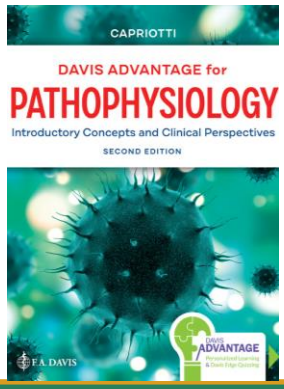
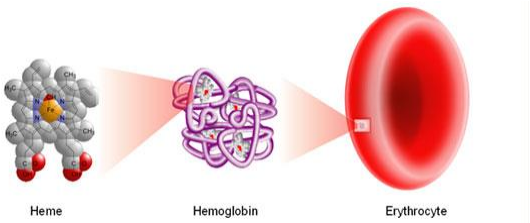


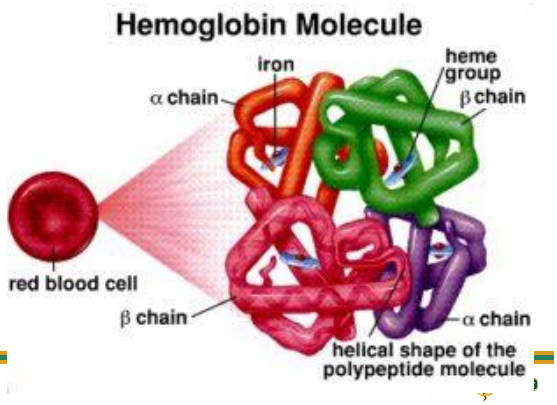
Chapter 13

Disorders of Red Blood Cells

Basic Concepts

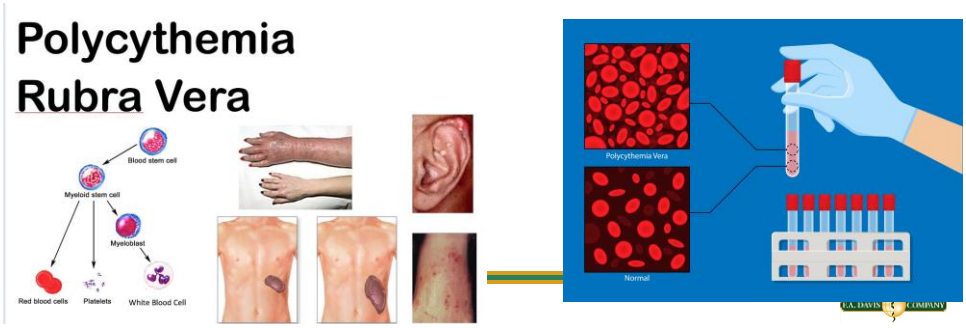
- RBC (erythrocyte)
  - Contain the protein hemoglobin (Hgb)
    - Aids in oxygen transport





Basic Concepts

- RBC two major pathologies:
  - polycythemia and anemia
- Polycythemia: overproliferation of all blood cells in bone marrow
  - Less common than anemia



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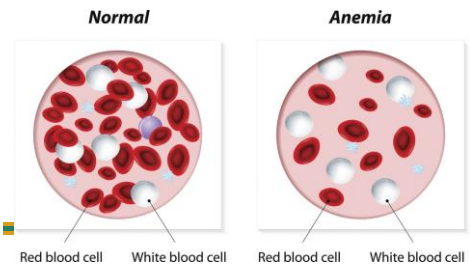
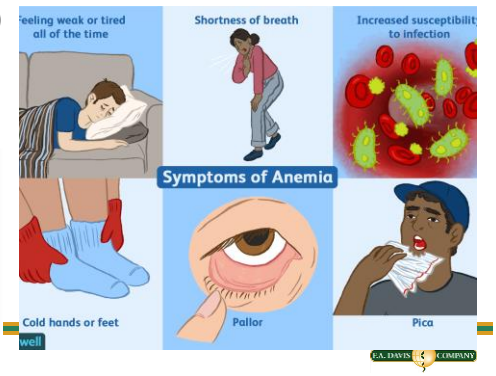
Basic Concepts (continued)

- Anemia
  - Lack enough healthy red blood cells to carry adequate oxygen to your body's tissues.
  - Some races and ethnic groups have increased risk of some forms of anemia
    - *Example:* Sickle cell anemia (SCA)





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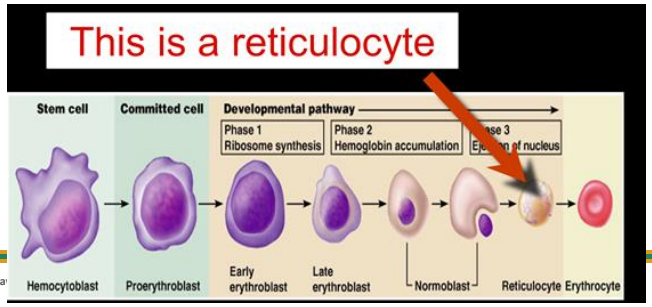
Erythrocyte Synthesis

- Erythropoiesis is the production/synthesis of RBCs → Arise from pluripotent stem cells in bone marrow → to mature red blood cel
- A mature RBC has no nucleus - Average lifespan: ~120 days
  - Spleen: removes aged, lysed, dead RBCs
- Reticulocyte = Immature RBC
  - Reticulocytosis refers to increased reticulocyte levels in blood
    - Indicate increased RBC synthesis in bone marrow



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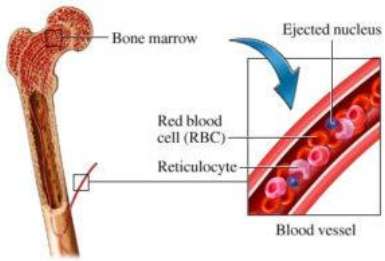
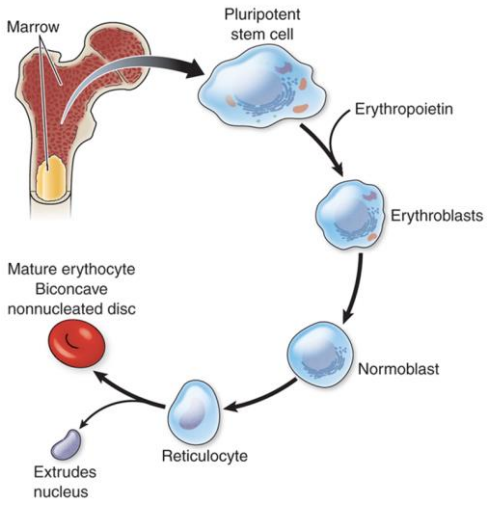
Erythrocyte Synthesis (continued_2)

A **HIGH RETICULOCYTE COUNT (Reticulocytosis)** may mean that your bone marrow needs to produce more red blood cells.

Causes: This can occur after a lot of bleeding, a move to a high altitude, or certain types of anemia → all these states cause hypoxia (low levels of O2) in the tissues.





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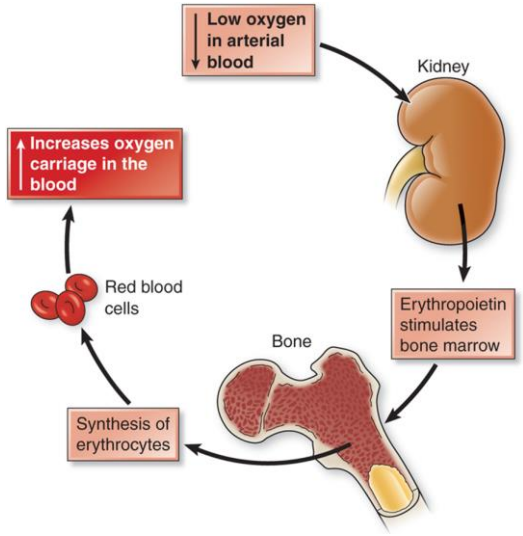
Erythropoietin

In case of hypoxia:

- Kidney releases erythropoietin (EPO)
- EPO simulates bone marrow to produce RBCs
- the increased RBCs is a body's effort to compensate for the hypoxia



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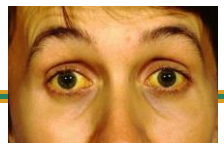
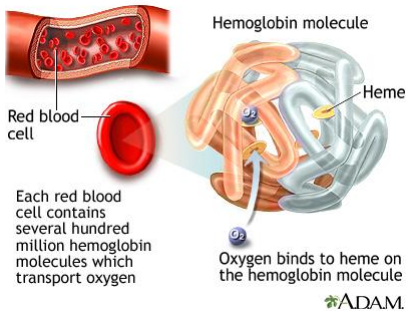
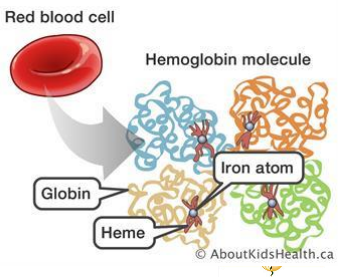
RBC Formation and Breakdown

- What do we need for RBC synthesis?
  - Protein, iron, vitamin B_{12}, folic acid
- Hemoglobin
  - Composed of heme (iron + porphyrin) and globin component
  - Porphyrin is metabolized to **biliverdin** (what colors urine, feces, ecchymoses)
  - Biliverdin brokes down to bilirubin (yellow pigment – a constituent of bile)
- Hyperbilirubinemia is the Accumulation of bilirubin in blood → Can lead to jaundice →







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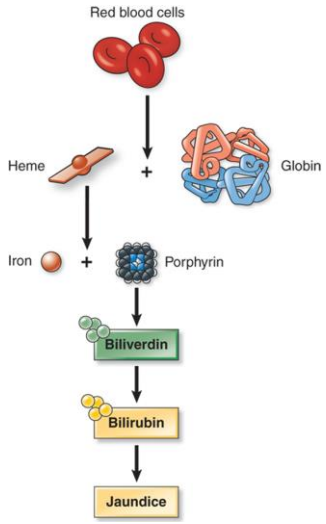
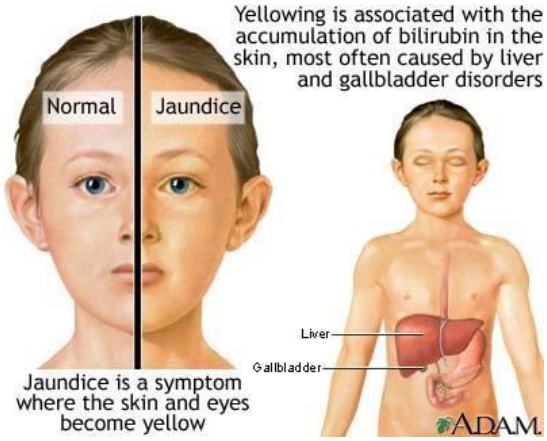
Red Blood Cell Breakdown





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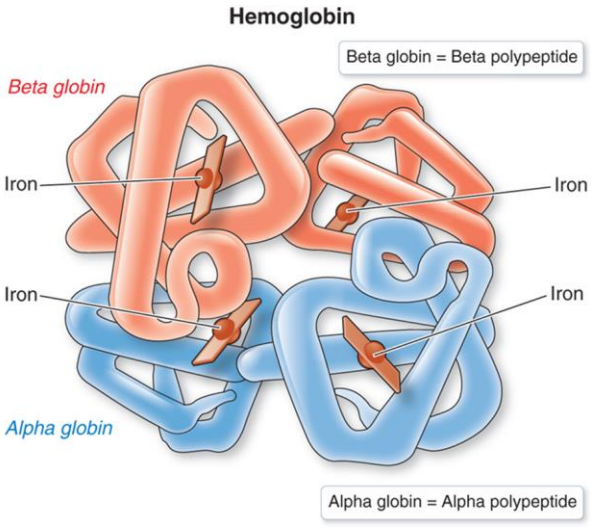
Hemoglobin

- Has high affinity for oxygen
- Is composed of 4 polypeptide chains (2 alpha and 2 beta)
  - Each chain contains an atom of iron
- Normal hemoglobin = Hgb A
- Fetal hemoglobin = Hgb F
- Hemoglobinopathy is Abnormal Hgb, due to genetic mutation.

Example: Sickle cell anemia (Hgb S)



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Iron Metabolism

- Iron required for RBC formation, specifically Hgb
- Transferrin: transports iron
- Total iron binding capacity (TIBC)
  - Elevates when iron levels are low (more spaces for iron to bind)
- Iron stored in ferritin complexes
  - Present in all cells
  - Most common: bone marrow, liver, spleen
- Iron from RBCs is recycled

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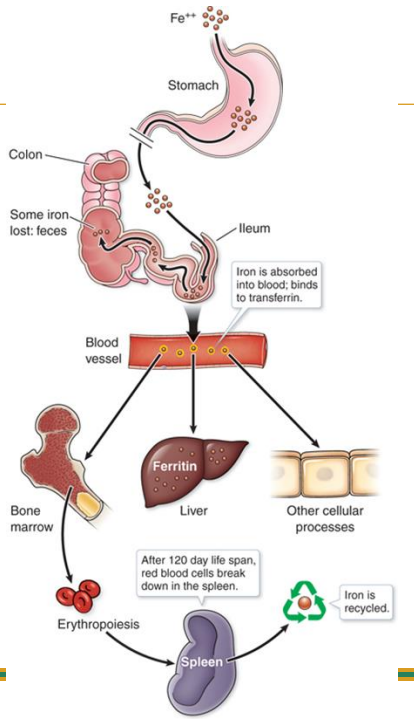
Iron Metabolism

- IRON is needed in the diet:
  - To synthesize Hgb in RBCs and myoglobin(a component of muscle cells)
  - For function of cellular enzymes, used in various metabolic processes
- Iron is absorbed in the duodenum and upper jejunum
- When absorbed into the bloodstream from the gastrointestinal (GI) system, iron is transported by a protein called TRANSFERRIN.
- Transferrin carries iron to the bone marrow for erythropoiesis.



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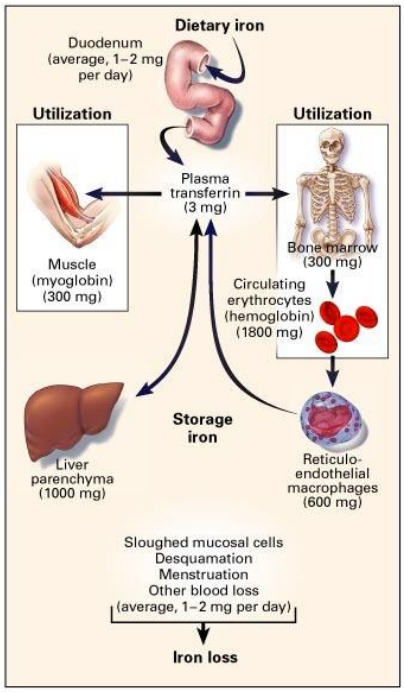
Iron Metabolism

- Transferrin binds with receptors on erythroid precursors in the bone marrow.
  - Up to 20% of absorbed iron goes into a storage pool in cells of the reticuloendothelial system, which is made up of the macrophages throughout the body.
  - The storage of iron occurs in ferritin complexes, most commonly found in the bone marrow, liver, and spleen.
- The liver's stores of ferritin are the primary physiological source of reserve iron in the body.



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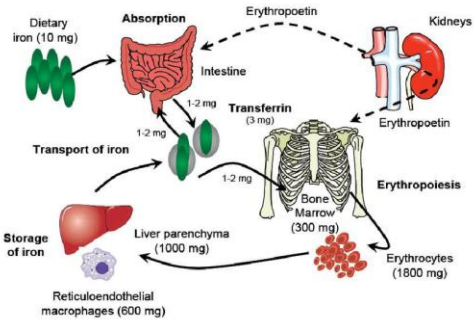
- Citrate and vitamin C → increase absorption of iron
- tannates in tea → decrease iron absorption.
- Meat → is the most readily absorbed kind of iron.
- Iron homeostasis → is closely regulated via intestinal absorption.
- Most of the iron in the body is recycled when old RBCs are taken out of circulation and destroyed → The RBC iron is scavenged by macrophages within the reticuloendothelial system and spleen and returned to the storage pool for reuse.



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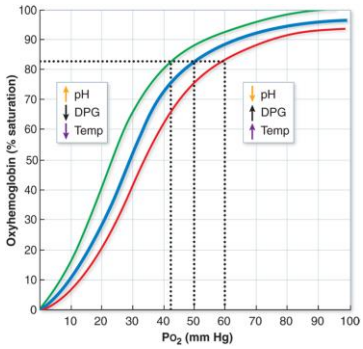
Oxyhemoglobin Dissociation Curve

- Represents the relationship between PO_2 and O_2 saturation of Hgb
- Low oxygen saturation compromises O_2 delivery
- Several factors affect the dissociation curve:
  - "Shift to the right" = decreased oxygen affinity
    - Increased CO_2, decrease pH (Bohr effect), increased 2,3 diphosphoglycerate (2,3 DPG), fever
  - "Shift to the left" = increased affinity for oxygen
    - Opposite conditions as above
- Carbon monoxide (CO) has high affinity for Hgb



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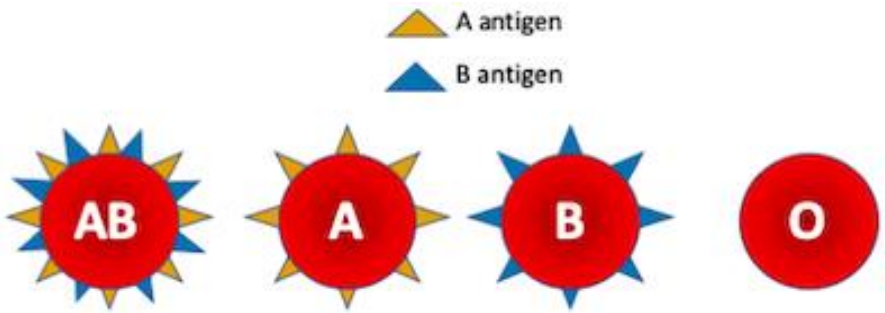
Blood Types

- All body cells, including RBCs, contain surface antigens.
- Specific types of antigens on the surface of RBCs are called agglutinogens.
- There are two types of agglutinogens: A and B
- ABO blood type classification is based on these agglutinogens. We can have: A, B, AB, O
- Note that the "O" blood type has no antigen



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Blood Types

- Another antigen on the surface of RBCs is Rh factor, also called D antigen.
- Rh+ → If the RBC surface has the Rh factor (positive)
- Rh- → if the RBC does not have the Rh factor (negative)

- Individuals inherit their blood type from their parents.
- The A and B antigens are encoded by different alleles, one from the mother and the other from the father.

	Group A	Group B	Group AB	Group O
Red blood cell type				
Antibodies in plasma	 Anti-B	 Anti-A	None	 Anti-A and Anti-B
Antigens in red blood cell	 A antigen	B antigen	 A & B antigens	None

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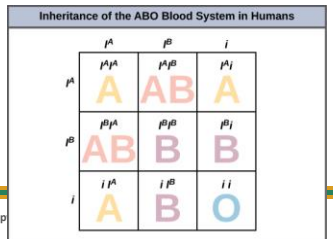
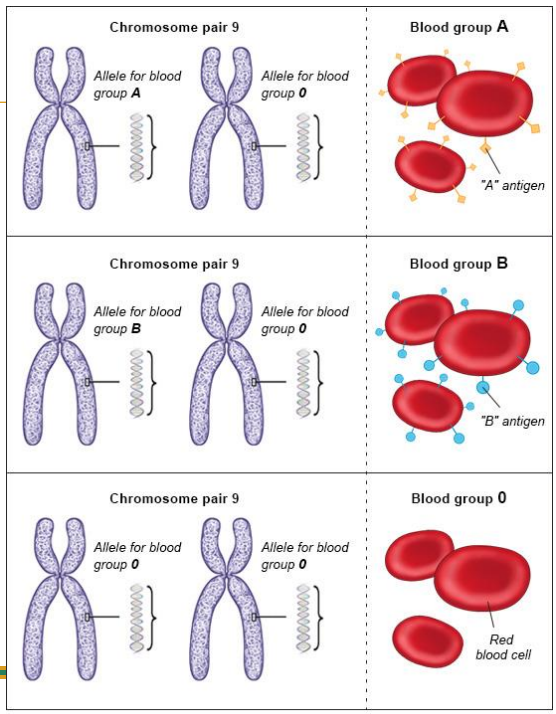
Blood Types

- A gene called the O allele codes for a nonfunctional protein that does not produce surface molecules.
- The person with O blood has no antigens on RBCs.
- The possible combinations of alleles that can yield the blood type of offspring can be configured with a Punnett square





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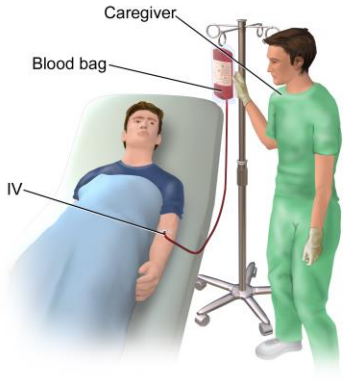
Blood Types (continued)

- Type O: can donate for any ABO type → universal donor (does not antigens. But cannot receive from A or B types, or will create antibodies for these foreign antigens)
- Type AB: universal recipient (has all antigens- A and B – will not be attacked by a "foreign" antigen)
- Rh- → has not the D antigen (cannot receive Rh+)
- Antibodies are important in Blood Transfusion
  - Recipient's antibodies can attack donor cells, and this causes dangerous blood transfusion reactions.



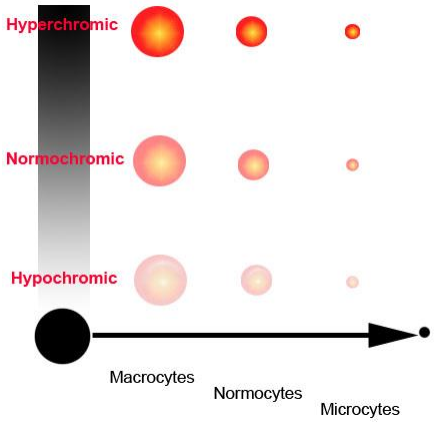
Blood Transfusion

Assessment of RBCs

- Hemoglobin (Hgb)
  - Amount of Hgb in blood (g/dL)
  - Males: 13 to 18 g/dL; females: 12 to 16 g/dL
- Hematocrit (Hct)
  - Percentage of whole blood consisting of RBCs
  - Males: 45%–52%; Females: 37%–48%
- Total RBCs
  - Number of RBCs per cubic milliliter
  - Males 4.5 to 5.5 X 10^6; females: 4.0 to 4.9 X 10^6

Assessment of RBCs (continued_1)

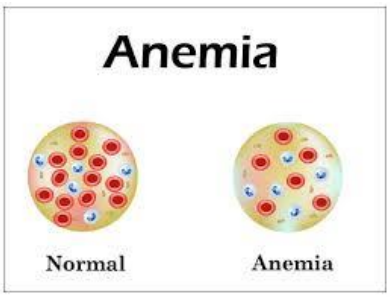
- Reticulocytes
  - Immature RBC's (1% of total RBCs)
- Mean corpuscular volume (MCV) – SIZE
  - MCV refers to the size of RBC
  - Macrocytic (megaloblastic),
  - Normocytic (normal size),
  - Microcytic (too small)
- Mean corpuscular hemoglobin (MCH) – COLOR – refers to the color of RBC
  - Hyperchromic (too red),
  - Normochromic (normal),
  - Hypochromic (too pale)



- NCNC = normochromic, normocytic (size and color are normal)

Anemia

- Possible etiologies
  - Deficiencies of Iron, vitamin B_{12}, folic acid
  - Blood loss - Chronic or acute
  - Hemoglobinopathies
  - Medications
  - Hemolysis



Anemia Signs and Symptoms

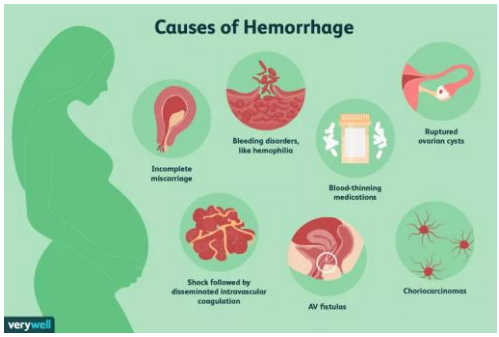
- Can be asymptomatic
- GI tract blood loss
- Heavy menstrual periods (menorrhagia)
- Pale complexion
- Tachycardia
- Jaundice
- Splenomegaly
- Nutritional anemias can cause glossitis, cheilitis, koilonychia, or pica

Anemia (continued)

- Diagnosis
  - Complete blood count: Hb, Hct, RBC count
  - Peripheral blood smear: size, shape, color of RBCs
  - Bone marrow aspiration
  - Echocardiogram/electrocardiogram
  - Nutritional status assessment
- Treatment
  - Varies based on cause

Anemia Caused by Decrease in RBC Mass

- Adult total blood volume: 5 liters
- Can lose 500 mL of blood without serious effects
- Loss of 1,000 mL or more:
  - Serious adverse effects
  - Hypovolemic shock
  - Cerebral hypoperfusion



Anemia of Acute Blood Loss

- Trauma, hemorrhage, clotting disorder
- Diagnosis
  - NCNC with reticulocytosis
  - FOBT to determine GI blood loss
- Treatment
  - For blood loss, establish hemostasis and fluid volume
    - IV: normal saline
    - Blood transfusion

Anemia of Acute Blood Loss (continued)

Signs and symptoms depend on loss of blood volume

- Less than 15% → Orthostatic hypotension and anxiety
- 15%–30% → SNS activity, increased HR; activation of RAAS; release of ADH; restlessness and change in consciousness
- 30%–40% → HR greater than 120 bpm, hypotension, urine output 5 to 15 ml/hr
- Greater than 40% → severe hypotension, decreased consciousness, HR greater than 140 bpm, no urine output

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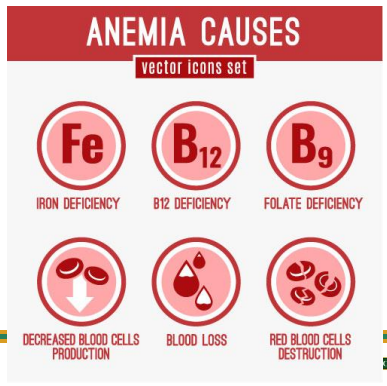
Anemia Caused by Chronic Blood Loss

- Causes
  - GI bleed (melena—dark stool), menorrhagia, hemolysis
  - Medications
    - NSAID's may lead to GI bleeding
- Signs and symptoms
  - Because blood loss is slow, patient may report no noticeable changes
- Diagnosis
  - Iron depletion often occurs
  - Microcytic and hypochromic anemia
  - Low iron, low ferritin, increased TIBC
  - Low Hgb and Hct
- Treatment
  - Remedy reason for blood loss
  - Replace iron: oral ferrous sulfate



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Hemolytic Anemias

- Erythrocyte destruction outpaces replacement

- Various causes:
  - Hemoglobinopathies → Inherited disorder of Hgb
  - Autoimmune disorders, blood transfusion reactions, hereditary spherocytosis, hemolytic disease of the newborn (HDN), and lead poisoning
  - Antibody Reactions → Warm agglutinin syndrome
    - IgG antibodies, hemolysis any temperature
    - Cold agglutinin syndrome - IgM antibodies, hemolysis at low temperatures
  - Alloimmune hemolysis → Antibodies against RBC antigens
    - Transfusion reactions → very important for nurses
    - Hemolytic disease of newborn

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Hemolytic Anemias (continued_2)

- Signs and symptoms
  - Typical anemia signs PLUS jaundice, dark urine (urobilinogen), enlarged spleen due to elevated RBC breakdown
- Diagnosis
  - Elevated reticulocytes to replace lost cells, peripheral smear will show misshapen and damaged RBCs
- Treatment
  - Depends on underlying causes

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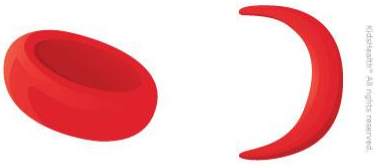
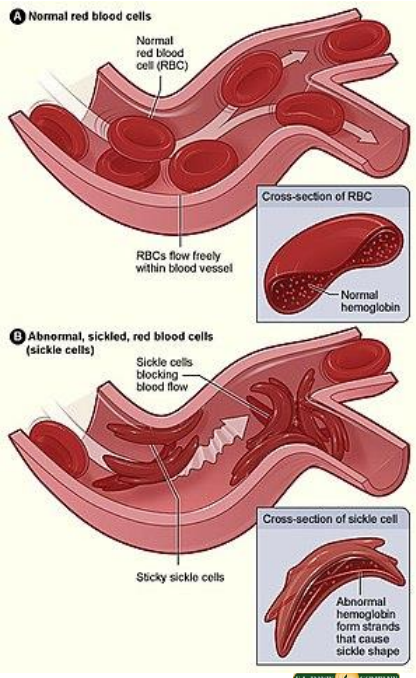
Sickle Cell Anemia (SCA)

- Autosomal hemoglobinopathy
- Homozygous and heterozygous forms (HbS)
  - Homozygous form more severe
- SCA increases resistance to malaria, thus genetic expression has remained high
- Signs of SCA do not appear until fetal Hgb levels begin to decline
- After age 10 years, complications increase
  - Renal disease is a major concern



Normal Red Blood Cell Sickle Cell



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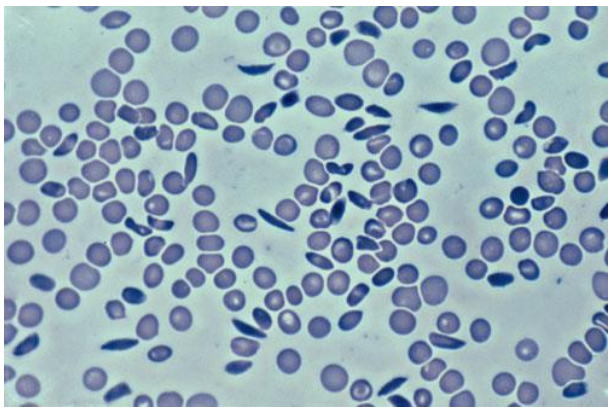
Sickle Cell Anemia (SCA) (continued_1)



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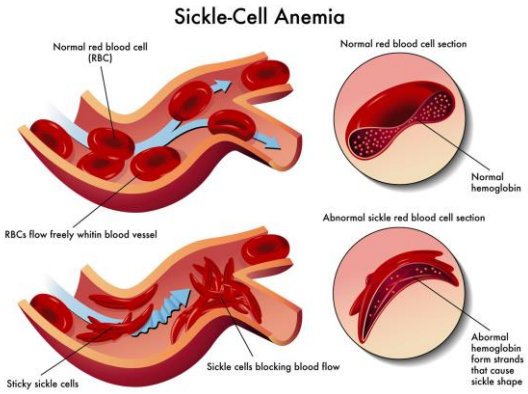
Sickle Cell Anemia (SCA) (continued_2)

- SCA causes RBCs to be fragile and misshapen
  - Sickle-cell appearance noted on peripheral blood smear
- What can make it worsen → Hypoxia, dehydration, severe stress and infection increase risk of distorted cell shapes
- Abnormal RBCs have lifespan of 10–20 days
  - Reticulocyte percentage increases to replace lost cells

Sickle Cell Anemia (SCA) (continued_3)

- **VASCO-OCCLUSIVE CRISES**
  - Misshaped RBC can lodge in capillaries, causing hypoxia in tissue
  - **Very painful**
  - Chronic damage to liver, spleen, kidneys, and eyes
  - **Hand-foot syndrome → Decreased blood flow to extremities**
  - Spleen may become damaged, requiring removal



Sickle Cell Anemia (SCA) (continued_4)

- Clinical presentation
  - Typical anemia signs, hyperbilirubinemia and enlarge spleen may be present
- Diagnosis
  - Electrophoresis revealing HbS
- Treatment
  - Avoid triggers of vaso-occlusive crises
  - Folic acid supplement to assist in RBC synthesis
  - Blood transfusions to replace lost cells (watch that iron levels do not elevate too much)
  - Bone marrow transplant

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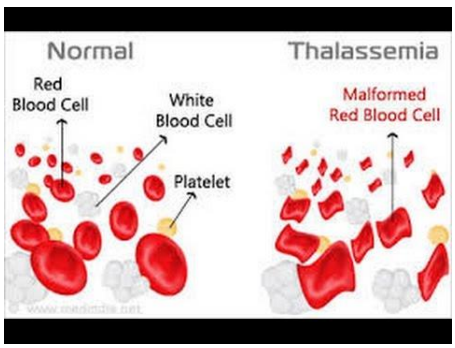
Thalassemia

- Autosomal hemoglobinopathy
  - Major form: homozygous
  - Minor form: heterozygous
- Genetic defect leads to abnormal polypeptide chains of Hb
  - Thalassemia alpha: alpha chain affected
  - Thalassemia beta: beta chain affected



CLINICAL PRESENTATION

- Typical anemia signs
- Bone pain may be present as bone marrow works to replace lost RBC's
- Hyperbilirubinemia and jaundice
- Splenomegaly may develop
- Heinz bodies may be present ➔ Pathognomonic for thalassemia (Collection of polypeptide chain in RBC's)

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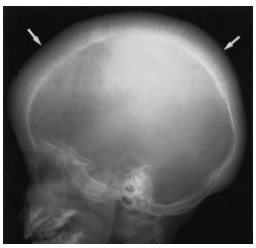
Thalassemia (continued_1)

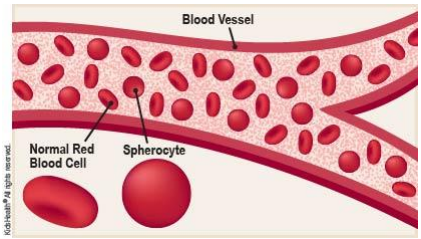
- Children
  - "Chipmunk" cheeks ---------->
  - "Hair-on-end" appearance of skull bones*
- Diagnosis
  - Electrophoresis
- Treatment: depends on severity
  - Transfusions
  - Splenectomy may be needed

*"Hair-on-end" appearance of skull →



Hereditary Spherocytosis

- Autosomal disorder
- Abnormal membrane proteins in RBC's
  - Spherical shape to RBC's
  - Increased fragility
  - Damaged cells gather in spleen



- Jaundice, bilirubin gallstones, aplastic anemia may develop
- Treatment
  - Blood transfusions, splenectomy, folic acid supplementation

Blood Transfusion Reactions

- Known as hemolytic transfusion reactions
  - Recipient blood-type antibodies attack transfused cells
- Mandatory that 2 clinicians double check donor-recipient blood types
- If transfusion reaction suspected, stop transfusion
- Nonhemolytic febrile reactions and mild allergies are the most common transfusion reactions

Blood Transfusion Reactions (continued)

Anaphylactic reactions can occur

- Severe cases
  - Hypotension, oozing from the IV site, diffuse bleeding, oliguria, shock, and renal failure
- Fever, chills, flushing, burning at IV line, joint pain, tachycardia

Hemolytic Disease of the Newborn (HDN)

- Mother's antibodies and newborn's RBCs antigens
- During delivery, maternal and infant blood may mix
- Mother's Rh antibodies attack RBCs of infant leading to mild hyperbilirubinemia and jaundice
- Sunlight and phototherapy are used to break down the bilirubin

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Hemolytic Disease of the Newborn (HDN) (continued)

- Unlike the antibodies to ABO antigens, the antibody to the Rh antigen can cross the placenta during pregnancy
  - Lead to development of erythroblastosis fetalis (see next slide)
  - Rhogam: covers the Rh-positive RBCs

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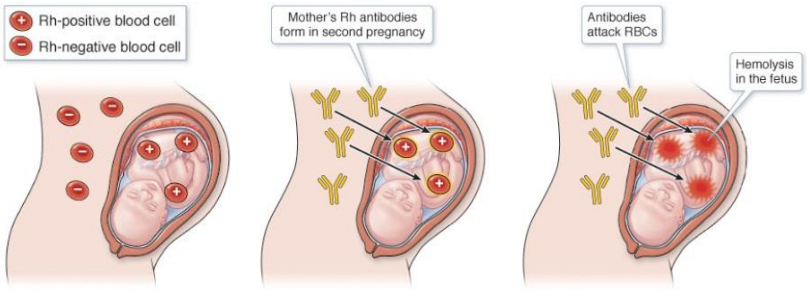
Erythroblastosis Fetalis



Anemia Due to Lead Poisoning

- Lead impairs hemoglobin synthesis, triggers hemolysis
- Lead is toxic to neurological system of children
- May cause iron deficiency anemia
- Blood test to check for lead levels
- Chelation therapy

RBC Maturation Defects

- Many factors can contribute to a lack of RBC maturation
- Typical signs of anemia may develop, along with specific signs and symptoms based on the etiology

- Iron deficiency
- Vitamin B_{12} deficiency
- Folic acid deficiency

Iron Deficiency Anemia

- Most common cause of anemia worldwide
- Women of childbearing age, infants and children, elderly, vegetarians, and those with GI bleeding
- Most common cause: menorrhagia, GI bleed, inadequate iron intake
- Signs and symptoms
  - Typical anemia signs and symptoms plus
    - Hair loss, glossitis, nail changes (koilonychias: spoon-shaped), pica (craving of ice, clay, starch, dirt)

Iron Deficiency Anemia (continued)

- Diagnosis
  - CBC
  - Peripheral blood smear
    - Pale (hypochromic)
    - Small (microcytic)
  - Serum iron and ferritin are decreased
  - FOBT should be done to rule out GI bleed
- Treatment
  - Oral ferrous sulfate (with correction of underlying etiology)

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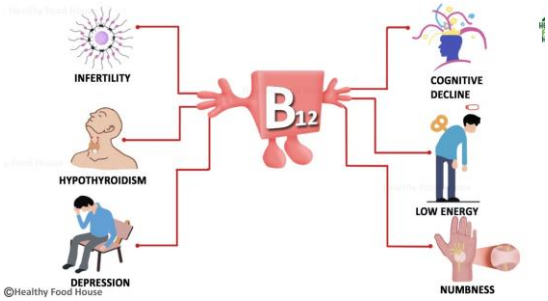
Vitamin B_{12} Deficiency

- Cofactor in RBC DNA synthesis and myelin sheath
  - Deficiency results in anemia and neurological issues
- Deficiency may develop due to:
  - Lack of intrinsic factor (*IF*) (see next slide)
    - *IF* needed for B_{12} absorption
    - Pernicious anemia: can not absorb needed B12
- Other causes: Dietary deficiency, gastric atrophy, chronic Helicobacter pylori infection, chronic alcoholism, gastric bypass surgery, Crohn's disease



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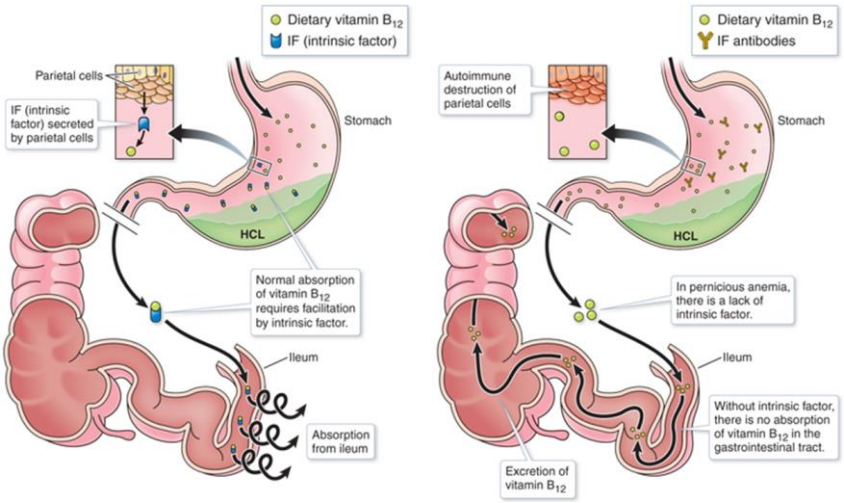
Pernicious Anemia

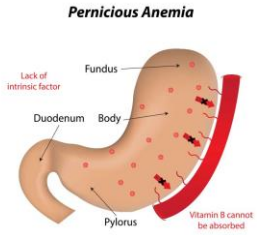


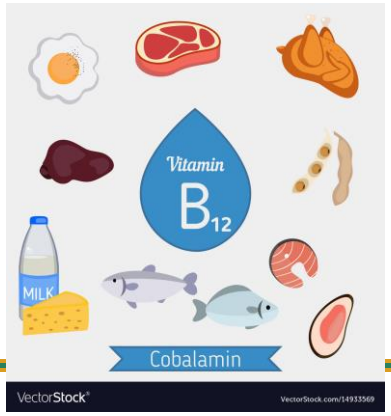
Vitamin B_{12} Deficiency (continued_1)

- Needed for folic acid metabolism and RBC DNA
  - Lack of B_{12} results in megaloblastic RBCs
- Neurological system
  - Typical signs of anemia along with glossitis, numbness and tingling, unsteady gate
- Diagnosis
  - CBC, peripheral blood smear reveals large cells
  - Folate, homocysteine, and methylmalonic acid levels should be examined

Vitamin B_{12} Deficiency (continued_2)

- Treatment
  - Address underlying etiology
  - Intramuscular B_{12} injections may be needed





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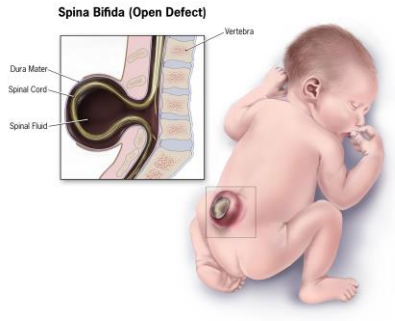
Folic Acid Deficiency

- Patients at risk include pregnant and lactating women, alcohol abusers, elderly, celiac disease sufferers
- Deficiency causes megaloblastic anemia → Folate along with vitamin B_{12} needed for RBC DNA synthesis
- Other uses for folic acid
  - Decreased incidence of spina bifida
  - Folic acid breaks down homocysteine (high homocysteine associated with increased risk of CVD)
- Patients may be asymptomatic
- Important to note both folic acid levels and vitamin B_{12} levels with megaloblastic anemia (as adequate B_{12} needed for successful folate metabolism)
- Treatment → Oral replacement of folic acid



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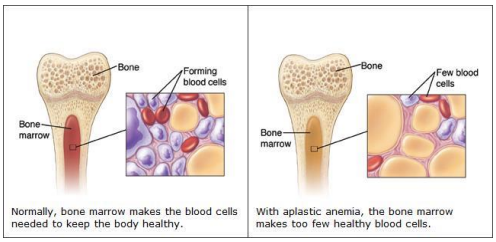
Lack of Bone Marrow Production of RBCs

- Lack of erythropoietin (EPO)
  - Usually due to kidney failure, hypothyroidism may also decrease EPO
  - Recombinant EPO can be given
- Aplastic anemia
  - Bone marrow fails: anemia, leukopenia, and thrombocytopenia
  - Caused by infection, radiation, chemicals (benzene), certain drugs or immune disease
  - Signs and symptoms may develop gradually or abruptly
  - Diagnosis begins with CBC
  - Blood transfusions necessary
  - Treatment: bone marrow transplant

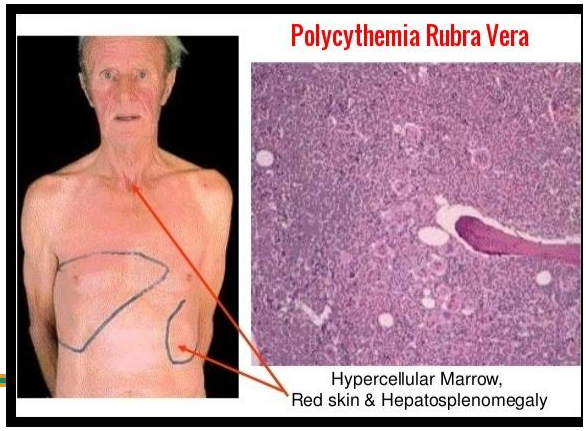


Lack of Bone Marrow Production of RBCs (continued_2)

- Anemia of chronic disease
  - Decreased RBC survival time, blunted EPO response, impaired iron metabolism
  - Lack of iron makes response to EPO less than desirable
  - Signs and symptoms of anemia are present
  - Transfusions not recommended, **EPO administration is preferred treatment** (higher than normal dose may be needed)

Primary Polycythemia

- AKA: polycythemia vera
- Hyperproliferation of all blood cells; increased clot risk
- Etiology unknown, may be chromosomal abnormality
- Rare
- CBC may show Hct of 60%, patient may present with hypertension, deep vein thrombosis,
  erythromelagia (ischemia and infarction in extremities)
- EPO level is low



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Secondary Polycythemia (erythrocytosis)

- More common than primary form
- Caused by prolonged hypoxia, i.e., COPD
- Signs and symptoms develop slowly, spleen may enlarge
- EPO levels are HIGH
- Correcting underlying hypoxia will reverse the condition

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