HLS

SHEET NO. 1

PATHOLOGY

كتابة: دكتور 021

تدقيق: ياسمين حمدان و فرح ظاهر

الدكتور: طارق العديلي

POLYCYTHEMIA

- **Increase in total RBC mass above normal range.**

- **Erythrocytosis: increased RBC s number.**

-Notice that the mass is a different term than the number! Erythrocytosis is related to an increase in number (count) whilst polycythemia is related to an increase in mass.
-Mostly, erythrocytosis is related to polycythemia, meaning that if the number of RBCs increases the mass also will increase. But there is an exception, if the patient is suffering from empty RBCs and there is no hemoglobin inside it, there will be erythrocytosis but with no change in mass.

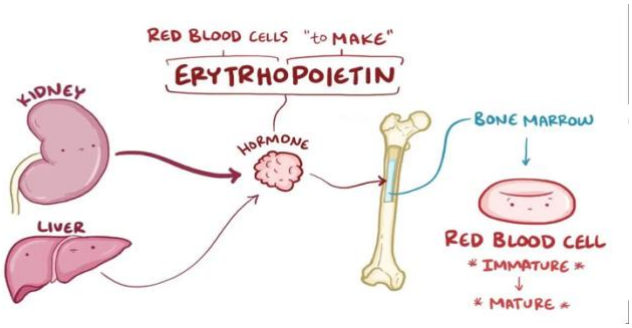
-**Polycythemia can be classified as the following:**
1-Relative polycythemia.
2- Absolute polycythemia .

- **Relative polycythemia: secondary to decreased plasma volume (water deprivation, severe diarrhea, diuretics) .**

-Relative polycythemia is described as a loss of fluid and increased RBCs concentration.

- **Absolute polycythemia**(true polycythemia)**: true increase in RBC mass, secondary to increased BM** (bone marrow) **production.**
- **Can be primary or secondary.**
- **Primary: autonomous high bone marrow production** (the problem is in the bone marrow itself produces a high amount of cells without any need, it is mainly a neoplastic disease "neoplasm in the bone marrow")**(polycythemia vera), erythropoietin is low** (due to negative feedback as the bone marrow is producing a large number of RBCs).

- **Secondary: systemic hypoxia —> high erythropoietin —> increased erythropoiesis** (synthesis of RBCs)



(bone marrow tries to correct hypoxia)

- **Secondary polycythemia has many causes listed below:**

1- Adaptive: living in high altitude (low oxygen)**, cyanotic heart disease** (congenital heart defect disease with insufficient oxygen pumping), **chronic pulmonary diseases eg: sleep apnea** (obstruction of respiration during sleep —> hypoxia).

Further clarification;

-high altitudes involve decreased oxygen density which makes it even harder to breathe so this will direct the bone marrow to increase the production of RBCs, thus hemoglobin will be increased.

2- Paraneoplastic: renal cancer, liver cancer the tumor secretes larger amount of hormones, as erythropoietin "EPO" which is mainly secreted by kidneys and a bit by liver. (No hypoxia)

Paraneoplastic :a tumor(either benign or malignant which produces larger amount of hormones or abnormal hormones, eg: lung tumor producing endocrine hormones)

3- Surreptitious (blood doping): endurance athletes (many athletes take EPO or androgens as a supplement or blood doping which is extracting some of their blood and injecting it back so that will increase the number of RBCs and thus increase oxygen carrying capacity and delivering it to tissues "منشطات").

4- Alcohol (multifactorial)**: frequent urination, depressed respiration**

5- Smoking. (Lung diseases)

- **In secondary polycythemia: no splenomegaly.**

* *Polycythemia Vera* (which is an absolute primary polycythemia).

- **It is classified as a type of: Myeloproliferative neoplasm .**
- Myelo refers to the bone marrow
- Myeloproliferative Disorders: cancers caused by changes in the stem cells inside bone marrow. Polycythemia vera is the most common myeloproliferative neoplasm. It makes your bone marrow produce too many blood cells, most predominantly erythrocytes.
- **Mutation in tyrosine kinase JAK2 in bone marrow stem cells** (99% of patients have this mutation)
- **JAK2 Normally acts in the signaling pathway of erythropoietin receptor and other growth factor receptors** +it is important for the proliferation of all bone marrow cells)

  -This mutation is stimulatory, so the protein becomes permanently active, leading to the proliferation of all bone marrow cells especially RBCs without the need for erythropoietin.
- **Hematopoietic cells become less dependent on growth factors.**

- **Excessive proliferation of erythroid, myeloid cells** (WBCs) **and megakaryocytes. (panmyelosis)** pan means all.
- **Erythrocytosis is most prominent, results in polycythemia.**
- **Splenomegaly is common** As neoplastic cells migrate to the liver and spleen and proliferate there.

*Symptoms of polycythemia (general)

- **Plethora/ cyanosis**

-**Plethora** is redness of skin especially the face.

-**cyanosis** is a bluish color of the skin due to the deoxygenated blood

- **Headache and dizziness (from hypertension)** due to increased blood mass and in some cases this may lead to heart failure .
- **Slow circulation and hyperviscosity** (due to the high cellularity) **cause cyanosis, blurred vision** retina is involved(abnormal circulation to retina) leading to blindness**, tissue ischemia .**
- **Thrombosis, or bleeding (disturbed function of vWF** Von Willebrand factor is a clotting factor)

-**Due to** increased RBCs, the blood becomes more viscous. As a result, the incidence of blood clotting increases making thrombi.

*In polycythemia vera: similar symptoms plus:

- **Pruritus (aquagenic)** (as leukocytosis occurs, histamine is released in large amounts, it appears as intense itching after a hot shower that's why it is aquagenic).
- **Peptic ulcer** (also due to histamine release).
- **Secondary gout (arthritis, kidney stones, tophi**(solid crystals in the tissue)**).** due to high turnovers of RBCs which results in higher-than-normal uric acid production .

BM with hypercellularity (panmylosis) —> cells die more frequently —> more DNA will be scattered —> turns into purine that turns into uric acid.

- Polycythemia **is a Chronic disease.**

- **Spent phase**(advanced)**: occurs after an interval of 10 years of symptoms, BM becomes fibrotic, hematopoiesis shifts to spleen** spleen becomes the main site for hematopoiesis leading to splenomegaly)
- **Blast crisis: transformation to acute myeloid leukemia (rare)** by gaining more mutations.

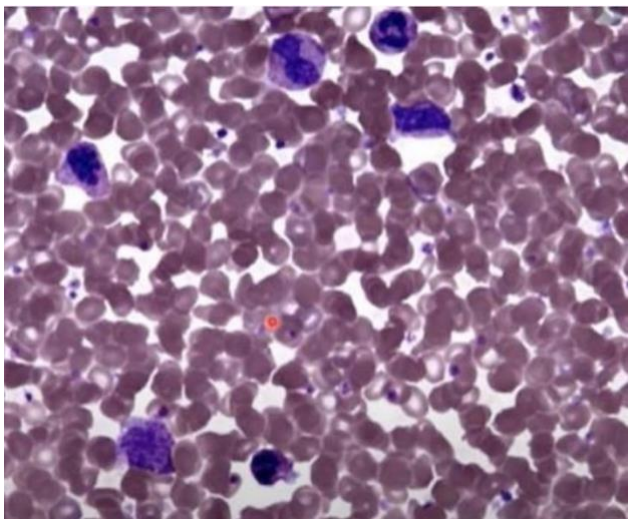
**Laboratory findings of polycythemia :*

- **High hemoglobin concentration (>16.5 g/dL in men, 16 in women) and high hematocrit (>49% in men, 48% in women).**
  RBCs contain hemoglobin, so if we measure hemoglobin concentration we also measure RBCs mass.
- **High RBCs count** erythropoiesis.
- **These tests might be masked if iron deficiency develops .**

Patients with polycythemia may develop iron deficiency as the high count of RBCs will consume iron so hemoglobin concentration will drop below expected criteria.
Further explanations: as we said before patients with polycythemia will have high Hb concentration (around 16.5 g/dl)
However patients with polycythemia who developed iron deficiency will have lower Hb concentration because the iron is low (Hb around 16) and that's what we call 'masking effect' .
So we conclude that if the Hb concentration wasn't high we cannot exclude polycythemia, the patient may suffer from iron deficiency.

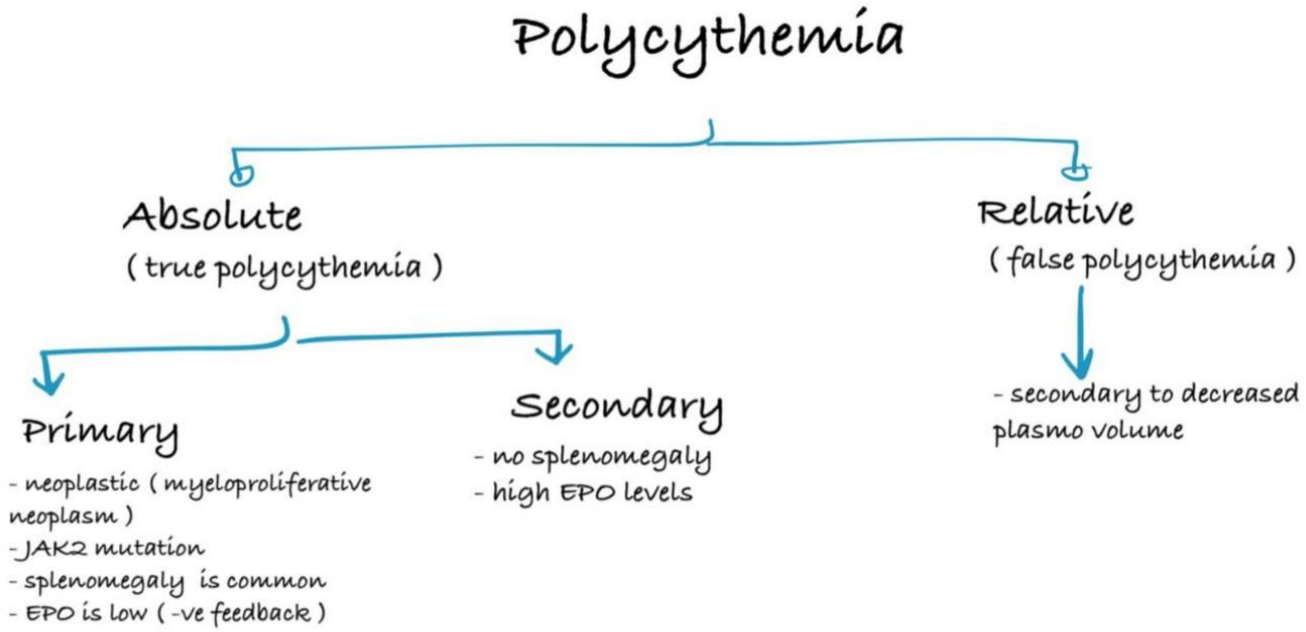
**In polycythemia vera: additional findings:*

- **Leukocytosis and thrombocytosis are common.**
- **JAK2 mutation** in 99% of patients in molecular tests.
- **Low erythropoietin level** negative feedback .
- **Hypercellular bone marrow with panmyelosis.** We take a biopsy from BM.



Peripheral blood smear in polycythemia : packed red blood cells

To sum up..



Highly recommend Link

https://youtu.be/jFxCZ91sDpI?si=jKWe2RoyIKZuDpUL