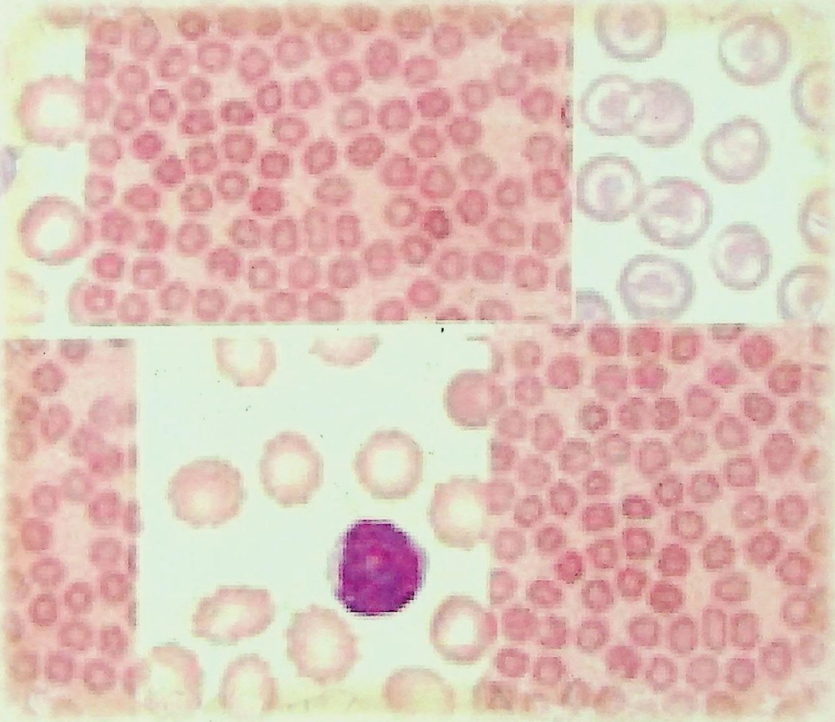
Clinical Hematology Study Guide

Study Topic Part 1: Erythropoiesis, RBC Morphology, Anemias



Kippy Shortsox

Preface

What is this thing written by Kippy Shortsox?
This is part 1 of a 3 part series of study topics about hematology. Part 1 covers **red blood cells, hematopoiesis, and anemias,** Part 2 covers white blood cells, and Part 3 covers coagulation and hemostasis.

This study guide was designed specifically for medical laboratory students and those studying for ASCP certification as an MLT. It uses a unique approach and leaves out the gobbledygook and concentrates only on the stuff that you need to know. It begins with a thorough learning outline that leave a space for notes on each opposing page. This allows a student to add information and taylor it to their own specific needs. It ends will a thorough multiple choice and Q & A section.

Serious attempts have been made to make learning this detailed topic as unfrustrating as possible. (Yea, I know unfrustrating is not a word).

The usual disclaimer
We have done everything in our power to ensure the accuracy of this study tool. However, we are human and mistakes are always possible.

Can you say website?
Feel free to email kippy at kippy@kippyshortsox.com with any questions, concerns, or requests for corrections.

A supplement website is available at:

http://kippyshortsox.com/blog

Please look for other study topics to include clinical chemistry, immunology and serology, parasitology, microbiology, and blood bank.

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DEDICATION

Fueled by late night vigils, sleepless nights, and awesome study buddies.

You know who you are!

Clinical Hematology

Study Guide

Clinical Hematology Study Guide

STUDY TOPIC PART 1: ERYTHROPOIESIS

RBC MORPHOLOGY

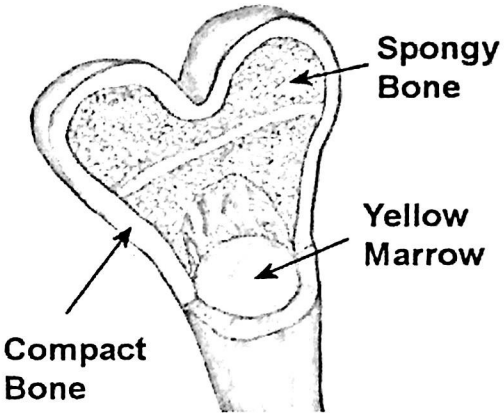
ANEMIA

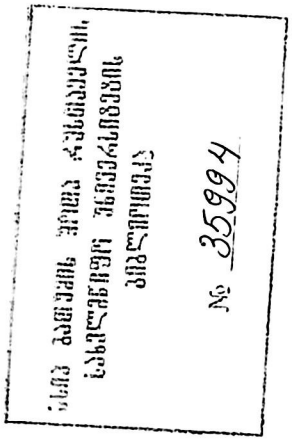
Study Topics for MLT Student and Certification
by Kippy Shortsox

Roasted bone marrow recipe!

Obtain some marrow bones from your local butcher Place bone marrow bones upright on a foil-lined baking sheet. Roast at 450 degrees for approximately 15 minutes Scoop out marrow and serve on toast and top with sea salt

YUM! YUM!





1. VOCABULARY

Acidosis

- A decrease in pH (increase in hydrogen ions)

Agglutination

- Clumping of cell

Alkalosis

- An increase in pH (decrease in hydrogen ions)

Anemia

- Body's response to diminished-oxygen carrying capacity of the blood

Aplastic crisis

- Severe drop in hemoglobin

Cholelithiasis

- Formation of gallstones

Erythrocyte sedimentation rate

- ESR-Screening test indicative of inflammation. Measures the distance that RBCs will fall in a vertical tube in a given period of time

Erythropoiesis

- Production of red blood cells

Ferritin

- It is the major iron storage protein of the body
- Measuring ferritin levels is an indirect way to measure the amount of iron stored by the body

Transferrin

- Transports iron

Transferrin saturation

- Transferrin saturation reported as a percentage - (serum iron divided by TIBC) X 100

2. ERYTHROPOEISIS

- Production, differentiation, and maturation of red blood cells
- The hematopoietic system includes:
  - Bone marrow
  - Liver
  - Spleen
  - Lymph nodes
  - Thymus
  - Stem cells

Stem cells

- Totipotent cells
  - Have the ability to develop into any human cell type, including developing into a fetus

- Pluripotent stem cells
  - Have the ability to develop into any human cell type except develop into a fetus.

- Multipotent stem cells - committed to a specific cell line
  - Hematopoietic progenitor cells (HPCs)

  - Lymphocytic committed cells (LSCs)
    - Develop into T cells (cellular immunity)
    - Develop into B cells (humoral immunity)

- Non-lymphocytic committed cells (myeloid) - CFU-GEMM
  - Granulocyte
  - Erythrocyte
  - Monocyte
  - Megakaryocyte

- Cytokines and interleukins
  - Responsible for regulating and directing the differentiation and maturation of a cell to a committed pathway
  - Interleukins are cytokines that encourage hematopoietic growth
  - Some cytokines are available as pharmaceutical products
    - Used to stimulate production of a specific cell line
    - Recovery from neutropenia
    - Bone marrow therapy
    - Increase white counts of AIDS patients

Red Cell Maturation

- Red cell proceeds through nucleated stages and completes maturation within approximately 5 days
- Size of red cell becomes smaller as it matures
- N:C ration decreases
- Nuclear chromatin condenses
- Hemoglobinization (cytoplasm changes color)
- Red cell anucleates in bone marrow due to successive cell divisions

CAP (ASCP) Maturation Stages

- **Pronormoblast** (Rubriblast)
  - 12 - 19 µm
  - N:C (nucleus to cytoplasm) = 4:1
  - 0 - 2 nucleoli
  - Dark with fine chromatin pattern
  - Cytoplasm stains basophilic blue with Wright stain
  - The blue color reflects RNA activity
- **Basophilic normoblast** (Prorubricyte)
  - 12 - 19 µm
  - N:C = 4:1
  - Chromatin begins clumping
  - Nucleoli are no longer apparent
- **Polychromatophilic normoblast** (Rubricyte)
  - 1-15 µm
  - N:C = 1:1
  - Hemoglobin makes it first appearance
  - Cytoplasm contains varied amounts of pink coloring providing a light, grayish color
- **Orthochromic normoblast** (Metarubricyte)
  - 8-12 µm
  - Chromatin is tightly condensed (pyknotic)
  - Reddish, pink cytoplasm indicating increased quantities of hemoglobin

- **Reticulocyte**
  - May be seen in the blood smear as polychromasia
  - Phase begins in the bone marrow and continues in the circulating blood
  - In Wright stain, residual RNA gives off a blue appearance known as polychromatophilia
  - Lacks nucleus but contains mitochondria and ribosomes.
  - Loss of mitochondria and ribosomes marks final transition to a mature red blood cell
- **Erythrocyte** (AKA discocyte)
  - 6-8 μm
  - Biconcave disc that is roughly the size of a lymphocyte's nucleus
  - Lacks nucleus
  - Hemoglobin performs oxygen-carbon dioxide transport (heme portion)
  - MCV = 80-100 fL
  - MCHC = 32%-36%
  - 120-day lifespan

Erythropoietin (EPO)

- Cytokine that is produced by the kidneys and in the liver in small amounts
- Regulates the production of red blood cells as a result of hypoxia
- Allows reticulocytes to be released from the bone marrow early
- Can reduce time needed for cells to mature in the bone marrow
- Prevents apoptosis

Life stages of hematopoiesis

- Yolk sac - 2 weeks to 2 months of fetal life
- Spleen and liver - 2 to 7 months of fetal life
- Thymus, lymph nodes, and spleen - 7 months of fetal life to birth
- Bone marrow - 7 months of fetal life through adult (bone marrow is the primary site)

Spleen (largest lymphoid organ)

- Fist-shaped organ that weighs approximately 8 ounces consisting of:
  - **Red pulp**
    - Red blood cell filtration
  - **White pulp**
    - Lymphocyte processing
    - Contains lymphocytes, macrophages, and dendritic cells
  - **Marginal zone**
    - Stores white blood cells and platelets
  - **Spleen has four functions:**
    - (1) Reservoir
      Holds - 1/3 platelets and 1/3 granulocytes
    - (2) Filtration (pitting and culling)
      Spleen removes imperfections such as:
      - Inclusions
      - Parasites
      - Abnormal hemoglobin
      - Abnormal membrane
    - (3) Immunologic role
      - Spleen is the largest secondary lymphoid organ
      - Promotes phagocytic activity by providing opsonizing antibodies which strip the capsule from bacterial surface
    - (4) Hematopoietic role
      - Extramedullary hematopoiesis

Bone Marrow (largest organ in the body)

- Bone Marrow contents
  - Yellow marrow
    - Composed mostly of adipose tissue
  - Red marrow
    - Contains all developing blood lines, progenitor cells, and macrophages
- M:E ratio (3:1 to 4:1)
  - Ratio of myeloid elements and their precursors and erythroid elements and their precursors
    - **Myloid** is the granulocyte precursors
    - **Erythroid** is nucleated red blood cells and their precursors
  - Fluctuations associated with certain disease states and conditions such as:
    - Iron deficiency anemia
    - Thalassemia
    - Iron overload disorders
    - Anemia of chronic disorders

Intramedullary hematapoeisis

- Normal process
- Hematopoiesis within the bone marrow
- Respond to anemic stress by premature release of reticulocytes into blood stream

Extramedullary hematapoeisis

- Always considered an abnormal process
- Hematopoiesis that takes place outside of the bone marrow in the spleen and liver
- Bone marrow is unable to keep up with demand
- Hepatosplenomegaly is common
- Seen in conditions such as:
  - Dysfunctional bone marrow
  - Aplastic anemia,
  - Infiltration by malignant cells
  - Overproliferation of a cell line (leukemia)

Hemolysis

- Red cell **senescence**
  - Natural death at the end of 120-day lifespan
  - Loss of an RBCs nucleus is most responsible for limited lifespan
  - Contents of cell are returned to circulation for recycling
  - Macrophages remove senescent red blood cells
  - Iron recycling by macrophages in spleen
- Evidence of hemolysis
  - Increased reticulocyte count
  - Increased polychromasia
  - nRBCs
- Extravascular hemolysis - (90%)
  - Occurs when macrophages clear senescent red blood cells
  - Most normal RBC death occurs in the spleen
  - Also occurs in liver, lymph nodes, and bone marrow
  - Heme and globin are recycled

- Intravascular hemolysis - (10%)
  - Red cells are being lysed in blood stream
  - 10% of hemolysis
  - Hemoglobin is released into the plasma
  - Hemoglobinemia (red-tinged plasma)
    - Seen only in intravascular lysis
  - Hemoglobinuria (hemoglobin in urine)
    - May be complement mediated
  - Laboratory
    - Decreased Hgb, Hct, and red blood cell count
    - Increased bilirubin
    - Decreased haptoglobin
    - Hemoglobinemia and hemoglobinuria may be present
    - Elevated reticulocyte count
    - Symptoms of anemia: pallor, fatigue, tachycardia

3. HEMOGLOBIN

RBC membrane and transport mechanisms

- Integral proteins
  - Example: glycophorin A, B, C
  - Expand through membrane and penetrate outer edge of RBC
  - Purpose is transport and supporting structure
  - Provides net negative charge
  - Some antigens located here
- Peripheral proteins
  - Confined to RBC membrane skeleton
  - Cytoskeleton is responsible for deformability and cellular integrity
  - Average RBC is 6 - 8 μm wide and have ability to fit through arterioles that are 1-3 μm
  - Examples include: spectrin and ankyrin
    - RBC deformability is major contributor to RBC survivial

Purpose of hemoglobin

- Primary purpose is oxygen delivery
  - Deoxyhemoglobin - hemoglobin without oxygen
  - Oxyhemoglobin - hemoglobin with oxygen
- Secondary purpose is pulling carbon dioxide away from tissues and assist in maintaining pH

Hemoglobin synthesis

- Hemoglobin synthesis takes place during the red cell maturation process
- Major components of hemoglobin are heme and globin
  - Red bone marrow and liver most common sites of heme synthesis
  - Heme is produced by red blood cell precursors located in the bone marrow
  - Enzymatic process that produces heme is called porphyrin synthesis

Types of hemoglobin

- **Embryo Hgb**
  - Synthesized and remain in embryo for 3 months
  - Does not participate in oxygen delivery
  - Hgb Gower and Hgb Portland
- **Fetal hemoglobin**
  - Synthesized beginning at 3 months of fetal life through birth
  - Hgb F
- **Adult hemoglobin**
  - Hgb A (95%-98%)
  - Hgb A2 (3%-5%)
  - Hgb F (<1%)

Hemoglobin structure

- Two primary structures
  - Heme portion
    - Two-thirds of body's total iron is bound to heme
  - Globin portion
    - Consists of amino acids linked together to form a polypeptide chain
    - Most significant chains are the alpha and beta chains
    - Heme and globin portions of the hemoglobin molecule are linked together by chemical bonds.
- Each normal adult hemoglobin molecule consists of 4 polypeptide chains
  - Two alpha chains
    - Has 141 amino acids in each alpha chain
    - Which has 2 attached heme groups
    - Two iron atoms Fe2+
    - Two oxygen molecules
  - Two beta chains
    - Has 146 amino acids in each beta chain
    - Which has 2 attached heme groups
    - 2 iron atoms Fe2+
    - 2 oxygen molecules

2,3-diphosphoglycerate (2,3-DPG)

- Produced during the Embden-Meyerhof pathway during anaerobic glycolysis
- Regulates oxygen affinity
- Oxygen affinity is responsible for the ease at which oxygen can be loade in the lungs and unloaded in the tissues

Abnormal Hemoglobin

- Electrophoresis is used for the preliminary identification of abnormal hemoglobin
- Abnormal hemoglobin consists of:
  - **Methemoglobin**
    - Iron is oxidized as Fe^{3+} instead of Fe^{2+}
    - Unable to bind oxygen
    - May be caused by metabolic defect of abnormal hemoglobin structure
  - **Carboxyhemoglobin**
    - Results from the combination of carbon monoxide with heme iron
    - Affinity for hemogobin is more than 200 times that of oxygen
    - No oxygen delivery to tissues
    - Carbon monoxide poisoning is increased in smokers
    - Highly toxic in unventilated spaces
  - **Sulfhemoglobin**
    - Cannot convert to normal hemoglobin and persists for life of cell
    - Can result in denaturization and heinz bodies
    - Cannot transport oxygen
    - Elevated concentration results in cyanosis
    - Toxic at levels exceeding 10%

4. OXYGEN DISSOCIATION CURVE

- Represents relationship between oxygen content and partial pressure of oxygen
- The higher the partial pressure, the higher the deficit of oxygen to tissue
- The affinity of hemoglobin for oxygen is dependent upon the partial pressure of oxygen (PO)
- 2,3-DPG controls hemoglobin's affinity for oxygen

Shift to left

- Increase in oxygen affinity
- Alkalosis
- Decreased 2,3-DPG
- H+ decreases
- P-CO_2 decreases
- Body temperature decreases

Shift to the right

- Decrease in oxygen affinity
- Acidosis
- Increased 2,3-DPG
- H+ increases
- P-CO_2 increases
- Body temperature increases

5. RED BLOOD CELL MORPHOLOGY

Acanthocytes (spur cell)

- Irregular-spaced projections that vary in width and length
- Acanthocytes arise from either of two mechanisms.
  - Alterations in membrane lipids that is seen in abetalipoproteinemia
  - Defeciency of lipids and Vitamin E causing abnormal morphology of RBCs
  - Liver dysfunction
    - Deficient lipoprotein accumulates in plasma causing increased cholesterol in RBCs
    - This causes abnormalities of membrane of RBC causing remodeling in spleen and formation of acanthocytes
- Seen in:
  - Abetalipoproteinemia
  - Cirrhosis of the liver
  - Following heparin administration

Bite cells (Helmet cells)

- Abnormal red cell structure resembling a bite
- Bites result from removal of denatured hemoglobin by macrophages in th spleen
- Usually associated with spherocytes and blister cells.
- Disease:
  - Microangiopathic hemolytic anemia
  - Thrombocytopenia purpura
  - DIC
  - Severe burns
  - Renal graft rejections

Blister cells

- When the red cell membrane around a bite cell repairs, a blister-like structure forms
- Disease:
  - Individuals with red-cell enzymopathies (most notably G6PD deficiencies)

Codocytes (target cells)

- Characteristic distribution of hemoglobin in the center of the cell with a target-like appearance
- Codocytes can be thought of as cells whose membrane is too large for their hemoglobin content
- Considered antithesis of spherocytes, which have too little membrane for their volume and hence increased susceptibility to lysis or increased "osmotic fragility"
- Usually seen in defective globin chain synthesis, for example hemoglobinopathies
- Disease
  - Liver disease
  - Thalassemia
  - Hyposplenism
  - Hemoglobinapathies
  - Hemolytic anemias and iron deficient anemia
  - Postsplenectomy

Dacrocyte (tear drop cells)

- Form as a result of removal of an inclusion from the cell as it moves through the spleen
- Red cells are very flexible and usually return to their normal shape following pitting, in this case the membrane may have been stretched too far and cannot return to its original shape.
- Disorders:
  - Megaloblastic anemia
  - Homozygous beta-thalassemia
  - Myeloproliferative syndromes
  - Pernicious anemia

Elliptocytes (ovalocytes)

- Cigar-shaped erythrocyte
- Associated with weakening of membrane skeleton and defects in proteins that hold the skeleton together (ankyrin and spectrin)
- The function of elliptocytes appear to be unaffected in most cases
- Disease:
  - Hereditary elliptocytosis
  - Thalassemia major
  - Iron deficiency anemia
  - Megaloblastic anemia

Spherocytes

- Erythrocytes that have lost their normal biconcave shape
- Intense orange-red color when stained
- May appear as artifacts if a slide is examined at the thinning end of a normal blood smear
- Occurs as the ratio of surface area to the volume of the cell contents decreases
- May be formed due to an inherited structural defect or from physical trauma such as heat or chemical injury
- Clinical disorders include:
  - Acquired hemolytic anemia
  - Blood transfusion reactions
  - Congenital spherocytosis
  - DIC
  - Hereditary spherocytosis

Schistocytes (fragmented cells)

- Red cell fragments that are irregularly shaped
- Clinical disorders include:
  - Hemolysis
  - Hemolytic anemias related to burns
  - Aplastic anemia
  - Renal transplant rejections
  - DIC

Stomatocytes

- Caused from increased sodium and decreased potassium ion concentrations within the cytoplasm of the red blood cell
- Clinical disorders include:
  - Acute alcoholism
  - Infectious mononucleosis
  - Lead poisoning or thalassemia minor
  - Hereditary stomatocytosis

6. INCLUSIONS

Basophilic stippling

- RNA and mitochodrial remnants that appear as granules throughout the cytoplasm
- Associated with defective heme synthesis, lead poisoning, and severe anemia

Cabot rings

- Thought to be microtubules from a mitotic spindle or remnants from the nuclear membrane
- Distinguished from the ring forms of Plasmodium by their larger size and by absence of a red chromatin mass
- Disease:
  - Lead poisoning
  - Leukemia
  - Pernicious anemia (anemia caused by Vitamin B deficiency)
  - Megaloblastic anemia

Howell-Jolly bodies

- Remnants of DNA
- During maturation in the bone marrow erythrocytes normally expel their nuclei, but in some cases a small portion of DNA remains.
- Usually are the result of a damaged spleen.
- Seen in:
  - Postsplenectomy
  - Autosplenectomy (sickle cell anemia)

Heinz bodies

- Formed from denatured hemoglobin
- The presence of bite cells are evidence that a Heinz body has been formed and removed by spleen

Pappenheimer bodies

- Iron found inside blood cells
- Appear as dark-staining beads on the periphery of red cells
- Seen in patients with thalassemia major and post-spleenectomy
- Called **siderocytes** when observed with Prussian blue stain
  - Siderocyte is a mature erythrocyte containing free iron (unbound)
  - If iron granules circle the nucleus, it is a ringed sideroblast
  - **Sideroblast** is an immature nucleated erythocyte (erythroblast) containing granules of ferritinn (unbound storage form of iron)

7. ANEMIA

Serum iron

- Ferritin and hemosiderin are the primary storage forms of iron
  - **Ferritin** is measured in plasma and found in the liver, spleen, skeletal muscle, and bone marrow
  - **Hemosiderin** is measured in urine and bone marrow
    - Hemosiderin often forms after bleeding. When blood leaves a ruptured blood vessel, the red blood cell dies resulting in the release of hemosiderin.
    - Excessive systemic accumulations of hemosiderin may occur in macrophages in the liver, lungs, spleen, kidneys, lymph nodes, and bone marrow. This may be due to excessive RBC destruction

- **Transferrin**
  - Protein used for transport of iron
- **Total iron bind capacity** (TIBC)
  - Ability to bind transferrin
- **Transferrin saturation**
  - (Serum iron ÷ TIBC) X 100

The iron store is evaluated through the use of the Prussian Blue stain

- Two types of iron:
  - Noneheme iron
    - Iron from food in the form of iron salts
  - Heme iron
    - Derived from the hemoglobin and myoglobin of meat
    - Two-thirds of the body's total iron is bound to heme

Factors affecting iron

- Iron ingested
- Iron absorbed
  - Fe^{3+} is converted to Fe^{2+} by stomach acid
  - Fe^{2+} is transported to bone marrow by transferrin
- Iron recycled
  - Globin is returned to amino acid pool
  - Heme is returned to bone marrow
- Storage forms (ferritin and hemosiderin)
  - Ferritin is the major storage form of iron and measured in plasma
  - Hemosiderin is measured in urine and bone marrow
    - Can be found in the liver, spleen, bone marrow and skeletal muscle
  - Hepcidin is a hormone produced by the liver and regulates iron transit
    - Iron is stored mostly in the liver

Anemia causes

- Decrease in the number of red blood cells or
- Decrease in the amount of hemoglobin contained within the red blood cells or
- Decrease in oxygen-carrying capacity of the blood
  - Insufficient hemoglobin (most common)
  - Hemoglobin is not functioning properly

- Anemia is not a disease. It is a symptom of a disease or physiological process
- Moderate anemias may not have clinical symptoms
- Severe anemia (Hemoglobin < 7 g/dL)
  - Pallor
  - Dyspnea
  - Vertigo
  - Headache
  - Muscle weakness
  - Lethargy
  - Hypotension and tachycardia

Hypoxia

- Inadequate hemoglobin content results in reduced delivery of oxygen to the tissues
- Erythropoietin stimulates RBC precursors resulting in more RBCs being released into circulation
- Chronic anemia results in physiological adaptations
  - Increased heart rate, respiratory rate, and cardiac output
  - Triggers increase in 2,3-DPG
- Patients with chronic anemia may be asymptomatic with hemoglobin concentrations as low as 6 g/dL which places strain on heart
- Production of red blood cells
- In healthy individuals, approximately 1% of the body's RBCs are removed due to senescence
- Bone marrow continuously replaces lost RBCs
- RBC production requires:
  - Iron
  - Vitamin B12
  - Folic acid (folate)
- Ineffective erythropoiesis
  - Production of defective erythroid progenitor cells
  - Normally defective cells destroyed in bone marrow prior to release into circulation

8. CLASSIFICATION OF ANEMIAS

Classification by red cell morphology

- Normocytic/normochromic anemia
  - MCV: 80 - 100 fL (normocytic - normal size)
  - MCHC: 31% - 36% (normochromic - normal color)
  - Typical of hypoproliferation
  - Examples:
    - Iron deficiency anemia (some)
    - Anemia of chronic disorders
    - Autoimmune disorders
    - Bone marrow disorders
- Microcytic/hypochromic anemia
  - MCV: < 80 fL (microcytic - small size)
  - MCHC < 30% (hypochromic - lacking color)
  - Red cells are smaller and have reduced hemoglobin content
  - Typical of maturation defects
  - Examples:
    - Iron deficiency anemia
    - Thalassemia
    - Anemia of chronic inflammation
    - Sideroblastic anemia
- Macrocytic/normochromic anemia
  - MCV > 100 fL (macrocytic - large size)
  - MCHC: 31% - 36% (normochromic - normal color)
  - Typical of maturation defects
  - Examples:
    - Megaloblastic
    - Vitamin B12 deficiency
    - Folic acid deficiency
    - Nonmegaloblastic
    - Chronic liver disease (alcoholism)
    - Hypothyroidism

Classification by pathophysiological characteristics

- Blood loss
  - Acute
  - Chronic
- Impaired production
    - Iron deficiency (Impaired hemoglobin synthesis)
    - Sideroblastic anemia (Impaired hemoglobin synthesis)
    - Anemia of chronic disease (Impaired hemoglobin synthesis)
    - Megaloblastic (problem with DNA synthesis)

- Membrane defects
  - Hereditary spherocytosis
  - Hereditary elliptocytosis
  - Pyropoikilocytosis
  - Paroxysmal nocturnal hemoglobinuria
- Enzyme deficiency
  - G6PD deficiency
  - Pyruvate kinase deficiency

- Globin abnormality
  - Sickle cell anemia and other hemoglobinopathies

- Acquired disorders
  - Acute blood loss
  - Immune related
  - Chemical
  - Drugs
  - Burns

Anemia evaluation

- Peripheral blood slide examination
  - Evaluate RBC diameter, shape, color, and inclusions
  - Dimorphism and uniformity
  - Shape abnormalities
  - Review of white blood cells and platelets
- Bone marrow examination
  - When cause of anemia from results of laboratory tests is unclear, a bone marrow examination may be indicated
  - Evaluates hematopoiesis and abnormal infiltration of the marrow
- Other laboratory tests
  - Urinalysis (detects hemoglobinuria or increase in urobilinogen)
  - Microscopic analysis of urine (detects hematuria or hemosiderin)
  - Analysis of stool (detects occult blood or parasites)

9. ANEMIAS

Anemia of chronic disease and inflammation

- Second most common anemia after IDA (iron deficiency anemia)
- Common complication in inflammation, infection, malignancy, or systemic diseases
- Believed to be related to Hepcidin
  - Hepcidin is key in controlling iron absorption and recycling
  - Hepcidin is released by the liver
- Treatment includes
  - Treating underlying condition

Aplastic Anemia

- Characterized by total bone marrow failure with pancytopenia and rapid progression to death
- Not a common disease
- Secondary to some disease states:

Cold Agglutinin Syndrome

- Rare hemolytic disorder
- Affects patients > 50
- Caused by IgM autoantibody
- Complement is fixed on the red cells during cold temperatures: 0-5° C
- Then red cells agglutinate and hemolyze as body temperature rise 20-25 C

Diamond-Blackfan Anemia (DBA)

- Bone marrow lacks bone marrow precursors with a slightly decreased number of leukocytes
- Characterized by:
  - Bone marrow failure
  - Low stature
  - Birth defects
  - Cancer predisposition
- Also known as:
  - Congenital pure red cell aplasia
  - Congenital hypoplastic anemia
- Shares many aspects with Fanconi anemia
- Severely anemic by 6 months of age with most patients being diagnosed by 1st birthday

- Diagnostic criteria
  - Anemia appearing prior to first birthday
  - Variable platelet counts, usually increased
  - Macrocytosis
  - Characterized by progressive and refractory anemia
  - No leukopenia or thrombocytopenia
  - Notable characteristic: elevated red blood cell adenosine deaminase level
- Treatment includes steroids and transfusional support

Fanconi anemia

- Congenital form of aplastic anemia
- Accounts for approximately 25% to 30% of childhood aplastic anemia
- Bone marrow shows a macrocytic process with thrombocytopenia and leukopenia
- Only therapy is bone marrow transplant
- Clinical manifestation:
  - Short stature
  - Skeletal disorders
  - Renal malformations
  - Microcephaly
  - Mental retardation
- Therapy:
  - Bone marrow transplant
  - Steroids

Glucose-6-Phosphate Dehydrogenase Deficiency

- Most common aerobic erythrocyte enzyme deficiency
- G6PD-enzyme necessary for RBC metabolism
- X-linked recessive disorder
- Protection from malaria
- Four clinical conditions:
  - (1) Drug-induced acute hemolytic anemia
  - (2) Favism
    - Affiliated with eating young fava beans or broad beans
  - (3) Neonatal jaundice
    - 2-3 days after birth
    - Show more jaundice than hemolysis
    - Phototherapy
  - (4) Congenital nonspherocytic anemia
- Laboratory findings:
  - Decreased G6PD
  - Presence of Heinz bodies

Hereditary Elliptocytosis

- Defect in membrane skeleton (Spectrin deficiency)
- Characterized by overabundance of red cells
- In symptomatic patients, splenectomy may be indicated
- Four subtypes
  - (1) Common hereditary elliptocytosis
    - Mild - No clinical symptoms
    - Severe: Fragmented cells, jaundice, and moderate hemolysis
  - (2) Southeast Asian ovalocytosis
  - (3) Spherocytic hereditary elliptocytosis
  - (4) Hereditary pyropoikilocytosis
    - Rare recessive disorder
    - Hemoglobin < 6.5 g/dL and Low MCV (50-75 fL)

Hereditary Hemochromatosis

- Genetic error of metabolism that produces a 2X to 3X greater than normal GI absorption of iron
  - Iron overload - autosomal recessive disorder on chromosome 6
  - Dueodenal mucosa is primary site for iron absorption regulation
  - Over course of decades excess iron accumulation damages organs and tissues
  - Transferrin amounts may decrease in presence of liver disease
    - Transferrin is produced in the liver
- Treatment
  - Therapeutic phlebotomy
- Symptoms:
  - Increased iron and increased transferrin saturation
  - Normal TIBC and normal transferrin
  - Cirrhosis of liver
  - Presence of disease confirmed with liver biopsy

Hereditary Spherocytosis

- Heterogeneous form of hemolytic anemia
  - Usually transmitted as an autosomal dominant trait
- Membrane protein deficiency of spectrin and ankyrin which is responsible for elasticity and deformability of red blood cells
  - Cells are unable to expand
  - Cell ion and gas transportation is disrupted
- Manifests at any age
- Symptoms:
  - Jaundice and anemia
  - Splenomegaly and spherocytes
  - Slightly elevated RDW and MCHC > 36% (50% of patients)
  - Cholelithiasis and increased bilirubin

Hereditary Stomatocytosis

- Rare hemolytic disorder
- Deficiency in membrane protein stomatin
  - Stomatin regulates ions across membrane
  - Red cells swell due to increase in intracellular sodium
- Seen in thalassemia, lead poisoning, HS, and in alcoholism

Iron Deficient Anemia (IDA)

- Treat with oral iron supplements

- Three-stage process of IDA
  - Stage 1
    - Iron stores depleted
    - Decreased ferritin level
    - Increased TIBC
  - Stage 2
    - Iron-deficient erythropoiesis
    - Slight microcytosis
    - Slight decrease in hemoglobin
  - Stage 3 (usually no symptoms until this stage develops)
    - Decreased iron
    - Decreased ferritin
    - Increased TIBC and decreased transferrin saturation
- Lab values
  - Decreased Hgb
  - Decreased Hct
  - Decreased MCV
  - Decreased MCHC

Paroxysmal Nocturnal Hemoglobinuria (PNH)

- A type of hemolytic anemia
- Red cells are destroyed while patients sleep and upon arising, the patient notices bloody urine
- Nine cell surface proteins are missing from cells, including proteins that offer protection to red cells against lysis by complement
- Intravascular lysis
- Treatment includes transfusion support and bone marrow transplants
- Clinical symptoms include:
  - Pancytopenia
  - Hemolytic anemia
  - Bone marrow failure
  - Thrombosis
  - Elevated levels of hemoglobin F
  - Elevated reticulocytes but not appropriate with respect to level of anemia
- Screening procedures:
  - Sugar water test
    - 50% solution of patient's washed EDTA red cells are mixed with ABO/ Rh compatible serum and sugar solution
    - Solutions are incubated for 30 minutes and then centrifuged
    - Percent hemolysis is determined by spectrophotometry
    - Normal cells show less than 5% hemolysis and suspect cells show between 10% and 80% hemolysis
  - The Ham test
  - Flow cytometry

Paroxysmal Cold Hemoglobinuria

- Rare hemolytic anemia caused by anti-P
- Attaches to the red blood cells at lower temperatures and then activates complement at warmer temperatures
- Lysis occurs at body temperature
- Occurs almost exclusively in children as a result of viral disorders
- Results of cold reacting IgG autoantibody
- Severe lysis causes:
  - Hemoglobinemia
  - Hemoglobinuria
  - Increased back pain
  - Fever
  - Chills
  - Abdominal pain
- Screening test: Donath-Landsteiner test

Pyruvate Kinase Deficiency (PK)

- Second most common inherited erythrocyte enzyme deficiency
- Autosomal recessive trait
- Pennsylvania Amish have a high frequency of PK deficiency
- Red cells are unable to generate ATP from ADP resulting in cell shrinkage
- Leads to premature destruction of red cells in the spleen and liver as well as hemolytic anemia
- Produces rigid, inflexible cells
- Laboratory findings
  - Normochromic, normocytic
  - Varying degrees of reticulocytosis
  - Elevated 2,3-DPG because of abnormal enzyme deficiency
  - Moderate hemolysis
  - Marked polychromasia
  - Hct between 18% - 36%
  - Few nRBCs
- Fluorescent screen is used for identification

Sickle Cell Anemia

Hemoglobin C Disease and Trait

- Hemoglobin C disease is the substitution of lysine for glutamic acid
- Homozygous inheritance - Hemoglobin C disease
- Heterozygous inheritance - Hemoglobin C trait
- No hemoglobin A is produced
- 90% Hgb C
- 2% Hgb A_2
- 7% Hgb F
- Milder symptoms than sickle cell
- Clinical manifestation:
  - Usually normochromic normocytic
  - Usually > 50% target cells
  - Possible mild hypochromia
  - ***Bars of gold crystals***
  - Mild, chronic hemolytic anemia with splenomegaly

Hemoglobin SC Disease

- Combination of hemoglobin S and hemoglobin C
- Abnormal C gene from one parent and abnormal sickle gene from another
- Less severe than sickle cell anemia
- Laboratory findings:
  - Target cells
  - Folded erythrocytes
  - ***Washington monument crystals***

Sickle disease and sickle trait

- Homozygous (disease)
  - Valine replaces glutamic acid
  - Resistant to Plasmodium falciparum
  - Inherited from both parents and results in sickle cell disease
  - No hemoglobin A is produced (instead abnormal hemoglobin S is produced)
    - 80% hemoglobin S
    - 20% hemoglobin F
- Heterozygous (trait)
  - Results in sickle cell trait
  - Resistant to Plasmodium falciparum
  - 60% hemoglobin A
  - 40% hemoglobin S
  - normal amounts of hgb A_2 and hgb F
- Spleen
  - Eventually spleen loses it ability to clear abnormalities resulting in autosplenectomy
- Laboratory
  - ***Sickle cells***
  - Anisocytosis and poikilocytosis
  - Hypochromia and microcytes
  - ***Target cells*** (commonly seen in hemoglobinapathies)
  - Basophilic stippling, Howell-Jolly bodies and sickle cells (drepacoyctes)
- Diagnosis
  - Dithionate solubility test
    - Based on the principle of hemoglobin S precipitates
    - If no Hgb S present, no precipitate forms
  - Hemoglobin electrophoresis
    - Sickle patients will show two bands: Hgb F and S
    - Sickle trait patients will show three bands: Hgb F, A, and S

Sideroblastic Anemia (inherited or acquired)

- Excess iron accumulation due to ferritin aggregates in the cytoplasm of immature erythrocytes
- Body has plenty of iron but is incapable of using it in hemoglobin synthesis
- Iron enters the developing red cell but then accumulates in the mitochrondria
- Dimorphic picture:
  - Normochromic and hypochromic cells
  - Macrocytes, normocytes, and microcytes
- Defect in enzymes regulating heme synthesis
- Ringed sideroblasts are the result of the heme enzyme abnormalities
  - 10% to 40% of nRBCs in the bone marrow are ringed sideroblasts
- Possible causes:
  - Acquired
    - Lead poisoning
    - Alcoholism
    - Thalassemia
  - Hereditary
    - Defective sex-linked recessive gene
- Diagnosis:
  - Hypochromic
  - Dimorphism
  - Normal or increased platelets
  - Increased serum iron, serum ferritin, and % saturation
  - Erythrocytes may contain Pappenheimer bodies
  - Target cells may be present
  - Basophilic stippling may be seen
  - Increased ferritin and iron

Thalassemia

- Globin chain disorder; not enough functional Hgb A produced
- Microcytic process with normal iron status
- Alpha thalasemia
  - Barts hydrops fetalis (no alpha chains)
    - Most severe
    - No hgb A is formed
    - 80% Barts hemoglobin produced (unable to carry oxygen)
    - Incompatible with life
  - Hgb H disease (1 functional alpha chain)
    - 30% Hgb H formed
    - Heinz bodies and rigid RBCs are destroyed by the spleen
  - Alpha thalassemia trait (2 functional alpha chains)
    - Mild anemia or asymptomatic
  - Silent carrier (3 functional alpha chains)
    - Hematologically normal
- Beta thalassemia
  - Beta thalassemia major - little or no beta chains
    - Also known as Cooley's anemia
    - Results in excess of alpha chains (no hemoglobin A is produced)
      - 90% Hemoglobin F
    - Microcytic/hypochromic with polychromasia
    - nRBC
    - Changes in facial structures
    - Low Hgb levels (6-9 g/dL)
    - Transfusion may lead to iron overload
    - Enlarged spleen
  - Beta thalassemia trait (1 abnormal beta gene)
    - Microcytic hypochromic with low Hgb and Hct levels
    - Hgb A_2 increased
    - Hgb A decreased
    - Mimics IDA values but RBC count may be elevated due to bone marrow compensa- tion

QUESTION AND ANSWER

1. **Acidosis**

   A decrease in pH (increase in hydrogen ions)

2. **Agglutination**

   Clumping of cells

3. **Alkalosis**

   An increase in pH (decrease in hydrogen ions)

4. **Aplastic crisis**

   Severe drop in hemoglobin

5. **Erythrocyte sedimentation rate**

   ESR-Screening test indicative of inflammation. Measures the distance that RBCs will fall in a vertical tube in a given period of time

6. Hemoglobinopathy

Genetic defect that results in abnormal structure of one of the globin chains in a hemoglobin molecule

7. Polychromasia

Blue tinge to a red blood cell indicating its premature release from the bone marrow

8. Polycythemia

An increased concentration of red blood cells

9. Reticulocyte

Immature RBC. Reticulocyte count > 2.5% is indicative of increased erythropoiesis

10. Thrombus

Clot

11. What is the difference between extravascular hemolysis and intravascular hemolysis?

Extravascular hemolysis occurs when macrophages clear senescent red blood cells. RBC death normally occurs in the spleen (may also occur in the liver, lymph nodes, and bone marrow). RBCs are phagocytized and hemoglobin is broken down into its components. Iron is returned to the bone marrow and the amino acids from the globin chains are returned to the amino acid pool. Intravascular hemolysis occurs when red cells are lysed in the bloodstream. Hemoglobin is released into the plasma and breaks down into dimers. Haptoglobin binds free hemoglobin dimers and quickly becomes saturated. If intravascular hemolysis continues, the hemoglobin dimers will filter through the glomerulus causing hemoglobinuria. Abnormal hemoglobin concentrations will cause visible discoloration of plasma resulting in hemoglobinemia.

12. List the organs involved in hematopoiesis.

Bone marrow, liver, spleen, lymph nodes, and thymus

13. List the stages of red blood cell development from least mature to most mature.

CAP: pronormoblast, basophilic normoblast, polychromatophilic normoblast, orthochromic normoblast, reticulocyte, erythrocyte

ASCP: rubriblast, prorubricyte, rubricyte, metarubricyte, reticulocyte, erythrocyte

14. Normal hemoglobin levels are influenced by _____, _____, and _____.

Normal hemoglobin levels are influenced by age, sex, and altitude

15. State the normal ranges and the formulas for calculating the following:

MCV

MCV = (Hct ÷ RBC) X 10 Normal value: 80-100 fL

MCH

MCH = (Hgb ÷ RBC) X 10 Normal value: 27 to 31 pg

MCHC

MCHC = (Hgb ÷ Hct) X 100 Normal value: 32% - 36%

16. The rule of three

RBC X 3 = Hgb Hgb X 3 = Hct ± 3

Hgb normal value:14 to 18 g/dL Hct Normal Value: 42-52%

17. State the values for MCV and MCHC for the following types of anemia and give examples for each.

Normocytic/normochromic anemia:

normocytic/normochromic anemia: MCV: 80 - 100 fL MCHC: 32% - 36%

Examples include: aplastic anemia, blood loss anemia, hemolytic anemia

Microcytic/hypochromic anemia

Microcytic/hypochromic anemia: MCV < 80 fL MCHC < 32%

Examples include: iron deficiency anemia, thalassemia, anemia of chronic disease, sideroblastic anemia, lead poisoning

Macrocytic/normochromic anemia

Macrocytic/normochromic anemia: MCV > 100 fL MCHC: 32% - 36%

Examples include: Megaloblastic anemia (vitamin B12 and folic acid deficiency) and nonmegaloblastic anemia

18. Name some factors that will effect the ESR.

Factors that will effect the ESR are: plasma proteins, type of anticoagulant, poikilocytosis, age of the specimen, temperature, position and size of the tube being used

19. _____ and _____are two tests that are used to establish the presence of hemolysis.

Serum unconjugated bilirubin and serum haptoglobin are two tests that are used to establish the presence of hemolysis.

20. Define medullary hematopoiesis.

Medullary hematopoiesis is hematopoiesis that takes place in the bone marrow

21. In which immature red blood cell are the nucleoli most visible?

pronormoblast

22. What is the average diameter of a normal erythrocyte?

7 - 8 μm

23. Where is EPO produced?

kidney

24. What does the M:E ratio represent?

The ratio of granulocytes and their precursors to nucleated erythrocytes and their precursors. An increased ratio is indicative of infections and chronic myelogenous leukemia; a decreased ratio may mean decreased leukopoiesis. The M:E ratio is used with other factors to determine significance.

25. What is the precursor to the platelet?

megakaryocyte

26. Where does hematopoiesis take place in a child?

In the bone marrow

27. Where does hematopoiesis take place in the fetus?

yolk sac - during 2 - 8 weeks gestation

liver and spleen - 2nd - 5th month

bone marrow begins to function after the 5th month

28. Iron is stored as _____ in the bone marrow.

Iron is stored as hemosiderin in the bone marrow.

29. If a patient's hemoglobin is 10 g/dL, what would you expect the hematocrit to be?

30%

Hgb X 3 = Hct ± 3

30. Erythroblasts located in the bone marrow containing bright-blue specks when stained are called _____.

Erythroblasts located in the bone marrow containing bright-blue specks when stained are called sideroblasts. Sideroblasts are abnormal nucleated erythroblasts with granules of iron that have accumulated in the cell's mitochondria.

31. In a normal individual, what percent of erythrocytes are replaced daily?

approximately 1%

32. What is the last nucleated stage in a developing RBC?

metarubricyte

33. What is an easy way to judge the size of a normal erythrocyte?

A normal RBC is approximately the same size as the nucleus of a mature lymphocyte

34. What is the term used to describe a variation in shape of erythrocytes?

poikilocytosis

35. Another name for a sickle cell is _____.

drepanocyte

36. Another name for a tear drop cell is _____.

dacrocyte

37. What is the difference between a siderocyte and a pappenheimer body.

They are the same thing. On a Prussian blue stain they are called siderotic granules. On a Wright stain they are called Pappenheimer bodies

38. Which of the following can be seen on a Wright stain: howell jolly bodies, heinz bodies, reticulocytes, or siderocyts?

Of those listed, only howell jolly bodies can be seen on a Wright stain. However, pappenheimer bodies can also be seen on a Wright stain. Heinz bodies and reticulocytes are seen with a supravital stain - Heinz bodies = crystal violet and reticulocytes = new methylene blue or brilliant cresyl blue. Siderocytes can be seen with a Prussian blue stain

39. What are common anemias that are classified as hypochromic/ microcytic?

iron deficiency anemia, thalassemia, and anemia of chronic disease

40. _____ are commonly seen with megaloblastic anemia.

ovalocytes

41. A patient has an increased MCV and marked polychromasia, what else will be abnormal

Their would be an increased reticulocyte count

42. What are some examples of a supravital stain

new methylene blue, brilliant cresyl blue;, and crystal violet

43. An increased ESR is typically seen with which conditions?

Infections and rheumatoid arthritis

44. Where is hemoglobin produced?

in nucleated RBCs in the bone marrow

45. What are the normal hemoglobins?

Hemoglobin A $\alpha_2\beta_2$

Hemoglobin A_2: $\alpha_2\delta$

Hemoglobin F: $\alpha_2\gamma_2$

46. What are the values for the normal hemoglobins

Hemoglobin A $\alpha_2\beta_2$

Adult: 97% newborn: 20%

Hemoglobin A_2: $\alpha_2\delta$

Adult: 2% newborn: 2%

Hemoglobin F: $\alpha_2\gamma_2$

Adult 1% newborn: 80%

47. Proteins that extend from the outer surface and span the entire RBC membrane are called _____.

Proteins that extend from the outer surface and span the entire RBC membrane are called integral proteins

48. An iron-saturated, nucleated RBC is called _____.

Siderocyte

A sideroblast is a nucleated normoblast with unbound iron (not bound to hemoglobin

49. _____ is defined as a variation in the size of an RBC.

Anisocytosis

50. What is polychromasia?

A condition in which RBCs have a grayish color on a blood smear. It occurs when RBCs are released prematurely from the bone marrow.

51. Decreased serum haptoglobin can indicate _____.

Haptoglobin binds free hemoglobin in plasma after red cells lyse in circulation. When significant intravascular hemolysis takes place, haptoglobin is depleted which can be measured in plasma

52. An RBC has a decreased central area of pallor. What is this called?

Hypochromasia

53. A patiet with lead poisoning will typically have numerous red blood cells with _____.

Basophilic stippling

54. Pappenheimer bodies are also called _____.

Siderotic granules

55. How does the body respond to anemic stress?

You will see an increased number of reticulocytes in circulating blood. An increased number of reticulocytes in circulating blood is an indication of the bone marrow responding to anemic stress. Normal retic counts are 0.5% to 2.0%

56. What is the most stable parameter of the CBC?

MCV. The MCV is the most stable parameter of the CBC because it has less than 1% variability over time. Normal values are 80 to 100 fL

57. Name two normal hemoglobin types.

Deoxyhemoglobin and oxyhemoglobin

Carboxyhemoglobin, methemoglobin, and sulfhemoglobin are all abnormal hemoglobin. Increases in any of these can be potentially fatal. The oxygen dissociation curve represents oxygen saturation and the ease of which oxygen is released to tissues under both normal and abnormal conditions.

58. Macrophages in the liver are called _____.

Kupffer cells

59. What are the names of some hematopoietic growth factors?

Interleukins, and cytokines such as thrombopoeitin and erythropoeitin

60. What is the primary factor that stimulates the production of EPO?

Hypoxia (decreased oxygen levels in the tissues)

61. Heinz bodies are associated with _____.

denatured hemoglobin

62. The color of an EDTA tube is _____.

purple

63. The color of a sodium citrate tube is _____.

blue

64. What does the M:E ratio represent?

The ratio of myeloid elements and their precursors to erythroid elements and their precursors

65. Iron is stored as _____ in the bone marrow

hemosiderin

Ferritin is the major storage form of iron and measured in plasma. Hemosiderin is measured in urine and bone marrow and can be found in the liver, spleen, bone marrow and skeletal muscle. Iron is stored mostly in the liver as ferritin

66. _____ is typically used to coat capillary tubes.

heparin

67. Sideroyctes are typically seen in patients _____.

Sideroytes are typically seen in patients who have had splenectomies and in iron overload conditions

MULTIPLE CHOICE

68. Which RBC morphology is associated with abetalipoproteinemia?

A. Normocytes
B. Skipacytes
C. Acanthocytes
D. Dracoocytes

Answer: c

A normacyte is a normal red blood cell. A skipaycyte is a red or white blood cell that you skip (when in the school campus lab) because you are unable to identify it. A dracocyte is a tear drop cell.

69. A loss of RBC membrane deformability may be due to:

A. Decrease in spectrin
B. Increased ATP production
C. Krebs cycle
D. All of the above

Answer: a

Spectrin is a peripheral protein that is responsible for deformability and cellular integrity

70. The storage form of iron is called:

A. Ferritin
B. Hemosiderin
C. Protoporphyrin
D. Imastressin
E. Both A and B

Answer: e

Both ferritin and hemosiderin are storage forms of iron, However, ferritin is the storage form that is most metabolically available. It is plasma ferritin assays that are used in the laboratory to assess adequate iron stores.

71. _____ accounts for 70% of the body's iron.

A. Ferritin
B. Hemosiderin
C. Hemoglobin
D. Ferric iron

Answer: c

About 70 percent of the human body's iron is found in hemoglobin Ferritin and hemosiderin are storage forms and ferric iron is a type of iron

72. One molecule of hemoglobin can carry _____ molescules of oxygen.

A. Four
B. Three
C. Two
D. One

Answer: a

Each heme group is capable of carrying one molecule of oxygen. There are four heme groups in one molecule of hemoglobin.

73. Heme is produced in the _____.

A. Liver
B. Spleen
C. Yellow marrow
D. RBC precursors in the bone marrow

Answer: d

Heme is produced by red blood cell precursors located in the bone marrow

74. In a left shift of the oxygen dissociation curve, hemoglobin _____.

A. Has a lower affinity for oxygen resulting in more oxygen being delivered to the tisssues
B. Has a higher affinity for oxygen resulting in more oxygen being delivered to the tissues
C. Picks up more oxygen in the lungs and delivers more oxygen to the tissue
D. Picks up more oxygen in the lungs but delivers less to the tissue

Answer: d

A shift to the left results in high oxygen affinity. Oxygen will be loaded more easily in the lungs, however, it holds onto it more tightly in tissue resulting in less oxygen delivery.

75. Which of the following will cause a shift to the right on the oxygen dissociation curve?

A. A decrease in 2,3-BPG levels
B. Acidosis
C. Severe anemia
D. Both b and c
E. None of the above

Answer: d

Acidosis is an increase in hydrogen ions. Both acidosis and severe anemia will cause a shift to the right. A decrease in 2,3-BPG levels will cause a shift to the left. As acidity increases so does the concentration of hydrogen

76. The affinity of hemoglobin for oxygen is dependent upon _____.

A. A left or right shift on the oxygen dissociation curve
B. Transferrin saturation
C. The partial pressure of oxygen
D. None of the above

Answer: c

Hemoglobin's affinity for oxygen is dependent upon the partial pressure of oxygen which is the amount of oxygen needed to saturate 50% of the body's hemoglobin.

77. Which of the following hemoglobins are incapable of transporting oxygen?

A. Sulfhemoglobin
B. Methemoglobin
C. Carboxyhemoglobin
D. Deoxyhemoglobin
E. All of the above
F. Three of the above

Answer: F

Sulfhemoglobin, methemoglobin, and carboxyhemoglobin are all incapable of transporting or delivering oxygen

78. Which of the following forms the red blood cell's cytoskeletal system and is also responsible for cellular integrity?

A. Integral proteins
B. Peripheral protein
C. DNA
D. Ribosomes

Answer: b

The peripheral proteins, spectrin and ankyrin, are responsible for RBC deformability and elasticity which are crucial for the RBC to maneuver through vascular spaces which have diameters of only 1-3 μm. The RBC has a diameter of 6-8 μm.

79. Which of the following will cause a shift to the right on the oxygen dissociation curve?

A. A decrease in 2,3-BPG levels
B. Acidosis
C. Severe anemia
D. Both b and c
E. None of the above

Answer: D

Acidosis is an increase in hydrogen ions. Both acidosis and severe anemia will cause a shift to the right. A decrease in 2,3-BPG levels will cause a shift to the left

80. Two thirds of the body's total iron is bound to the _____ of a hemoglobin molecule.

A. Heme
B. Globin chains
C. ransferrin
D. Glycophorin A and B

Answer: a

81. The MCV is calculated with which of the following formulas?

A. (Hgb ÷ RBC) X 100
B. (Hct ÷ RBC) X 10
C. (Hct ÷ RBC) X 100
D. (Hct ÷ Hgb) X 10

Answer: b

82. An erroneous Hct will not affect _____.

A. MCV
B. MCHC
C. MCH
D. RDW

Answer: c

MCH is calculated as (Hgb ÷ RBC) X 10 so it would not be affected by an erroneous Hct. RDW is calculated with electronic cell counters. However, they calculate the RDW from the MCV and RBC results. Since the MCV uses the Hct in its calculation, an erroneous Hct result will affect the RDW result.41.

83. Which of the following will affect the ESR (erythrocyte sedimentation rate)?

A. Blood drawn in a sodium citrate tube
B. Blood drawn in an EDTA tube
C. Increased quantities of hemoglobin C
D. Anisocytosis or poikilocytosis
E. Plasma proteins
F. B and E
G. E and D

Answer: G

ESR is directly proportional to RBC mass and indirectly proportional to surface area. RBC shape, size, as well as fibinogen and globulin levels can cause an increase or decrease in ESR.

84. The body will compensate for anemia by _____.

A. A decrease in 2,3-DPG
B. An increase in 2,3-DPG
C. Decreased reticulocyte production
D. Increased reticulocyte production
E. B and D

Answer: E

The body will attempt to compensate for anemia by increasing 2,3-DPG and by increasing production of reticulocytes and releasing them early from the bone marrow

85. What are schistocytes?

RBC fragments. They are seen commonly seen in DIC, hemolysis, and burns

MORE QUESTION & ANSWERS

86. In what disease process is an increase in hemoglobin F seen?

Hemoglobin F is the predominant fetal hemoglobin. In adults, increased levels are seen with hemoglobinopathies and thalassemias. The highest levels of hgb F are seen in beta thalassemia major

87. What is the substitution in hemoglobin S?

Valine is substituted for glutamic acid

88. What is the substitution in hemoglobin C?

Lysine is substituted for glutamic acid

89. What is a diagnositic feature of megaloblastic anemia?

hypersegmentation of neutrophils

90. Why is the reticulocyte count increased in hemolytic anemia?

Bone marrow is trying to compensate for the blood loss by releasing immature erythrocytes into the blood

91. What is PNH?

paroxysmal cold hemoglobinuria. It is caused by the Donath-Landsteiner antibody (anti-P)

In PCH, the Donath-Landsteiner antibody binds to the RBCs if exposed to the cold and causes them to lyse when they return to body temp. It is often a secondary process to some viral diseases

92. What is Fanconi's anemia?

It is the hereditary form of aplastic anemia

93. What is polycythemia vera?

An increase in all blood lines (granulocytes, lymphocytes, RBCs, and platelets

94. Describe the electrophoresis pattern for sickle cell anemia.

80 - 95% hemoglobin S

1 - 10% hemoglobin F

2 - 3% hemoglobin A_2

No hemoglobin A is produced

95. Describe the blood smear for sickle cell anemia patients.

The blood smear will commonly show:

Sickle cells - Normal red blood cells are disc-shaped and easily change shape to facilitate their moving easily through your blood vessels. Red blood cells contain hemoglobin which carries oxygen from the lungs to the rest of the body. Sickle cells contain abnormal hemoglobin, hemoglobin S. This abnormal hemoglobin causes the cells to develop a sickle shape. Sickle cells are stiff and sticky and block blood flow in the blood vessels of the limbs and organs. In sickle cell anemia, sickle cells usually die after only about 10 to 20 days. The bone marrow can't make new red blood cells fast enough to replace the dying ones which results in anemia.

Target cells - these cells are commonly seen in individuals without a spleen. Since sickle cell patients often exhibit autosplenectomy, target cells are a typical finding

nRBCs - nRBCs (or normoblasts) are not normally seen in the peripheral blood. However, sometimes normoblasts may escape the bone marrow and enter the blood stream. Under normal conditions they are immediately destroyed by the spleen. This is not the case with many patients with sickle cell anemia. Sickle cell anemia patients who have undergone autosplenectomy will show nRBCs in their blood smear.

Howell-Jolly bodies - Howell-Jolly bodies are seen in cases where there is marked decreased splenic function. Common causes include splenectomy, trauma to the spleen, and autosplenectomy caused by sickle cell anemia.

Basophilic stippling - Occurs in conditions in which the synthesis of hemoglobin is impaired; the stippled particles are aggregates of ribosomes. Several diseases are associated with basophilic stippling and include lead poisoning, thalassemia, megaloblastic anemia, sickle cell anemia, and sideroblastic anemia.

96. What is the hallmark feature of beta thalassemia minor?

An elevated hemoglobin A_2

97. What is anemia of chronic disease (ACD)?

This is an anemia that is the result of inflammation, chronic infection, or malignancy. It is frequently seen in patients with tuberculosis, rheumatoid arthritis, systemic lupus, and chronic liver disease. Frequently seen as hypochromic/ microcytic

98. Which anemia has the distinguishing feature of a dimorphic population?

Sideroblastic anemia

99. Echinocytes include _____ and _____ cells.

Echinocytes include crenated and burr cells. They are caused by changes in osmotic pressure. They have evenly spaced round projections. They are commonly seen in liver disease and pyruvate kinase deficiency

100. What causes ringed sideroblasts?

Impaired heme synthesis

101. What causes acanthocytes (spur cells)?

Spur cells are caused by excessive cholesterol in their cell membrane. They are commonly seen in liver disease caused by alcoholism, post-splenectomy, and abetalipoproteinemia.

102. How can spur cells be distinguished from burr cells?

Spur cells have unevenly spaced projections whereas the projections in burr cells are evenly spaced

103. Spherocytes are associated with _____.

Spherocytes are associated with defects of the red cell membrane usually cell membrane proteins. This is seen in hereditary spherocytosis. They are also seen in sickle cell anemia, hemoglobin C, and thalassemia resulting in increased susceptibility of RBCs to damage causing spherocytes

104. What is one of the best indicator's of the body's iron stores?

Serum ferritin

105. Whole blood includes _____, _____, _____, and _____.

erythrocytes, leukocytes, platelets, and plasma

106. Explain the difference between extramedullar and intramedullary hematopoiesis.

In intramedullary hematopoiesis blood is produced within the bone marrow. Extramedullary hematopoiesis: is where blood cell production takes place outside the bone marrow. It occurs when the bone marrow cannot meet body requirements and occurs mainly in the liver and spleen. It is always an abnormal process and is usually accompanied by hepatomegaly and/ or splenomegaly

This study guide was designed specifically for medical laboratory students and those studying for ASCP certification as an MLT. It uses a unique approach and leaves out the gobbledygook and concentrates only on the stuff that you need to know. It begins with a thorough learning outline that leave a space for notes on each opposing page. This allows a student to add information and taylor it to their own specific needs. It ends will a thorough multiple choice and Q & A section.

Feel free to email kippy at kippy@kippyshortsox.com with any questions, concerns, or requests for corrections.

A supplement website is available at:

http://kippyshortsox.com/blog

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