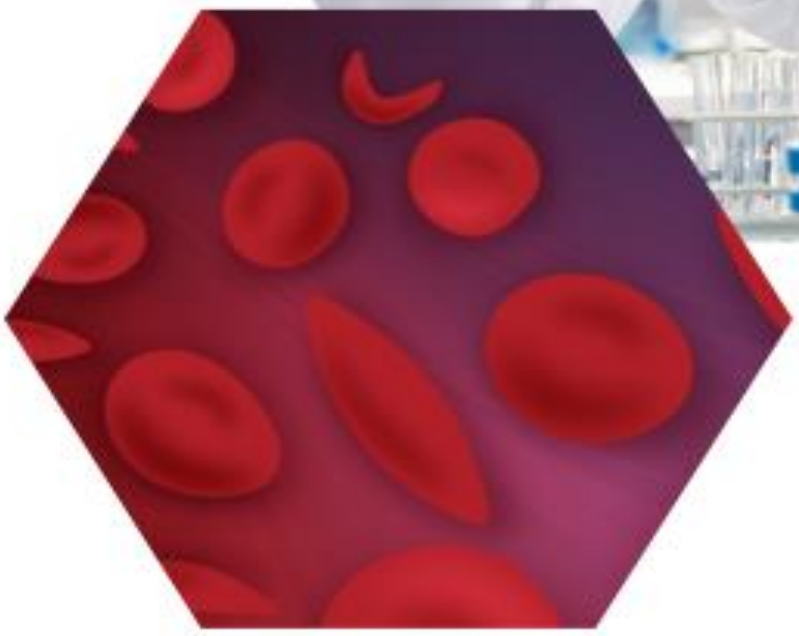
Doctor.021

no.1

HLS PATHOLOGY



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POLYCYTHEMIA

- **Increase in total RBC mass above normal range.**(the normal is not a fixed number).
- **Erythrocytosis: increased RBC s number.**(most of the time erythrocytosis leads to polycythemia).

-Notice that the mass is a different term than number! Erythrocytosis is related to increase in number whilst the polycythemia related to increase in mass.
-Mostly, erythrocytosis is accompanied with polycythemia but there is an exception, if the patient is suffering from another condition like iron deficiency, there will be erythrocytosis but with a paradoxic decrease 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 false increase in the concentration of RBCs, so it is not a true hematologic disease.

- **Absolute polycythemia**(true polycythemia)**: true increase in RBC mass, secondary to increased BM production .**
- **Can be primary or secondary.**
- **Primary: autonomous high bone marrow production** (primary 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 large number of RBCs).
- **Secondary: systemic hypoxia —> high erythropoietin —> increased erythropoiesis** over all results in polycythemia.

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

1- **Adaptive: living in high altitude, cyanotic heart disease, chronic pulmonary diseases eg: sleep apnea** (obstruction of respiration during sleep).

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.
-As for cyanotic heart disease which is a disease that is characterized by defect in heart in infants.

2- **Paraneoplastic: renal cancer, liver cancer** (as erythropoietin is secreted mainly by kidneys and a bit by liver)
3- **Surreptitious (blood doping): endurance athletes** (many athletes take EPO as a supplement or do blood doping)

Extra information

about doping: Athletes extract some of their blood couple of days before a race and inject it back a day before so that will increase number of RBCs and thus increasing oxygen carrying capacity and delivering it to tissues).

4- **Alcohol: frequent urination** (mainly relative polycythemia), **depressed respiration**

5- **Smoking.**

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

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

- **It is classified as a type of: Myeloproliferative neoplasm .**
- Polycythemia vera is the most common myeloproliferative neoplasm. It makes your bone marrow produce too many blood cells, most predominantly erythrocytes in the case of polycythemia vera.
- **Mutation in tyrosine kinase JAK2 in bone marrow stem cells** 99% of people with PV develop this mutation.
- **Normally acts in the signaling pathway of erythropoietin receptor and other growth factor receptors.** This mutation is stimulatory(gain of function) so the protein becomes permanently active.
- **Hematopoietic cells become less dependent on growth factors.**
- **Excessive proliferation of erythroid, myeloid cells and megakaryocytes. (panmyelosis)** pan means all.
- **Erythrocytosis is most prominent, results in polycythemia.**
- **Splenomegaly is common** As neoplastic cells migrate to liver and spleen and proliferate there.

*Symptoms of polycythemia (general)

- **Plethora/ cyanosis**

-**Plethora** is redness of skin.

-**cyanosis** is a bluish color of the skin due to the deoxygenated blood seen mainly in digits, ear and nose.

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

-**Due to** increased of RBCs, the blood becomes more viscous as a result the incidence of blood clotting increases making thrombi or emboli such as in cases of DVT, MI and Pulmonary Embolism.

*In polycythemia vera: similar symptoms plus:

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

-Furthur explanation :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: occurs after an interval of 10 years of symptoms, BM becomes fibrotic, hematopoiesis shifts to spleen** spleen (becomes the main site for hematopoiesis).

-Further explanation on BM fibrosis, in polycythemia vera atypical megacaryocyte hyperplasia takes place thus secreting cytokines such as TGF-b in huge amount activating fibroblast resulting in an obliteration of bone marrow with fibrosis.

- **Blast crisis: transformation to acute myeloid leukemia (rare)** 10%.

Note: bone biopsy must be taken in order to differentiate between spent phase and blast crisis.

*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)** test of blood mass (total blood not just RBCs).
- **High RBCs count** erythropoiesis.
- **These tests might be masked if iron deficiency develops .**

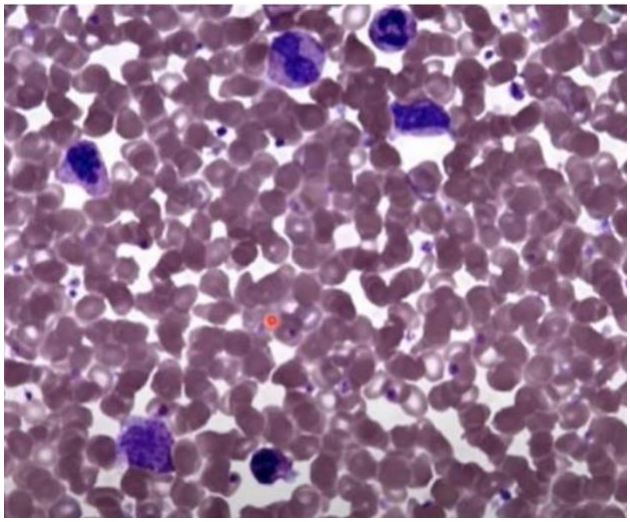
Patients with polycythemia may develop iron deficiency as the high count of RBCs will consume iron so hemoglobin concentration will drop below expected criteria.
Further explanations: as we said before patients with polycythemia will have high Hb concentration (around 18-19 g/dl)
But patients with polycythemia who developed iron deficiency will have lower Hb concentration (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 we need to check the size of RBCs and if they were small (microcytic) with very high cell count (erythrocytosis)it means that the patient has polycythemia.

***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.**

-Remember that as we become older, part of our bone marrow is going to be replaced with adipose tissue and that occurs normally, which is not the case in polycythemia as the bone marrow is completely hypercellular and there is no adipose.

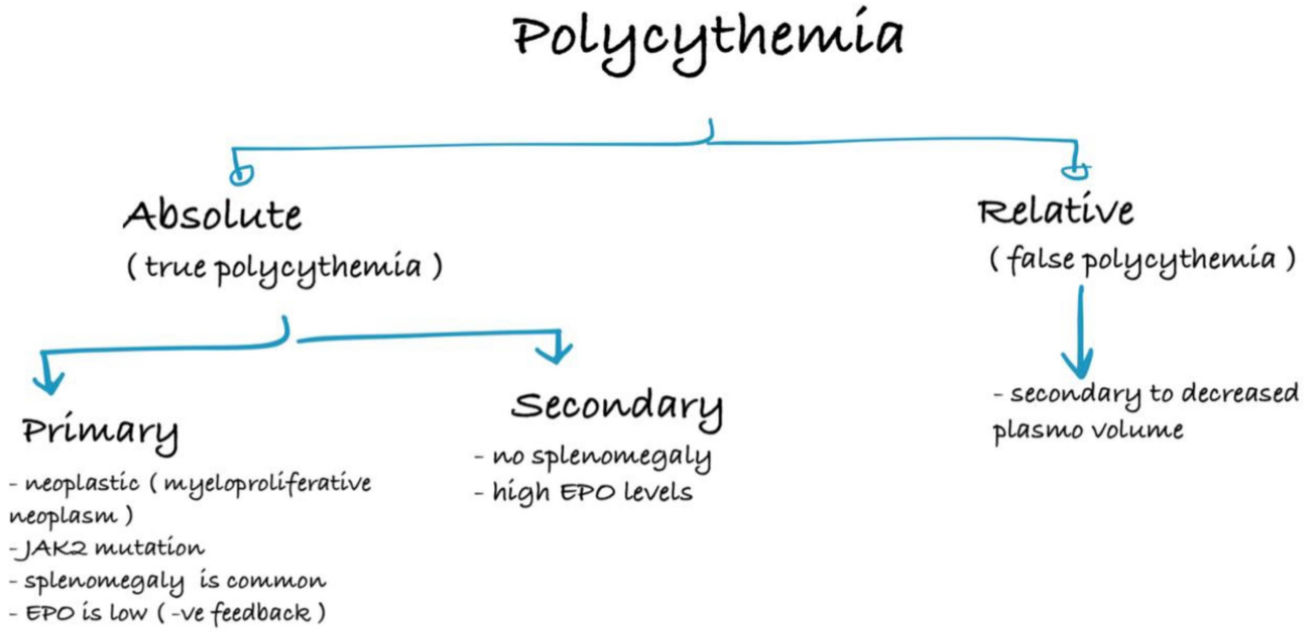
- This cannot be implicated clearly on children as they already don't have obvious amounts of adipose tissue in BM .



Periphral blood smear in polycythemia : packed red blood cells

-Notice the crowded RBCs and the thick smear due to viscosity

To sum up..



Links that might be useful..g

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

https://youtu.be/pWGRT17SazA?si=B4VOdxEP3grQY7HM

سأحمل روحي على راحتي ..... و ألقي بها في مهاوي الردى

فإمّا حياة تسرّ الصديق ..... و إمّا ممات يغيظ العدى

PRAY FOR GAZA

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