

## RBC and WBC Morphology

### Hematopoiesis

- Hematopoietic Tissues
  - Embryo
    - Third week: yolk sac
    - Third month: liver
  - Fetal
    - Fourth month: bone marrow
  - Birth
    - The bone marrow is virtually the sole source of blood cells
  - Childhood
    - Up to the age of puberty, all bone marrow is red and hematopoietically active
  - Adult (~18 years of age)
    - Vertebrae, ribs, sternum, skull, pelvis, and proximal epiphyseal regions of the humerus and femur
  - Hematopoiesis
    - Stem cells
    - CFU (colony forming unit)
    - BFU (burst forming unit)
- **Erythrocyte** (*red blood cell*)
  - An anucleate cell, which is the vehicle for the transportation of hemoglobin.
    - The function of hemoglobin is the transportation of oxygen and carbon dioxide
  - **Erythron**
    - The combined population of erythrocytes and their precursors, whether mature or immature, in blood, bone marrow, or extravascular spaces
  - Normoblastic Maturation (*will not be asked on the exam*)
    - Pronormoblast (proerythrocyte)
    - Basophilic normoblast (early erythroblast)
    - Polychromatophilic normoblast (late erythroblast)
    - Orthochromatic normoblast (normoblast)
    - Reticulocyte
  - **Factors Influencing Red Cell Production**
    - **Erythropoietin**
      - A hormone which affects the production of increased numbers of red cells
      - Glycoprotein
      - Produced mainly in the kidney
      - **Action**
        - Induces committed progenitor cells in the marrow to proliferate and differentiate into pronormoblasts
        - Shortens the generation time of normoblasts
        - Promotes early release of reticulocytes into the circulation



- Distribution of cells
    - Estimate
    - Enumeration
  - Myeloid:Erythroid ratio
    - Ratio of total # of granulocyte precursors to total # of red cell precursors
      - Increased: Erythroid hypoplasia, infection, myelogenous leukemia
      - Decreased: erythroid hyperplasia, depressed granulopoiesis
  - Megakaryocytes: number
  - Number and location of lymphoid aggregates
  - Presence or absence of iron
  - Presence or absence of rare or abnormal cells
  - Structure of bone
- **Basic Hematologic Tests**
  - **Hemoglobin**
    - Conjugated protein which is the transport vehicle for oxygen and carbon dioxide
    - Measured spectrographically
    - Reference range:
      - Males: 14 – 18 g/dl
      - Females: 12 – 16 g/dl
  - **Hematocrit**
    - The ratio of the volume of erythrocytes to that of whole blood
    - Methods:
      - Automated: calculated from MCV and RBC
      - $HCT = MCV \times RBC$
    - Reference range
      - Males: 41- 53 %
      - Females: 36 – 46%
  - **Erythrocyte Count (RBC)**
    - Expressed as # of cells per unit volume of whole blood
    - Automated
      - Electrical impedance
      - Light Scattering
  - **Wintrobe Indices**
    - **Mean Cell Volume (MCV)**
      - The average volume of the red cells
      - $MCV = HCT/RBC$
      - Measured in femtoliters (10-15 )
      - Reference range: 76 – 96 fl
    - **Mean Cell Hemoglobin (MCH)**
      - The content (weight) of hemoglobin of the average red cell
      - $MCH = HGB/RBC$
      - Reference range: 27 – 33 pg

- Picogram = 10-12 grams
  - **Mean Cell Hemoglobin Concentration (MCHC)**
    - The average concentration of HGB in a given volume of packed red blood cells.
    - **MCHC = HGB/HCT**
    - Reference range: 30 –35 g/dl
- **Red Cell Distribution Width (RDW)**
  - Measure of the variability of MCV distribution
  - Increased in conditions with large variation in red cell size
  - Early indicator of iron deficiency

## White Blood Cell Morphology

- **Leukopoiesis**
  - The maturation of leukocytes from pluripotential stem cells in the bone marrow
  - Granulopoiesis: generation of granulocytes
  - Monocytes
  - Lymphocytes
  - Granulocyte and Macrophage Colony Stimulating Factors
    - Glycoprotein factors which react with specific receptors on stem cells to direct their differentiation into committed stem cells
  - CSF-GM (Colony Stimulating Factor-Granulocyte-Monocyte)
    - Plays a role in granulopoiesis analogous to that of erythropoietin in erythropoiesis
    - Produced in endothelial cells in the bone marrow
    - Concentration dependent effect
      - Low concentrations—monocytes
      - High concentrations--granulocytes
  - Stages of Granulocyte Maturation
    - Myeloblast
    - Promyelocyte
    - Myelocyte
    - Metamyelocyte
    - Band forms
    - Segmented neutrophil
  - Cytoplasmic Granules
    - Primary granules
      - Appear initially in promyelocytes
      - Stain magenta
    - Secondary granules
      - Appear in myelocytic stage
      - Small, difficult to see with light microscopy
      - Pale pink to gray
- Laboratory Tests
  - WBC
    - # white blood cells/mm<sup>3</sup>

- Includes all types of white cells
  - Differential Count
    - Percentage of each cell type is determined
  - Bone Marrow
- **White Cell Disorders**
  - Leukocytosis
    - An increase in the total WBC above the upper limit of the reference range
      - Neutrophilia: increase in neutrophils
        - The primary factors influencing the neutrophils count are
          - Rate of inflow of cells from the bone marrow
          - Proportion of neutrophils in the marginal and circulating pools
          - Rate of outflow (or destruction) from the blood
        - Physiologic Neutrophilia
          - Exercise
          - Stress
          - Epinephrine
        - Pathologic Neutrophilia
          - Infection
          - Toxic
          - Tissue destruction or necrosis
          - Hematologic disorders
          - Inflammatory disorders
      - Eosinophilia: increase in eosinophils
        - Allergic disorders
        - Parasitic infections
        - Hematologic : CML
        - Hypereosinophilic syndrome
          - Persistent eosinophilia with no known cause
        - Drugs : digitalis, sulfonamides
      - Monocytosis: increase in monocytes
      - Lymphocytosis: increase in lymphocytes
    - Basophilia
      - Myeloproliferative disorders
    - Neutropenia
      - A reduction of the absolute neutrophil count
      - Causes
        - Bone marrow: lack of production
        - Ineffective granulopoiesis
        - Decreased survival/increased destruction
  - Leukemoid Reaction
    - Neutrophilic Leukemoid Reaction

- Hemolysis
  - Hemorrhage
  - Malignancy with bone marrow involvement
  - Infections
  - Severe burns
  - Hodgkin's Disease
- Definition: an excessive leukocytic response. It includes:
  - Leukocytosis of  $50 \times 10^9 /L$  or higher with a shift to the left
  - Lower counts, even below normal, with considerable numbers of immature forms
- Differentiation From Leukemia
  - Lack of eosinophilia and basophilia of CML
  - Presence of more mature granulocytic forms
- Leukoerythroblastic Reaction
  - Circulating normoblasts accompanied by a neutrophilic leukemoid reaction
  - Major causes
    - Metastatic carcinoma involving the bone marrow
    - Sickle cell anemia
- Lymphocytic Leukemoid Reaction
  - Extremely high counts of normal appearing lymphocytes may occur in pertussis
  - Atypical lymphocytic leukemoid reaction
    - Infectious mononucleosis
- **Abnormal WBC Morphology**
  - **Auer Rods**
    - Linear or spindle-shaped red-purple inclusions in blasts or promyelocytes
    - Usually seen only in pathologic conditions
      - AML (acute myelogenous leukemia)
    - Derivative of azurophilic granules
  - **Toxic Granulation**
    - Dark blue to purple cytoplasmic granules
    - Peroxidase positive
    - Found in severe infections or other toxic conditions
  - **Dohle Inclusions Bodies**
    - Small oval inclusions in the peripheral cytoplasm of neutrophils which stain pale blue with Wright's stain
    - Remnants of free ribosomes or rough endoplasmic reticulum
    - Frequently accompanies toxic granulation
  - **Hypersegmentation**
    - Normal neutrophils have 2 – 5 lobes connected by a thin chromosome strand
    - Hypersegmentation occurs if :
      - > 5% of neutrophils have 5 lobes or more

- Or if 1% of neutrophils have 6 or more lobes
  - Seen in megaloblastic anemia
- **May-Hegglin Anomaly**
  - Rare, autosomal dominant condition
  - Pale blue inclusions resembling Dohle bodies in neutrophils
  - Giant platelets
  - Thrombocytopenia
- **Pelger – Huet Anomaly**
  - Autosomal dominant
  - Failure of normal segmentation of granulocytic nuclei
  - Most nuclei are band shaped or bilobed