Approach to Anemia

- Pathologic state due to insufficient erythrocytes.

**Easiest way to classify:**
- Secondary to loss
- Secondary to lack of production
- Secondary to destruction

**Symptoms:**
- Tachycardia, exertional dyspnea, pallor of nails/conjunctiva, fatigue, reduced exercise tolerance.

**Labs:**
- CBC

**Pathology:**
- To make RBC, require: Epo (Made in Kidney), Iron, Cobalamin, Vitamin B12, marrow microenvironment.

**Approach:**
- Look at MCV (micro/normo/macrocytic)
- Peripheral blood smear (always look at smear).
- **Reticulocyte Count:** (tells you if the marrow is working).
  - Typically a % of normal erythrocytes
  - Now done with flow cytometry.
  - Patients with anemia have LOW total erythrocytes
  - Often corrected as reticulocyte index as bone marrow stress causes increased Epo production --> doubles of half-life of circulating reticulocytes (multiply by 0.5).
    - Therefore, must correct to \( \text{reticulocyte index} = \% \text{retics} \times \text{hematocrit} (\div 45 \times 0.5) \)
    - (last part is the correction factor for the doubling of retics)

**Absolute Retic Counts:**
(some labs do FLOW cytometry, which reports Absolute Number--> eaier to use, less available)

<table>
<thead>
<tr>
<th>Retic Count</th>
<th>Retic Index</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>23,000–90,000/μL</td>
<td>&lt;2%</td>
<td>Normal (Inappropriate Response to Anemia)</td>
</tr>
<tr>
<td>&gt; 100,000/μL</td>
<td>&gt;3%</td>
<td>Appropriate Anemia Response</td>
</tr>
</tbody>
</table>

(Retic Index numbers: wikipedia, Retic count numbers: MKSAP 16)
• Mentzner index to distinguish thalassemia vs iron def anemia
  ○ MCV/RBC -->
    ▪ <13 - thalassemia (bone marrow still produces enough RBC)
    ▪ >13 - Iron def anemia (bone marrow cannot produce as many, so there are few RBCs and microcytic)
Microcytic Anemia

DDx TAILS

- Thalassemia
- Anemia of Chronic Disease
- Iron Deficiency Anemia
- Lead Poisoning
- Sideroblastic Anemia

Standard Workup:

- Blood Film
- Ferritin
- Retics
- B12 (Folate low yield)

Can use RDW to help distinguish etiologies:

- Iron Deficiency: increased RDW (anisocytosis)
- Thalassemia minor: normal RDW (also expect high RBC count)
Thalassemia

- Risk factors:
  - Thalassemia major --> only in kids
  - B-thalassemia --> Mediterranian, Middle eastern.
- Labs:
  - Microcytic anemia but Normal Ferritin.
  - Persistently low MCV (MCV not changing if you trend it).
  - Low RDW
  - Hemoglobin electrophoresis
    - If normal can still be alpha-thalassemia (B-thal will show up). Need to do genetic testing.
    - Genetic testing = Definitive.

Normocytic Anemia

- Nutritional (Can be IDA, folate, B12, sick cell, methotrexate)
- Renal Failure (Often CKD stage 4) EPO deficiency. If giving Epo, ensure has iron too.
- Active Bleed

Macrocytic Anemia

- EtOH Use
- Myelodysplastic Syndrome
- Folate Deficiency
- B12 Deficiency (also glossitis, weight loss, macroovalocytes, hypersegmented PMNs, hemolysis, posterior columns neuro deficits).
- etc...

Multiple Myeloma

- Pt may have history of fractures
- sPEP and uPEP (Serum Protein ElectroPhoresis, and urine Protein Electrophoresis)
- sPEP --> 80% sensitivity
  - adding uPEP --> raises sensitivity to 80-95% sensitivity
  - for uPEP they do spot urine for Bence Jones Proteins (even thought called uPEP)
- 5% of patients with MM will have normal sPEP and uPEP

Pancytopenia

Causes

- Primary BM Failure: (MDS, Aplastic Anemia)
- Malignancy: (Leukemia)
- Infiltrative Process (TB, Amyloidosis, Sarcoidosis)
- Drugs (Chemotherapy)

Aplastic Anemia

- Destruction of hematopoietic cells in BM leading to pancytopenia and hypocellular bone marrow.
- Etiology: (BROAD!)
  - Congenital
    - Fanconi’s Anemia (genetic DNA repair problem, leads to leukemias and BM failure in Ashkenazi)
    - Shwachman-Diamond Syndrome (BM failure and pancreatic insufficiency)
  - Acquired
    - Idiopathic (T-cell mediated - 1/3 to 2/3 of cases)
    - Drugs (Chemotherapeutic agents, and idiosyncratic rxns chloramphenicol, phenylbutazone)
    - Toxins (Benzene, organic solvents, DDT, insecticides)
    - Ionizing Radiation
    - Post-Viral Infection (parvovirus B19, EBV, HDV, HEV, HHV6, HIV)
    - Autoimmune (SLE) - rare
    - Paroxysmal nocturnal hemoglobinuria (PNH) - associated with aplastic anemia, but not cause.
- Investigations:
  - No LAD, can be acute or insidious
• Anemia, neutropenia, Thrombocytopenia +/- pancytopenia.
• Blood film (decreased number of RBC)
• Bone Marrow (Hypocellular, hypoplasia, fat replacement)

Treatment:
• Remove Offending Agent
• Supportive care (transfusions, antibiotics)
• Immunosuppression (anti-thymocyte globulin - 50-60% respond, cyclosporine).
• Allogenic BM transplant.

Notes
• Bone Marrow Suppression causes 10 g/L/week loss of Hb. NOT MORE!
• High RDW associated with:
  • Iron deficiency anemia, hemolytic anemias, myelofibrosis, blood transfusion