Polycythemia

**Definition**
Female: > 16.5/48
Male: >18.5/52

**Relative polycythemia:** isolated decrease in plasma volume causes elevation in Hgb/Hct

**Absolute polycythemia:**

1. **Primary polycythemia** - Acquired or inherited mutation. i.e. polycythemia vera

2. **Secondary polycythemia** - Circulating plasma factor stimulating erythropoiesis, usually erythropoietin,
   a. oxygen sensitive EPO response o hypoxia
   b. EPO secreting tumor

3. **Inapparent polycythemia:** both RCM and plasma volume increased

4. **Combined polycythemia:** RCM increased and plasma volume increased

**Physiology Key points**

1. EPO is a trophic hormone that stimulates differentiation of erythroid progenitor cells
2. 90% of epo synthesized by kidneys in response to hypoxic signal
   a. Trigger for this signal is likely anemia, oxygen saturation (hypoxemia), oxygen release, oxygen delivery
   b. Negative feedback, Increase in oxygen delivery decreases EPO production

**Initial Evaluation**

1. Repeat test
2. History: Pulmonary etiologies and symptoms, high altitudes, home oxygen, intra-cardiac or intrapulmonary shunts, fh, use of steroids, epo injections, smoking, chronic exposure to CO, occupational,
3. Physical Exam: pulse ox after minimal exertion, sleep studies, evidence of cyanosis, clubbing, murmurs/bruits (pulmonary av shunts), hsm,
4. Lab findings
   a. High rbc count and decreased hbg/hct= think thalassemia minor
   b. Elevated total wbc and/or platelet and/or mcv= think polycythemia vera
   c. Microscopic hematuria= think EPO secreting renal cell carcinoma
   d. Hyperglycemia/electrolyte disturbances= think endocrine tumors
   e. Abnormal lft’s= think hepatoma (esp if previous diagnosis of cirrhosis, viral hepatitis, hemochromatosis
5. chest x-ray: AVM’s, chronic obstructive lung, pulm htn

**Further Evaluation:**

1. suspect CO (tobacco smoke, engine exhaust) measure blood carboxyhemoglobin
2. suspect hypoxia: pulse ox, arterial oxygen sat, arterial oxygen tension (pO2), when tension is normal but sat is low suggests carboxyhemoglobin/methemoglobinemia
3. measure serum epo concentration
4. blood volume measurement

* Source of info and tables is Up To Date
**Major Causes of Erythrocytosis**

**Autonomous (inappropriate) increase of Epo** – inappropriately high serum Epo
- Erythropoietin-producing neoplasms
- Renal cell carcinoma
- Hepatocellular carcinoma
- Hemangioblastoma
- Uterine fibroids
- Erythropoietin-producing renal lesions
- Following renal transplantation (some cases are independent of erythropoietin)

**Appropriate increases in erythropoietin** – appropriately high serum erythropoietin
- Hypoxemia secondary to:
  - Chronic pulmonary disease
  - Right-to-left cardiac shunts
  - Sleep apnea
- Massive obesity (Pickwickian syndrome)
- High altitude
- Red cell defects
  - Some cases of congenital methemoglobinemia
  - Chronic carbon monoxide poisoning (including heavy smoking)
  - Cobalt

**Germinine and somatic mutational causes of polycythemia**
- Polycythemia vera
- Activating mutations of the erythropoietin receptor
- Chuvash polycythemia
- Methemoglobinemia
- Idiopathic familial polycythemia
- High oxygen affinity hemoglobin
- Absence of or decrease in 2,3 BPG mutase

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**Diagnostic Approach to Suspected Erythrocytosis: Presence of PV-Related Feature**

**Suspected erythrocytosis**

- PV-related features present
  - Check serum EPO
  - Elevated
  - Normal
  - Low
  - Secondary erythrocytosis
  - Obtain bone marrow
  - PV
  - Diagnose for PV
  - Non-diagnose for PV
  - Repeat serum EPO and Hb in 3 months

- PV-related features absent
  - See next figure
  - PV

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**Diagnostic Approach to Suspected Erythrocytosis: Absence of PV-Related Features**

**Suspected erythrocytosis**

- PV-related features present
  - Check serum EPO
  - Low
  - Obtained bone marrow
  - PV
  - Repeat serum EPO
  - Repeat Hb in 3 months
  - Ventilatory for secondary erythrocytosis
  - Secondary erythrocytosis

- PV-related features absent
  - See previous figure
  - PV
  - Repeat Hb in 3 months

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*PV-related features include increased red cell mass with arterial oxygen saturation <92 percent, splenomegaly, thrombocythemia, and leukocytosis

*If PV is strongly suspected and the initial EPO level is normal, repeat testing in 3 months is suggested before additional testing is performed.

Abbreviations: PV = polycythemia vera; EPO = erythropoietin; Hb = hemoglobin; M = male; F = female

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