**Anemia**

Anemia is defined as:
Hgb (per WHO): <13 in men and <12 in women

<table>
<thead>
<tr>
<th>Hemoglobin Type</th>
<th>Chains</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hgb A</td>
<td>Alpha 2, Beta 2</td>
</tr>
<tr>
<td>Hgb A2</td>
<td>Alpha 2, Delta 2</td>
</tr>
<tr>
<td>Hgb F</td>
<td>Alpha 2, Gamma 2</td>
</tr>
<tr>
<td>Hgb H</td>
<td>Beta 4</td>
</tr>
<tr>
<td>Hgb Barts</td>
<td>Gamma 4</td>
</tr>
<tr>
<td>Hgb S</td>
<td>Alpha 2, Beta S 2</td>
</tr>
<tr>
<td>Hgb C</td>
<td>Alpha 2 Beta C 2</td>
</tr>
<tr>
<td>Hgb SC</td>
<td>Alpha 2, Beta C/Beta S</td>
</tr>
</tbody>
</table>

Two major ways to approach anemia:
1. Morphologic Features
2. Mechanisms of Loss

**Approach #1 – Morphologic Features**

**Microcytic Anemias**

Retic Count <2%
- Iron Deficiency Anemia
Mechanisms:
- Chronic loss (e.g. menstruation, GI Bleed) or malabsorption (e.g. IBD, celiac disease, bowel resection)
- Exam: palor, glossitis, stomatitis, conjunctival pallor, koilonychias (spooning of nails)
- Low Ferritin, high TIBC

Retic Count >2%
- Thalassemia
  - General: mutations that lead to decreased or absent synthesis of either the alpha or beta chain → results in an imbalance in chains with precipitation of excess chain and hemolysis, additionally results in ineffective erythropoiesis
  - Alpha Thal
    - Epi: African, Mediterranean, southeast Asian, middle eastern descent
  - Beta Thal
    - Epi: Mediterranean, southeast asia, india, pakistan
- Sideroblastic Anemias

Normocytic Anemias
Retic Count <2%
- Anemia of Chronic Inflammation
  - High ferritin, low TIBC
- Anemia of Kidney Disease
  - Treatment: ESA with goal hgb of 11
  - Risks of ESA: thrombosis, HTN
- Acute Blood Loss
- Drugs

Retic Count >2%
- Membranopathies
  - Hereditary Spherocytosis
    - Classic form is autosomal dominant but there are recessive forms
    - Varies from severe and diagnosed infancy to more benign forms diagnosed in adulthood
  - Hereditary Elliptocytosis
  - PNH
    - Mechanism: CD59 inserts itself into C9 in complement cascade to prevent MAC formation, this is not expressed on cell surface in PNH and leads to an increased susceptibility to activated complement
    - Clinical Manifestations: hemolysis, pancytopenia, venous thrombosis
    - Treatment: eculizumab (MAB to C5), or BMT
- Sickle Cell
- Genetics: point mutation on beta globin chain
- Spectrum of disease (Hgb SS, HgbSBeta +, HgbSBeta null, Hgb SC)
- Clinical Manifestations: vaso-occlusive crises, splenic sequestration, acute chest, CVA, priapism, CHF, pulm HTN, AVN, etc.

- Enzymopathies
  - Pyruvate Kinase: problems with glycolytic pathway, presents in childhood
  - G6PD
    - Enzyme: catalyzes NADP to NADPH providing redox potential for glutathione
    - Inheritance: X-linked
    - Epi: subtropical parts of the world (Africa, southern Europe, middle east, southeast Asia)
    - Precipitants: drugs (sulfonamides, nitrofurantoin, some quinolones)

- MAHA
  - General Features: fever, anemia, thrombocytopenia, renal failure, neuro changes, schistocytes on smear
  - TTP-HUS
    - Mechanism: ADAMTS13 deficiency → normally cleaves large vWF into smaller vWF multimers, deficiency leads to accumulation of larger multimers, small vessel platelet thrombi
  - DIC
    - Mechanism: blood exposure to massive amounts of TF, resulting thrombin production, triggering of coagulation
    - Diagnosis: elevated d-dimer levels, low fibrinogen, coagulopathy
    - Treatment: treat precipitant, supportive therapy

- Autoimmune Hemolytic Anemias
  - Intravascular
    - General Mechanism: antibody to a red cell antigen, antibodies coat red cells, Fc portion of antibody recognized by Fc receptor on macrophages trigerring erythrophagocytosis
  - Extravascular
    - General Mechanism: antibody (usually IgM) binds antigen and activates complement, formation of membrane attack complex and red cell destruction
  - General Treatments
    - First Line: steroids
    - Second Line: rituximab, splenectomy
    - Third Line: IVIG, cyclosporine, azathioprine
  - Warm: IgG mediated
  - Cold: Cold agglutinin – IgM mediated (mycoplasma pneumonia, waldenstroms), Paroxysmal Cold Hemoglobinuria (IgG)

Macrocytic Anemias
Reticulocytosis
Myelodysplastic Syndromes

Abnormal Nucleic Acid Metabolism
- Drugs
  - B12/Folate Deficiency
    o Mechanism: Unable to convert dUMP to dTMP, resulting in impaired DNA synthesis
    o Smear: hypersegmented neutrophils

Lipid Abnormalities
- Hypothyroidism
- Cirrhosis

ETOH: mechanism unknown

Anemia Keywords
- Schistocytes: MAHA
- Spherocytes: warm antibodies or hereditary spherocytosis
- Bite Cells: G6PD Deficiency
- Target Cells: Thalassemia
- Inclusions: Malaria
- Heinz Bodies: G6PD (denatured, oxidized Hgb)