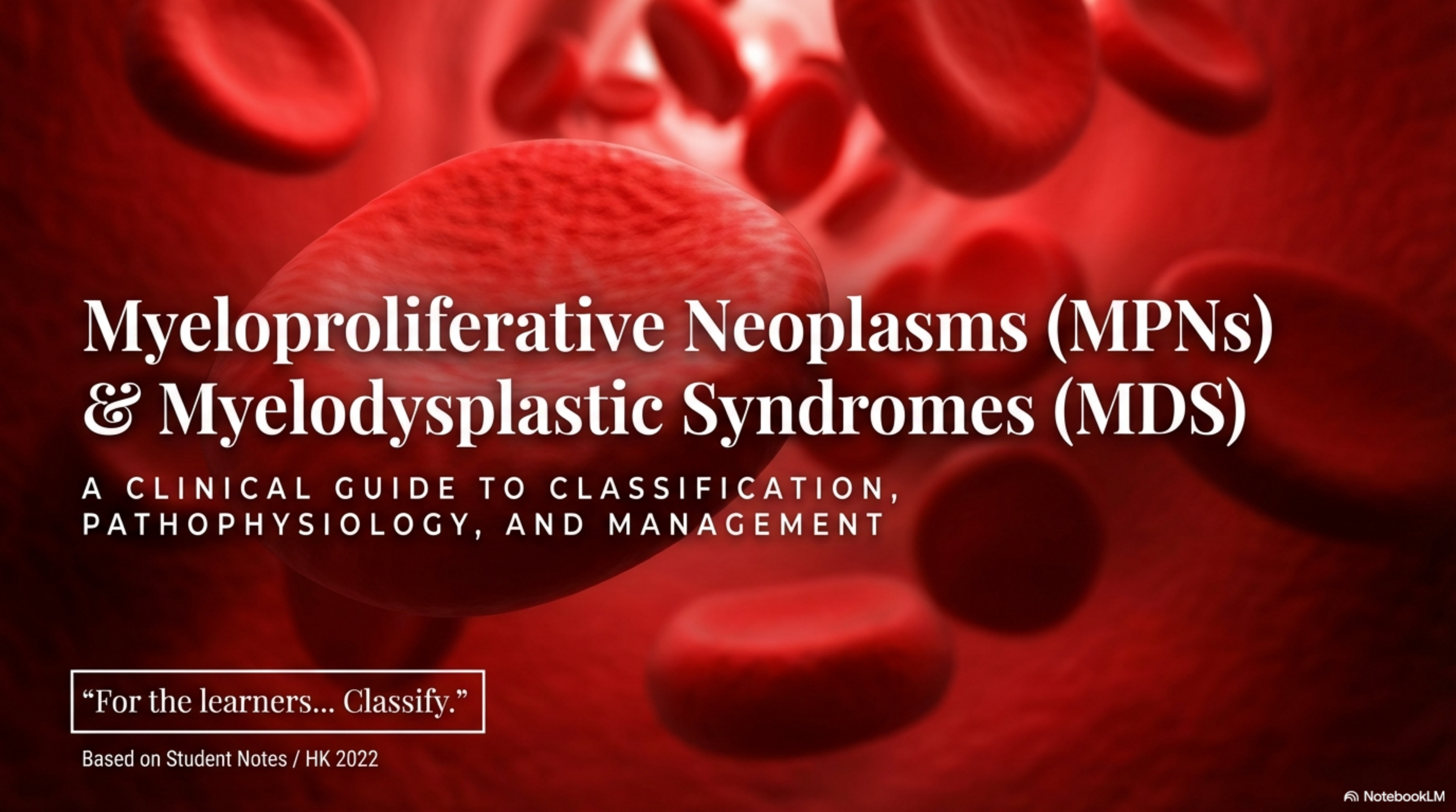


Myeloproliferative Neoplasms (MPNs) & Myelodysplastic Syndromes (MDS)

A CLINICAL GUIDE TO CLASSIFICATION, PATHOPHYSIOLOGY, AND MANAGEMENT

"For the learners... Classify."

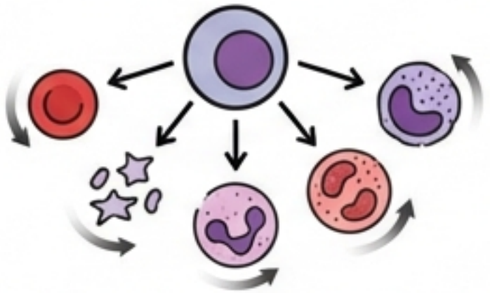
Based on Student Notes / HK 2022

Deconstructing the Pathology

MYELO-PROLIFERATIVE NEOPLASM

Myeloid Lineage Origin

Non-Lymphoid: RBCs, Platelets, Neutrophils, Eosinophils, Basophils.



Increased Numbers

Manifests as -cytosis, -cythemia, or -philia.

Clonal Mutation

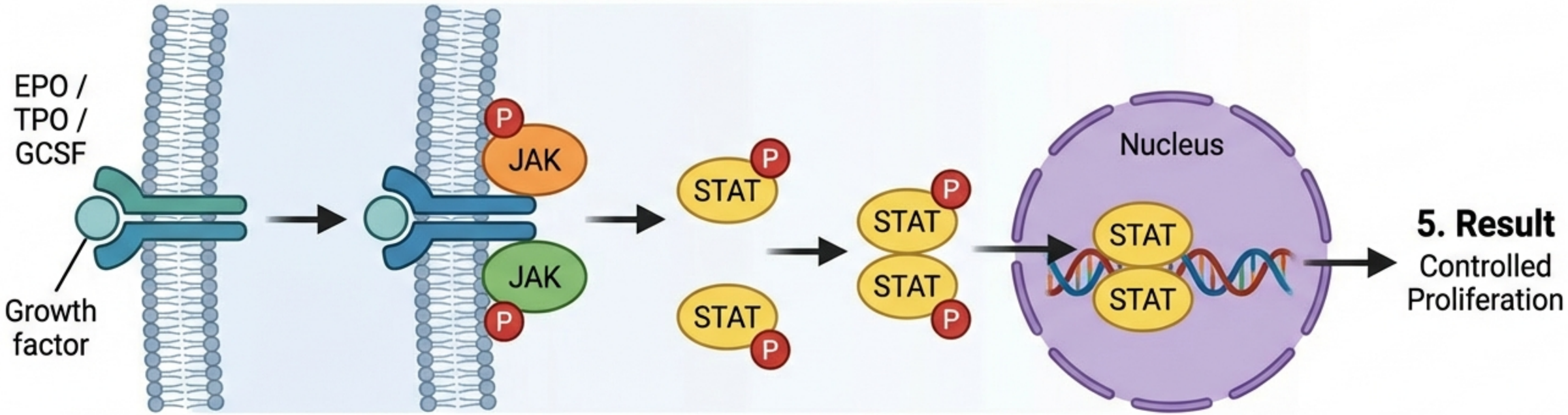
Autonomous growth.
NOT Reactive.
NOT Secondary.

Key Insight: Cancer is a clonal, genetic disease that arises from a normal counterpart.

The Physiology of Proliferation

Normal Regulation: Supply Meets Demand

Hematopoietic progenitors only proliferate when the body requests it via cytokines.



1. Ligand Binding

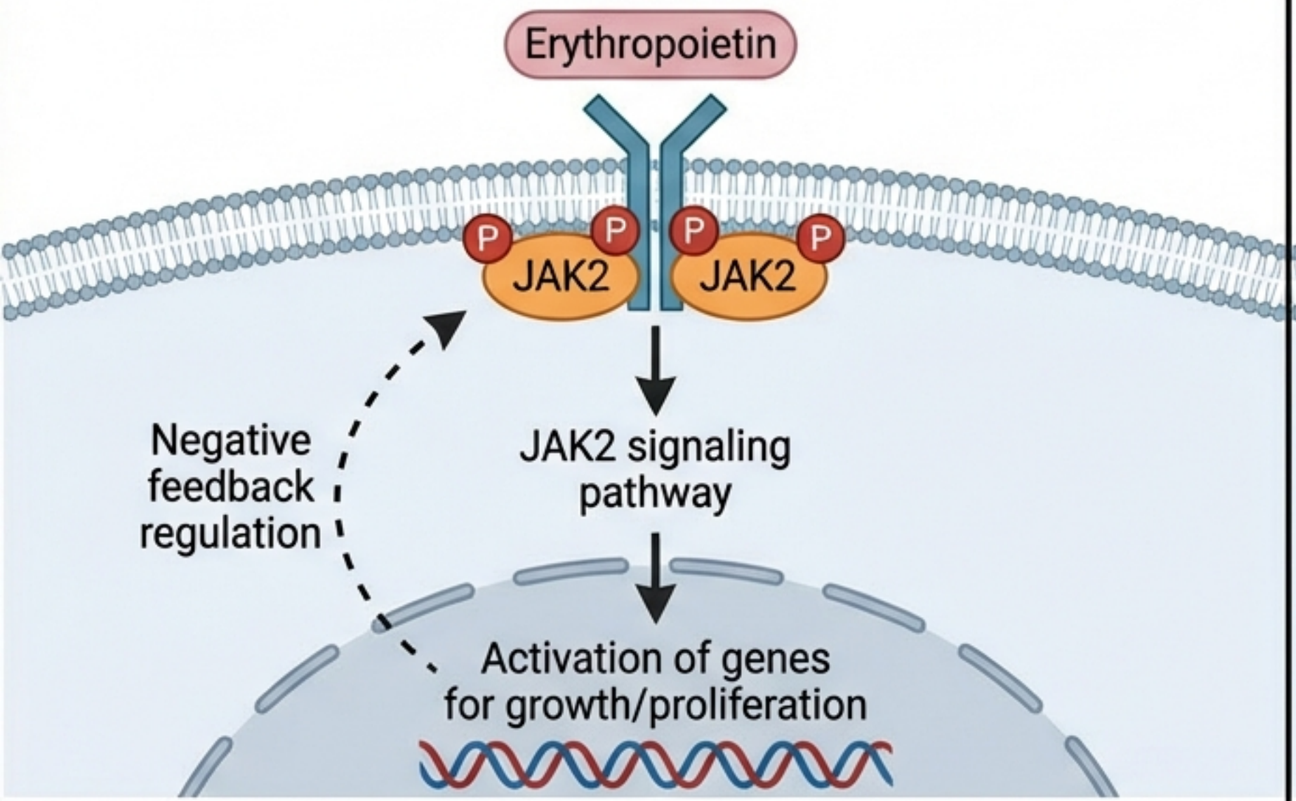
2. Activation
Phosphorylation

3. Signal Transduction
STAT Dimerization

4. Gene Expression
STAT Binds to DNA

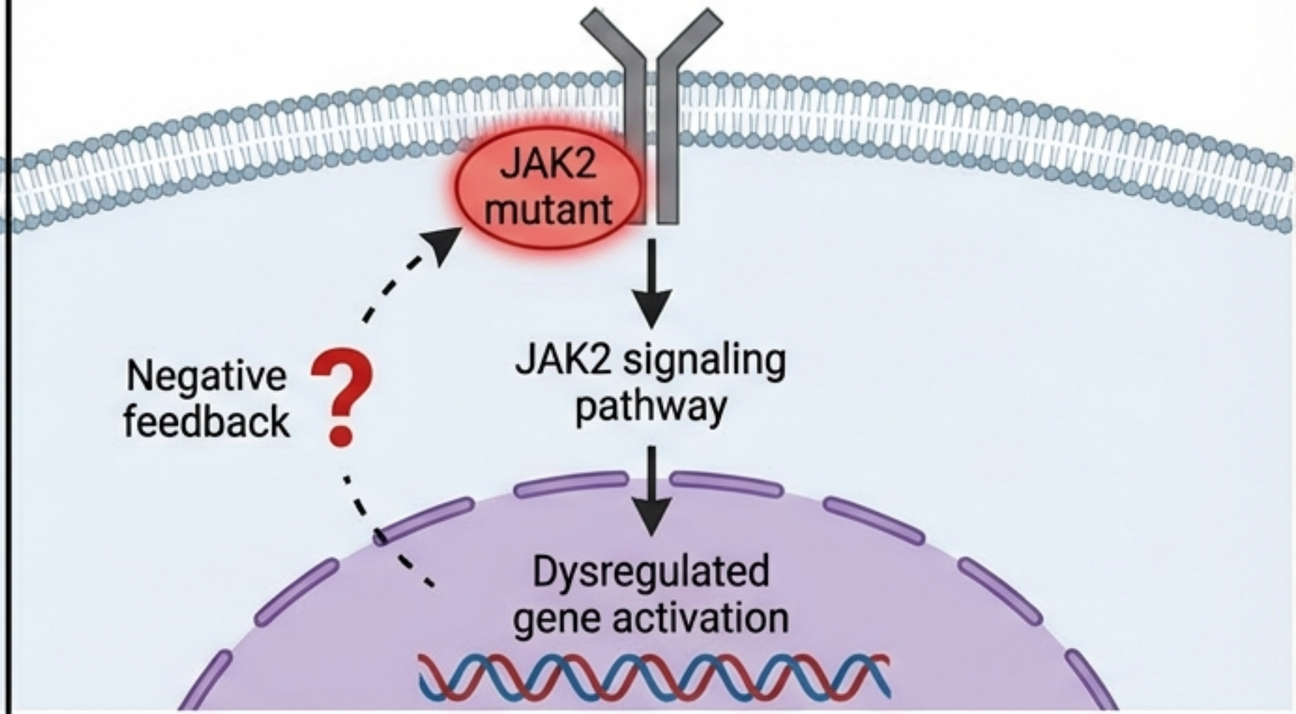
The Pathophysiology: A Broken Switch

Normal Regulation



Dependent on Growth Factors.

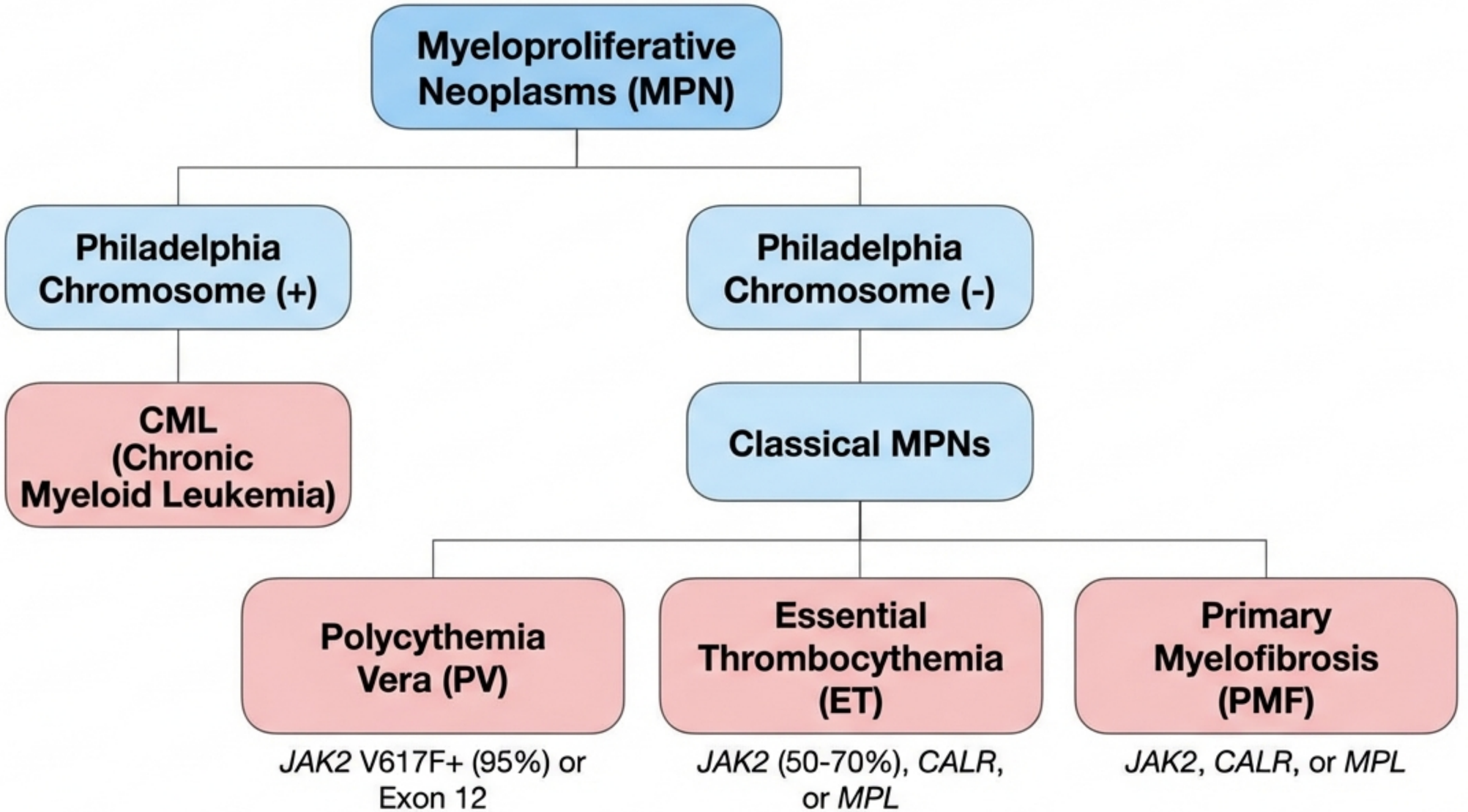
Polycythemia Vera (MPN)



Constitutive Activation (JAK2 V617F).
Independent of Growth Factors.

The Result: Unregulated, clonal production of blood cells.

The WHO Classification of Myeloid Neoplasms



The Diagnostic Challenge: Reactive vs. Clonal

Is this high count secondary to stress, or is it cancer?

REACTIVE
(Secondary)

- Infection
- Inflammation
- Tissue Necrosis
- Stress/Hypoxia
- Smoking
- Medications

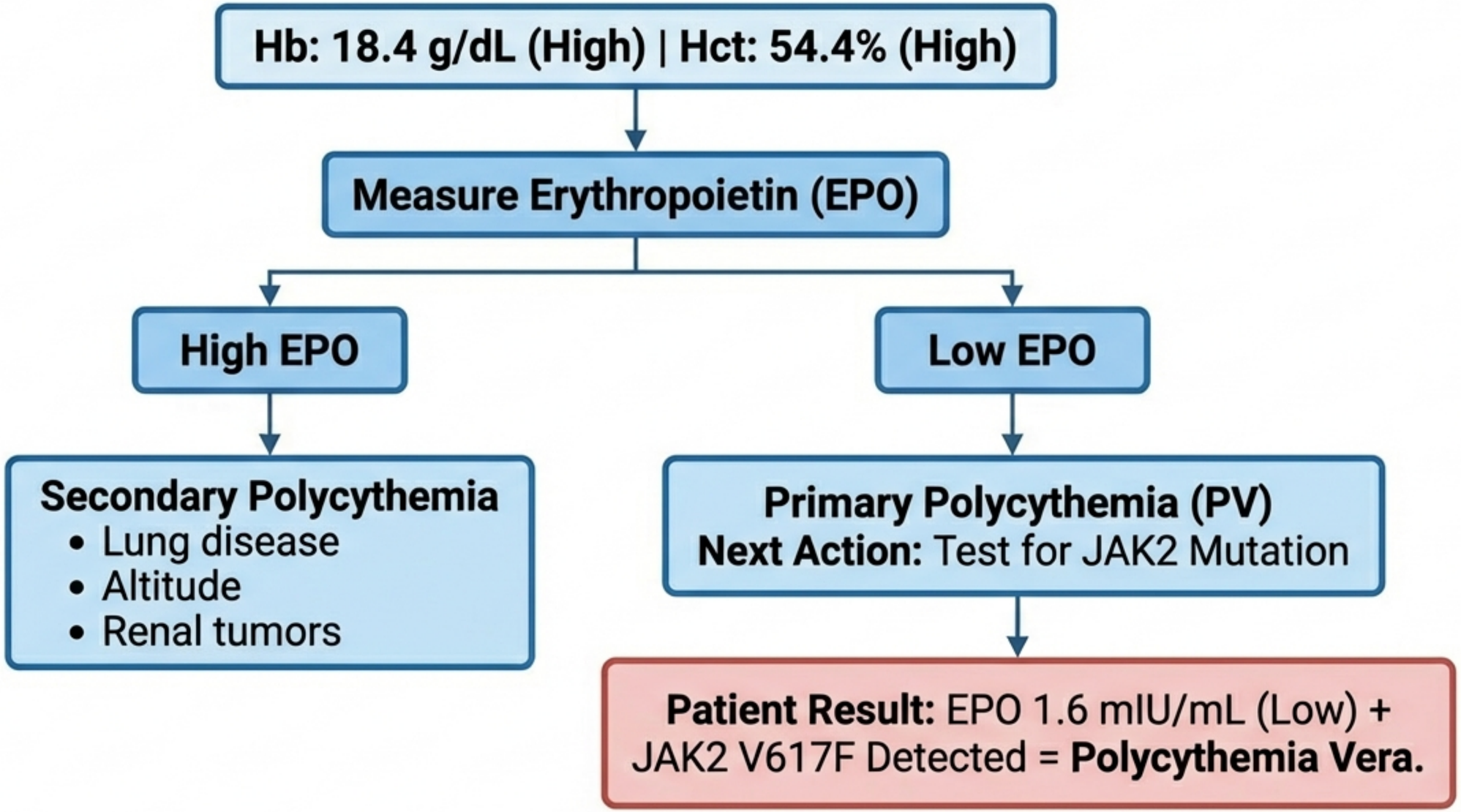
Neutrophil counts >50k usually indicate non-reactive etiologies.

CLONAL
(Primary)

- Myeloproliferative Neoplasms (Mutations)

The Clinical Question: Differentiating the cause of Cytosis/Cythemia.

Case Study 1: Erythrocytosis (Polycythemia)



Case Study 2: Neutrophilia & Splenomegaly

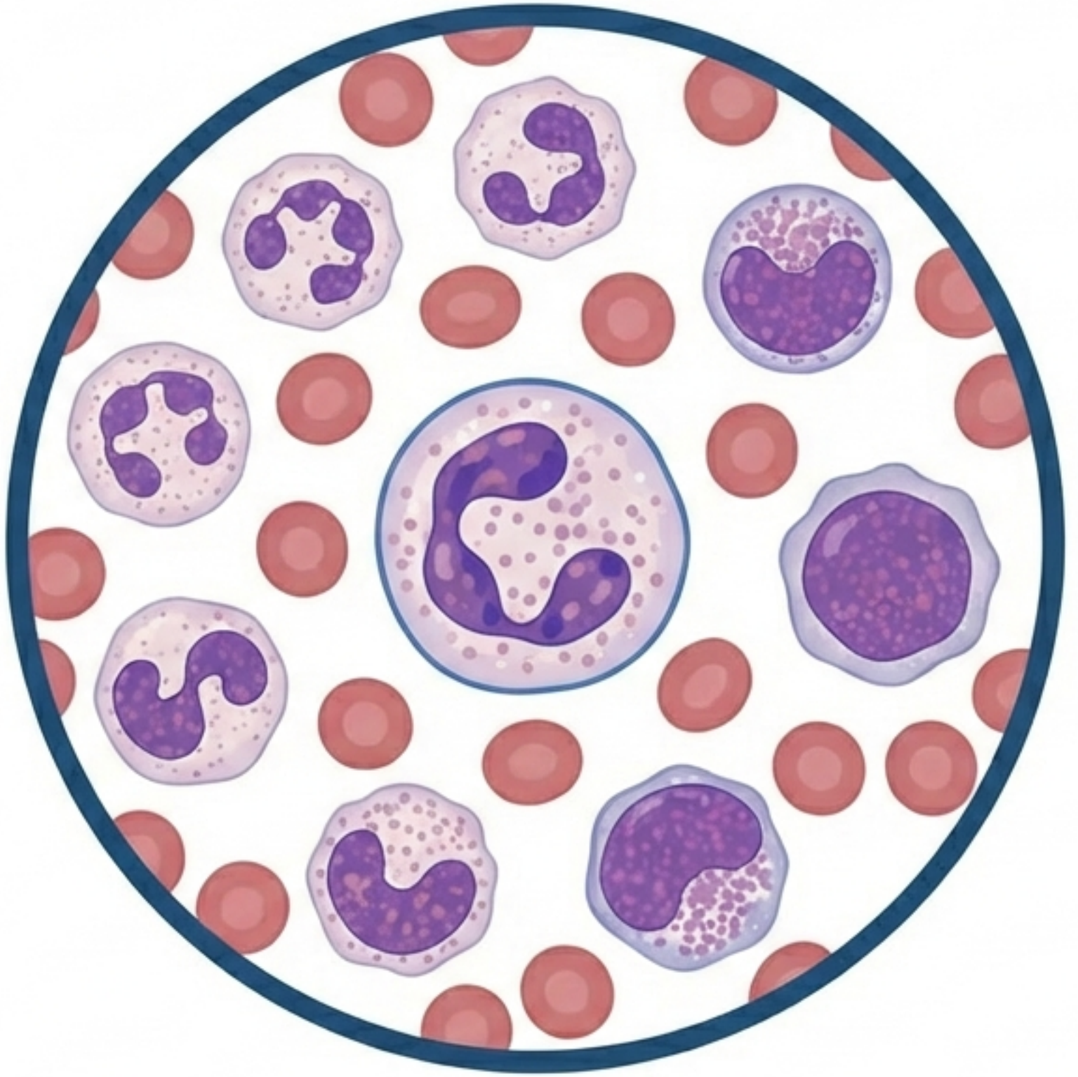
Patient Profile: 31-year-old male. Incidental abnormal CBC.

Key Finding: Palpable Splenomegaly (50-90% of cases).

Diagnosis: Chronic Myeloid Leukemia (CML).

Clinical Features:
- Insidious onset, fatigue, weight loss.
- Hyperleukocytosis is tolerated due to mature, small cells.

Phases: Chronic -> Accelerated -> Blast Phase.



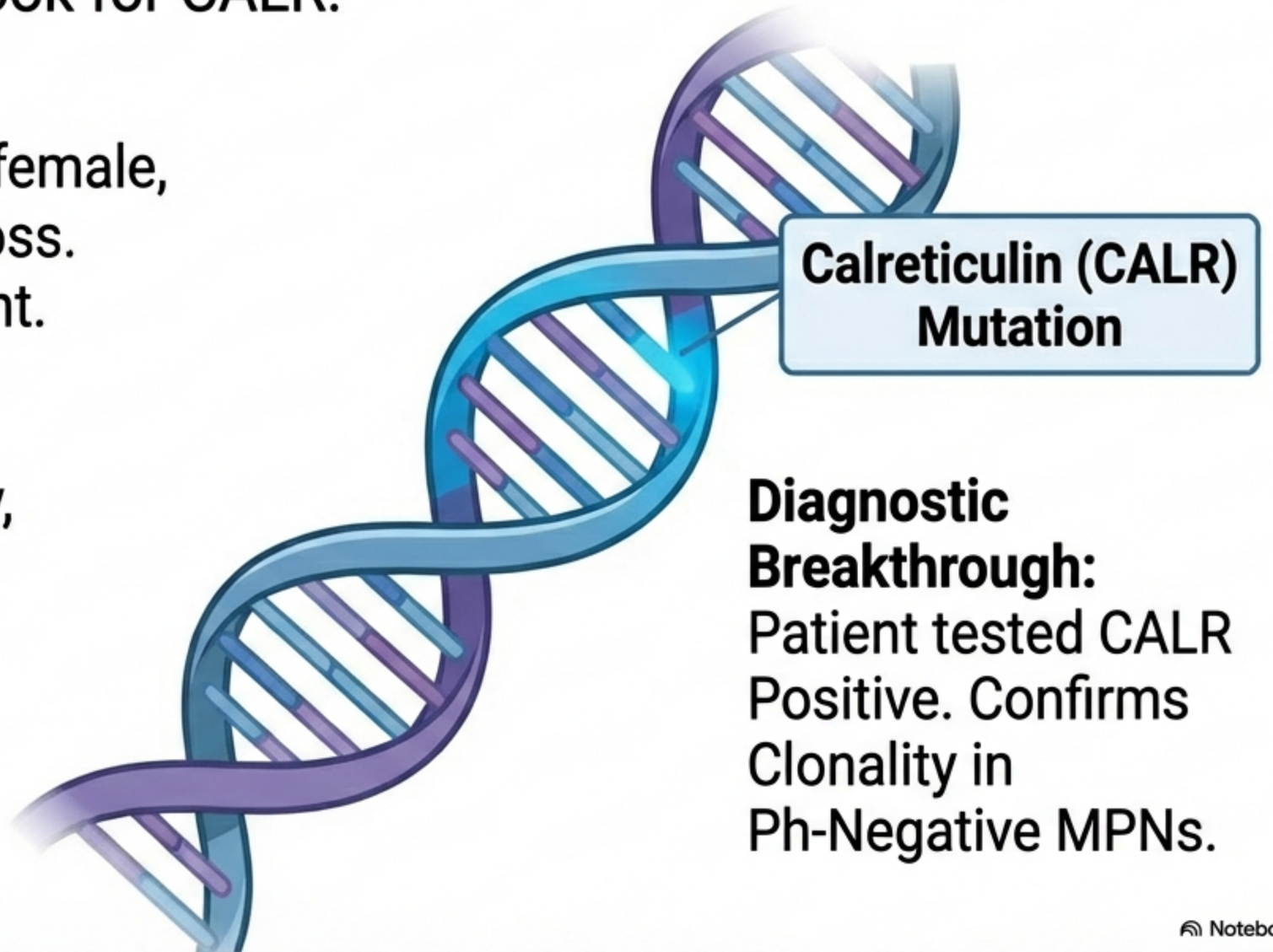
Case Study 3: Thrombocytosis

When JAK2 is negative, look for CALR.

Patient Profile: 30-year-old female, history of early pregnancy loss. Persistent high platelet count.

Differential Diagnosis:

- **Reactive**: Iron deficiency, Infection, Inflammation.
- **Primary:** Essential Thrombocythemia (ET).



Diagnostic Breakthrough: Patient tested CALR Positive. Confirms Clonality in Ph-Negative MPNs.

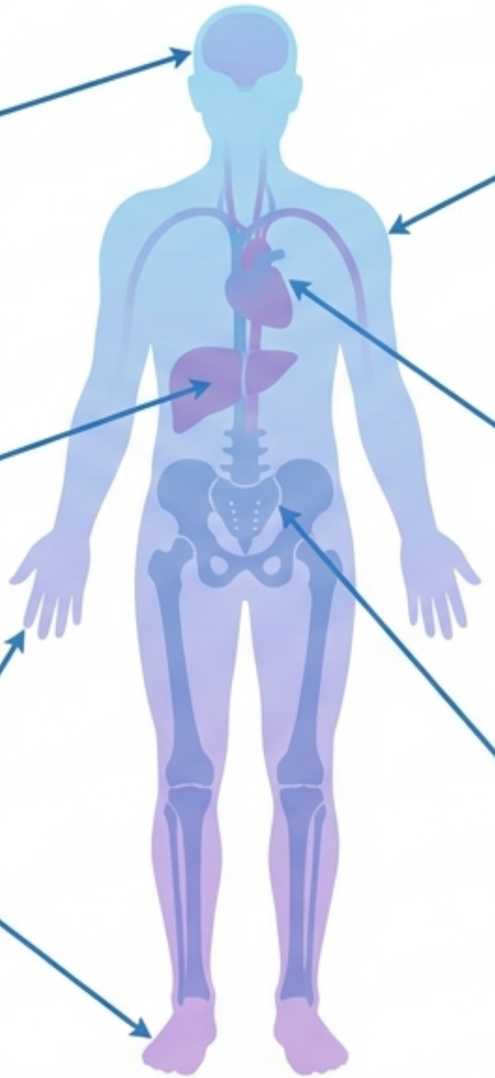
Clinical Features & Complications

The **burden** of disease beyond the blood counts.

CNS Symptoms (Headache, Dizziness, Visual disturbances)

Budd-Chiari Syndrome (Hepatic vein thrombosis) – A Red Flag for MPN

Erythromelalgia (Burning pain), Gout



CNS Symptoms (Headache, Dizziness, Visual disturbances)

Thrombosis (Stroke, MI, DVT) - 20% Risk

Progression to Fibrosis or Acute Leukemia (Blast Phase)

The Counterpoint: Myelodysplastic Syndromes (MDS)

MPN: Effective Proliferation

Mutation | Clonal Cytosis | **UP** (High Counts)

MDS: Ineffective Proliferation (Dysplasia)

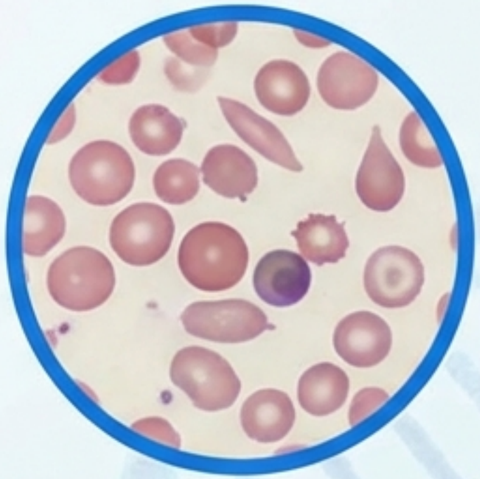
Mutation | Clonal Cytopenia | **DOWN** (Low Counts)

Key Features List for MDS:

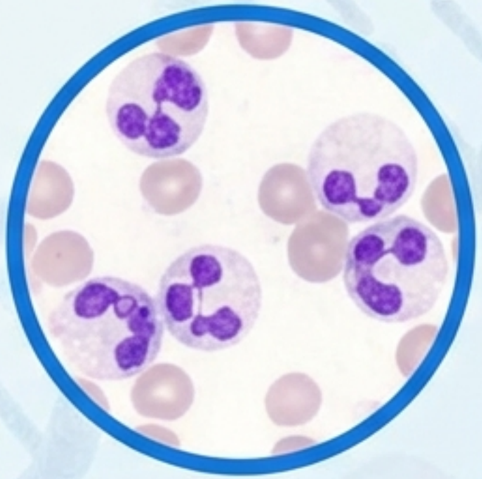
- Acquired somatic mutations in stem cells.
- Dysplasia: Abnormal maturation/morphology.
- Disease of aging.
- Presentation: Pancytopenia or single lineage cytopenia.

Case Study: MDS & Refractory Anemia

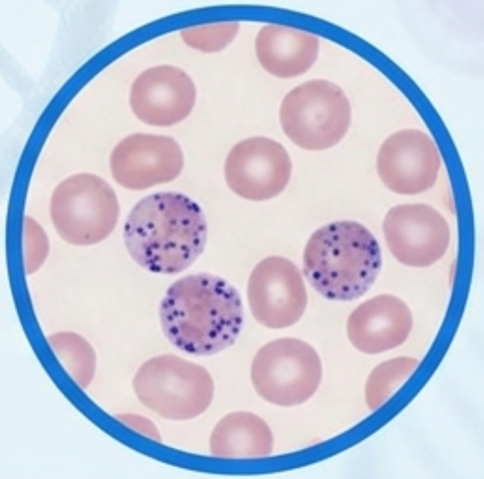
- **Patient:** 80-year-old woman.
- **Presentation:** Macrocytic anemia (Hb 7.4 g/dL, MCV 119.9 fL).
- **History:** Failed Vitamin B12 treatment (Rules out nutritional cause).
- **Bone Marrow:** Hypercellular (trying to grow) but Ineffective.



Anisopoikilocytosis
(Size/shape variation)



Hypogranulated Neutrophils
(Abnormal, 'washed out' appearance)



Basophilic Stippling

Management Strategy for MPNs

Primary Prevention

Aspirin (Vascular event reduction)

Thrombosis Management

Systemic Anticoagulation

Cytoreduction

Hydroxyurea, Interferon

Venesection (Phlebotomy) for Polycythemia Vera

Targeted Therapy

JAK2 Inhibitors (Ruxolitinib) for MPN

TKIs (Imatinib) for CML

Summary & Recap

1. **Context:** The majority of high blood counts are Reactive/Secondary, not cancer.
2. **Definition:** MPNs are Clonal, autonomous, and growth-factor independent.
3. **Genetics:** JAK2 V617F, CALR, and MPL are the diagnostic keys for Classical MPNs.
4. **Differentiation:** MDS represents clonal but ineffective hematopoiesis (Dysplasia + Cytopenia).
5. **Risk:** Management focuses on preventing Thrombosis and monitoring for Fibrosis/Leukemic transformation.

Questions & References

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Thank you.