Red Blood Cell Disorders

ANEMIA

I. BASIC PRINCIPLES
   A. Reduction in circulating red blood cell (RBC) mass
   B. Presents with signs and symptoms of hypoxia
      1. Weakness, fatigue, and dyspnea
      2. Pale conjunctiva and skin
      3. Headache and lightheadedness
      4. Angina, especially with preexisting coronary artery disease
   C. Hemoglobin (Hb), hematocrit (Hct), and RBC count are used as surrogates for RBC mass, which is difficult to measure.
      1. Anemia is defined as Hb < 13.5 g/dL in males and < 12.5 g/dL in females (normal Hb is 13.5–17.5 g/dL in males and 12.5–16.0 g/dL in females).
   D. Based on mean corpuscular volume (MCV), anemia can be classified as microcytic (MCV < 80 µm³), normocytic (MCV = 80–100 µm³), or macrocytic (MCV > 100 µm³).

MICROCYTIC ANEMIAS

I. BASIC PRINCIPLES
   A. Anemia with MCV < 80 µm³
   B. Microcytic anemias are due to decreased production of hemoglobin.
      1. RBC progenitor cells in the bone marrow are large and normally divide multiple times to produce smaller mature cells (MCV = 80–100 µm³).
      2. Microcytosis is due to an “extra” division which occurs to maintain hemoglobin concentration.
   C. Hemoglobin is made of heme and globin; heme is composed of iron and protoporphyrin. A decrease in any of these components leads to microcytic anemia.
   D. Microcytic anemias include (1) iron deficiency anemia, (2) anemia of chronic disease, (3) sideroblastic anemia, and (4) thalassemia.

II. IRON DEFICIENCY ANEMIA
   A. Due to decreased levels of iron
      1. ↓ iron → ↓ heme → ↓ hemoglobin → microcytic anemia
   B. Most common type of anemia
      1. Lack of iron is the most common nutritional deficiency in the world, affecting roughly 1/3 of world’s population.
   C. Iron is consumed in heme (meat-derived) and non-heme (vegetable-derived) forms.
      1. Absorption occurs in the duodenum. Enterocytes have heme and non-heme (DMT1) transporters; the heme form is more readily absorbed.
      2. Enterocytes transport iron across the cell membrane into blood via ferroportin.
      3. Transferrin transports iron in the blood and delivers it to liver and bone marrow macrophages for storage.
      4. Stored intracellular iron is bound to ferritin, which prevents iron from forming free radicals via the Fenton reaction.
D. Laboratory measurements of iron status
1. Serum iron—measure of iron in the blood
2. Total iron-binding capacity (TIBC)—measure of transferrin molecules in the blood
3. % saturation—percentage of transferrin molecules that are bound by iron (normal is 33%)
4. Serum ferritin—reflects iron stores in macrophages and the liver
E. Iron deficiency is usually caused by dietary lack or blood loss.
1. Infants—breast-feeding (human milk is low in iron)
2. Children—poor diet
3. Adults (20–50 years)—peptic ulcer disease in males and menorrhagia or pregnancy in females
4. Elderly—colon polyps/carcinoma in the Western world; hookworm (*Ancylostoma duodenale* and *Necator americanus*) in the developing world
5. Other causes include malnutrition, malabsorption, and gastrectomy (acid aids iron absorption by maintaining the Fe$^{2+}$ state, which is more readily absorbed than Fe$^{3+}$).
F. Stages of iron deficiency
1. Storage iron is depleted—↓ ferritin; ↑ TIBC
2. Serum iron is depleted—↓ serum iron; ↓ % saturation
3. Normocytic anemia—Bone marrow makes fewer, but normal-sized, RBCs.
4. Microcytic, hypochromic anemia—Bone marrow makes smaller and fewer RBCs.
G. Clinical features of iron deficiency include anemia, koilonychia, and pica.
H. Laboratory findings include
1. Microcytic, hypochromic RBCs with ↑ red cell distribution width (RDW, Fig. 5.1)
2. ↓ ferritin; ↑ TIBC; ↓ serum iron; ↓ % saturation
3. ↑ Free erythrocyte protoporphyrin (FEP)
I. Treatment involves supplemental iron (ferrous sulfate).
J. Plummer-Vinson syndrome is iron deficiency anemia with esophageal web and atrophic glossitis; presents with anemia, dysphagia, and beefy-red tongue

### III. ANEMIA OF CHRONIC DISEASE

A. Anemia associated with chronic inflammation (e.g., endocarditis or autoimmune conditions) or cancer; most common type of anemia in hospitalized patients
B. Chronic disease results in production of acute phase reactants from the liver, including hepcidin.
1. Hepcidin sequesters iron in storage sites by (1) limiting iron transfer from macrophages to erythroid precursors and (2) suppressing erythropoietin (EPO)