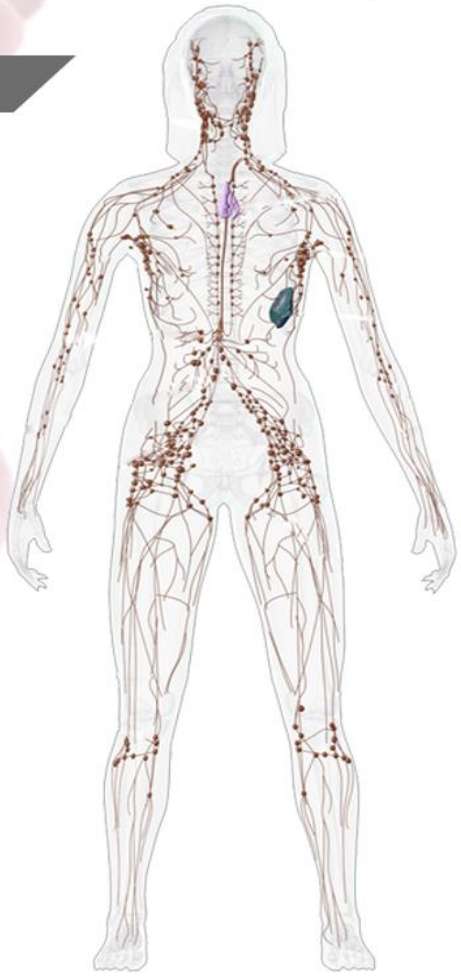
Sheet #

Hematology and Lymphatic system

Subject | Pathology



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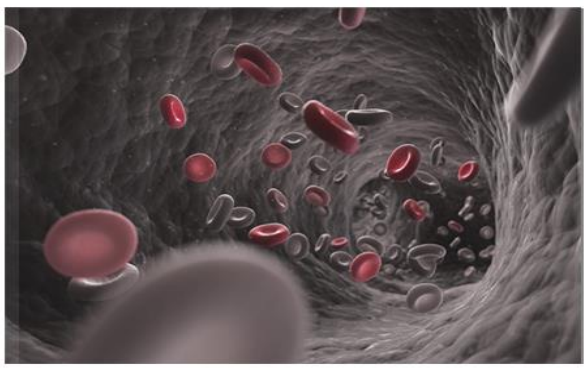


Polycythemia: denotes an abnormally high red cell count, usually with a corresponding increase in the hemoglobin level

- Polycythemia is opposite to Anemia
- Classification of polycythemia to:

1- Relative
2- Absolute: two types :
a- Primary.
b- Secondary. Or called relative absolute polycythemia

Relative Polycythemia:

Stem from decrease plasma volume rather than change in total RBC mass. means RBCS within reference range it did not change .The change happened at level of plasma volume .

Cause of decrease plasma : dehydration, diarrhea, diuretic therapy, excessive vomiting, excessive sweating .so decrease in plasma cause increase HCT and increase hemoglobin concentration.

Absolute Polycythemia:

- in absolute polycythemia, the increase of RBC count is due to overproduction of RBCs in the bone marrow
- To differentiation between primary and secondary polycythemia used erythropoietin level
- erythropoietin is a hormone produced from kidney to promote production of RBCs and hemoglobin

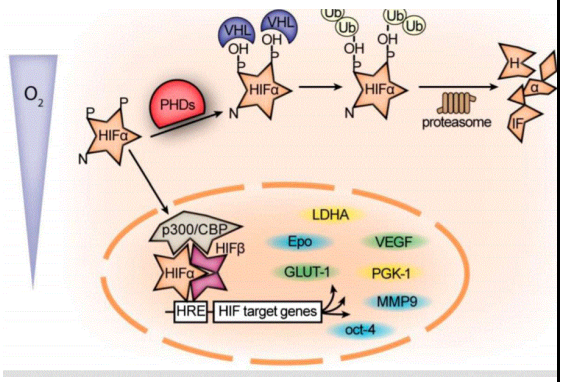
-**Primary** polycythemia is associated with **low** erythropoietin levels.

-**Secondary** polycythemia is associated with **elevated** erythropoietin levels.

- The relationship between O_2 and hemoglobin

-in right upper half of the picture, the concentration of oxygen is high so hypoxia induced factor alpha will be Destroyed.

- If the concentration of **oxygen** is **low** ,hypoxia induced factor alpha will not be destroyed and will combine with other molecules resulting in activation of downstream signals including the production of **erythropoietin.**



- Causes of Secondary polycythemia :

  A)The **most** important cause is hypoxia

  There are two types of hypoxia:

  1-General hypoxia :

  - Smoking
  - High altitude
  - High affinity hemoglobin

  2-Localized hypoxia

  - Renal artery stenosis: if the kidney senses renal artery stenosis it will assume it's happening in the whole body so it will produce high amounts of erythropoietin.
  - Polycystic kidney disease

  B) Certain neoplasms

  - Wilms tumor: kidney malignant tumor ,which occur in child in average of 3years old.
  - Renal cell carcinoma
  - Cerebellar hemangioma/hemangioblastoma
  - Hepatocellular carcinoma

Primary absolute polycythemia

Erythropoietin production will be low. because of disease abnormalities in level of stem cell. So the production of erythroid precursor cells is independent on erythropoietin. High production of RBCs cause suppression of erythropoietin hence erythropoietin in serum is low.

The most common cause of primary absolute polycythemia is **polycythemia Vera**.

- **polycythemia Vera**.

- is characterized by increased marrow production of red cells, granulocytes, and platelets (panmyelosis), so when we take a bone marrow biopsy, we will see proliferation of all myeloid cells. but the increase in red cells (polycythemia) that is responsible for most of the clinical symptoms.

-The main characteristic of malignant polycythemia is polycythemia Vera

- Pan=all
- Myelosis=increase in myeloid cells

- Strongly associated with JAK2 mutation (Valine-to-phenylalanine substitution at residue 617 *this is from the slides*) . Such mutation is present in more than 97% of PV cases.
- These patients are more prone to thrombosis because of high viscosity of blood but also to bleeding! despite increase platelets and that's because these platelets are nonfunctional which results in bleeding.
- At the beginning of the disease, the spleen is mildly enlarged however at later stages it becomes massively enlarged which is called spent phase.
- Hypercellularity in the bone marrow
- Complications of the disease is severe fibrosis affecting the bone marrow and organomegaly; this phase is called spent phase
- Spent phase(massive splenomegaly and fibrosis in Bone Marrow)

Clinical manifestation of polycythemia.

• Pruritis
• Headache dizziness
• Hyperuricemia and gout
• increased risk of both major bleeding and thrombotic episodes.
• Deep venous thrombosis
• Stroke
• Myocardial infarction
• Bowel infarction
• Budd-Chiari syndrome

if complication bleeding appear it might suffer epistaxis and bleeding gums
Major hemorrhage can occur in ~10% of the patients.

Treatment

Phlebotomy(to remove some of hemoglobin and RBCs; technically it's drawing some blood from the patient) and JAK2 inhibitors.
• 2% might transform to acute myeloid leukemia.

Diagnosis of polycythemia Vera

Uses criteria set forth by WHO classification of tumors.

- In order to diagnose polycythemia Vera, you need **all three major criteria** or the **first two major and the minor criterion**) .

• Major criteria:

1. Elevated hemoglobin
2. hypercellularity of MB with panmyelosis
3. Presence of JAK2 .

- Minor criteria
  1. Serum erythropoietin level below

The Doctor's Questions:

1- Relative polycythemia occurs in the setting of:

A. Wilms tumor

B . **Dehydration**

C. Renal cell carcinoma

D. Polycythemia Vera.

E. Hypoxia

2- All of the following are examples of secondary absolute polycythemia, except:

A. Smokers B.

B. Renal artery stenosis

C. Polycystic kidney

D. Polycythemia Vera

E. High altitude

3- The risk of acute myeloid leukemia in polycythemia Vera is:

A. 2%

B. 10%

C. 30%

D. 50%

E. 70%

4- One of the following is a minor criterion for PV:

A. High hemoglobin

B. Hypercellular bone marrow

C. Low erythropoietin level

D. High erythropoietin level

E. Endogenous erythroid colony formation in vitro

Best of luck