1. **Peripheral cytopenia (Low HB ± Low WBC & Low PLT)**[2]
2. **Dysplasia (abnormal morphology)**
3. **Ineffective hematopoiesis (hypercellular marrow)**[3]
4. **Progression to AML (pre leukemic disease)**
5. **Enhanced apoptosis**



Many subtypes according to:

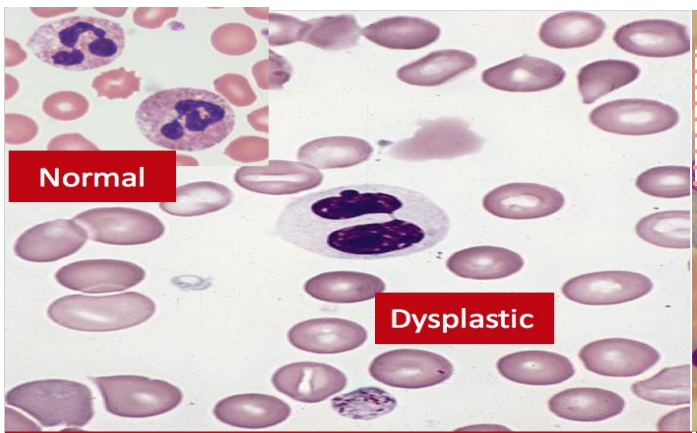
1-Blast count (MDS related to AML)

2-Degree of dysplasia [4]

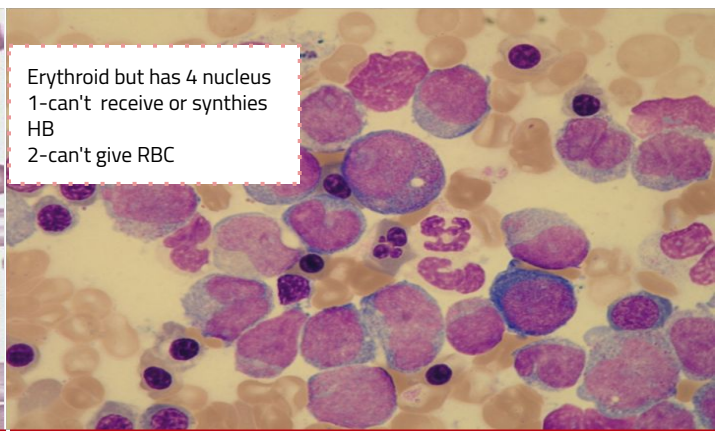
3-Genetics

- **Variable genetic abnormalities mainly -5, -7**
- **Treatment : supportive +/- chemotherapy**[5]

-5:monosomy, good prognosis, more in female
-7: monosomy, bad prognosis.



Blood: Pancytopenia with dysplasia



Erythroid but has 4 nucleus
1-can't receive or synthies HB
2-can't give RBC

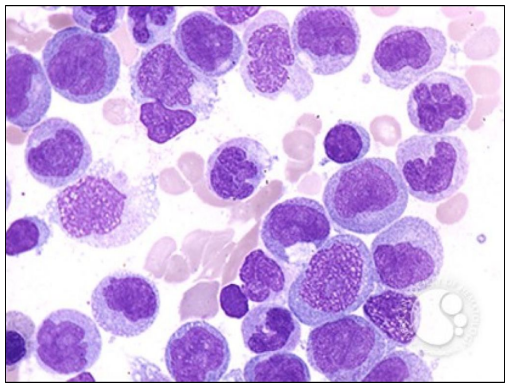
BM: Hypercellular with dysplasia

Proliferation — **Apoptosis** = **Ineffective Hematopoiesis**

[1] production of abnormal morphological cells.
[2]In MPN will have peripheral cytosis.
[3]Because of ineffective hematopoiesis→BM produce cell but not functioning will die in peripheral blood that is why he will have 1- cytopenia 2- hypercellular BM
[4] may come with pancytopenia affect WBCs, RBCs,Platelet or may one of them (unilinear , unilinage)
[5] we give him transfusion RBCs or Antibody or platelet depending on the problem

Chronic Myelomonocytic Leukemia (CMML)[1]

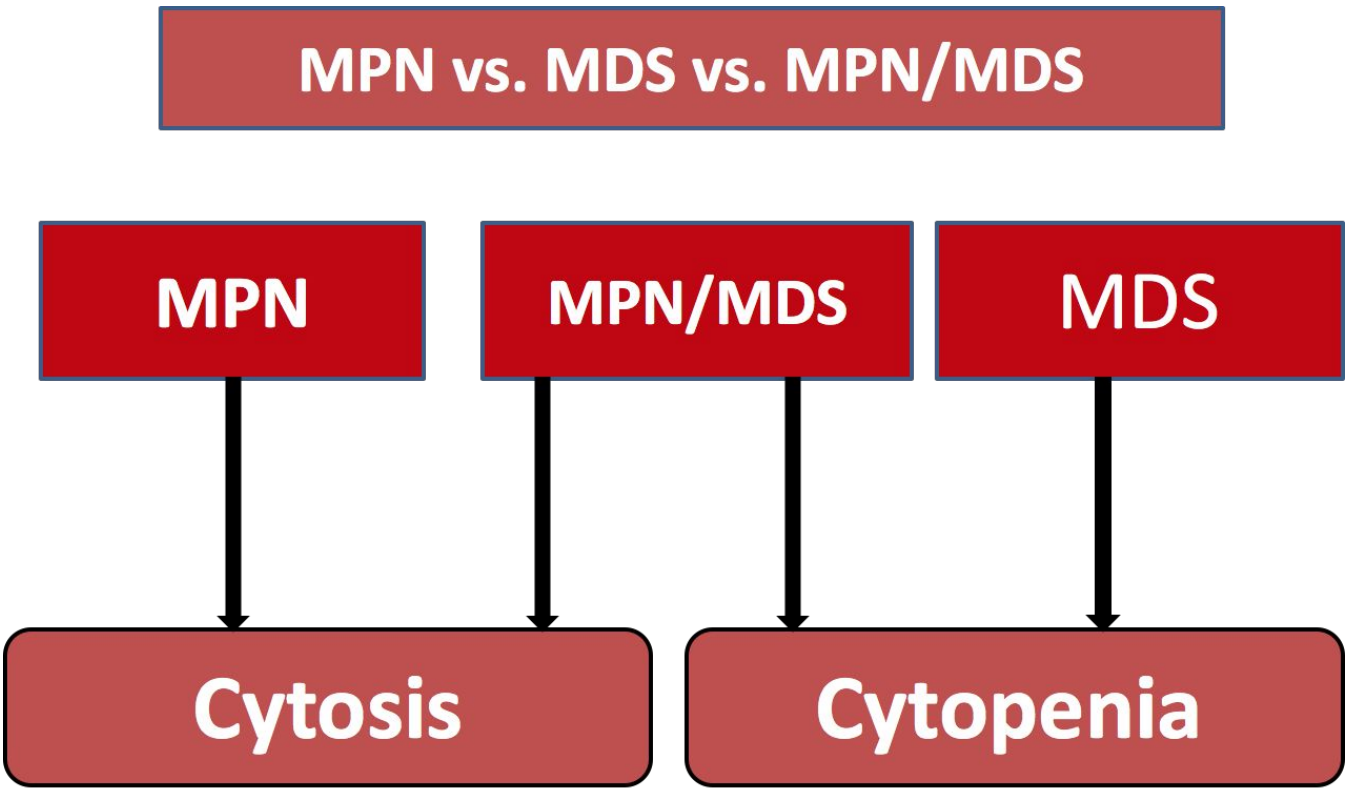
- Clonal Hematopoietic malignancy characterized by proliferation **of both monocytes and neutrophils.**[2]
- MDS/MPN disease:



* **Features of MDS (dysplasia& enhanced apoptosis)**

***Features of MPN (marked proliferation)**

- **Philadelphia chromosome must be negative**[3]
- Blast must be less than 20%.
- Aggressive course (survival rate around 2.5 y)
- Treatment : Chemotherapy ±SCT[4]



[1]will present with very severe anemia and cytosis
[2] reduction of platelet and RBC
[3] positive = CML
[4] stem cell transfusion