

# Myeloproliferative Neoplasms

## 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

## MPN features

- **Cytosis**
- **Organomegaly (mainly splenomegaly)**
- **High uric acid**
- **Hypercellular bone marrow**
- **Progression to acute leukaemia (mainly AML)**

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

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**BCR-ABL must be negative**

**2. Myeloid and lymphoid neoplasms with eosinophilia and abnormalities of *PDGFRA*, *PDGFRB*, and *FGFR1***

**3. MDS/MPN**

- 3.1. Chronic myelomonocytic leukemia (CMML)
- 3.2. Juvenile myelomonocytic leukemia (JMML)
- 3.3. Atypical chronic myeloid leukemia, *BCR-ABL*-negative (aCML)
- 3.4. MDS/MPN, unclassifiable

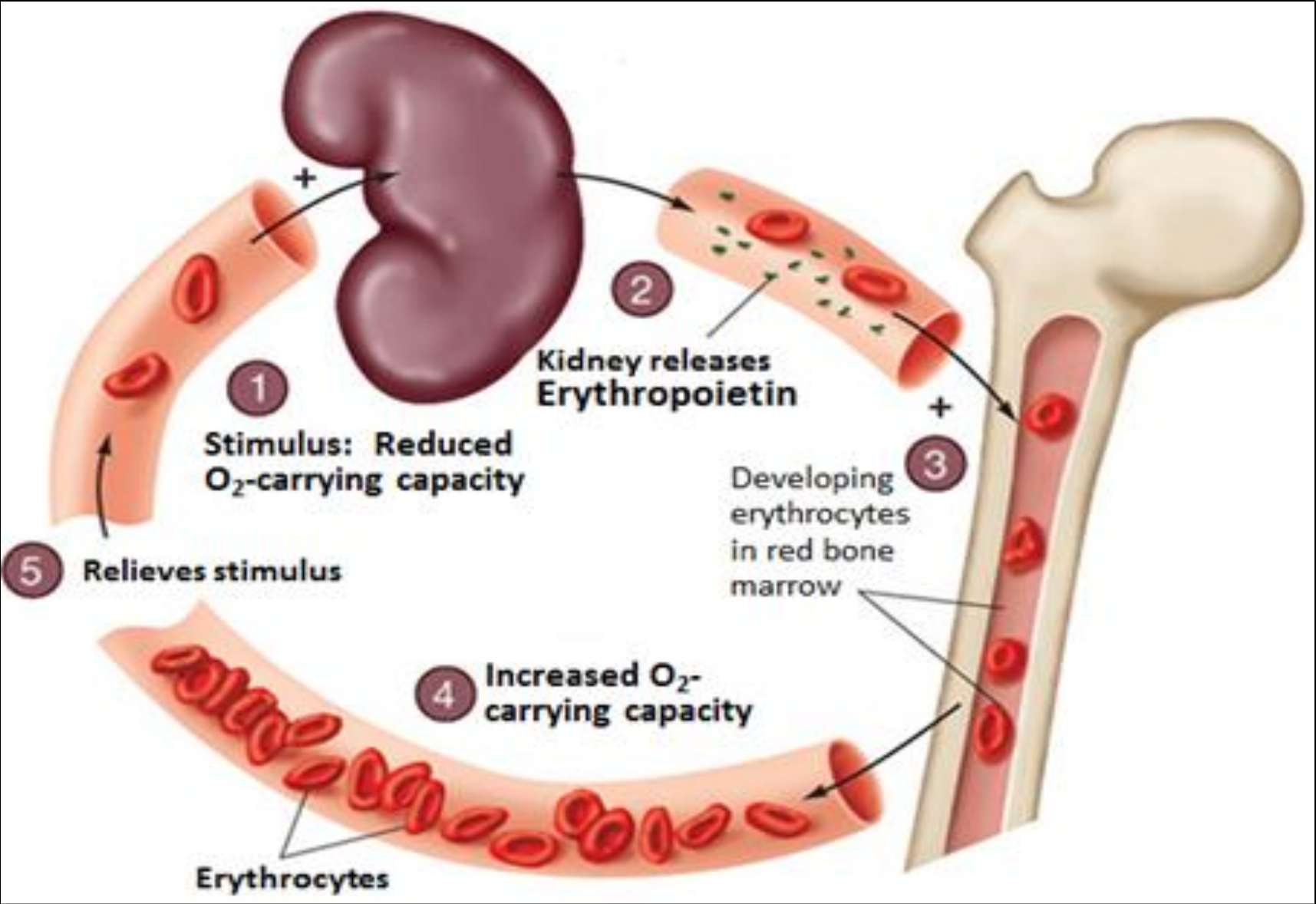
**4. Myelodysplastic syndromes (MDS)**

**5. Acute myeloid leukemia (AML)**

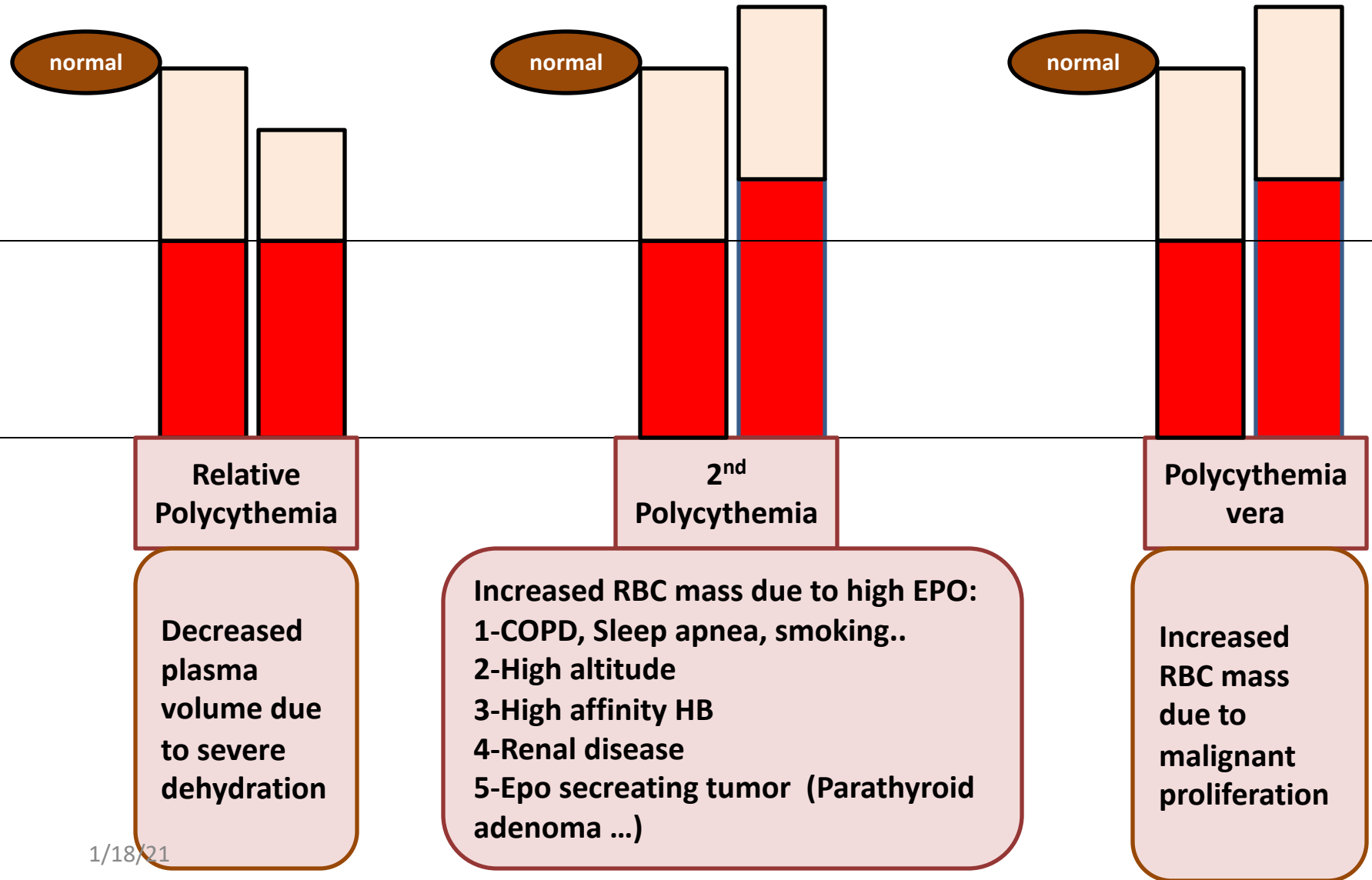
# Polycythemia

- 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 >16.5 or 18.5 g/dl in women and men, respectively.

# Regulation of Erythropoiesis

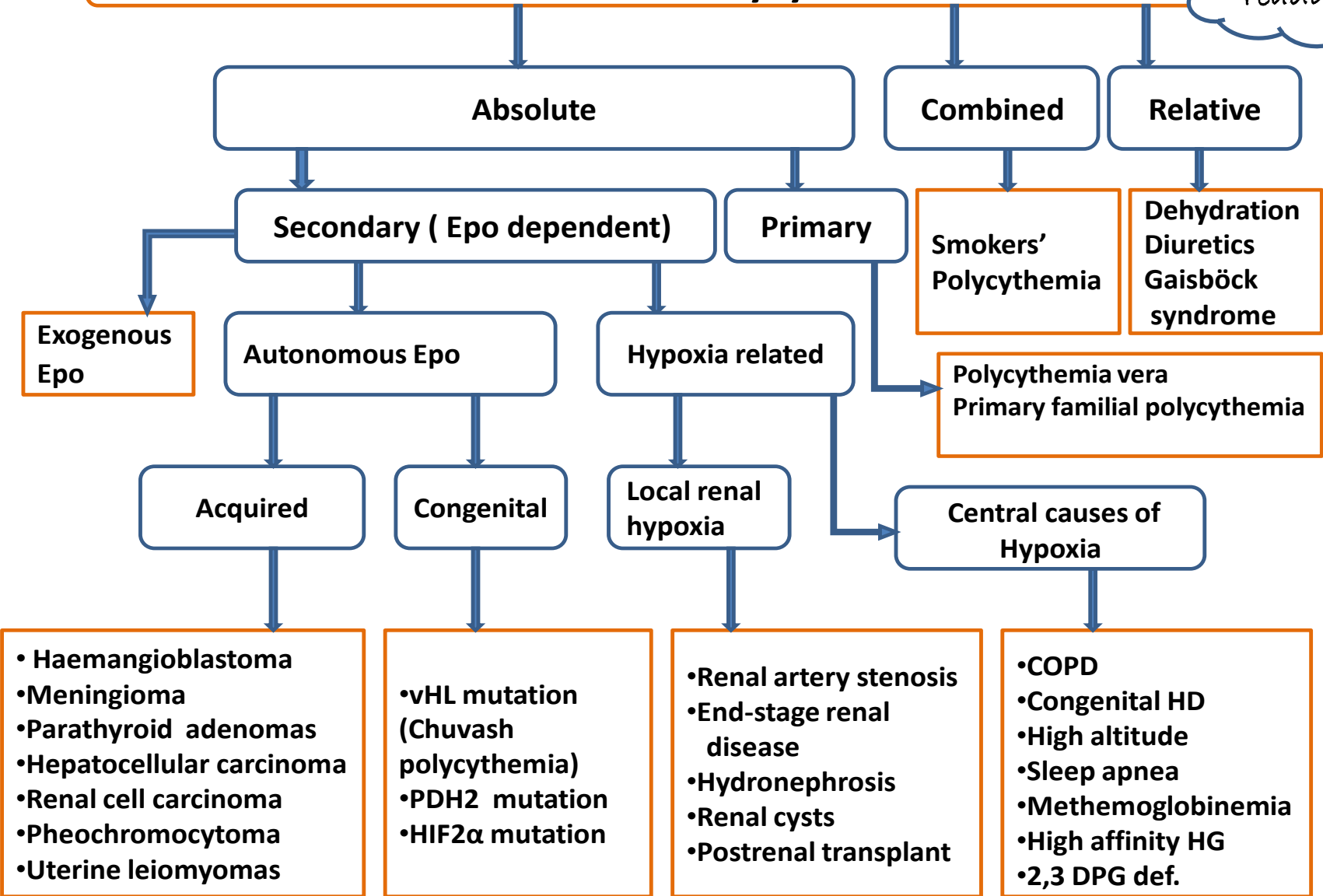


# Classification of Polycythemia



# Classification of Polycythemia

For reading



- Haemangioblastoma
- Meningioma
- Parathyroid adenomas
- Hepatocellular carcinoma
- Renal cell carcinoma
- Pheochromocytoma
- Uterine leiomyomas

- vHL mutation (Chuvash polycythemia)
- PDH2 mutation
- HIF2α mutation

- Renal artery stenosis
- End-stage renal disease
- Hydronephrosis
- Renal cysts
- Postrenal transplant

- COPD
- Congenital HD
- High altitude
- Sleep apnea
- Methemoglobinemia
- High affinity HG
- 2,3 DPG def.

# 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
- Hypercellular bone marrow
- JAK2 mutation in >95% of cases
- Low Serum erythropoietin level



# Clinical features of PV

## 1-Increased blood viscosity

- Hypertension
- Headache, dizziness, visual disturbances & paresthesia

## 2- Thrombosis

- Deep vein thrombosis
- Myocardial infarction
- Mesenteric, portal or splenic vein thrombosis

3-Splenomegaly in 70%

4-Hepatomegaly in 40%

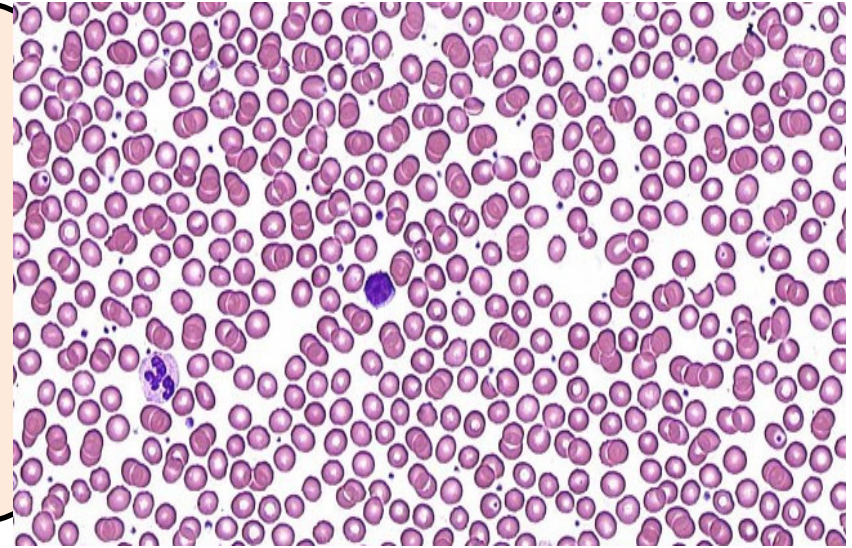
# Investigations

## CBC:

- \*RBC: increased
- \*Hb: increased
- \*WBC & PLT :mildly increased (usually)

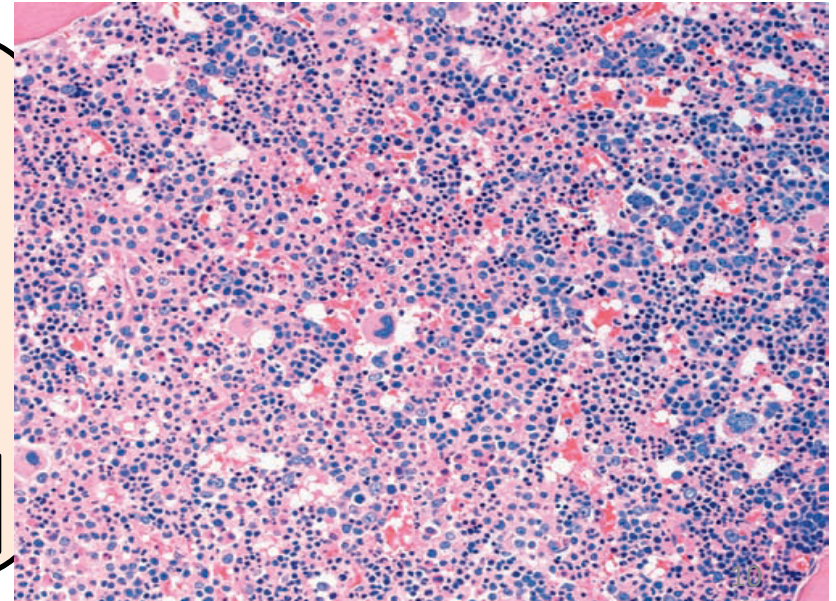
## Blood smear:

- Excess of normocytic normochromic RBC
- ±Leukocytosis &thrombocytosis



## Bone marrow

- Hypercellular
- Predominant erythroid precursors
- ± Increased megakaryocytes & Myeloid precursors.



↑ Blasts → AL transformation

# Complication & treatment

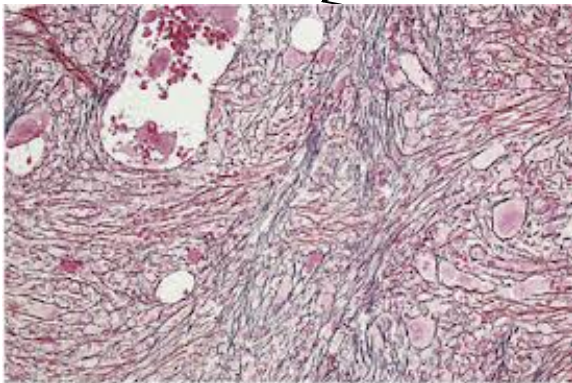
## Diagnosis of Polycythemia Vera

### Treatment:

- Venesection + Aspirin
- ± Myelosuppressive drugs (hydroxyuria)

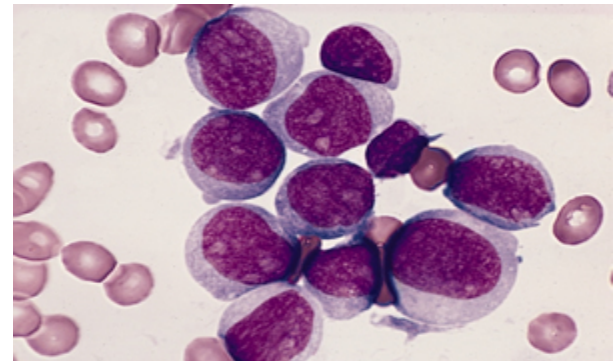
10-15 years

20%



1/18/21 **Myelofibrosis**

10%



**Acute leukemia**

# Primary Myelofibrosis

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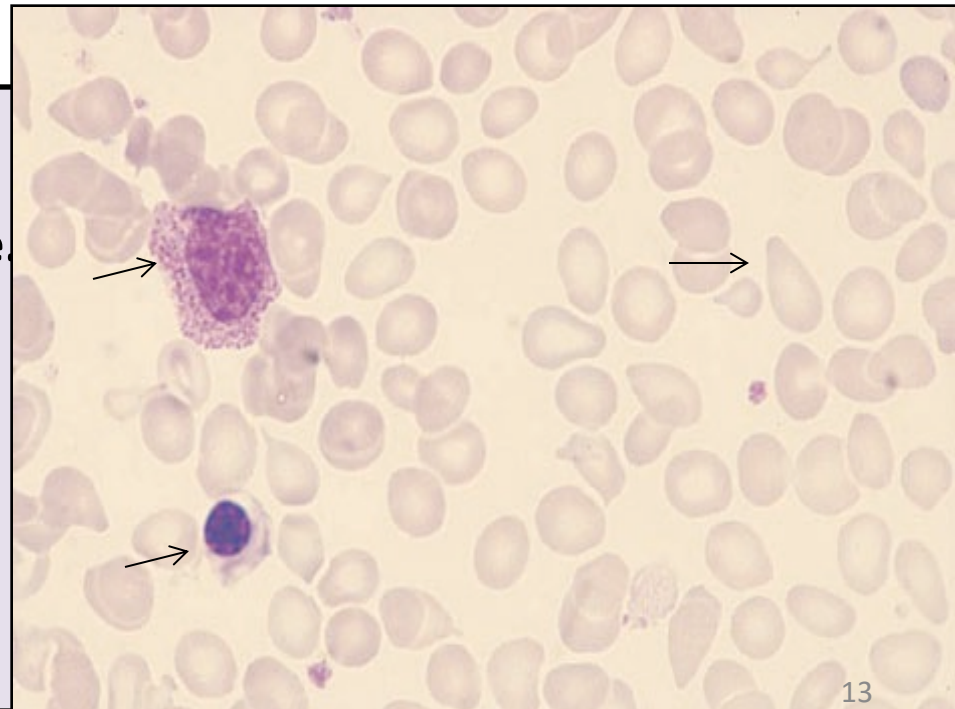
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# Primary Myelofibrosis

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

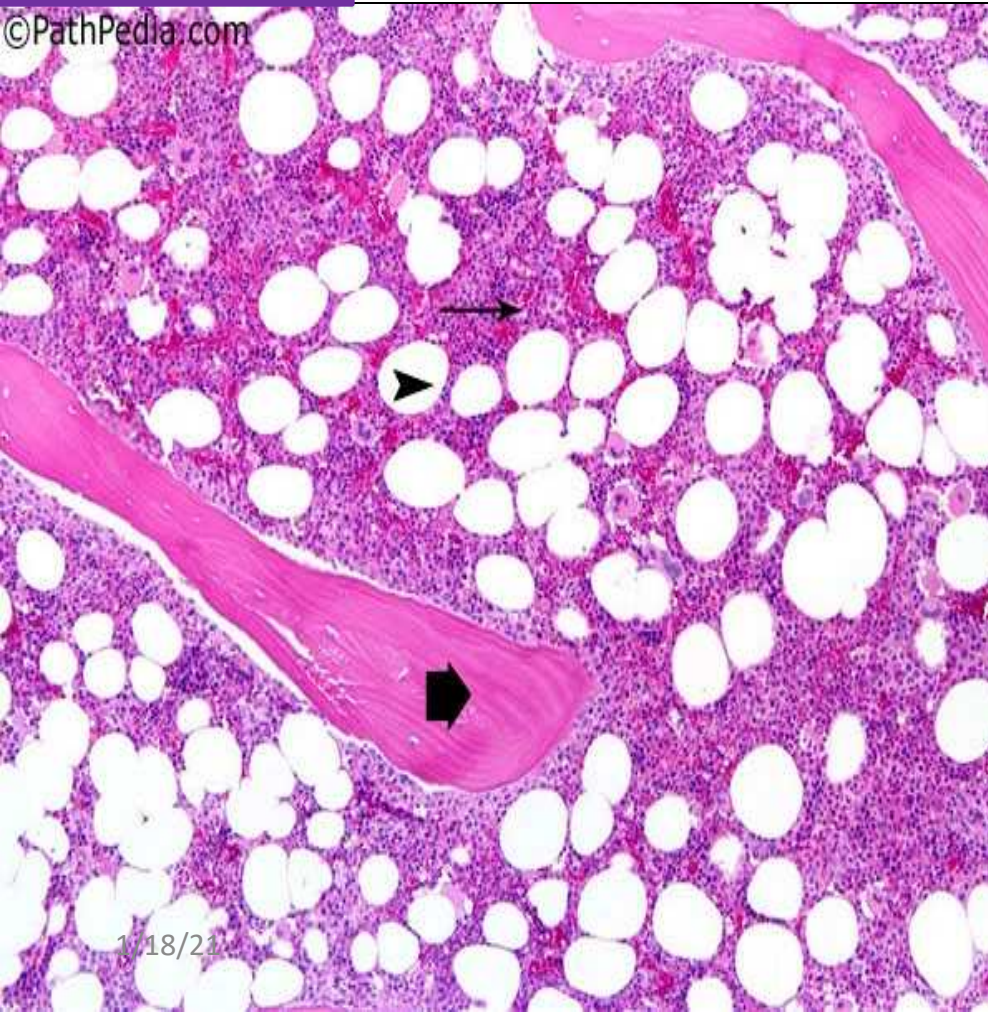
## Clinical features

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

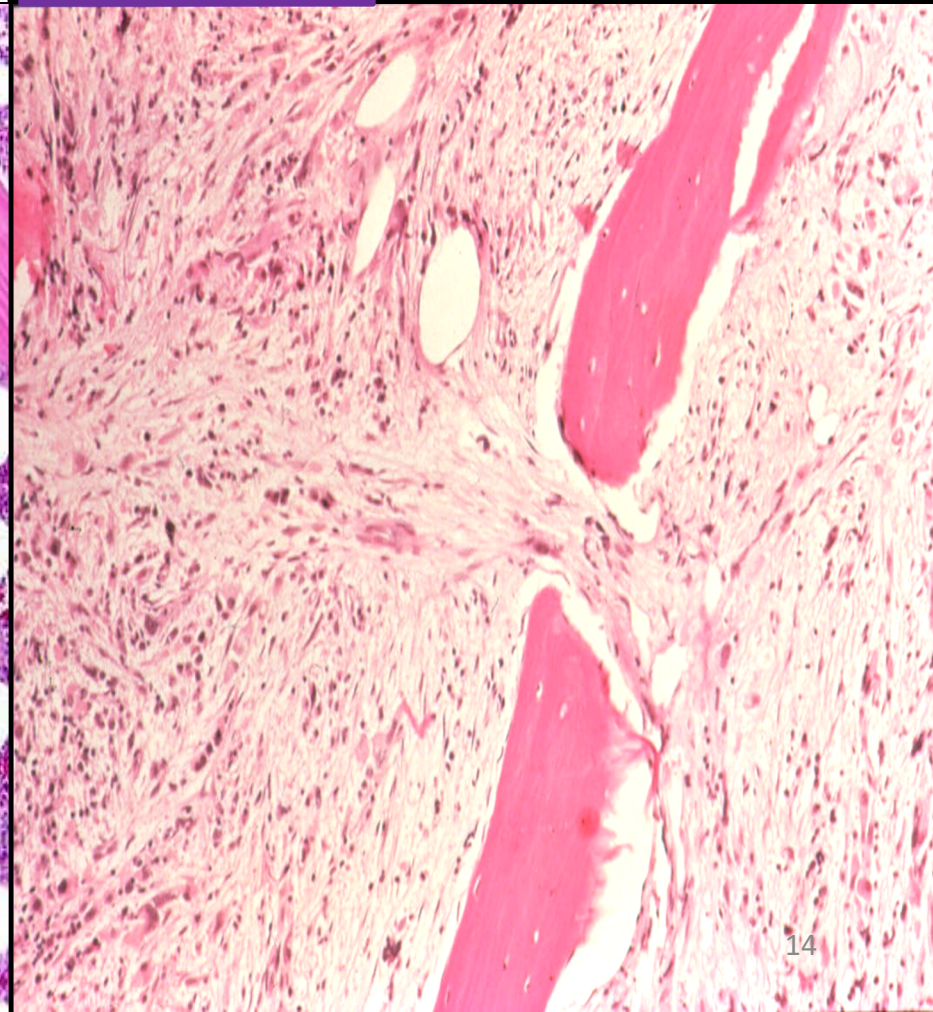


# Bone marrow in Myelofibrosis

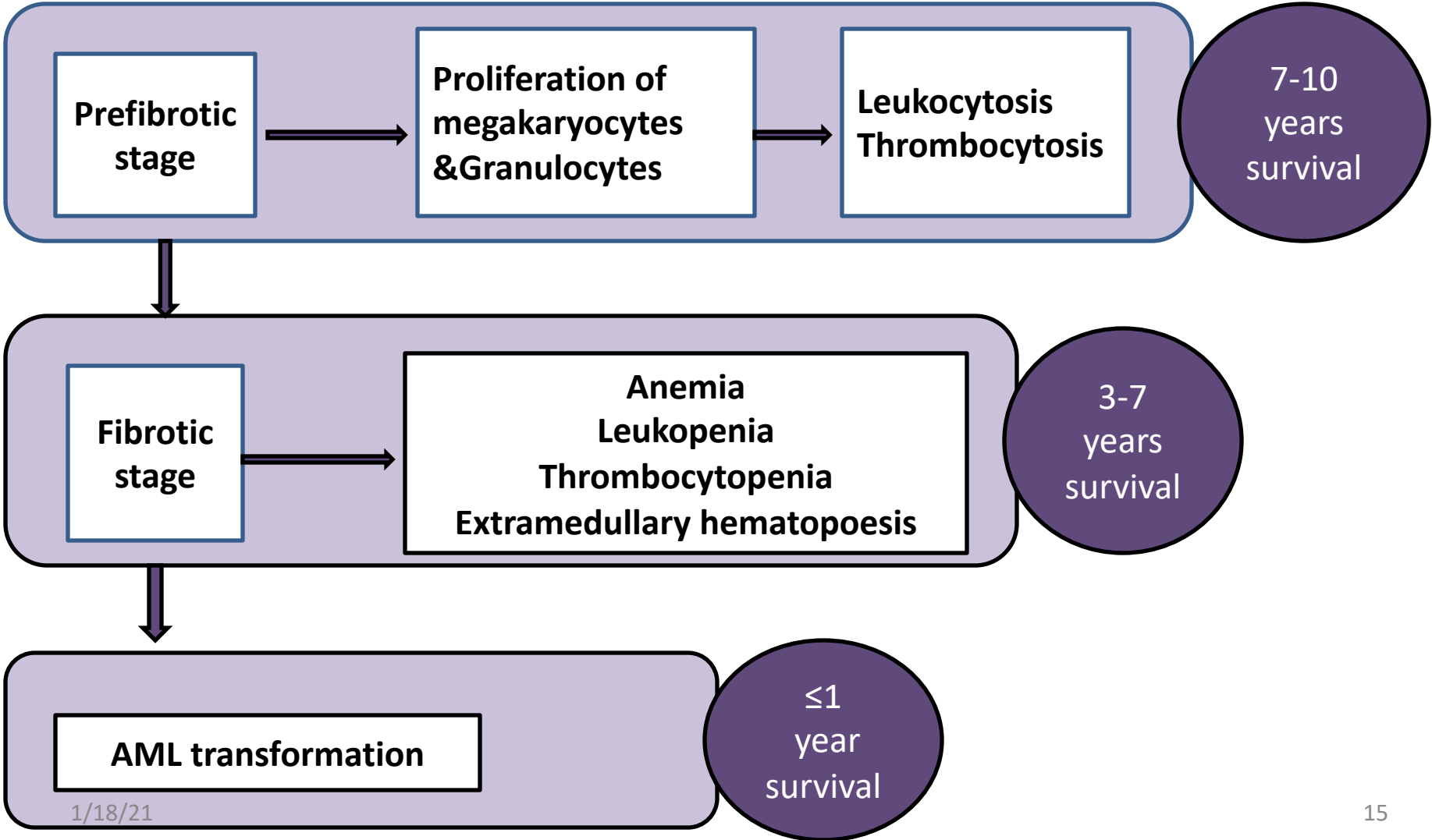
Normal BM



Fibrotic BM



# Stages of PMF



# Essential Thrombocythemia

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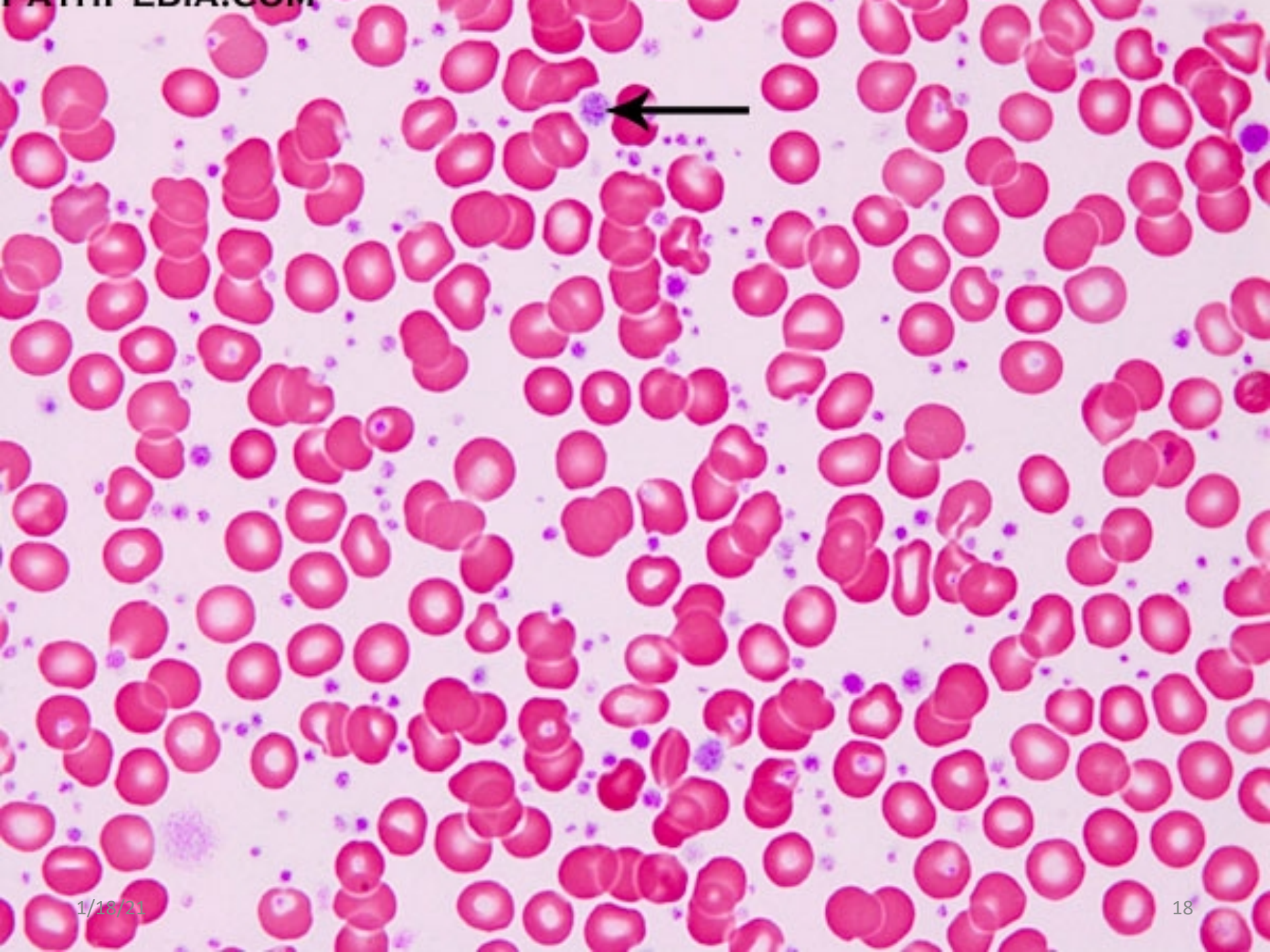
# Essential Thrombocythemia

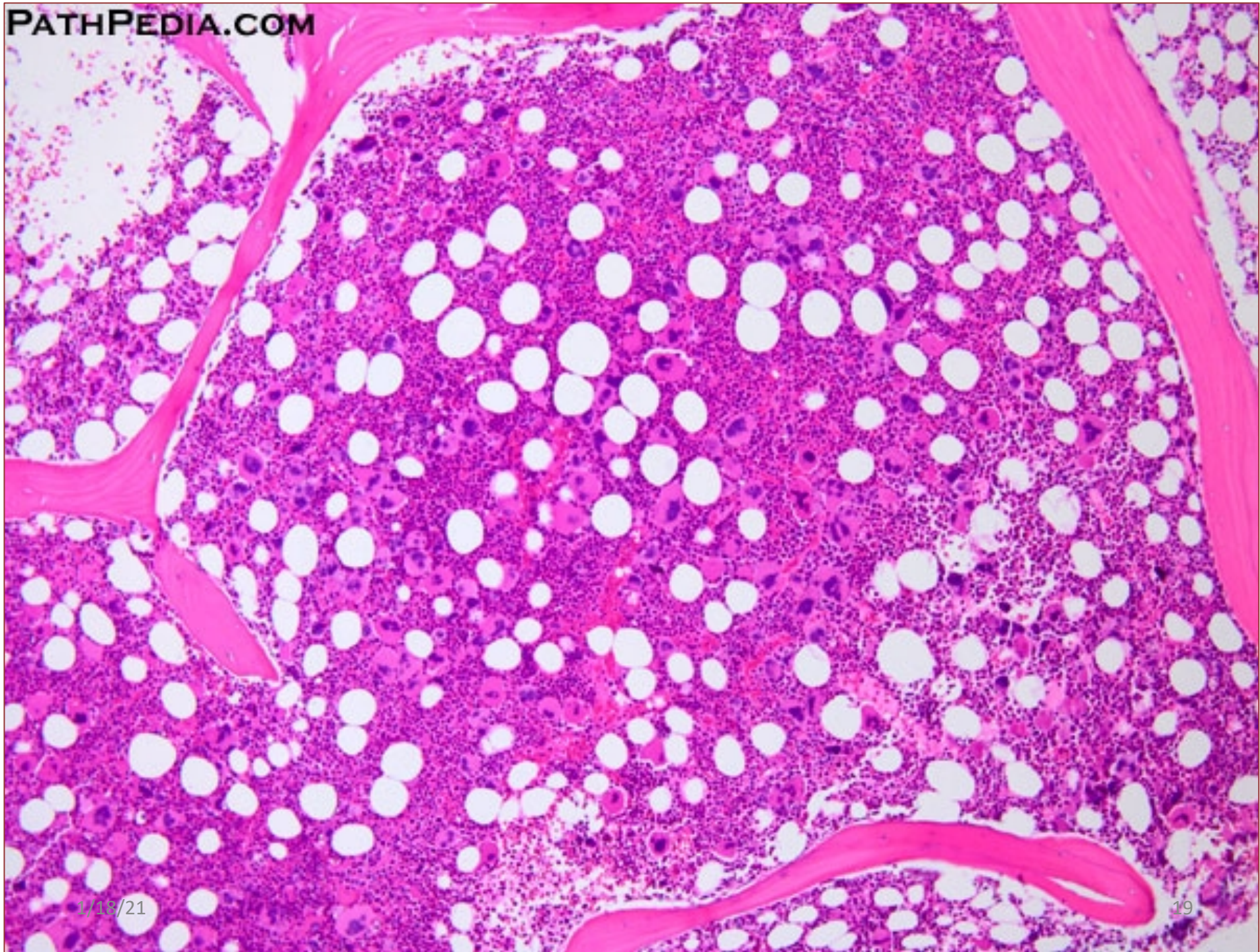
ET is MPN that involves primarily the megakaryocytic lineage. & characterized by sustained thrombocytosis .

## Diagnostic Features

- Sustained thrombocytosis  $\geq 450 \times 10^9$ .
- Hypercellular BM with megakaryocytic proliferation
- Exclusion of: CML, MDS, PV & Primary Myelofibrosis
- JAK2 mutation (60%), if negative; no evidence of reactive thrombocytosis:

Iron def. ,splenectomy, surgery, infection, autoimmune disease....





# Essential Thrombocythemia

## Clinical Presentation

- Asymptomatic (50%)
- Thrombosis
- Bleeding
- Mild splenomegaly (50%)
- Mild hepatomegaly (20%)

Very indolent  
(5% risk of AML transformation )

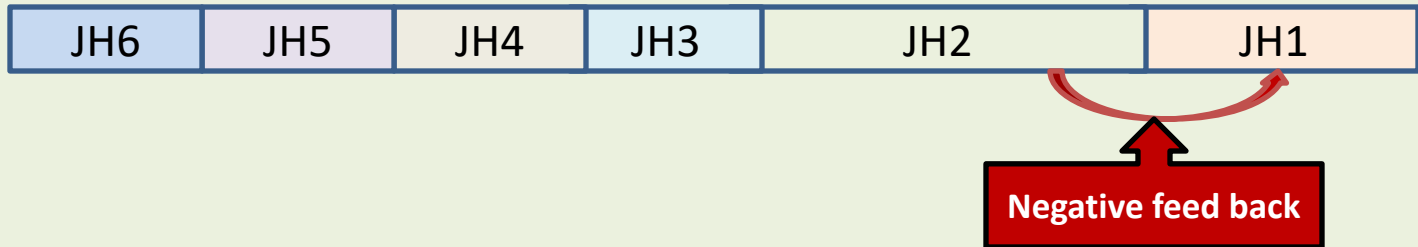
## Treatment

Aspirin ± Hydroxyuria

# JAK2 Mutation

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

JAK2 kinase domains structure



## **JAK2 mutation :**

**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,**

# JAK2 Mutation

