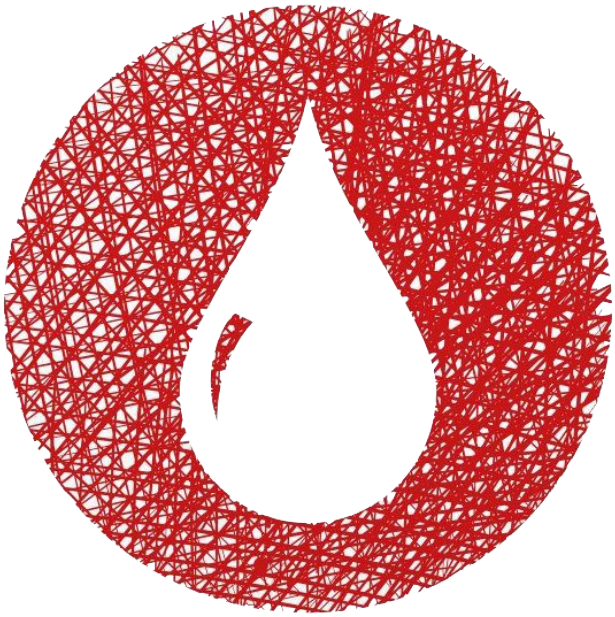


Polycythemia

Team leaders : Abdulrahman Alageel, Ebtesam Almutairi.
Done by : Rawan Mishal , Majd Albarrak

Impotent
Notes
Doctor's slides

Myeloproliferative Neoplasms

Myeloproliferative neoplasms (MPN)[1]

1. Chronic myelogenous leukemia, *BCR-ABL1-positive* (**CML**)
2. Polycythemia vera (PV)[2]
3. Essential thrombocythemia (**ET**) [3]
4. Primary myelofibrosis (**PMF**) [4]
5. Chronic neutrophilic leukemia (**CNL**)
6. Chronic eosinophilic leukemia, not otherwise specified (CEL-NOS)
7. Mast cell disease (MCD)
8. MPN, unclassifiable [5]

MPN features

- Cytosis
- Organomegaly (mainly splenomegaly)[6]
- High uric acid. [7]
- Hypercellular bone marrow
- Progression to acute leukaemia (mainly Acute Myeloid Leukemia)

Just Read

Classification of Myeloid Neoplasms According to the 2008 world health Organization Classification Scheme:

1. **Myeloproliferative neoplasms (MPN)**
   a. Chronic myelogenous leukemia, BCR-ABL1-positive (CML)
   b. Polycythemia vera (PV)*
   c. Essential thrombocythemia (ET)*
   d. Primary myelofibrosis (PMF)*
   e. Chronic neutrophilic leukemia (CNL)*
   f. Mast cell disease (MCD)*
   g. MPN, unclassifiable*
2. Myeloid and lymphoid neoplasms with eosinophilia and abnormalities of PDGFRA, PDGFRB, and FGFR1
3. MDS/MPN
   a. Chronic myelomonocytic leukemia (CMML)
   b. Juvenile myelomonocytic leukemia (JMML)
   c. Atypical chronic myeloid leukemia, BCR-ABL-negative (aCML)
   d. MDS/MPN, unclassifiable
4. Myelodysplastic syndromes (MDS)
5. Acute myeloid leukemia (AML)

***BCR-ABL must be negative**

[1] **Chronic disorders:** certain population of abnormality, expanded with different maturation stages, confined for a long period of time, will have a phase of transformation into acute leukemia eventually.
[2] increased erythrocytes.
[3] increased megakaryocytes.
[4] Fibrotic changes in bone marrow.
[5] overlapped features of the above.
[6] Extramedullary hematopoiesis (Outside BM).
[7] increased turnover of cells.

Clonal disorders: attributed to one clone of cell. One hematopoietic early cell faces a genetic abnormality so it produces a clone of abnormal cells. If it expands in a short time & gives confined to one population of cells it will give acute leukemia.

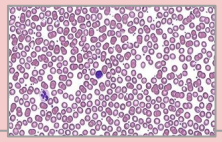
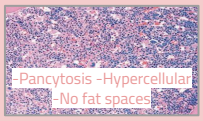
Polycythemia

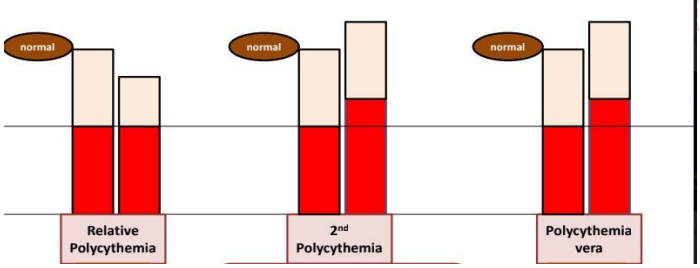
inrease risk of MI, DVT and strokes.

Characters		◇ In Greek "too many cells in the blood." ◇ Absolute increase in total body red cell volume (or mass) ◇ Manifests itself as a raised Hb or packed cell volume (PCV) ◇ Hb is >16.5or 18.5 g/dl in women and men, respectively.
Classification of Polycythemia	**Relative Polycythemia**	Decreased plasma volume due to severe dehydration. [1]
	Secondary Polycythemia Or reactive	Increased RBC mass due to **high erythropoietin**: ◇ COPD, Sleep apnea, smoking.. ◇ High altitude. ◇ High affinity HB. ◇ Renal disease. ◇ Erythropoietin secreting tumor (Parathyroid adenoma…)
	Polycythemia Vera	Increased RBC mass due to malignant proliferation.[2]

Polycythemia Vera

MPN characterized by increased red blood cell production independent of the mechanisms that normally regulate erythropoiesis.

Diagnostic Features		◇ HB >18.5g/dl in men ,16.5g/dl in women. [3] ◇ **Hypercellular** bone marrow . ◇ **JAK2 mutation** in >95% of cases. ◇ **Low Serum erythropoietin level**[4] It has nothing to do with MCH/MCV What's important here: RBC count, Hemoglobin level, PCV
Clinical features of Polycythemia Vera	**Increased blood viscosity**	◇ Hypertension. ◇ Headache, dizziness, visual disturbances & paresthesia.
	Thrombosis	◇ Deep vein thrombosis. ◇ Myocardial infarction. ◇ Mesenteric, portal or splenic vein thrombosis.
	Splenomegaly in 70%	
	Hepatomegaly in 30%	
Investigations	**CBC** 	◇ RBC: increased. ◇ Hb: increased. ◇ WBC & PLT :mildly increased (usually)
	Blood smear	◇ Excess of normocytic normochromic RBC. ◇ **±Leukocytosis & thrombocytosis.**
	Bone marrow 	◇ **Hypercellular**. ◇ Predominant erythroid precursors . ◇ ± Increased megakaryocytes & Myeloid precursors.



↑ Blasts (20% or above) → Acute leukemia transformation

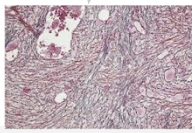
[1] Nothing wrong with cell production
[2] Clonal disorder with normal erythropoietin levels..
[3] high.
[4] already high RBC, no stimulation of EPO.

Complication & Treatment of Polycythemia Vera

Venesection + Aspirin ± Myelosuppressive drugs (hydroxyuria)

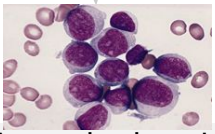
10-15 years

20%



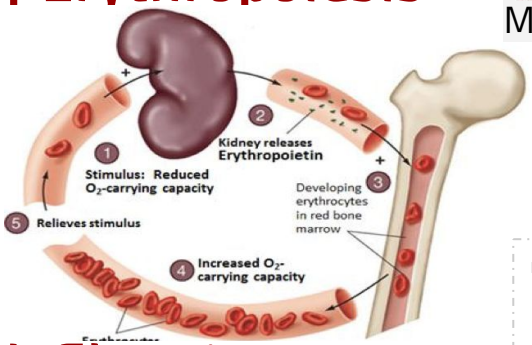
Myelofibrosis

10%



Acute leukemia

Regulation of Erythropoiesis



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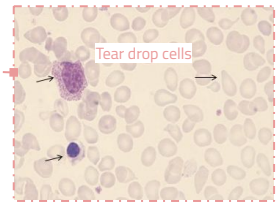
Primary Myelofibrosis

[The worst type of **Myeloproliferative neoplasms** in term of prognosis]

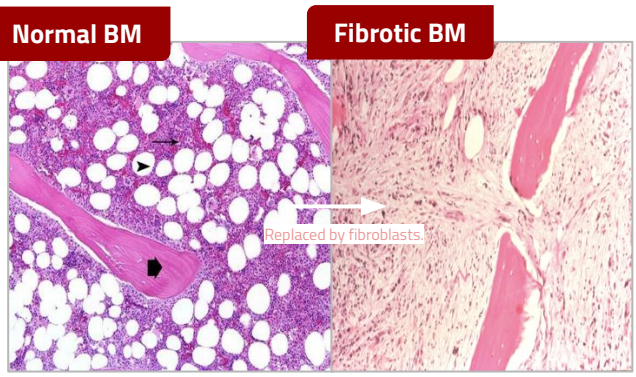
Clonal MPN characterized by a proliferation of megakaryocytes & granulocytes in the bone marrow that associated with deposition of fibrous connective tissue and extramedullary haematopoiesis.

Clinical features:

- Anemia
- Leukoerythroblastic blood picture.[2]
- **Massive splenomegaly**
- Fibrotic bone marrow
- **JAK2 mutation (50%)**
- **Risk of AML transformation (20%)**



Bone marrow in myelofibrosis:



Fat spaces & hematopoietic elements.

Losing hematopoietic elements, with reticulin & collagen fibers.

Stages of PMF

Prefibrotic stage → Proliferation of megakaryocytes & Granulocytes → Leukocytosis Thrombocytosis → **7-10 years** survival

Fibrotic stage → Anemia Leukopenia Thrombocytopenia Extramedullary hematopoiesis → **3-7 years** survival

→ AML transformation → **≤1** year survival

[1] has the worst prognosis.

[2] You will see early precursors of RBC's and WBC's in peripheral smear. (stressed/ infiltrated BM)

Essential Thrombocythemia

[Best type of MPN in term of prognosis]

Myeloproliferative neoplasms (MPN)

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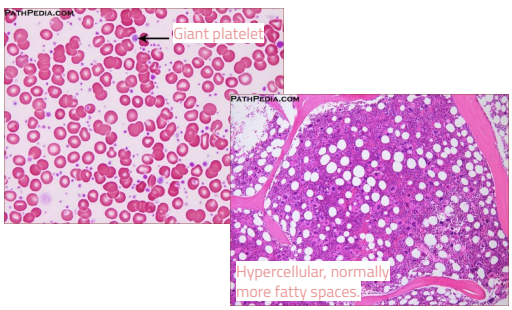
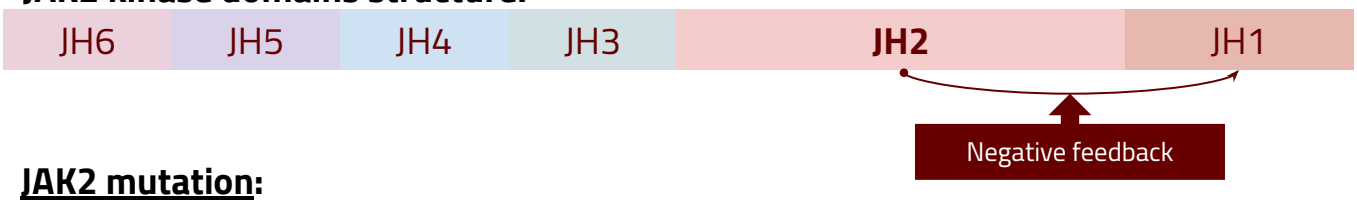
Characters	ET is MPN that involves primarily the megakaryocytic lineage. & characterized by sustained thrombocytosis.
Diagnostic Features	◇ Sustained thrombocytosis ≥450×10^9. ◇ Hypercellular BM with megakaryocytic proliferation ◇ Exclusion of: CML (how? CML is caused by a genetic abnormality BCR-ABL), MDS,PV & Primary Myelofibrosis ◇ JAK2 mutation (60%), if negative; no evidence of reactive thrombocytosis: ○ Iron def. ,splenectomy, surgery, infection, autoimmune disease….
Clinical Presentation	The following are Very indolent (5% risk of AML transformation) ◇ Asymptomatic (50%) ◇ Thrombosis ◇ Bleeding ◇ Mild splenomegaly (50%) ◇ Mild hepatomegaly (20%)
Treatment	Aspirin ± Hydroxyuria



JAK2 Mutation

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

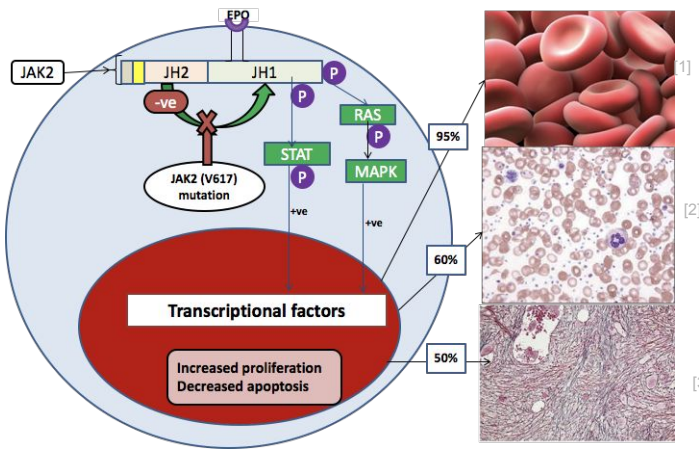
JAK2 kinase domains structure:



<u>JAK2 mutation</u>:

Point mutation (at codon 617 in JH2) leads to loss of auto inhibitory control over JAK2.

The mutated JAK2 is in a constitutively active state.



[1]polycythemia vera
[2]ET
[3]PMF

Quiz

Q1.Polycythemia vera is :
A) increased RBCs mass due to EPO.
B) increased in platelets mass due to malignancy.
C) increased in RBCs mass due to malignancy.

Q2.Most gene mutation in Polycythemia vera is :
A) JAK1
B) JAK2
C)JAK3

Q3. proliferation of megakaryocytes & granulocytes in the bone marrow is a characteristic of :
A) Primary Myelofibrosis
B)Essential Thrombocythemia
C)Polycythemia Vera

Q4. Parathyroid adenoma causes:
A) Primary Myelofibrosis
B)Essential Thrombocythemia
C)secondary Polycythemia

Q5. severe dehydration can cause:
A) relative Polycythemia
B)Essential Thrombocythemia
C)secondary Polycythemia

1) C
2) B
3) A
4) C
5) A