

APPROACH TO ANEMIA

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Definition of Anemia



- Reduced red blood mass
- RBC measurements: RBC mass, Hgb, Hct or RBC count
- Hgb, Hct and RBC count typically decrease in parallel except in severe microcytosis (like thalassemia)

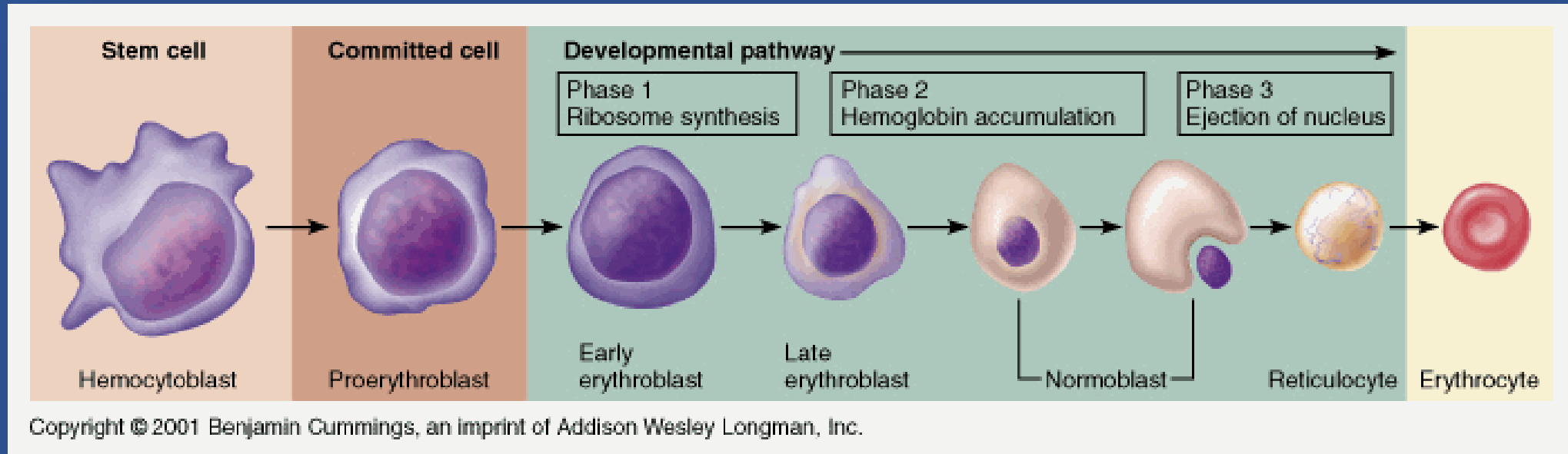
Normal Range of Hgb/Hct

- NL range: many different values:
 - 2 SD below mean: < Hgb 13.5 or Hct 41 in men and Hgb 12 or Hct of 36 in women
 - WHO: Hgb: <13 in men, <12 in women
 - Revised WHO/NCI: Hgb <14 in men, <12 in women
 - Scripps-Kaiser based on race and age: based on 5th percentiles of the population in question
 - African-Americans: Hgb 0.5-1 lower than Caucasians

Approach to Anemia

- Setting:
 - Acute vs chronic
 - Isolated vs combined with leukopenia/thrombocytopenia
- Pathophysiologic approach
- Morphologic approach

Reticulocytes



- Reticulocytes life span: 3 days in bone marrow and 1 day in peripheral blood
- Mature RBC life span: 110-120 days
- 1% of RBCs are removed from circulation each day
- Reticulocyte production index (RPI): $\text{Reticulocytes (percent)} \times (\text{HCT} \div 45) \times (1 \div \text{RMT})$:
 - <2 low

Pathophysiologic approach

- **Decreased RBC production**
 - Reduced effective production of red cells: low retic production index
 - Destruction of red cell precursors in marrow (*ineffective erythropoiesis*)
- **Increased RBC destruction**
- **Blood loss**

Reduced RBC precursors

- Low retic production index
- Lack of nutrients (B12, Fe)
- Bone marrow disorder => reduced RBC precursors (aplastic anemia, pure RBC aplasia, marrow infiltration)
- Bone marrow suppression (drugs, chemotherapy, radiation)
- Decreased trophic hormones (EPO, TSH, androgens)
- Anemia of chronic disease/inflammation

Ineffective erythropoiesis

- *Hallmark*: Bone marrow erythroid hyperplasia and relatively low reticulocytes
- Megaloblastic anemia
- Thalassemia
- Myelodysplastic syndrome
- Sideroblastic anemia

Increased destruction of RBC

- **Extravascular** destruction of RBC
 - Intrinsic RBC defects
 - Extrinsic RBC defects
- **Intravascular** destruction of RBC

Intravascular hemolysis

- Anemia and jaundice may be severe
- Circulatory collapse, renal damage
- Hemoglobinuria (RBC-free Hgb in urine)
- Hemoglobinemia (free Hgb in plasma)
- Hemosiderinuria (chronic intravascular hemolysis)

Intravascular destruction of RBC

- Microangiopathic hemolytic anemia (TTP, HUS, AS, prosthetic valve leak)
- Transfusion reaction
- Infection (clostridial sepsis)
- Hypotonic solutions
- Rho (D) immune globulin
- Copper poisoning, Wilson disease (high oxidant potential)
- Snake bites
- PNH (paroxysmal nocturnal hemoglobinuria)
- Paroxysmal cold hemoglobinuria, cold agglutinin disease

Extravascular hemolysis

- **Intrinsic RBC defects**

- Enzyme deficiencies (G6PD deficiency)
- Hemoglobinopathies (sickle cell disease, thalassemia)
- Membrane defects (spherocytosis)

- **Extrinsic RBC defects**

- Liver disease
- Hypersplenism
- Infections (Malaria, Babesia, Bartonella)
- Oxidant agents (dapsone, nitrites)
- Autoimmune hemolytic anemia (drugs, warm/cold Ab)
- LGL (large granular lymphocyte leukemia)
- IVIG
- Lead/copper/snake or spider bites

Chronic blood loss

- Most common cause of anemia
- Often difficult to quantitate:
 - Perioperative bleeding is often underestimated
 - Retroperitoneal or upper thigh bleeding may not be clinically obvious, more common in patients on anticoagulation

Morphologic approach

- Macrocytic anemia
- Microcytic anemia
- Normocytic anemia

Macrocytic anemia

- Reticulocytosis
- Abnormal nucleic acid metabolism
 - B12/folate deficiency
 - Drugs interfering with nucleic acid synthesis (zidovudine, hydroxyurea)
- Abnormal RBC maturation
 - MDS, acute leukemia, LGL
- ETOH
- Liver disease
- Hypothyroidism

Microcytic anemia

- Reduced iron availability
 - Iron deficiency
 - Anemia of inflammation
 - Copper deficiency
- Reduced globin production
 - Thalassemias and other hemoglobinopathies
- Abnormal heme synthesis

Normocytic anemia

- Systemic disorders
- Chronic renal disease
- Cardiorenal anemia
- Cancer-associated anemia
- Hospitalized patients

H&P

- Bleeding s/s
- Malignancy s/s
- Pallor
- Jaundice

Labs

- RBC indices
- Retic count
- Smear review
- WBC + diff
- nRBC
- Platelets

Anemia in elderly

- No different definition of anemia in elderly
- Elderly patients should undergo standard anemia evaluation
- NHANES III study:
 - 10% of men & women >65 were mildly anemic (2% Hgb <11)
 - 1/3: nutritional anemia: iron/B12/folate
 - 1/3: CKD/inflammatory d/o (arthritis, DM,...)
 - 1/3: Unexplained anemia

Athletes' anemia

- Dilutional anemia: plasma expansion
- Exercise – induced acute phase response: production of inflammatory cytokines
- GIB and iron deficiency
- Intravascular hemolysis from “march” hemoglobinuria
- Performance – enhancing agents (androgens and erythropoietin): may cause polycythemia masking anemia

Questions

RBC indices

- **RBC**: No. of RBCs in a specified volume of whole blood
- **Hgb**: concentration of Hgb in whole blood
- **HCT**: packed red cell volume: $[RBC \times MCV]/10$
- **MCV**: mean corpuscular volume: $MCV = 10 \times HCT \div RBC$
- **RDW**: red cell distribution width: $[SD/MCV] \times 100$
- **MCH**: mean corpuscular hemoglobin: average hemoglobin content in a RBC: $MCH = Hgb \times 10 \div RBC$
- **MCHC**: mean corpuscular hemoglobin concentration: $Hgb \times 100 \div HCT$