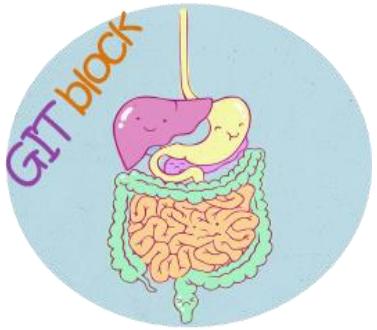


Chronic leukaemia

NOTE : THIS TEAMWORK DON'T VIEW EVERYTHING IN THE SLIDES ONLY
THE IMPORANT THINGS NOTED BY THE DOCTORS

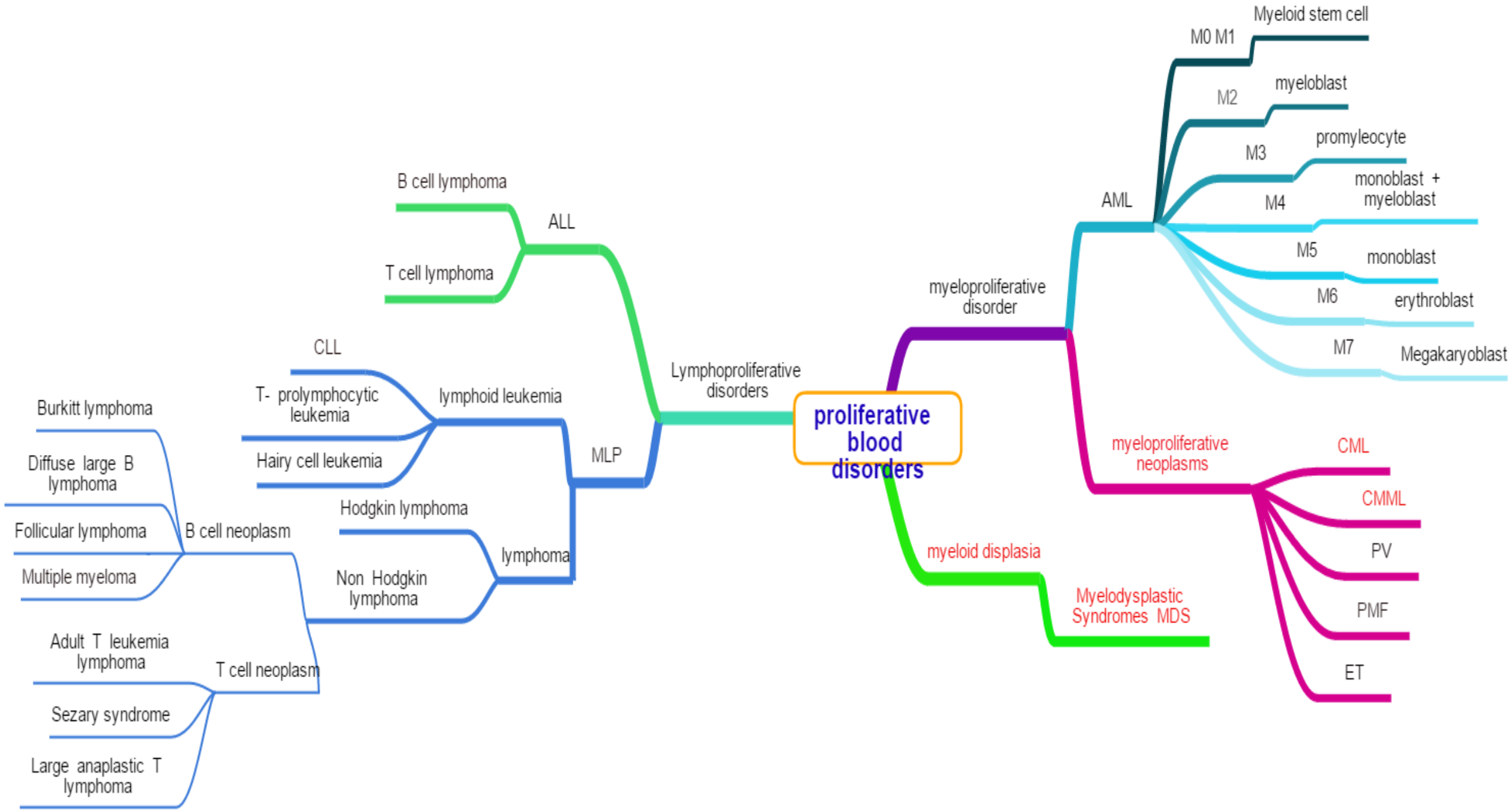
Color coding

- **important**
- **Extra info**
- **Notes from lecturer**

دعاء فبل المذاكرة :

(اللهم أني أسالك فهم النبين و حفظ الملرسلين و الملائكة المقربين اللهم اجعل السنتنا عامرة بذكرك و قلوبنا بخشيتك، أنك على كل شيئا قدير و حسبنا الله نعم الوكيل)

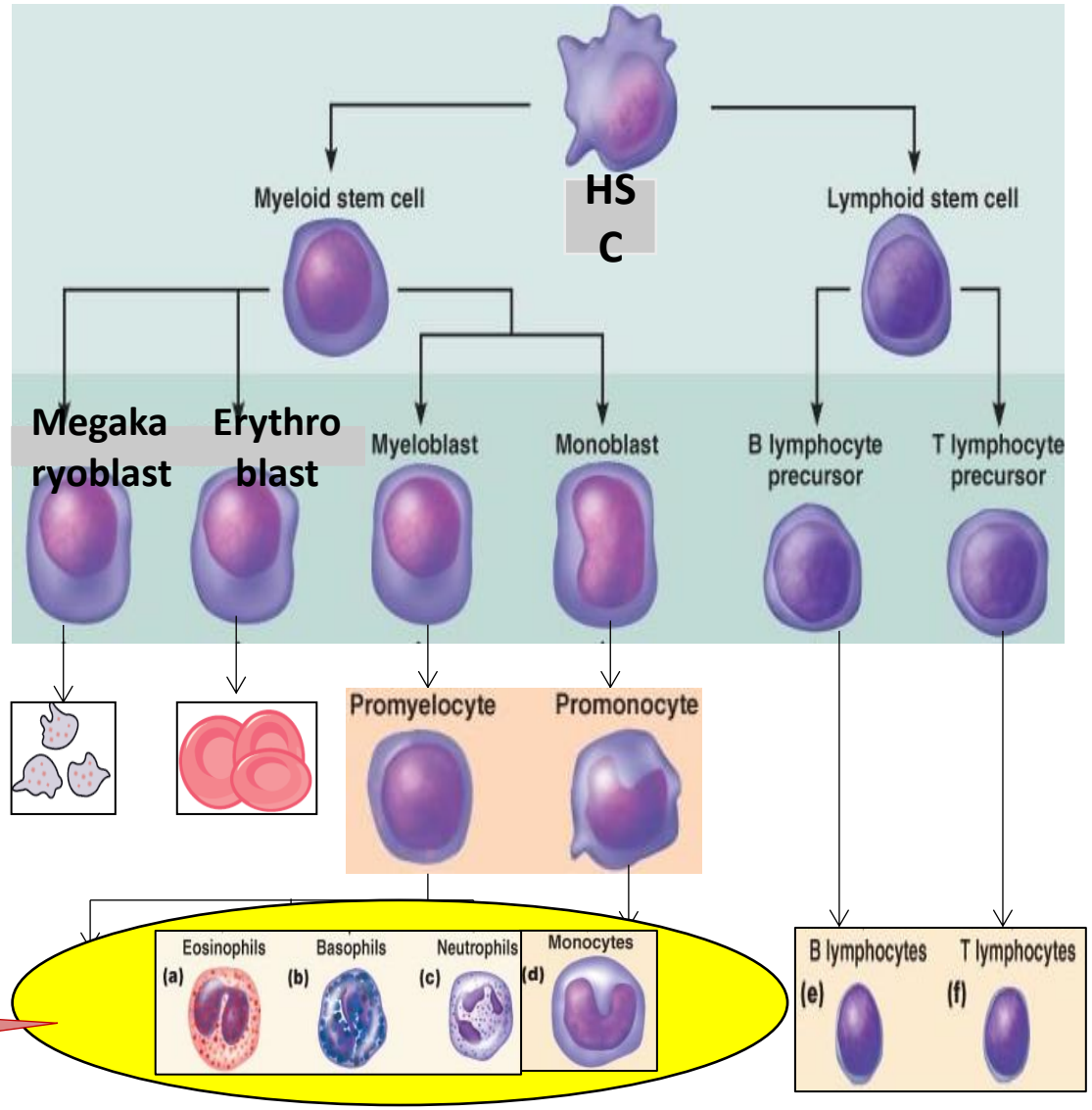
Please don't hesitate to contact us on:Haematology434@gmail.com


proliferative blood disorders
Lymphoproliferative disorders
ALL
B cell lymphoma
T cell lymphoma
MLP
lymphoid leukemia
CLL
T- prolymphocytic leukemia
Hairy cell leukemia
lymphoma
Hodgkin lymphoma
Non Hodgkin lymphoma
B cell neoplasm
Burkitt lymphoma
Diffuse large B lymphoma
Follicular lymphoma
Multiple myeloma
T cell neoplasm
Adult T leukemia lymphoma
Sezary syndrome
Large anaplastic T lymphoma
myeloproliferative disorder
AML
Myeloid stem cell
M0 M1
myeloblast
M2
promyleocyte
M3
monoblast + myeloblast
M4
M5
monoblast
M6
erythroblast
M7
Megakaryoblast
myeloproliferative neoplasms
CML
CMML
PV
PMF
ET
myeloid displasia
Myelodysplastic Syndromes MDS

Chronic leukaemia

- •Heterogeneous group of hematopoietic neoplasms
- • **Uncontrolled proliferation** and **decreased apoptotic activity** with variable degrees of differentiation (Chronic leukemia unregulated growth of mature cells unlike the acute leukemia which is immature “precursors”) .
- •**Composed of relatively mature cells**
- •Indolent: slow growing with mild pain ”chronic” (If untreated, the course is in months or years)
- •Occurs mainly in adults

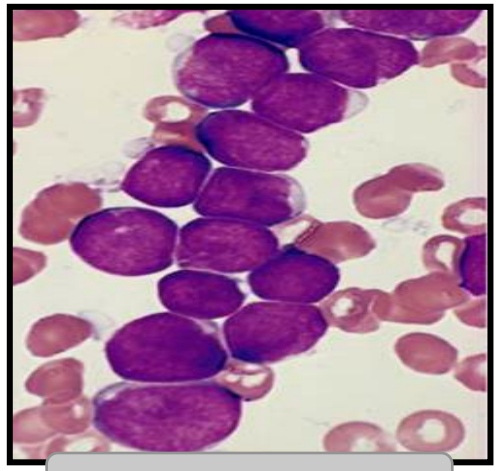
Variable differentiation and proliferation in this level of heamatopoiesis

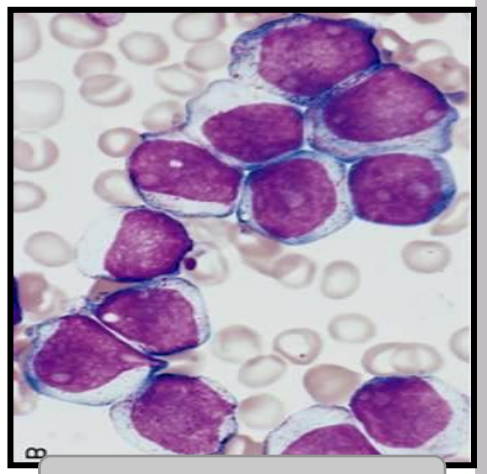


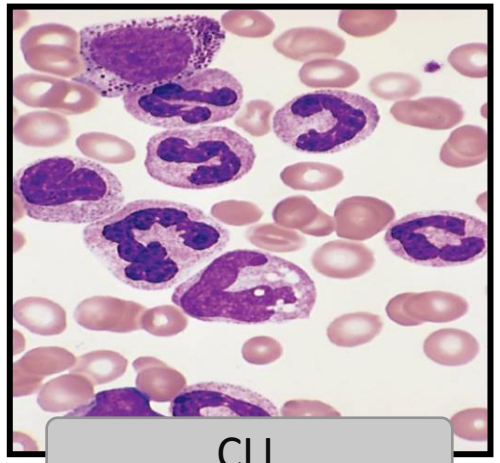
Main types of leukemia

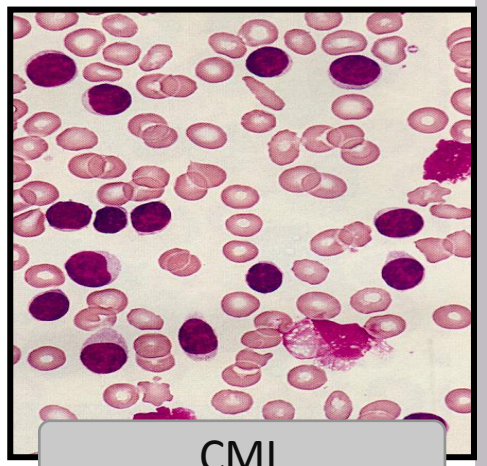
	Acute	Chronic
Lymphoid	ALL	LPN(CLL)
Myeloid	AML	MPN/MDS (CML)
Mixed	Acute Biphenotypic	
Non	Acute Undifferentiated	

*ALL: acute lemphocytic leukemia, AML: acute myeloid leukemia
*CLL: chronic lymphocytic leukemia, CML: chronic myeloid leukemia
*LPN: lymphoproliferative neoplasm, MPN: myeloprolferative neoplasm
*MDS: myelodysplastic syndrome
*Leukemia can be divided on the basis of the speed of evolution of the disease into acute (rapid,weeks to months) and chronic (slow,asymptomatic for years). Each of these is subdivided into myeloid and lymphoid according to the cell type involved


ALL


AML


CLL


CML

Myeloproliferation neoplasm(MPN)

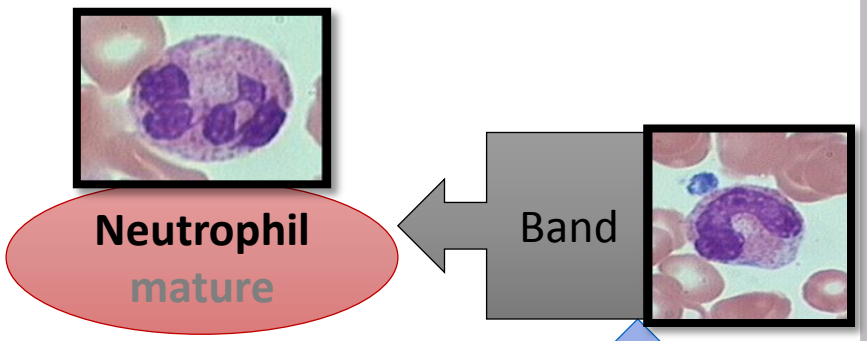
- **Malignant proliferation** of myeloid cells (maturing cells) which are mainly granulocytes (mostly neutrophils) in blood and bone marrow.
- • Occur mainly in adults
- • Slow onset and long course

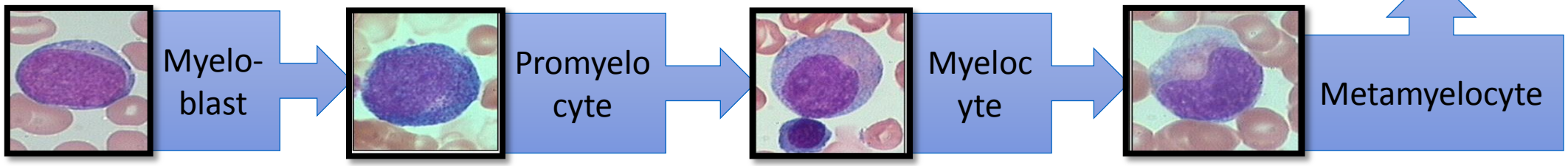
MPN features

Cytosis (increase in number of cells)
Organomegaly (mainly splenomgaly)
High uric acid (due to dystraction of blood cells, patients might develop gout)
Hypercellular bone marrow
Progression to acute leukemia mainly AML

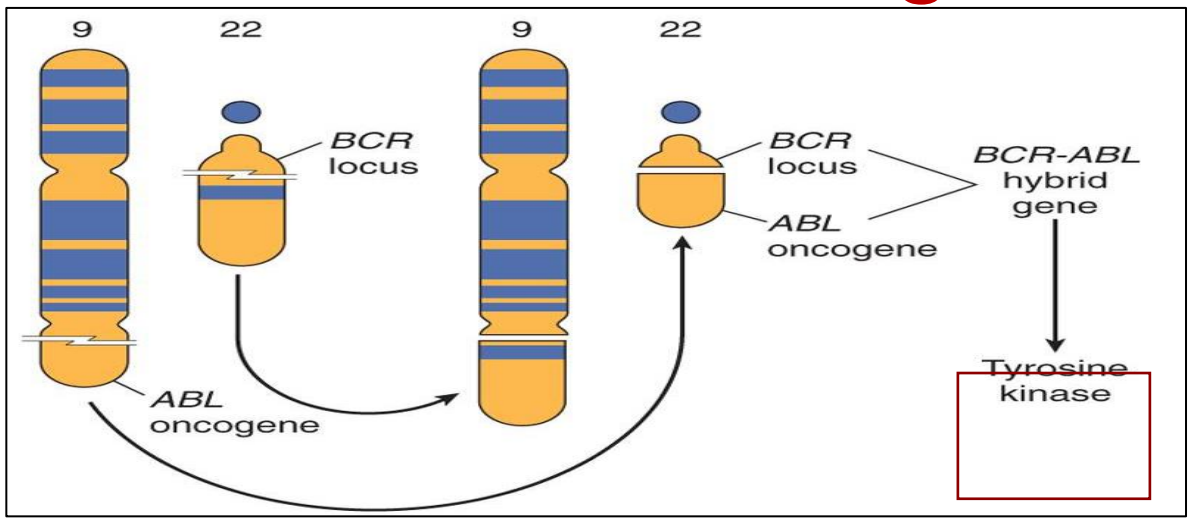
Chronic Myeloid Leukemia (CML)

- 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) .**

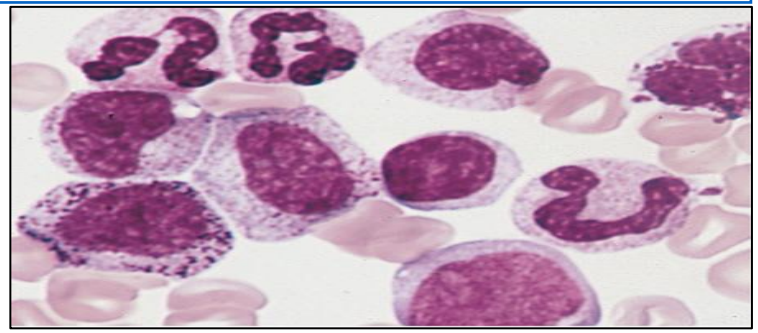




Pathogenesis of CML



Tyrosine Kinase : **is an enzyme involved in the activation of all steps of the transduction pathway of cellular proliferation.**
TK activity is increased abnormally when BCR gene and ABL1 gene are fused in Philadelphia chromosome which gives phosphate to transduction pathways that lead to (uncontrolled proliferation.)



Clinical presentation

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

splenomegaly

Main Differential Diagnosis

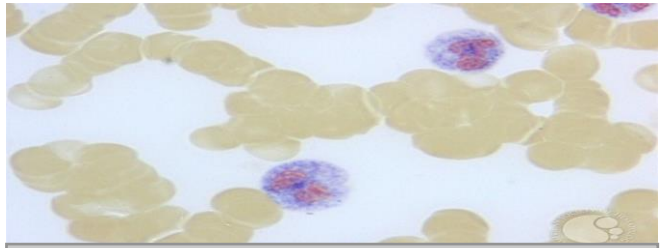
- **1- Chronic myelomonocytic leukemia (monocytosis, BCR-ABL negative).**
- **2- Leukemoid reaction: Leukocytosis due to physiological response to stress (inflammation) or infection.**

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

Neutrophil Alkaline phosphate (NAP) score

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

Low (negative): CML

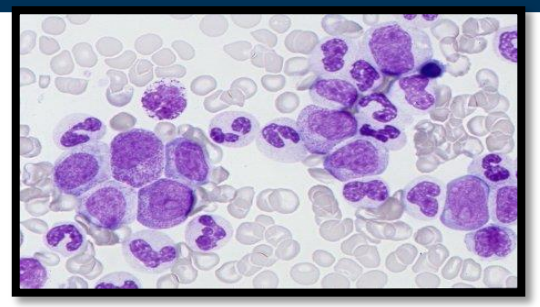


High: leukaemoid

Chronic myeloid leukaemia phases

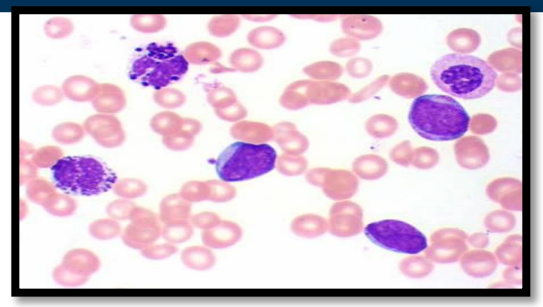
Chronic phase

Leukocytosis (12-1000x10^9/L).
Mainly neutrophils and myelocytes.
Blasts ∠10% ,Basophils∠ 20%.
Stable course (years).



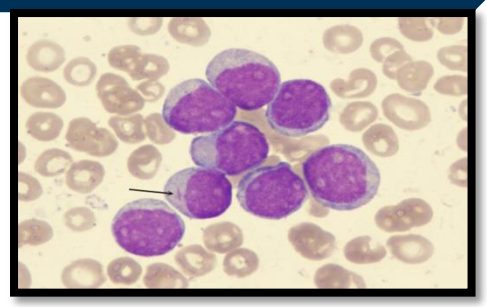
Accelerated phase

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



Blastic phase

≥20% blasts = Acute Leukemia.
80% AML and 20% all.
(coarse: Weeks).



Not important

Treatment

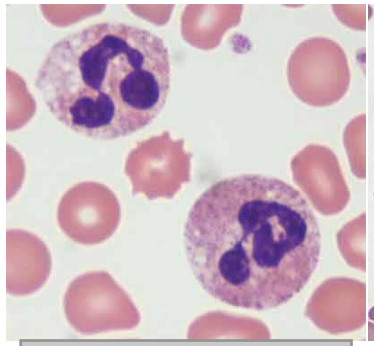
First line therapy: tyrosine kinase inhibitors like Imatinib.

- Excellent response (5 years survival >90%)

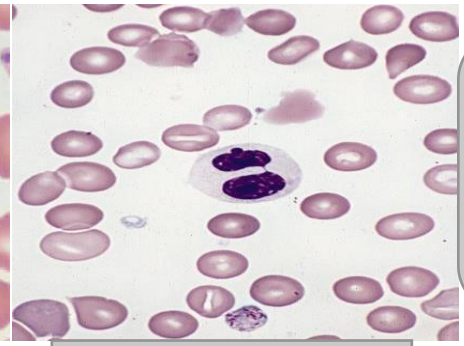
second line therapy: if no response => stem cell transplantation.

Myelodysplastic Syndromes (MDS)

- Group of myeloid neoplasm characterized by:
- **1- Peripheral cytopenia** (low HB +/- low WBC and low PLT).
- **2- Dysplasia** (abnormal morphology).
- **3- Ineffective hematopoiesis (hypercellular bone marrow).**
- **4- Progression to AML (preleukaemic disease).**
- **5- Enhanced apoptosis in the perepheral blood.**

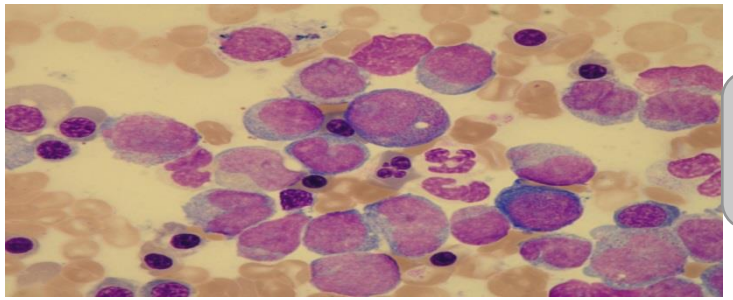


Normal blood



Dysplasia in blood

Blood: Pancytopenia with dysplasia



BM: Hypercellular with dysplasia

↑ proliferation - ↑ apoptosis = Ineffective Hematopoiesis

Many aubtypes according to:

1- Blast count.

2- Degree of dysplasia.

3- Genetics.

Variable genetic abnormalities mainly -5, -7.

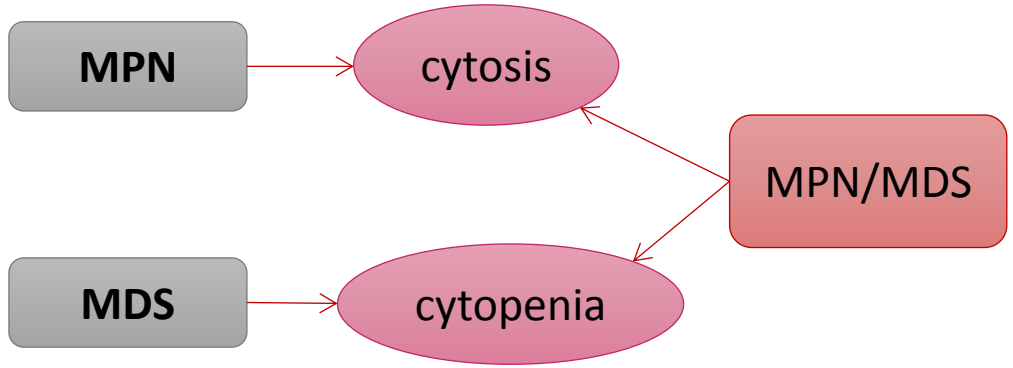
Treatment: supportive +/- chemotherapy.

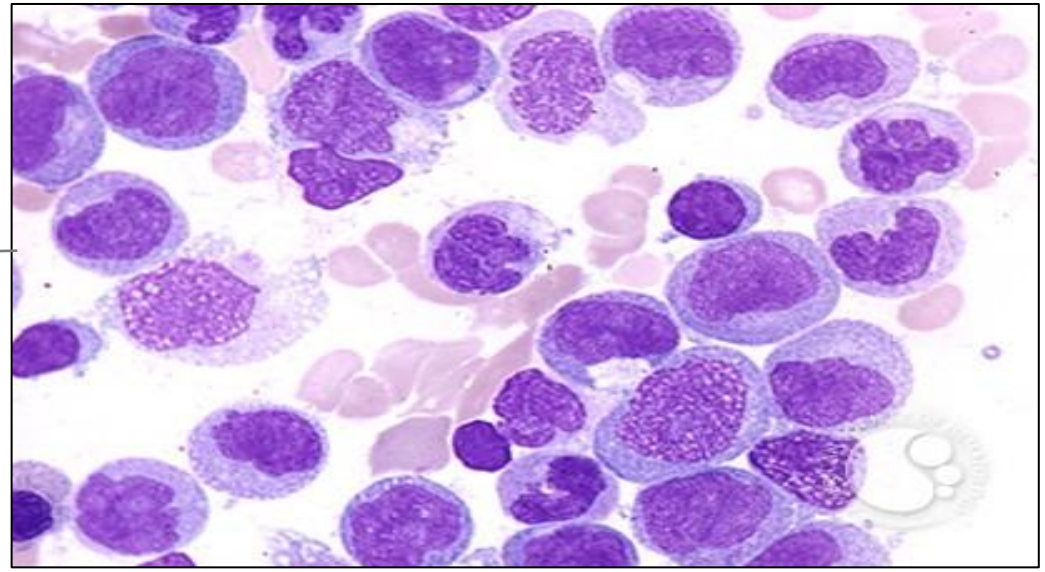
Chronic Myelomonocytic Leukemia (CMML)

- Clonal **Hematopoietic malignancy** characterized by **proliferation of both monocytes and neutrophils.**
- **MDS/MPN disease** (apoptosis & proliferation at the same time)

***Features of MDS** (dysplasia& enhanced apoptosis)
***Features of MPN** (marked proliferation)

- **Philadelphia chromosome must be negative**
- **Blast must be less than 20%** if more than 20% that means it is acute





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

1-in which level of heamatopoiesis chronic leukemia happens:

A. Platelet
B. B lymphocyte
C. Granulocyte
D. Erythrocyts

2- MPN : proliferation of immature cells:

A. false
B. true

3- which one is associated with BCR-ABL1 fusion gene

A. MPN
B. AML
C. MDS
D. CML

4- if NAP score was very low that indicate:

A. AML
B. CLL
C. leukaemoid
D. CML

5- MDS associated with:

A. Peripheral cytopenia
B. Hypercellular bone marrow
C. A & B
D. Non of the above

6-CMML characterized with:

A. Basophil proliferation
B. Monocyte proliferation
C. B lymphocyte proliferation
D. Eosinophil proliferation

1- C
2- A
3- D
4- D
5- C
6- B

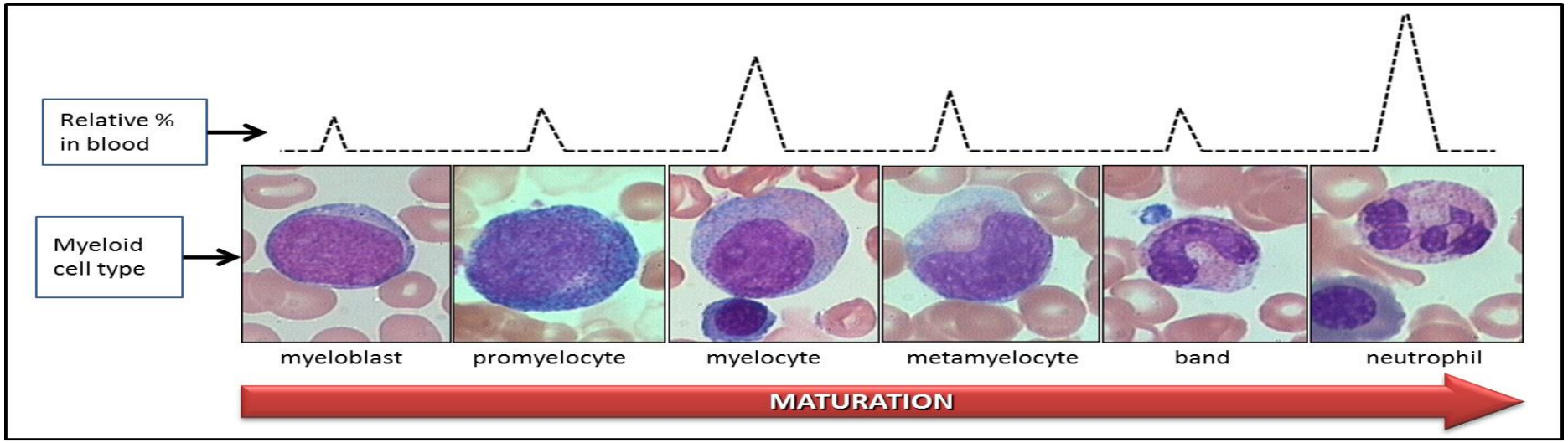
Q1 what is the function of TK enzyme?

an enzyme involved in the activation of all steps of the transduction pathway of cellular proliferation.

Q2 what are the MPN features?

- Cytosis (increase in number of cells)
- Organomegaly (mainly splenomgaly)
- High uric acid (patients might develop gout)
- Hypercellular bone marrow
- Progression to acute leukemia mainly AML but never to ALL

Q3what are the stages of neutrophil maturation?



Thank you for checking our work

Now you can check a lecture out :D

Done by:

Khalil alhindas

Salih albnyan

Abdulrahman alnoaem

Mohammed albadrany

Reviewed by:

Hadeel B.Alsulami

Abdullah M.albasha

دعاء بعد المذاكرة :

(اللهم اني أستودعتك ما قرأت وما حفظت وما تعلمت، فرده لي عند حاجتي اليه أنك على كل شيء قدير، وحسبنا الله ونعم الوكيل)