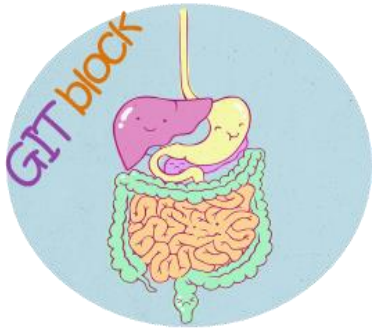


Myeloproliferative Neoplasms

Polycythemia vera (PV)–Essential Thrombocythemia (ET)- Primary Myelofibrosis (MF)

Color coding

- important
- Extra info
- Notes from lecturer

دعاء قبل المذاكرة :

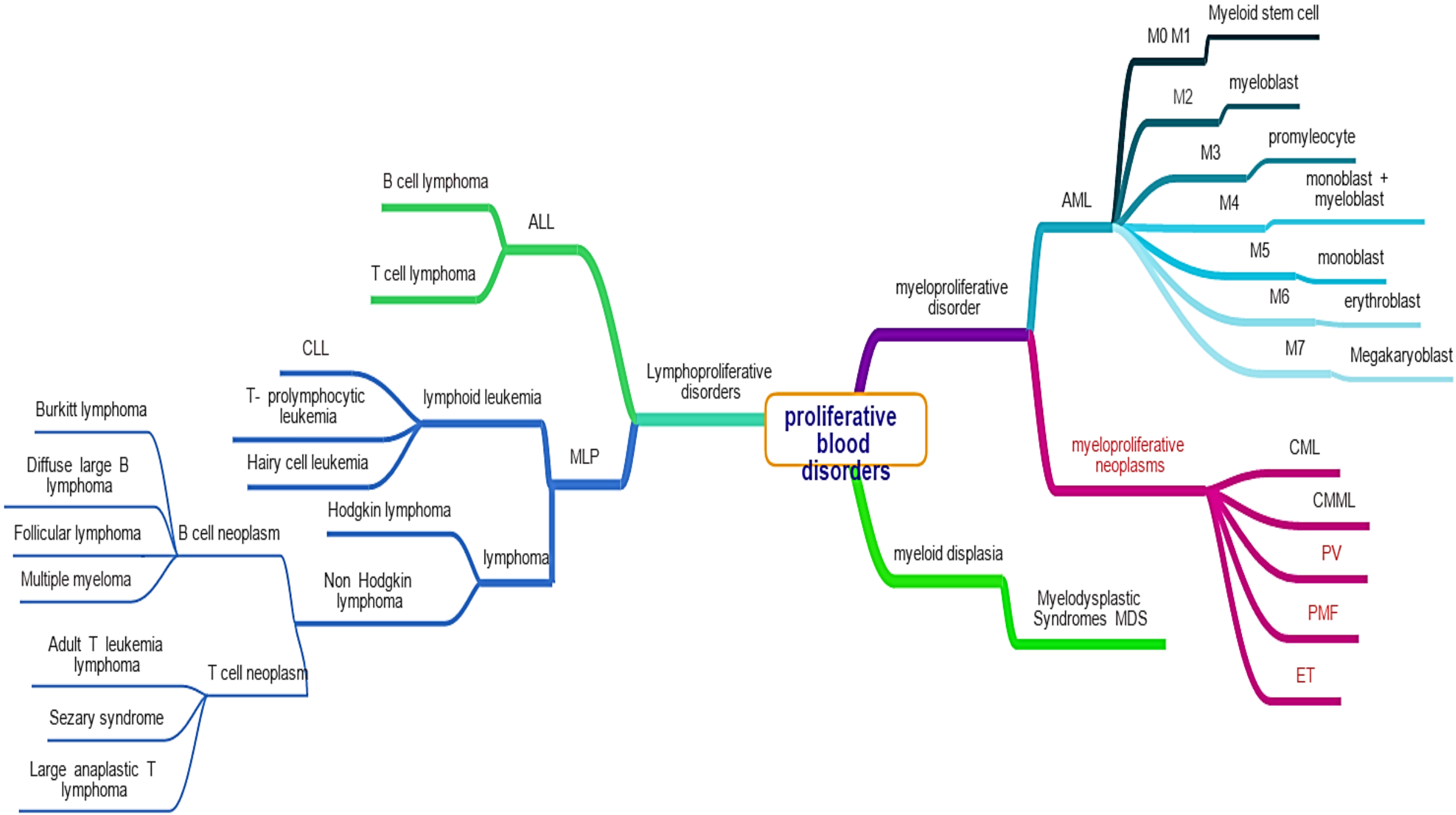
(اللهم أني أسالك فهم النبين و حفظ الملرسلين و الملائكة المقربين اللهم اجعل السنتنا عامرة بذكرك و قلوبنا بخشيتك، أنك على كل شيئا قدير و حسبنا الله نعم الوكيل)

DON’T FORGET to check our editing file : haematology edit

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

	Male	Female
Hemoglobin(g/dL)	13.5-17.5	11.5-15.5
Hematocrit (PCV) (%)	40-52	36-48
Red Cell Count ($\times 10^{12}$)	4.5-6.5	3.9-5.6
Mean Cell Volume (MCV) (fL)	80-95	
Mean Cell Hemoglobin (MCH) (pg)	30-35	
MCHC %	31 - 37	
Platelet count	140-450x10^3/L	
NORMAL PLATELET SIZE MPV	7.2-11.1 fl	
NORMAL PLATELET DIAMETER	1-2.5 µ	
WBC	4000-11,000 /L	
Segmented (neutrophils)	1.8-7.8	
Eos	0-0.45	
Baso	0-0.20	
Lymphs	1.0-4.8	
Monos	0-0.80	

A Good Doctor Knows normal CBC


proliferative blood disorders
Lymphoproliferative disorders
myeloproliferative disorder
MLP
ALL
B cell lymphoma
T cell lymphoma
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
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

MPN features

- Cytosis
- Organomegaly (mainly splenomgaly)
- High uric acid
- Hypercellular bone marrow
- Progression to acute leukaemia, mainly AML (About 80% will progress to AML)

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

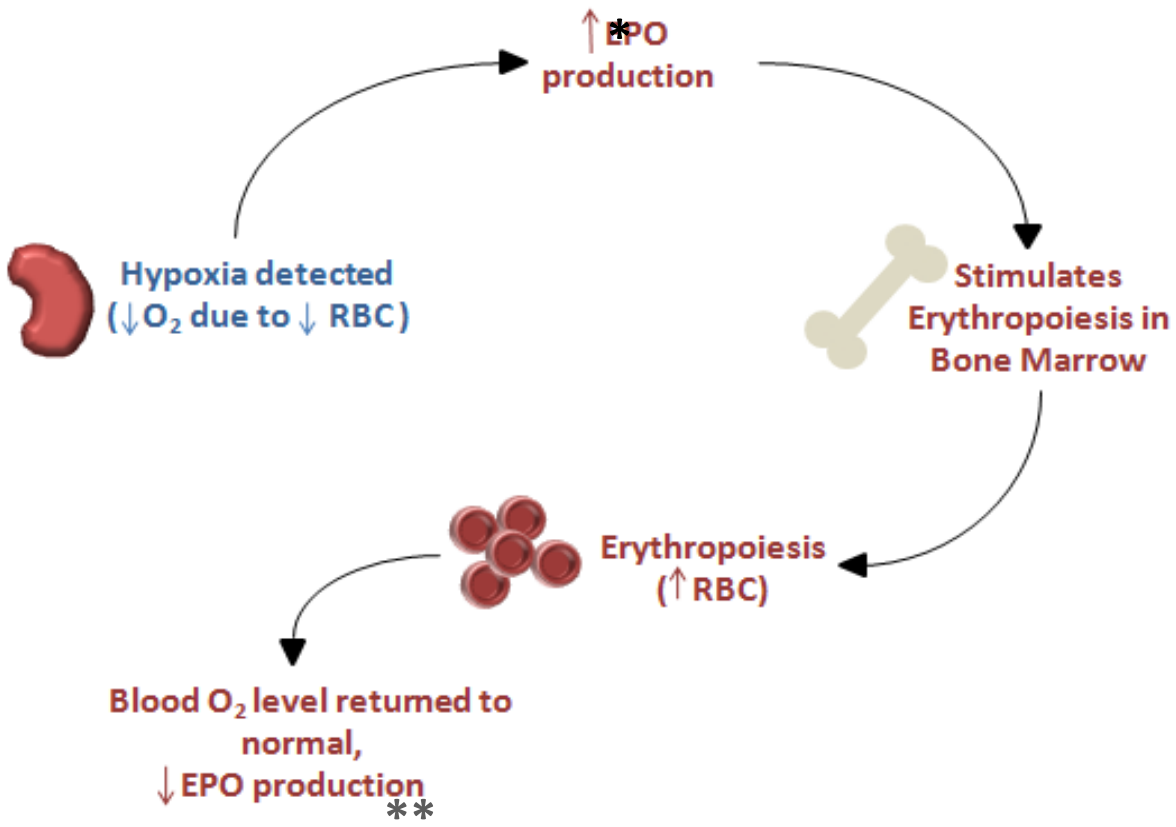
→ **2-8 BCR-ABL must be negative**

Polycythemia

It means "too many cells in the blood"

manifestations	
increase in total body red cell volume (or mass)	
High Hb or PCV	
Hb in Women	Hb in Men
More than 16.5 g/dl	More than 18.5 g/dl

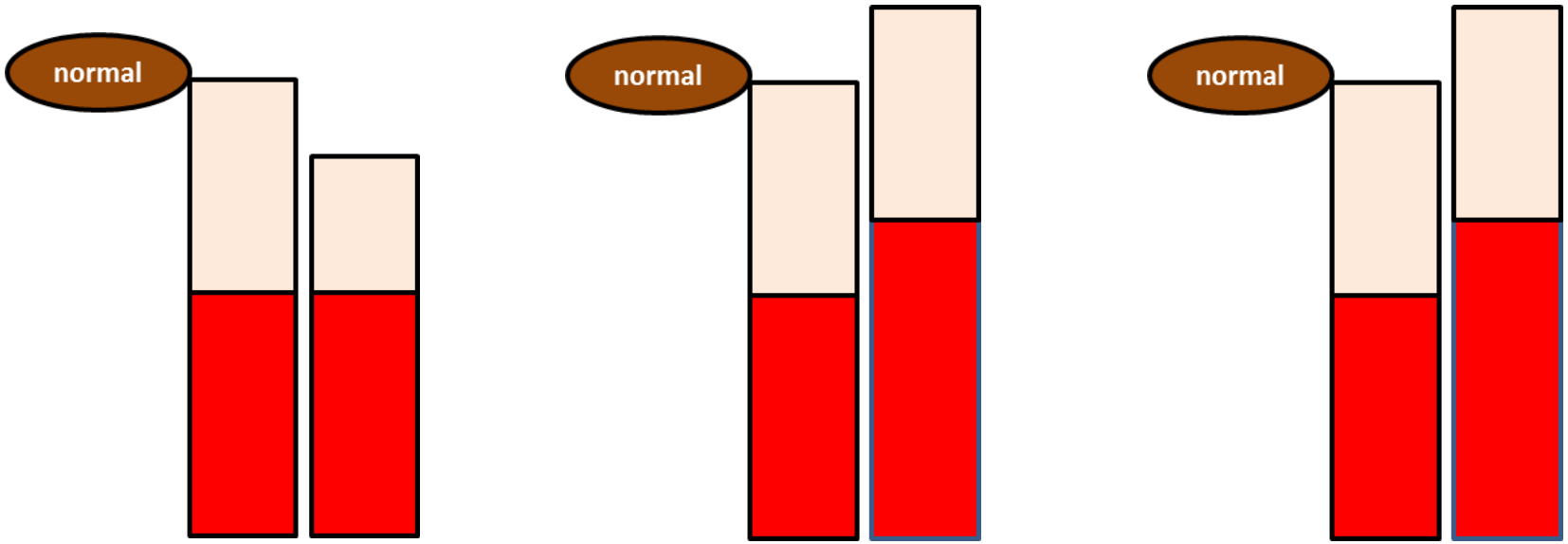
Regulation of Erythropoiesis



* Major site of Epo production is the kidney.

** When O2 increases the –ve feedback decrees the EPO production.

Classification of Polycythemia



Relative Polycythemia	2nd Polycythemia	Polycythemia vera
Decreased plasma volume due to **severe dehydration**	Increased RBC mass due to **high EPO**: • COPD, Sleep apnea, smoking • High altitude • High affinity HB • Renal disease • Epo secreating tumor (Parathyroid adenoma)	Increased RBC mass due to **malignant proliferation**

Polycythemia Vera

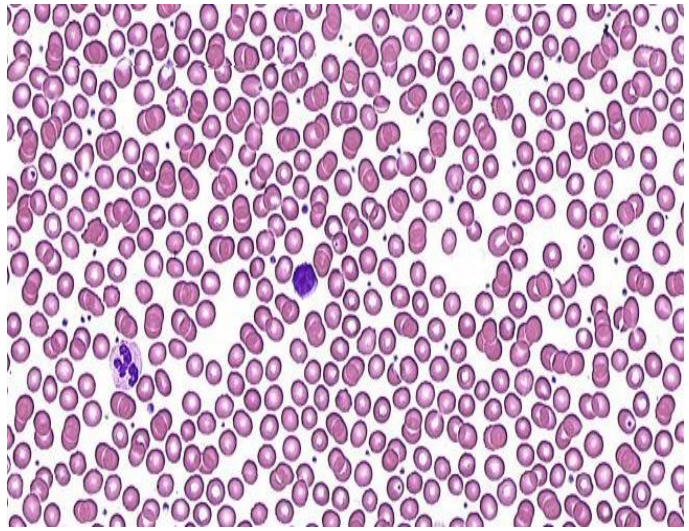
It is MPN characterized by **increased RBCs production independent of the mechanisms that normally regulate erythropoiesis.**

Diagnostic Features	Clinical features of PV
High Hb more than: 18.5g/dl in men . 16.5g/dl in women.	Increased blood viscosity will lead to: Hypertension. Headache, dizziness, visual disturbances & paresthesia.
Hypercellular bone marrow .	Thrombosis: Deep vein thrombosis. Myocardial infarction. Mesenteric, portal or splenic vein thrombosis.
JAK2 mutation in > 95% of cases.	Splenomegaly in 70% .
Low Serum erythropoietin level .(when we see this immediately we do the genetic studies)	Hepatomegaly in 40%.

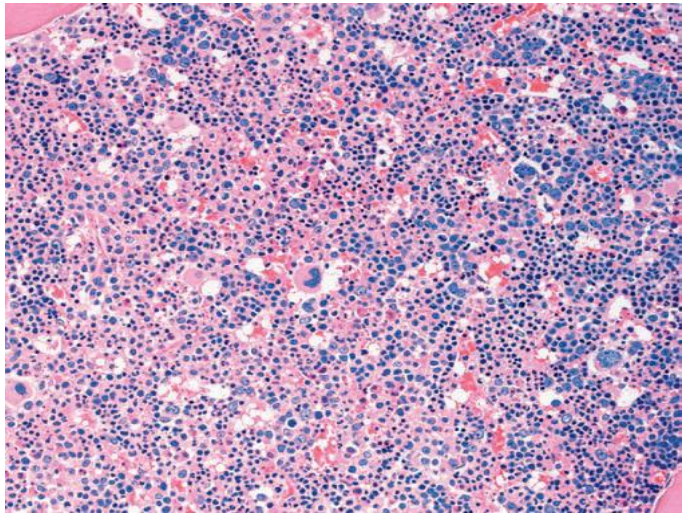
Investigations

CBC	
RBC	increased
Hb	increased
WBC & PLT	mildly increased

Blood smear
Excess of normocytic normochromic RBC
±Leukocytosis &thrombocytosis

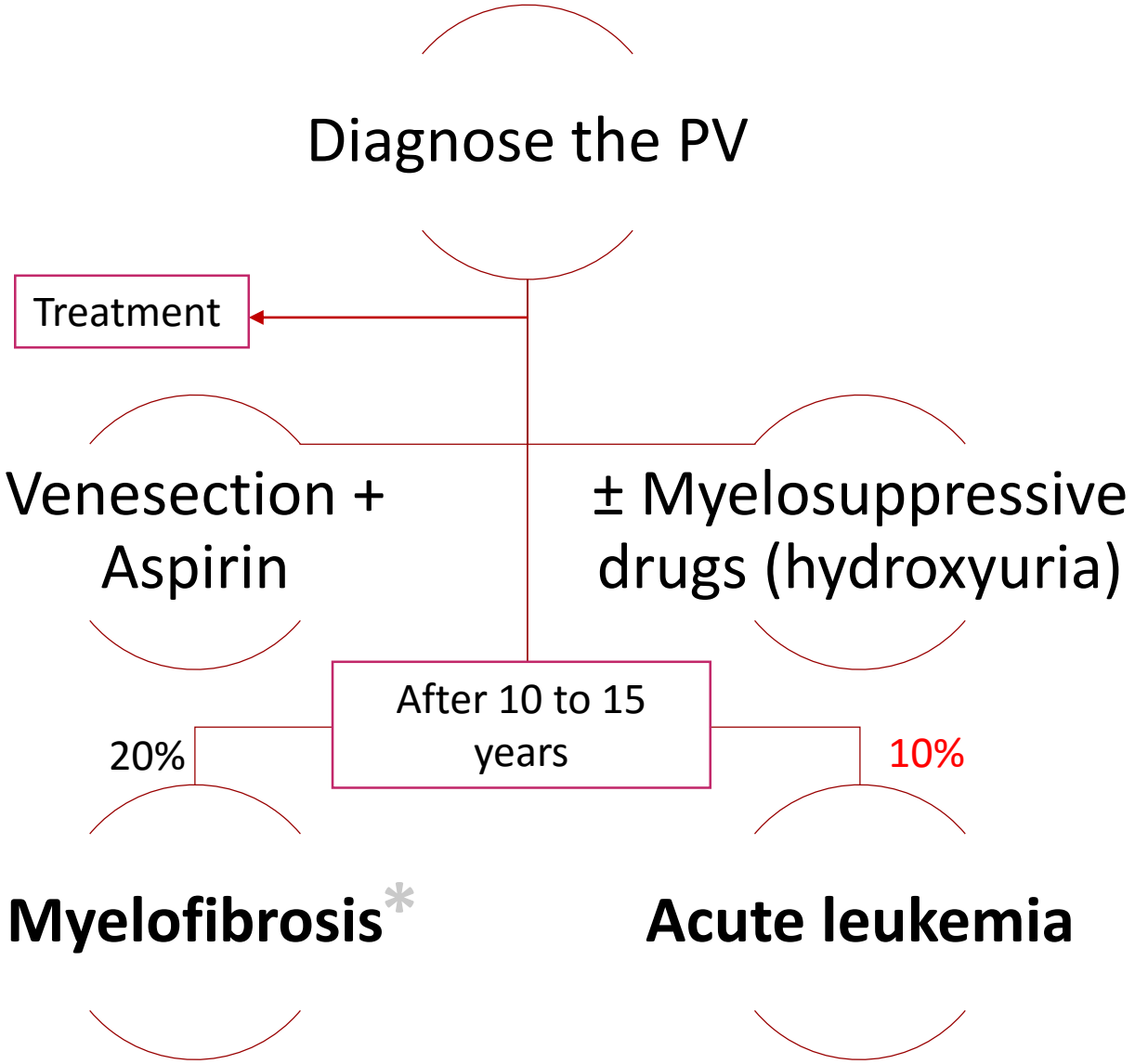


Bone marrow
Hypercellular
Predominant erythroid precursors
± Increased megakaryocytes &Myeloid precursors.



↑ Blasts → AL transformation

Complication &treatment



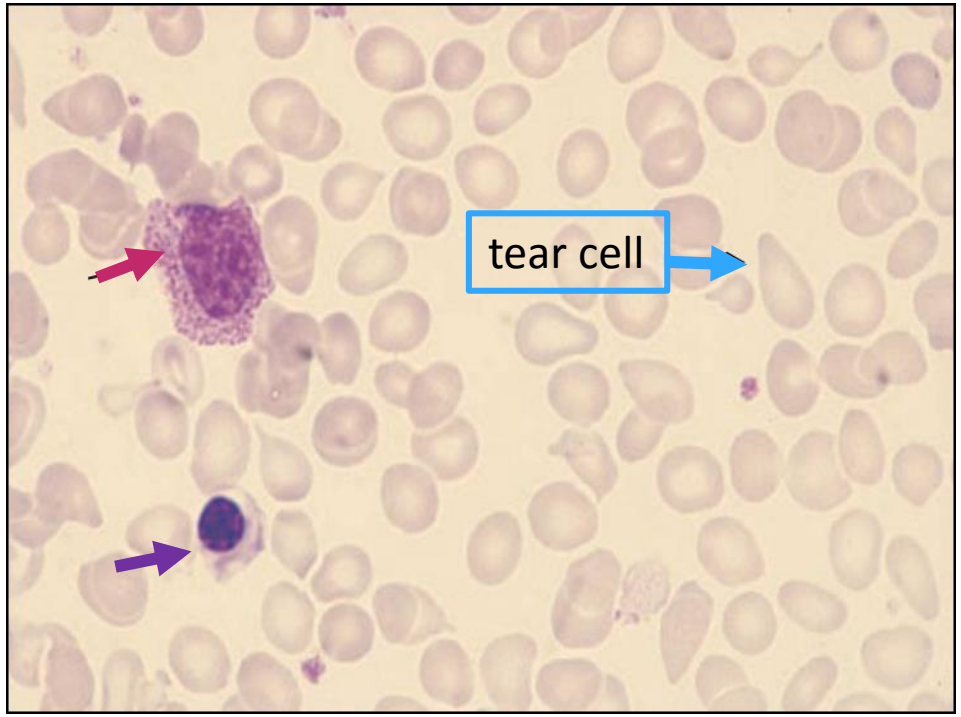
* Could progress to Acute leukemia

Primary Myelofibrosis

Clonal MPN characterized by a **proliferation of** megakaryocytes & granulocytes in the bone marrow **that associated with deposition of fibrous connective tissue and extramedullary haematopoiesis** (spleen and liver).

Clinical features :

- Anemia (because bone mostly produce megakaryocyte and granulocyte).
- Leukoerythroblastic blood picture (when we find precursor of granulocytes and erythrocytes)
- Massive splenomegaly. (CML and MF cause the massive splenomegaly)
- Fibrotic bone marrow
- JAK2 mutation (50%)
- Risk of AML transformation (20%)

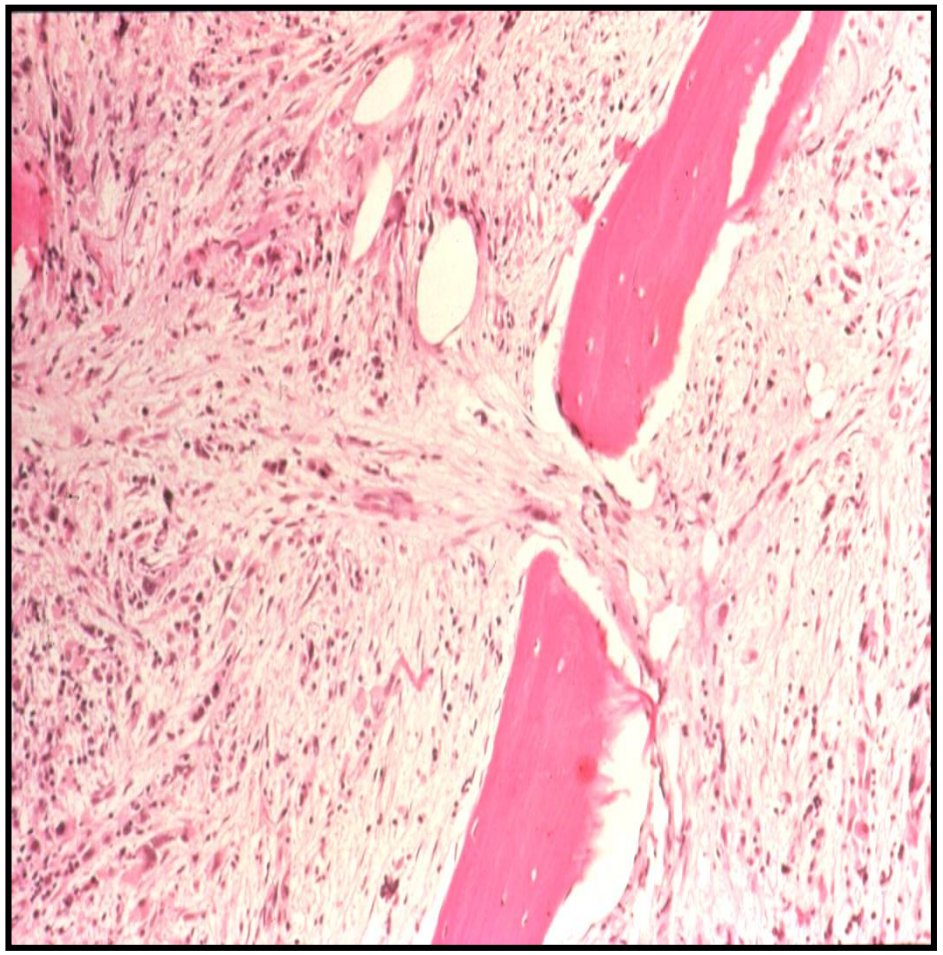


Bone marrow in Myelofibrosis

Normal BM

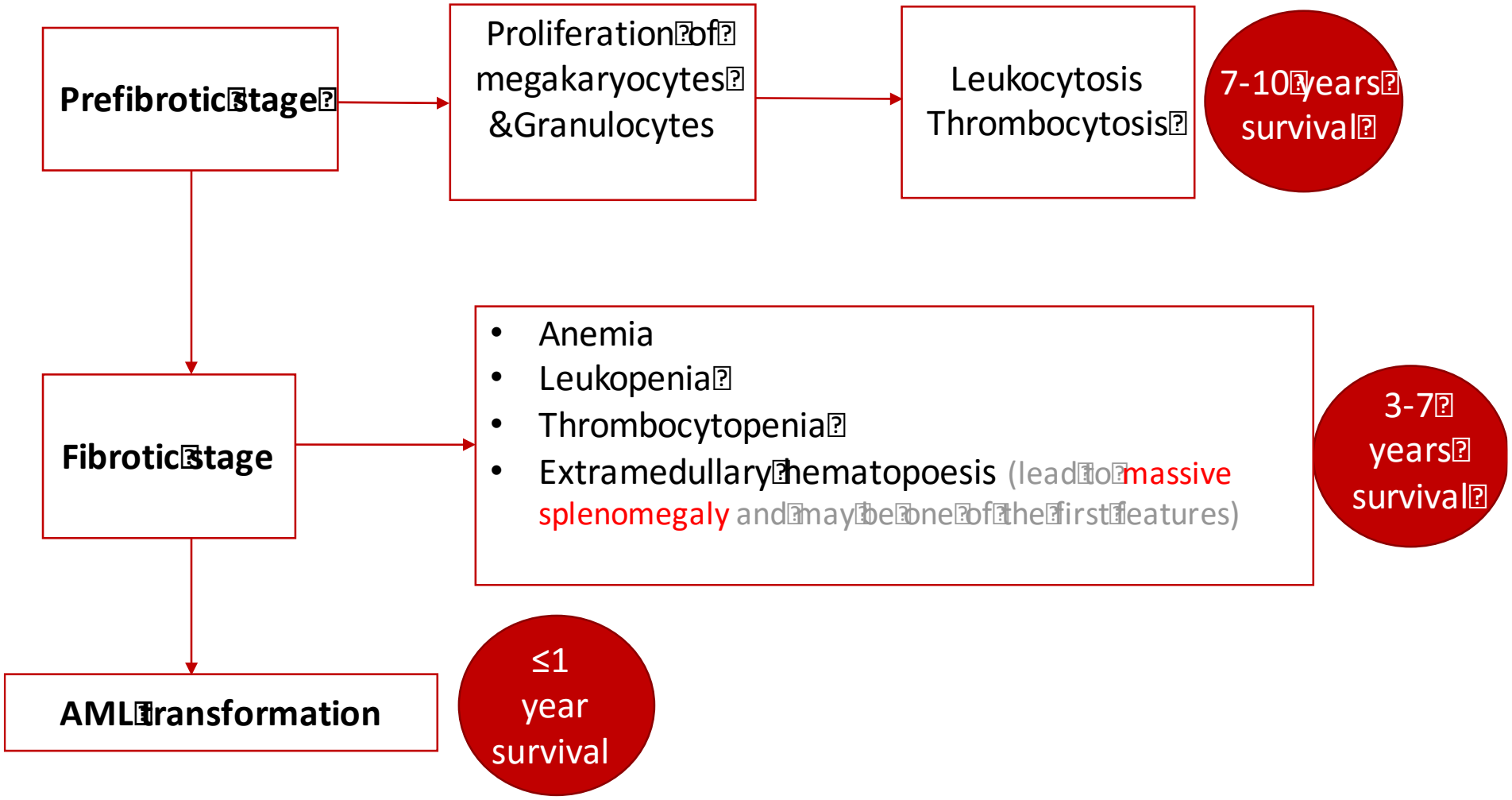
- Fat Cells
- Hematopoietic cells

Fibrotic BM



- No Fat cells
- Fibrosis
- No Hematopoietic cells

Stages of PMF



Essential Thrombocythemia

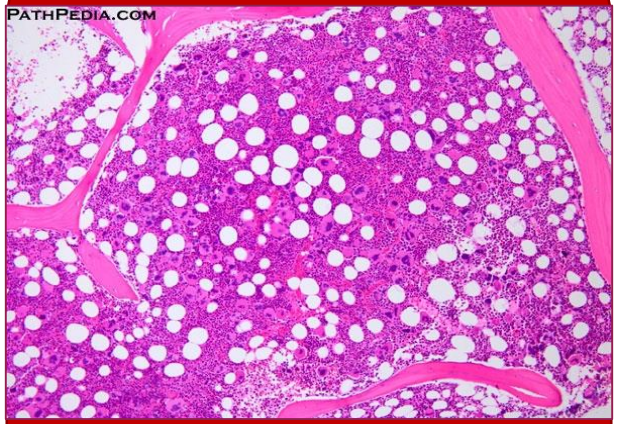
ET is MPN that involves primarily the **megakaryocytic lineage.** characterized by sustained thrombocytosis.

Diagnostic Features:
Sustained thrombocytosis ≥45O×10^9.
Hypercellular BM with megakaryocytic proliferation.
Deferential diagnosis Exclusion of CML, MDS,PV &Primary Myelofibrosis.
JAK2 mutation 60%. Before doing it we have to exclude the Reactive (secondary) Thrombocytosis do to (Iron def. ,splenoctomy, surgery, infection ,autoimmune disease).

Blood Film

High platelets count

Bone marrow



- Hyper cellular BM
- Increase megakaryocyte
- Decrease fat cells

Essential Thrombocythemia

Clinical Presentation

Asymptomatic (50%)

Thrombosis

Bleeding

Mild splenomegaly (50%)

Mild hepatomegaly (20%)

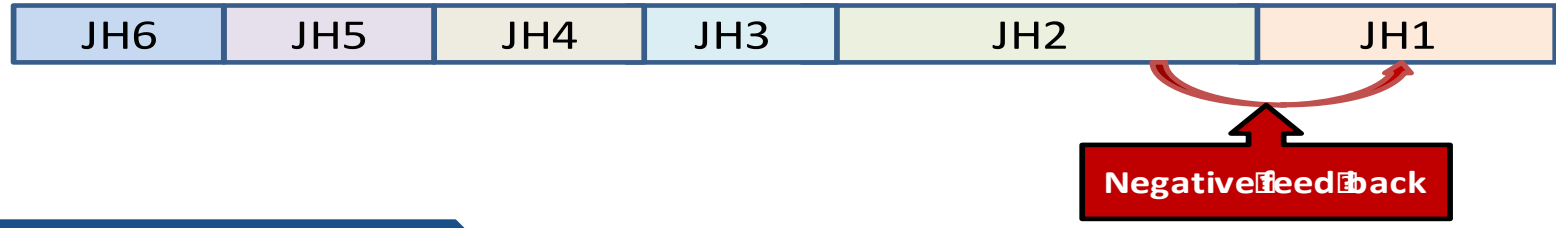
Very indolent(5% risk of AML transformation)

Treatment

Aspirin ±Hydroxyuria

JAK2 Mutation

JAK2: Non receptor protein tyrosine kinase involved in **signal transduction pathway**



JAC2 involved in the signal transduction pathway and it is responsible for its own activity by -ve feedback

point mutation at **codon 617 in JH2** will lead to continuous activity leading to lose of the auto inhibitory control over JAC2

Transcriptional factors increase leading to Increased proliferation and Decreased apoptosis

this is seen in **95% of polycythemia** cases , 60% in Essential Thrombocythemia and 50% in Primary Myelofibrosis

Q1 Which of the following can cause massive spleen ?

A. Polysathemia vera
B. Chronic Myelomonocytic Leukemia
C. Essential Thrombocythemia
D. Primary Myelofibrosis

Q2 What causes Primary Myelofibrosis MF ?

A. Proliferation displaced myeloid cells
B. proliferation of both monocytes and neutrophils
C. proliferation of megakaryocytes & granulocytes

Q3 Which of the following can Polycythemia vera develop to ?

A. Essential Thrombocythemia
B. Myelofibrosis
C. **Myelodysplastic Syndromes**
D. Chronic Myelomonocytic Leukemia

Q4 Which of the following is JAK 2 mutation ?

A. point mutation at codon 617 in JH2
B. t(9;22) forming *BCR-ABL1* fusion
C. Point mutation at codon 716 in JH2

Q5 Which of the following is important in diagnosis of Essential Thrombocythemia ET ?

A. Exclusion of CML, MDS,PV &Primary Myelofibrosis
B. JAK2 mutation
C. Thrombosis
D. hepatomegaly

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

A 60 yrs old male presented with high BP , headache and visual disturbances a CBC was done showed RCC of 7x10^12 and Hb of 18 what are possible findings in blood film smear and what is the most likely diagnosis?

- Excess of normocytic normochromic RBC
- Leukocytosis
- thrombocytosis

Name 3 things that can cause secondary Polycythemia?

- smoking
- High altitude
- Renal disease

A 75 year old female have being having PV for more than 10 years came with an enlargement in her spleen also developed anemia , blood film smear shows Leukoerythroblastic picture and CBC showed decrease in WBC and Platelets .What is your diagnosis and which stage ?

Primary Myelofibrosis Fibrotic stage due to :

The enlarged spleen / anemia / Leukopenia /Thrombocytopenia

Thank you for checking our work

Now you can check a lecture out :D

Done by :

Ghaida Almasaad

Reviewed by:

Hadeel B.Alsulami

Abdullah M. Albasha

دعاء بعد المذاكرة:

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