Anemia and Other Blood Disorders

(with a focus in the pediatric population)

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Approach to CBC:

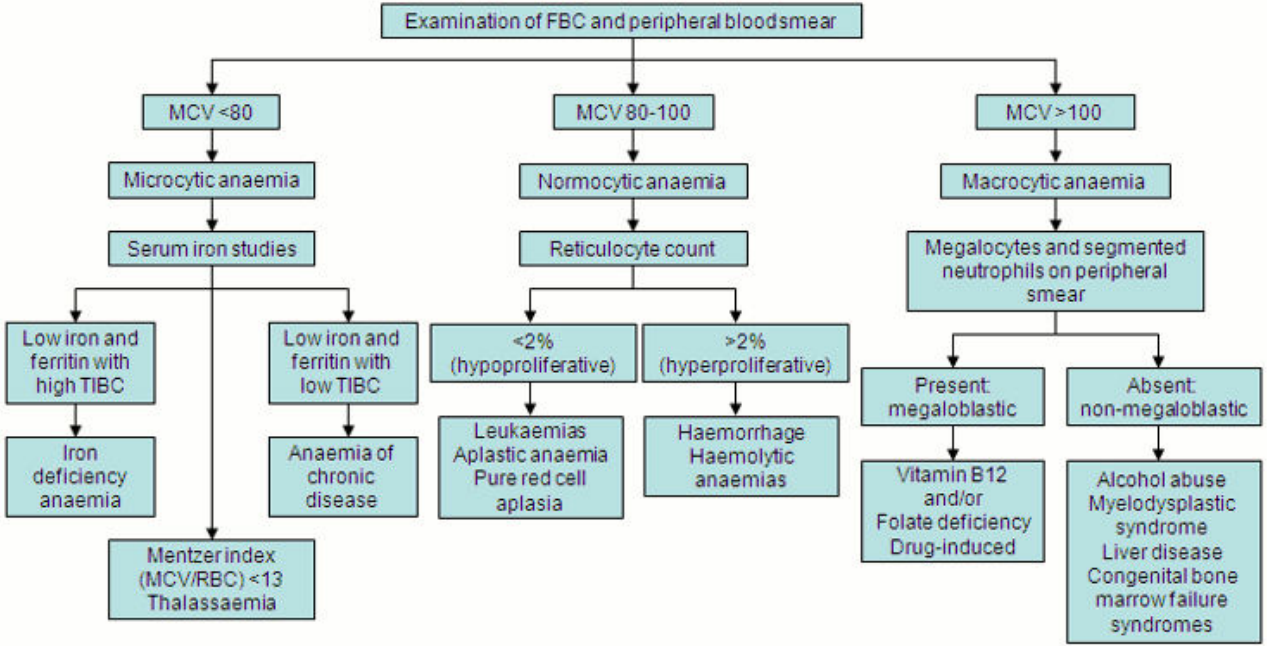
- A test that gives information about the **3 main types of cells** in the blood:
  - **RBCs:** carry oxygen to your body
  - **WBCs:** fight infections; multiple types and each works in a different way
  - **Platelets:** form clots after an injury to stop bleeding
- CBC measures the number of each of the 3 types of cells and determines if the levels are normal, low, or high
- Can show if your body is also making new cells
  - RBC: measured by hemoglobin, hematocrit, RBC count, size, shape, etc …
  - WBC: if differential is included, can measure the different types of white blood cells and show any abnormals
- If CBC shows something abnormal or needs further investigation, you can look at the cells under a microscope - **“blood smear”**

RBC Indices Terminology:

- **Hemoglobin:** protein that carries O2 in the RBCs
- **Hematocrit:** measures proportion of RBC in blood as related to total blood count (%)
- **RBC count:** number of cells
- **Reticulocyte count:** signifies RBC production

- **Mean Corpuscular Volume (MCV):** size of average red blood cell
- **Red cell distribution width (RDW):** a measure of the amount of variability in size of RBC
- **Mean Corpuscular Hemoglobin (MCH):** Hgb content in avg red blood cell
- **Mean Corpuscular Hgb Concentration (MCHC):** concentration of Hgb in avg red blood cell

Approach to Anemia



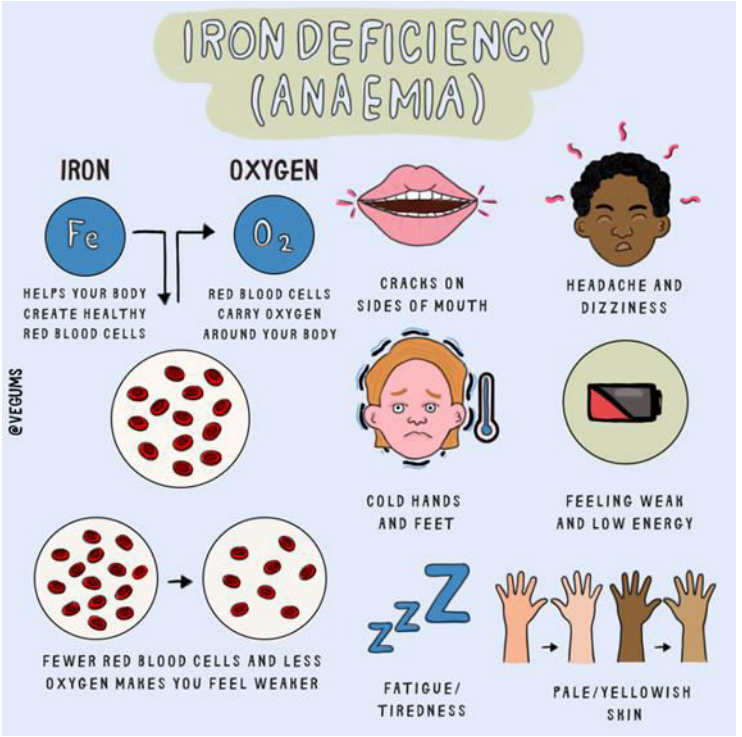
Microcytic Anemia (MCV <80)

1. Iron deficiency anemia
2. Lead Poisoning Anemia (Plumbism)
3. Alpha/Beta-Thalassemia

Iron Deficiency Anemia

- **MC cause** of anemia worldwide
- **Etiology:** decreased absorption such as diet, chronic blood loss such as excessive menstruation, occult GI blood loss
- **Risk Factors:**
  - Increased metabolic requirements: children, pregnant, and lactating women
  - Cow milk in young children: in infants <1yr and toddlers drinking large volumes of cow's milk
- **Pathophysiology:** decreased RBC production due to lack of iron and decreased iron stores (decreased ferritin)

- **Symptoms:**
  - Fatigue, weakness, exercise intolerance, dyspnea
  - CNS sx: poor concentration, apathy, irritation, poor school performance, cognitive disturbances
  - Pagophagia: craving for ice/ Pica: appetite for non-food substances
- **PE:**
  - Pallor, tachycardia
  - <u>Koilonychia:</u> brittle nails with spooning
  - Angular cheilitis
  - Atrophic glossitis: smooth tongue



➔ **Diagnosis:**
- **CBC:** microcytic hypochromic anemia, ↑RDW, ↓reticulocytes
- **Iron studies:** ↓ferritin, ↑TIBC (transferrin), ↓transferrin saturation <20-15%, ↓serum iron
- **Bone marrow:** absent iron stores (rarely performed)

➔ **Management**
- **Iron replacement** with oral iron (ferrous sulfate), iron-containing formulas in bottle-fed infants, iron-enriched foods and red meats, parental
- Take iron replacement with vitamin C, with water or orange juice and on an empty stomach to increase absorption.
  - Antacids impairs absorption
- AE: GI symptoms, such as nausea, vomiting, constipation, flatulence, diarrhea, dark stools

➔ Iron replacement results in ↑reticulocytes w/in 5-10 days, correction of anemia in 6-8wks and repletion of iron stores in 1-3 months

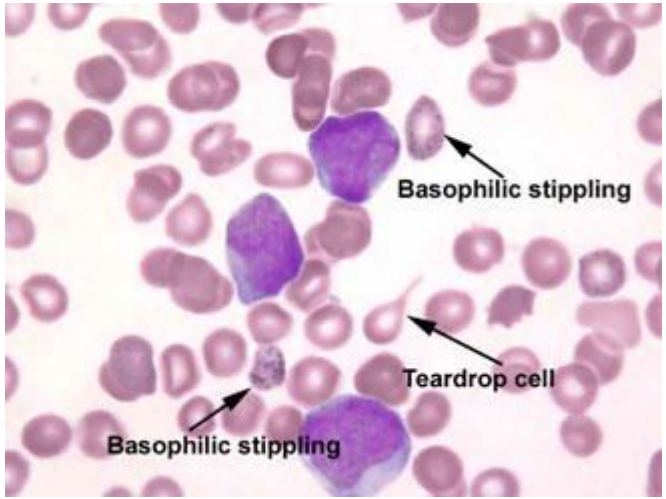
➔ Severe life-threatening anemia: red blood cell transfusion
- Hgb<7

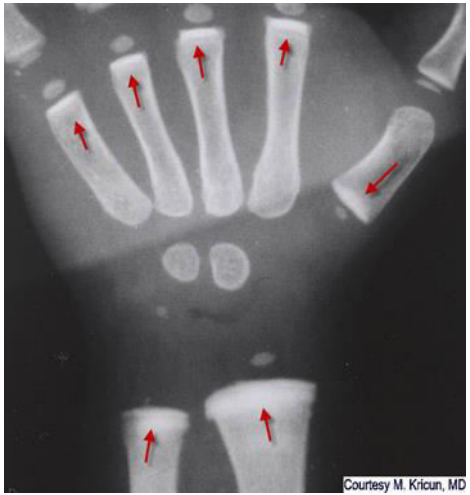
Lead Poisoning Anemia (Plumbism)

- **Pathophysiology:** lead poisons enzymes, causing cell death; shortens RBCs' lifespan; inhibits multiple enzymes needed for heme synthesis → **acquired sideroblastic anemia**
- **RFs:** most common in children (<6y/o) due to increased permeability of the blood brain barrier
- **Sources:** ingestion or inhalation of environmental lead (ie: paint chips or lead dust)
- **Clinical Manifestations:**
  - +/- asymptomatic/nonspecific symptoms
  - Neurologic Sx: ataxia, fatigue, learning disabilities, difficulty con, developmental delayed, hearing loss, peripheral neuropathy (wrist or foot drop), encephalopathy
  - GI sx: lead colic - intermittent abdominal pain, vomiting, loss of appetite, and constipation

➔ **Diagnosis:**

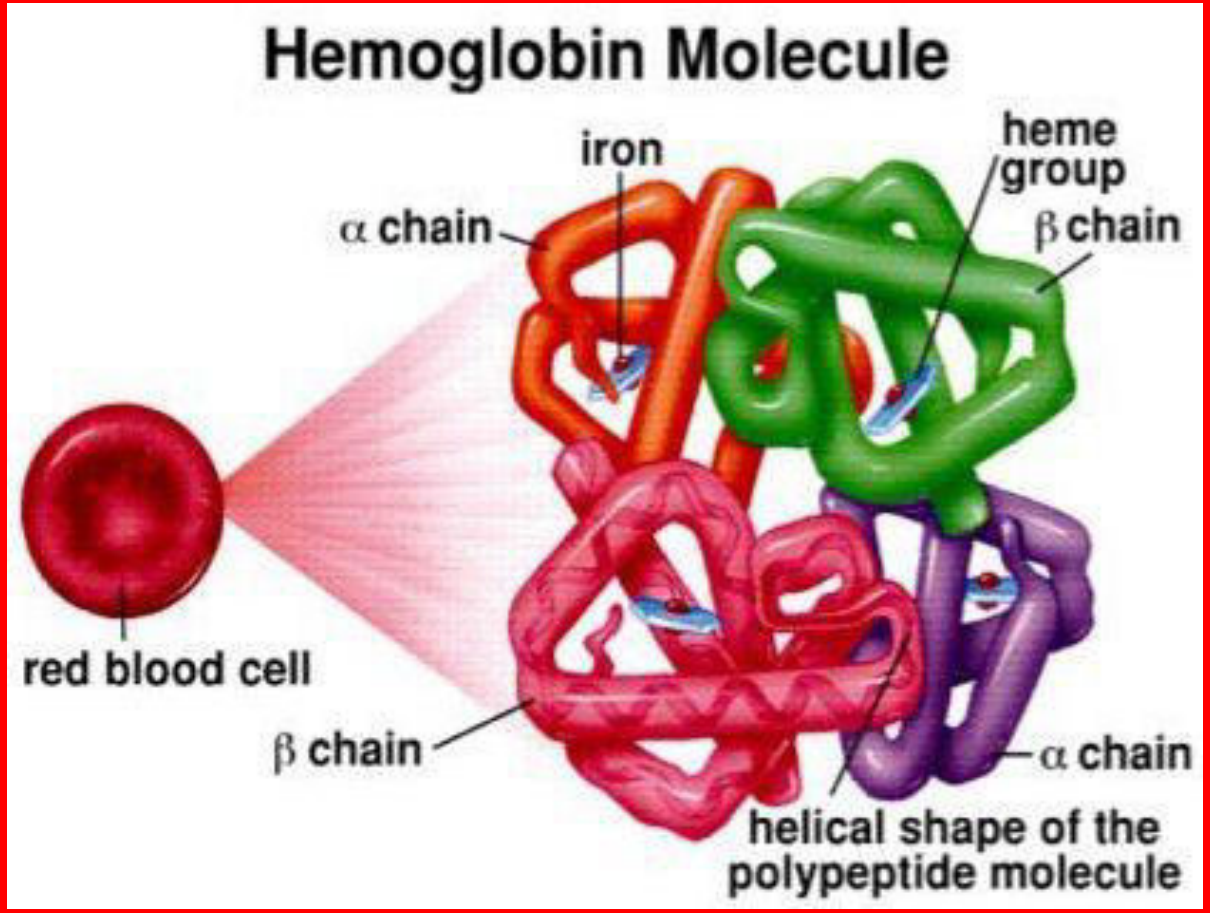
- **Serum lead levels: >10 mcg/dL** on venous sampling most accurate
- **Peripheral smear: microcytic hypochromic anemia** with **basophilic stippling** (dots of denatured RNA seen in RBCs), ringed sideroblasts in bone marrow
- Iron studies: normal or ↑serum iron, ↓TIBC
- Radiographs: "lead lines" - linear hyperdensities at the metaphyseal plates in children





➔ **Management:**

- Remove the source of lead!
- Mild (<44 mcg/dL): outpatient follow up and lifestyle modifications
- Moderate (45-69 mcg/dL): oral chelation as inpatient (Succimer)
- Severe (>70 mcg/dL): IV chelation and hospitalization (Succimer and Calcium disodium edetate)


Hemoglobin Molecule
iron
heme group
α chain
β chain
red blood cell
β chain
α chain
helical shape of the polypeptide molecule

Thalassemia

- ➔ Decreased production of globin chains
- ➔ Think thalassemia if microcytic anemia with normal/ ↑serum Fe or no response to Fe treatment

Alpha- Thalassemia

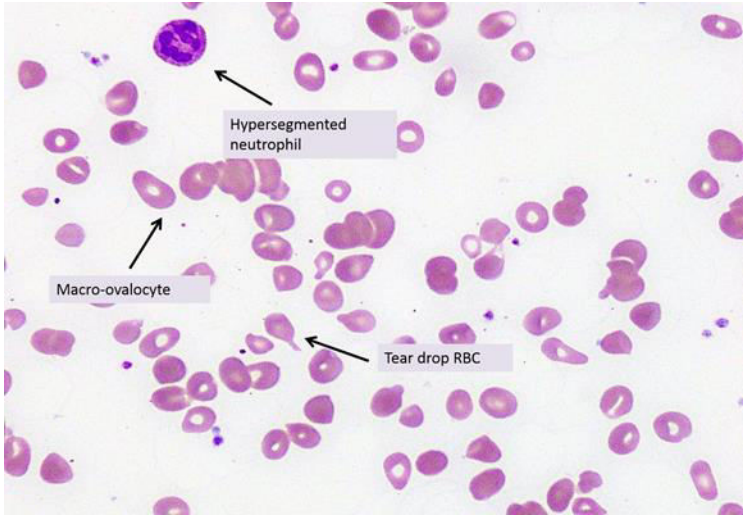
- ➔ **¾ gene deletions** causing decreased alpha chain production
- ➔ Patients usually **symptomatic at birth** (neonatal jaundice and anemia), **frontal bossing**, maxilla overgrowth
- ➔ **Dx:** Microcytosis, hemolytic anemia (**schistocytes,** tear drop cells, **↑reticulocytes**), target cells, **↑RBC count**, ↓Hgb, **+Heinz bodies**
  - ◆ Hemoglobin electrophoresis: presence of **HbH (beta chain tetramer)**
- ➔ **Episodic blood transfusions** during periods of increased hemolysis or severe anemia, vitamin C and folate supplementation, **iron chelating agents**, splenectomy, bone marrow transplant (in major)

Beta-Thalassemia

- ➔ **Minor/trait:** most common type; only 1 gene is defective
- ➔ **Major (Cooley's anemia):** both genes mutated
- ➔ Symptoms often **after 6 months of life: severe, chronic anemia, hepatosplenomegaly,** bony abnormalities (frontal bossing, abnormal ribs), osteoporosis by age 10, endocrine abnormalities, enlarged kidneys, cardiac dysfunction/heart failure
- ➔ **Dx:** ↓MCV, normal or ↑RBC count, normal or ↑serum iron; smear shows **target cells**
- ➔ Minor: no treatment
- ➔ Major: managed same as Alpha-thalassemia intermedia

Macrocytic Anemia (MCV >100)

1. B12 (Cobalamin) Deficiency
2. Folate Deficiency



B12 Deficiency

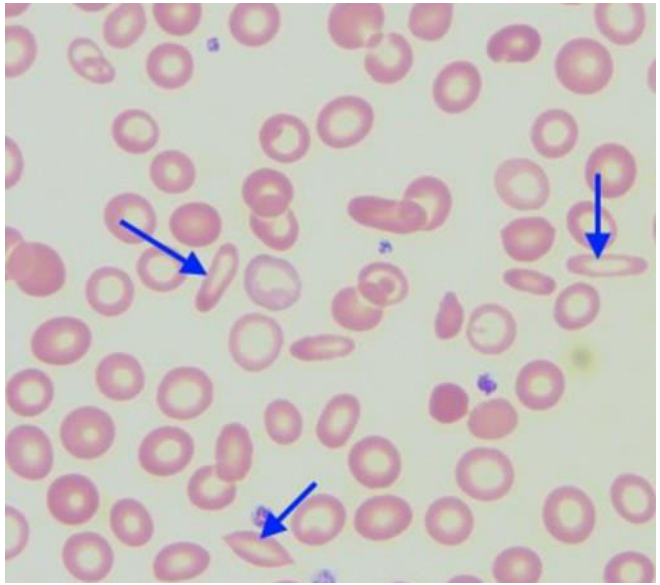
- **Etiology:** decreased absorption (**pernicious anemia (MC**), Crohn disease, celiac disease, chronic alcoholic use), decreased intake (**vegans**)
- **Sx:**
  - Anemia symptoms with **neurological abnormalities**
    - Fatigue, exercise intolerance, pallor
    - Symmetric paresthesias, vibratory, sensorym and proprioception deficits, decreased DTRs
  - Glossitis, diarrhea
- **Dx:**
  - CBC with smear: ↑**MCV,** hypersegmented neutrophils, macro-ovalocytes
  - Decreased serum B12 levels, increased LDH
- **Management:**
  - Dietary deficiency: oral B12 replacement
  - Symptomatic anemia or neuro findings: B12 IM

Anthropometric
Developmental delays/**fall in growth curves** Weight < 10th percentile Height < 10th percentile Head circumference < 10th percentile Unable to sit alone Unable to walk Involuntary movements Hyperpigmentation Abnormal fine and gross motor function

Normocytic Anemia (MCV 80-100)

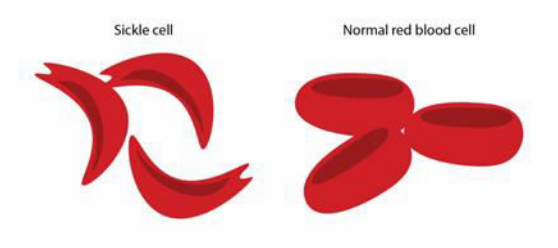
1. Anemia of Chronic Disease
2. Hemolytic Anemias
    a. Hereditary Spherocytosis
    b. Sickle cell trait/disease
    c. Thrombotic thrombocytopenic purpura (TTP)
    d. Hemolytic Uremic Syndrome (HUS)

Hereditary Spherocytosis



- **Deficiency in RBC membrane & cytoskeleton, leading to increased RBC fragility & sphere-shaped RBCs.** These abnormal RBCs are detected and destroyed by the spleen → hemolysis
- **Sx:**
  - Severe cases may present in infancy (neonatal jaundice), mild cases may present in adulthood
  - **Recurrent episodes of hemolysis** (anemia, jaundice, splenomegaly)
- Dx: **Negative Coombs testing**, hyperchromic microcytosis, 80% spherocytes, **increased MCHC**
- **Tx: Splenectomy** - curative
  - Folic acid: helps to sustain RBC production and DNA synthesis

Sickle Cell Trait/ Disease



- **Disease:** Homozygous sickle mutation
- Main clinical manifestations: hemolytic anemia and vaso-occlusion (acute or chronic pain, tissue ischemia or infarction)
  - Sx may begin early as 6 months
  - Dactylitis most common initial presentation, delayed growth and development, fever, infections
- Dx: peripheral smear: **sickle erythrocytes**, target cells, decreased hemoglobin
  - Howell-jolly bodies: functional asplenia
  - Hemoglobin electrophoresis
- Tx: Hydroxyurea (increases production of HbF)
  - Infection ppx in children: penicillin given as early as 2-3months until at least 5yrs to prevent infectious complications
  - Prevnar and Flu vaccines recommended

- **Trait:** heterozygous
- **Usually asymptomatic** and are not anemia unless exposed to severe hypoxia, extreme physical stress, high altitudes or dehydration
  - May develop episodic hematuria or isosthenuria
- **Dx:** hemoglobin electrophoresis - **presence of both HbA>HbS**
  - Peripheral smear usually associated with normal Hgb, Hct, reticulocyte count, and smear
- **Trait does not usually require treatment.** Painful crisis is not a component of trait

Neutropenia

- Decrease in the number of absolute neutrophil count (ANC) in blood
- **ANC:** mature granulocytes + neutrophil band cells
  - **Mild** neutropenia corresponds to an ANC between **1000 and 1500/microL**
  - **Moderate** between **500 and 1000/microL**
  - **Severe** with **<500/microL**.
  - The risk of infection begins to increase at an ANC below 1000/microL
- Neutrophil count must be stratified for age and even race
  - At birth - predominant but rapidly decrease in the first few days of life
  - Infancy - 20-30% of total lymphocyte count
  - At 5yrs - equal number of neutrophils and lymphocytes
  - In adults - characteristic 70% predominance of neutrophils during puberty

TABLE 6

Congenital causes of neutropenia[20]

Constitutional/ethnic neutropenia	-Mild, chronic (ANC >1000/mcL) -No history of recurrent infections -Mediterranean or African ancestry
Benign familial neutropenia	-Similar to constitutional, but not ethnically linked
Cyclic neutropenia	-Self-limited infections associated with nadir of neutropenia -Recurrence q2-5 weeks -Autosomal dominant

ANC, absolute neutrophil count.

- In infants and young children: several differential diagnoses
  - Transient mild to moderate neutropenia can be caused by a variety of common viral infections during childhood, including RSV, influenza, parvovirus, Epstein-Barr virus, and human herpes virus 6
  - Isoimmune neutropenia: due to antineutrophil antibodies transferred from the mother → presents as moderate to severe neutropenia
  - Severe congenital neutropenia: very rare, characterized by severe infections in 1st month of life
  - Cyclic neutropenia: neutropenic episodes 3-6 days every 21 days
- In older children:
  - Can be seen in absence of infection → Most causes of neutropenia are benign, especially if the ANC is above 800/microL. Usually due to medications, recent viral infection, gingivitis/tooth abscess → continue to observe and repeat CBC
  - Can be seen in recurrent infection → need to follow up → evaluate for collagen vascular disease and nutritional disorders and if unremarkable, bone marrow aspiration to look for myelodysplastic syndrome
- **Tx:** Depends on the cause and degree of neutropenia.
  - **Neutropenic fever:** In general, patients with an absolute neutrophil count (ANC) >1000/microL can be managed on an outpatient basis while those with an ANC of <500/microL and marrow aplasia may require inpatient treatment with parenteral antibiotics
  - Usually broad-spectrum abx treatment