HEALTHY PEOPLE 2020
This course aligns with the Healthy People 2020 initiative and discusses Blood Disorders and Blood Safety.
Hematology is the branch of internal medicine, physiology, pathology, clinical laboratory work, and pediatrics that is concerned with the study of blood, the blood-forming organs, and blood diseases. Hematology includes the study of etiology, diagnosis, treatment, prognosis, and prevention of blood diseases. The laboratory work that goes into the study of blood is performed by a clinical laboratory scientist.

INSTRUCTOR:
M. Lorraine Torres, Ed.D, MT (ASCP)
College of Health Sciences, Room 423
Phone: 747-7282
Office hours: MW 3:00 – 4:00 Friday 1:00 – 2:00 or by appointment
lorit@utep.edu

CLASS LOCATION
MW 8 - 9:20; College of Health Sciences 135

REQUIRED TEXTBOOKS:


COURSE DESCRIPTION
This course is the first part of a two part Hematology course series. Hematology I will cover the red cell series and Hematology II will cover the white cell series and hemostasis. Hematology I is designed to provide a basic understanding of the fundamental mechanisms involved in all facets of erythrocyte formation and function and etiology and treatment of red blood cell disorders. This course will examine normal and abnormal erythrocyte hematopoiesis and the resulting anemias, hemoglobinopathies, polycythemia, and other erythrocyte dyscrasias.
GOAL:
This course is designed to introduce the basic concepts of hematology and its clinical application to the Clinical Laboratory Science student. This course will provide the student with the knowledge to accurately identify normal and abnormal components of the hematopoietic system and identify various testing procedures to evaluate the patient results in light of clinical evidence.

OBJECTIVES
At the end of this course students will be able to:

1. Recognize and describe normal and abnormal hematopoiesis and its manifestation in bone marrow and peripheral smears.

2. Demonstrate their ability to differentiate between normal and abnormal blood cells in the peripheral blood.

3. Select the appropriate hematological analysis and evaluate results in light of patient abnormalities.

4. Given patient blood results / data, the student should be able to recall objectives at the basic taxonomic level and use this recall to interpret patient results to apply and examine knowledge gained and apply this knowledge in a problem-solving manner to correctly predict diagnosis of the patient.

5. Synthesize and appreciate the importance of accurate testing and evaluation in providing the patient and the clinician with the accurate tools for diagnosis, treatment and disease prevention by evaluating patient results and correlating these results to situations when erroneous results are obtained either though instrument error or apathy among laboratoriens.

NOTE: Each chapter of the book has written objectives. The student should answer these objectives in order to understand the material fully.

AFFECTIVE OBJECTIVES
Upon completion of this course, the student should be able to exhibit the appropriate responsible behaviors by demonstrating:

1. A positive attitude by being prepared for lecture and laboratory sessions completing assigned tasks on time and displaying self-motivation.

2. Organization by utilizing time effectively, sequencing and prioritizing tasks for completion with time constraints and maintaining a neat clean work.
3. Attention to detail by diligently pursuing accuracy and documenting data accurately and legibly.

4. Problem solving ability by explaining purpose of each step in diagnosis, interpretation, procedure, recognizing discrepancies in techniques or procedures and repeating necessary lab tests when necessary.

5. Dependability by following directions, working independently after being given directions.

6. Stability and self-confidence by approaching and performing routine tasks confidently without assistance and maintaining composure.

7. Appropriate interpersonal skills by cooperating and communicating effectively with classmates and instructors and displaying courteous, considerate behavior and appropriate appearance.

8. Ethical behavior and integrity by respecting confidentiality of patient information, complying with professional standards and code of ethics, adhering to safety policies and abiding by all rules and regulations of the institution.

Detailed Cognitive Objectives: Covered in Hematology I and II and Hematology Lab.
The objectives are listed beginning on page 10.

Psychomotor Objectives:
Refer to the Hematology Laboratory syllabus.

Class Attendance:
The student is expected to attend all classes. It is the responsibility of the student to notify the instructor of any absence. In the case of an emergency or illness, the instructor should be notified as soon as possible. When, however, in the judgment of the instructor, a student has been absent to a degree as to impair his or her status relative to credit for the course, the instructor may drop the student from the class with a W before the course drop deadline or with an F after the course drop deadline. The student will be dropped if they miss 4 or more classes. If a student is 10 minutes late this will be recorded as a tardy. Two tardies make one absence.

Test Policy:
There will be four examinations and a comprehensive final. The lecture exams may include brief essay questions and case studies along with multiple choice questions. No make-up exams will be offered. If you cannot attend an exam for a legitimate reason, (death, illness etc.) inform the instructor as soon as possible and the instructor will arrange a new time. If the
student does not make any arrangements (s)he will receive a ZERO on the exam. Please notice that our grade scale is different from the standard grade scale. In order to pass the course you must earn a 75% average and a 74.9% does not constitute a passing grade. Students in the CLS program cannot continue with the program with a grade of D or below.

EXAMINATIONS:
Four exams and a comprehensive final will be given. Exams are worth 40% of the total grade and the final is worth 40%. No make-up exams will be given. If an exam is missed (0%) the final grade will be based on the average of 4 exams. None of the test grades will be dropped. You must attend all classes. On a day that an exam is given in another class if you do not attend the hematology class 5 points will be taken off your next hematology exam.

GRADING SCALE:

<table>
<thead>
<tr>
<th>Grade</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>A</td>
<td>100 - 90%</td>
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<td>B</td>
<td>89 - 80%</td>
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<td>C</td>
<td>79 - 75%</td>
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<td>D</td>
<td>74.9 – 70%</td>
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<td>F</td>
<td>69 or below</td>
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FINAL GRADE CALCULATION:

<table>
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<tr>
<th>Component</th>
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<tbody>
<tr>
<td>Exams</td>
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<tr>
<td>Quizzes/ homework</td>
<td>20%</td>
</tr>
<tr>
<td>Final</td>
<td>40%</td>
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UNANNOUNCED QUizzes AND ASSIGNMENTS:
Tickets to Class and unannounced quizzes will be given throughout the course and will constitute 20% of the final grade. There are no make-up exams or quizzes. Late assignments will not be accepted and student will receive a grade of zero (0%) for that assignment.

This is the “Ticket to Class” You will need one each time class meets. You will not be allowed to enter the class without a ticket unless you have a “free” day. The tickets are posted on Blackboard and you are responsible for downloading them and completing the assignment.

University / CLS Policy on examinations:
When examinations are administered, students are to place backpack, papers and other personal belongings at the front or side of the room. Students will spread around the room when seating themselves. The Instructor may move you. No hats, caps, or bulky clothing may be worn. Phones may not be used as a calculator. Programmable calculators are not to be used in the CLS Program, only basic calculators will be allowed. Students will return examination papers in to the exam monitor before leaving the room for any reason; once a student has left the room, he/she may not continue with the examination. If a student misses an exam or a quiz, a make-up exam may be taken ONLY IF the student has informed the instructor of the
absence prior to the beginning of the examination, and only if the absence is approved by the instructor, only in rare instances will a student be excused from an examination or a quiz. If permission is given to take an exam or a quiz, it will be scheduled at the convenience of the instructor. Make-up exams/quizzes, while they may cover the same material may differ from the exam/quiz taken by the rest of the class in organization, format, or specific item data.

**MAKE UP EXAMS/QUIZZES (WITH INSTRUCTOR’S APPROVAL)**
Make up exams/quizzes will have an automatic deduction of 7 points. Make ups exams/quizzes, while they may cover the same material may differ from the exam/quiz taken by the rest of the class in organization, format, or specific item data.

**INSTRUCTIONAL STRATEGIES:**
Hematology is an entirely new subject for most students so it is imperative that the student keeps current in all the readings. MAKE A SPECIAL EFFORT TO LEARN ALL THE HEMATOLOGY VOCABULARY. Each assigned reading should be read at least twice. There will be a quiz and or a ticket to class at the beginning of almost every class. Each chapter of the book has written objectives. The student should answer these objectives in order to understand the material fully. At the end of the chapters there are review questions the student should answer to help assess the student’s grasp of the chapter content. The back of the chapter also includes a summary chart of the chapter to help the student recall the important subject matter.

**TIME NEEDED TO STUDY!**
For each hour you spend in class, you should spend 2-3 hours outside of class studying. Thursday is your study day and differential day (if you need more time)

**STUDENTS WITH DISABILITIES**
If you have a disability and need classroom accommodations, please contact The Center for Accommodations and Support Services (CASS) at 747-5148, or by email to cass@utep.edu, or visit their office located in UTEP Union East, Room 106. For additional information, please visit the CASS website at www.sa.utep.edu/cass. Accommodations are not given in retrospect.

**CELL PHONES/LAP-TOPS:**
All cell phones must be OFF or IN SILENCE MODE. Computers are allowed just for materials related to class. If a student is caught surfing the web or other unrelated subject/materials, he/she won’t be allowed to bring his/her computer to class again.

**ACADEMIC DISHONESTY:**
Won’t be tolerated. Any student suspected of academic dishonesty may be subject to disciplinary action, including the possibility of failure of the course and dismissal from the university. “Scholastic dishonesty includes but is not limited to cheating, plagiarism, collusion, the submission for credit of any work or materials that are attributable in whole or in part to
another person, taking an examination for another person, any act to give unfair advantage to student or the attempt to commit such acts.” Regent’s Rules and Regulations, Part One, Chapter VI, Section 3, Subsection 3.2, Subdivision 3.22. Since scholastic dishonesty harms the individual, all students, and the integrity of the university, policies on scholastic dishonesty will be strictly enforced.

Examples of “cheating” include (but not limited to):

- Copying from the homework, in-class work or exam paper of another student, engaging in written, oral, or any other means of communication with another student during an exam or homework assignment, or giving aid to or seeking aid from another student during a test;
- Possession and/or use during an exam or home test of materials which are not authorized by the person giving the test, such as class notes, books, or specifically designed “crib notes”;
- Using, obtaining, or attempting to obtain by any means the whole or any part of non-administered test, test key, homework solution, or computer program; using a test that has been administered in prior classes or semesters but which will be used again either in whole or in part without permission of the instructor; or accessing a test bank without instructor permission;
- Collaborating with or seeking aid from another student for an assignment without authority;
- Substituting for another person, or permitting another person to substitute for one's self, to take a test;
- Falsifying research data, laboratory reports, and/or other records or academic work offered for credit.

“Plagiarism” means the appropriation, buying, receiving as a gift, or obtaining by any means another's work and the unacknowledged submission or incorporation of it in one's own academic work offered for credit, or using work in a paper or assignment for which the student had received credit in another course without direct permission of all involved instructors. NOTE: This includes cutting-and-pasting and photocopying from on-line and other material.

“Collusion” means the unauthorized collaboration with another person in preparing academic assignments offered for credit or collaboration with another person to commit a violation of any provision of the rules on scholastic dishonesty.

Student Due Process
Students who believe they have been unfairly evaluated must:

Step 1: Attempt to resolve the difficulty with the faculty member.
Step 2: If the dispute cannot be resolved in Step 1, the student may within 5 school days appeal to the program director stating the evidence for the continued dispute in writing.

Step 3: If still unresolved a written complainant, evidence, and reason for the dissatisfaction must be submitted to the Assistant Dean of the College of Health Sciences. The Assistant Dean will call upon the Due Process Committee to review and make recommendations to the Assistant Dean based on statements, written evidence, and interviews with all parties involved.

Step 4: If the matter is still not settled, the complainant will notify the Dean, within five (5) school days. The Dean will then pursue the matter with the Vice President for Student Affairs.

The process will continue until the matter is resolved.

Part One and Three of the text book (chapters 1 - 5, 14 – 16) are the chapters on Hematology methods. The methods will be discussed mainly in the laboratory (CLSC 3257) however the student will be required to know the material from these chapters for the lecture class. Students need to be aware that this is a comprehensive course. The information in previous chapters we have covered and laboratory procedures will be built upon and tested over the information.

**TENTATIVE COURSE SCHEDULE**

<table>
<thead>
<tr>
<th>DATE</th>
<th>Topic to be covered</th>
<th>Chapter 6 review from general Bio.</th>
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<tbody>
<tr>
<td>Aug 27</td>
<td>Overview of Hematology &amp; Hematopoiesis</td>
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<tr>
<td>Aug 29</td>
<td>Bone Marrow / Red Blood Cell Structure &amp; Function</td>
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<tr>
<td><strong>Sep 3</strong></td>
<td><strong>Labor Day NO CLASS</strong></td>
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<tr>
<td>Sept 5</td>
<td>Erythrocyte structure &amp; function, hemoglobin</td>
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<tr>
<td>Sept 10</td>
<td>Erythrocyte structure &amp; function</td>
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<tr>
<td>Sep 12</td>
<td>Anemia: Diagnosis and Clinical Considerations (19)</td>
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<td>Sep 17</td>
<td>Evaluation of Cell Morphology / corpuscular constants</td>
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<td><strong>Sep 19</strong></td>
<td><strong>EXAM 1 (Chapters 6–10, 14, 17, &amp; 19)</strong></td>
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<td>Sep 24</td>
<td>Iron Metabolism</td>
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<tr>
<td>Sept 26</td>
<td>Hypochromic anemias / Fe deficiency</td>
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<tr>
<td>Oct 1</td>
<td>Hypochromic anemias</td>
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<tr>
<td>Oct 3</td>
<td>Megaloblastic anemia</td>
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<tr>
<td>Oct 8</td>
<td>Megaloblastic anemia</td>
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<tr>
<td>Oct 10</td>
<td><strong>EXAM 2 (chapters 6 - 11, 14, 17, 19- 21)</strong></td>
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Oct 15  Aplastic Anemia etc
Oct 17  Aplastic Anemia etc – **HOPE fair**
Oct 22  Hemolytic anemia: Intracorpuscular defects: Hereditary defects of membrane
Oct 24  Hemolytic anemia: Intracorpuscular defects: Hereditary defects of membrane
Oct 29  Hemolytic anemia: Intracorpuscular defects: Hereditary enzyme deficiencies
Oct 31  Hemolytic anemia: Intracorpuscular defects: Hereditary enzyme deficiencies
Nov 5    Principles of Automation
Nov 7    **EXAM 3 (chapters 6 - 11, 14 – 17, 19 -24)**

Nov 12  Hemolytic anemia: Intracorpuscular defects: The Hemoglobinopathies
Nov 14  Hemolytic anemia: Intracorpuscular defects: The Hemoglobinopathies
Nov 19  Hemolytic anemia: Intracorpuscular defects: Thalassemia
Nov 21  Hemolytic anemia Extracorpuscular defects
Nov 26  Hemolytic anemia Extracorpuscular defects
Nov 28  Hypoproliferative anemia
Dec 3    Quality Management, Quality Assurance and Quality Control
Dec 5    **EXAM 4 (chapters 6 - 11, 14 – 17, 19 - 28)**

DEC 13    Comprehensive final  9-12 Room TBD

**MLS Hematology cognitive objective covered in Hematology I, Hematology I Laboratory and Hematology II. Psycomotor objective performed in Preceptroship I and or II.**

Upon completion of this course, the student should be able to: Define, discuss, explain, identify and perform ... 

**Normal hematopoietic system**

Define hematopoiesis  Level 1

Theory of pluripotent stem cell development
Stem cell kinetics: Generative cell cycle
Hematopoietic inductive environment of regulatory growth factors and inhibitors
Apoptosis

Identify phases and site of origin for cellular development of active hematopoietic tissue in embryo and fetus  Level 1
Yolk sac
Mesoblastic phase
Hepatic phase (extramedullary)
Medullary/myeloid phase

Identify phases and site of origin for cellular development of active hematopoietic tissue in infant and young child  
Level 1
All red marrow spaces (all cell lines)
Thymus fully developed (T lymphs)
Secondary lymphoid tissue (B-cell, T-cell and NK-cell)

Identify phases and site of origin for cellular development of active hematopoietic tissue in adult  
Level 1
Red marrow (axial skeleton and proximal ends of long bones)
Primary and secondary lymphoid tissue (B-cell, T-cell and NK-cell)

Explain the role of other organ systems in hematopoiesis  
Level 2
Mononuclear phagocyte system
Spleen (Structure, blood flow, function)
Liver (Structure, blood flow, function)
Lymph nodes (Structure, blood flow, function)
Thymus (Structure, blood flow, function)

State the physical findings commonly present in hematologic disease  
Level 2
Splenomegaly
Hypersplenism
Hepatosplenomegaly
Lymphadenopathy

Bone Marrow Tissue

List indications for performing bone marrow examination  
Level 1

Describe bone marrow collection techniques  
Level 1
Aspiration
Core biopsy

Describe key terms and apply concepts used to assess bone marrow structure and function  
Level 2
Myeloid to erythroid ratio (M:E)/erythroid to granulocyte ratio (E:G)
Erythropoiesis
Granulopoiesis
Megakaryopoiesis
Non-hematopoietic cells
Cellularity: fat (yellow marrow) to cell (red marrow) ratio
Aplastic marrow
Hypoplastic marrow
Hyperplastic marrow

Describe concepts related to the assessment of iron stores and sideroblast population in the bone marrow

Type I
Type II
Type III

Perform differential count on normal bone marrow specimens

Distinguish between normal and abnormal hematopoietic elements found within the peripheral blood

Correlate bone marrow findings with peripheral blood evaluation

Prepare peripheral blood for routine hematologic procedure and smear analysis

Determine specimen acceptability

List appropriate anticoagulants and mechanism of anticoagulation

Identify acceptable ratio of anticoagulant to blood for specimens obtained from venipuncture and skin puncture

List reasons for rejecting specimens

Stain smears using Romanowsky dyes and techniques according to established procedures
   Manual, Automated

List and define components of stain and explain the principle

Judge the acceptability of blood smears through microscopic evaluation and established criteria
   Random distribution of cells
   Good stain quality
   Absence of artifact

Troubleshoot staining problems
Correlate peripheral blood evaluation with automated cell analysis Level 3

Enumerate and morphologically evaluate blood cells on Romanowsky stained smears Level 2

**Erythropoiesis**

Describe the distinctive features used to characterize developing cells Level 1
- Overall cell diameter or volume
- Nucleus (diameter or volume, relative diameter or volume, staining reaction, chromatin pattern, presence or absence of nucleoli)
- Cytoplasm (relative amount, staining reaction)
- Nuclear:cytoplasmic ratio

List the maturation sequence of developing erythrocytes given Romanowsky stained smears, electronic images or other visual means of representation of blood and bone marrow Level 1

Distinguish nucleated erythrocyte precursors from other hematopoietic elements Level 2

Categorize red cells Level 2
- Diameter or volume
- Shape
- Color
- Inclusions
- Distribution patterns

Describe nutritional and regulatory factors associated with erythropoiesis Level 2
- Erythropoietin (EPO)
- Iron
- Vitamins (B₁₂ / folate)

List hormones associated with erythropoiesis Level 1
- Estrogen/Androgens/Thyroxine/Growth hormone

Identify and discuss components of the mature red cell that are essential for survival and function Level 2
- Membrane composition
  - Lipids/Proteins/Skeletal proteins
- Membrane Function
  - Maintain RBC shape, deformability, and permeability
  - Support system for surface antigens
Transport and exchange of gases and ions (cationic pumps)

Describe metabolic pathways for maintenance of cell function
Embden-Meyerhof/glycolytic
Hexose monophosphate shunt
Methemoglobin reductase
Luebering-Rapoport

Level 1

**Erthrocytic Hemoglobin**

Summarize the mechanisms by which normal hemoglobin is structured and synthesized in the developing red cell

Iron transport, uptake, and supply
Protoporphyrin IX (heme) formation
Globin synthesis and genetic control (Chromosome 11 and 16)
Embryonic hemoglobins (Gower I, Gower II, Portland)
Adult hemoglobins (Hb A, Hb F, Hb A₂)

Describe normal hemoglobin-oxygen function using the oxygen dissociation curve (ODC)

Identify the effect various conditions can have on the oxygen dissociation curve
pH (Bohr effect)
Temperature
CO₂
2,3-DPG (2,3-BPG)
Hb S,F and other variants

Interpret the effect of various factors on the concentration of hemoglobin
Age and gender
Pregnancy
Altitude
Smoking
Associated disease
Altered hemoglobin derivatives
(carboxyhemoglobin/methemoglobin/sulfhemoglobin)

**Erythrocytic Catabolism**

Summarize the mechanism by which red cells are catabolized
Identify phases (extravascular, intravascular)
Trace the basic steps associated with each phase
Define terms associated with red cell destruction

Level 2

Level 1
Erythrocyte Evaluation

Describe procedures to evaluate erythrocytes and their physical properties using patient blood and quality control samples Level 1

Perform procedures to evaluate erythrocytes and their physical properties Using patient blood and quality control samples Level 2

State the clinical utility of histogram review in erythrocyte evaluation Level 1

Determine if results are in accordance with prescribed criteria for accuracy and precision Level 3

Discuss automated hemogram parameters used for erythrocyte evaluation Level 1

- Hemoglobin
- Hematocrit
- Mean cell volume (MCV)
- Mean cell hemoglobin (MCH)
- Mean cell hemoglobin concentration (MCHC)
- Red cell distribution width (RDW)

Calculate red blood cell indices when provided appropriate data Level 2

State the principles of method analysis for hemoglobin determination Level 1

- Hemoglobin measured at the point-of-care
- Cyanmethemoglobin method
- Other instrument methods for hemoglobin

Perform erythrocyte sedimentation rates Level 2

- Wintrobe
- Westergren and its modifications
- Automated
Perform standard reticulocyte assays
  Supravital smear method with Miller disc
  Supravital smear method without Miller disc
  Automated methods

Perform and interpret calculations associated with reticulocyte assays
  Corrected
  Absolute
  Production index (RPI)
  Reticulocyte hemoglobin concentration
  Reticulocyte mean volume
  Immature reticulocyte fraction (IRF) or reticulated hemoglobin content (CHr)

Determine the appropriate area of a peripheral blood smear to evaluate red blood cell morphology

Distinguish between normal and abnormal red blood cell morphology

List red blood cell count and indices reference values that account for variations in gender and age

Correlate automated hemogram parameters and calculated indices with each other and with peripheral smear exam results

Calibrate and perform preventive maintenance on instruments used to evaluate erythrocytes and their physical properties

Recognize and troubleshoot pre-analytical (pre-examination), analytical (examination), and post-analytical (post examination) causes of problems or unexpected results

Take corrective action to resolve unexpected results and/or events on instruments used to evaluate erythrocytes

Make decisions to recommend appropriate follow-up to prevent unexpected results and/or events from reoccurring

**Leukopoiesis**

State reference values that reflect variations in gender and age for the leukocyte counts in peripheral blood
  Total leukocyte count
  Relative and absolute values for neutrophil, lymphocyte, eosinophil,
basophil and monocyte counts

Identify factors that alter leukocyte values
   Physiologic variation
   Pathologic abnormalities

Enumerate and/or calculate leukocyte counts
   Relative values
   Absolute values

List morphologic features used to differentiate developing leukocytes
   Overall cell diameter or volume
   Nucleus
   Shape
   Relative diameter
   Nuclear to cytoplasmic ratio (N:C)
   Staining reaction
   Chromatin pattern
   Presence or absence of nucleoli
   Relative amount of cytoplasm
   Cytoplasmic staining properties
   Presence or absence of granules and staining reaction in cytoplasm

**Leukopoiesis: Granulocytes**

List the maturation sequence of neutrophils, eosinophils, and basophils

Differentiate distinguishing morphology for stages of developing blood granulocytes

Explain mechanisms that regulate and modulate granulopoiesis
   Regulatory growth factors and inhibitors
   Kinetics (life span, circulation)
   Biochemistry (granule content and surface membrane receptors, energy metabolism)

Explain the functions associated with granulocytes
   Chemotaxis
   Phagocytosis and killing
   Allergic response (eosinophils and basophils)
   Host defense against parasites (eosinophils)
   Hypersensitivity mediator (basophils and mast cells)
Leukopoeisis: Monocytes and Lymphocytes

Summarize structural and functional features that characterize monocytes and macrophages

Kinetics (life span, circulation, tissue phase)
Function (phagocytosis, antigen-presenting cells (APC), pathogen presenting cells)

List the maturation sequence of monocytes and macrophages

List the maturation sequence of lymphocytes

Summarize structural and functional features that characterize lymphopoiesis

Sites of formation and production (Bone marrow, Thymus, Lymph nodes and secondary lymphoid tissue)

Kinetics (Life span, Migration)
Function
Humoral immunity (B lymphocytes and subsets)
Cell mediated immunity (T lymphocytes and subsets)
Natural killing and antibody dependent cellular cytotoxicity

Recognize morphology of developing monocytes and macrophages

Recognize morphology of developing lymphocytes

Describe the use of monoclonal antibodies to differentiate lymphocytes by immunophenotype

B-cell lymphocytes and subsets
T-cell lymphocytes and subsets
Natural Killer (NK) cells
Plasma cells

Leukocyte Evaluation

Perform commonly used methods to evaluate leukocytes

State the principles and clinical utility of histogram/scatterplot review

Determine absolute and relative white cell counts on patient and control specimens using manual and automated methods in accordance with prescribed criteria for accuracy and precision

Calibrate and perform preventive maintenance on instruments used to evaluate white cells
Determine differential cell counting using automated methods Level 2

Evaluate white cell histograms and scatterplots for diagnostic and quality control purposes Level 3

Identify and classify normal and abnormal white cells on a properly stained Romanowsky blood smear Level 2

Correlate and verify automated cell counts and differentials with established criteria Level 3

Estimate the total white blood count from a smear Level 2

Correct leukocyte counts for the presence of nucleated red cells Level 2

Calibrate and perform preventive maintenance on instruments used to evaluate Level 2 leukocytes and their physical properties

Recognize and troubleshoot pre-analytical (pre-examination), analytical (examination), and post-analytical (post examination) causes of problems or unexpected results Level 3

Take corrective action to resolve unexpected results and/or events on instruments used to evaluate leukocytes Level 3

Make decisions to recommend appropriate follow-up to prevent unexpected results and/or events from reoccurring Level 3

Nonmalignant Leukocyte Disorders

Explain the classification of nonmalignant leukocytic disorders Level 1

Quantitative changes

Qualitative changes

Compare and contrast absolute values with relative values Level 2

Neutrophilia

Neutropenia

Eosinophilia

Eosinopenia

Basophilia

Associate quantiative and qualitative leukocyte disorders with expected results Level 1

Bone marrow production and release

Rate of entry into peripheral circulating pools
Shifts between circulating and marginating pools
Rate of exit into tissues

Identify morphologic changes in neutrophils that may accompany nonmalignant Level 2 neutrophilic disorders
  Shift to the left
  Toxic granulation
  Dohle bodies
  Vacuolization
  Leukemoid reaction
  Leukoerythroblastic reaction
  Agranulocytosis
  Hypossegmentation
  Hypersegmentation

State characteristic abnormalities and clinical features for the qualitative/functional disorders of neutrophils
  Pelger-Huet anomaly
  Alder-Reilly anomaly
  Chediak-Higashi anomaly
  May-Hegglin anomaly
  Chronic granulomatous disease (CGD)
  Myeloperoxidase deficiency
  Leukocyte adhesion deficiency

Describe qualitative and quantitative alterations of monocytes

Define monocytosis

Compare absolute monocyte values with relative values

Identify causes of monocytosis

Identify abnormal lipid accumulations within monocytes and macrophages

Identify causes of non-neoplastic disorders of lymphocytes and plasma cells

Define lymphopenia/lymphocytosis

Compare lymphocyte absolute values with relative values

Compare and contrast morphologic features of reactive lymphocytes and normal lymphocytes
  Size
Nucleus
Cytoplasm
Heterogeneity

Differentiate between reactive and resting lymphocytes on Romanowsky stained smears

Identify the causes of reactive lymphocytosis

**Red Blood Cell Disorders: Anemia**

Define anemia

State the clinical signs and symptoms of anemia
  - Hemoglobin
  - Hematocrit
  - Red blood cell count
  - RBC indices
  - Red cell distribution width (RDW)
  - Peripheral smear
  - Reticulocyte count
  - Bone marrow evaluation

List the categories used in a morphological classification of the anemias

Describe the expected laboratory results seen in the various pathophysiologic classifications of anemias
  - Decreased red cell production (Bone marrow failure, ineffective hematopoiesis, Myelophthsis)
  - Increased red cell destruction, hemolytic processes
  - Loss of red blood cells

Discuss the clinical utility of the RBC indices as relates to physiologic conditions

Explain sources of error of the red cell indices

Use the RBC indices as a quality control mechanism for assessing the validity of the erythrocyte count, hemoglobin, and hematocrit values

Define common terms used to describe red cell morphology
  - Anisocytosis
  - Poikilocytosis
  - Polychromatic
  - Rouleaux
  - Agglutination
Acanthocyte/Spur Cell
Codocyte/Target Cell/Leptocyte
Dacryocyte/Tear Drop Cell
Drepanocyte/Sickle Cell
Echinocyte/Burr Cell
Elliptocyte
Keratocyte
Schistocyte
Spherocyte
Stomatocyte
Basophilic stippling
Cabot rings
Heinz bodies
Howell-Jolly bodies
Malarial parasites
Pappenheimer bodies/siderotic granules
Hemoglobin crystals
Hemoglobin H

Describe the composition and morphology and list the possible pathologic conditions of various red blood cell inclusions

Red Blood Cell Disorders: Erythrocytosis (Polycythemia)

Define polycythemia

Differentiate between absolute polycythemia and relative polycythemia

Compare and contrast secondary polycythemia, and relative erythrocytosis

Etiology
Clinical features
Laboratory findings
Prognosis

Describe changes in the bone marrow and peripheral blood with polycythemia vera
**Red Blood Cell Disorders: Hypochromic Anemias**

Define hypochromic anemia  
List the causes of hypochromic anemias  
Discuss the etiology and pathophysiology of hypochromic anemias  
- Iron deficiency anemia  
- Sideroblastic anemia  
- Anemia of chronic disease  
- Hemochromatosis/ Hemosiderosis  
- Porphyrias  
- Thalassemia  

Compare and contrast laboratory findings in iron deficiency anemia, anemia of chronic disease/inflammation and sideroblastic anemia  
- Serum ferritin  
- Serum iron  
- Transferrin/ Total Iron Binding Capacity (TIBC)  
- Percent transferrin saturation  
- Bone marrow evaluation for ringed sideroblasts  
- Free erythrocyte protoporphyrin (FEP)/zinc protoporphyrin (ZPP)  
- Transferrin receptor tests  
- Hepcidin  

Outline a laboratory approach to the evaluation of a patient’s iron status  

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**Red Blood Cell Disorders: Megaloblastic Anemias**

Discuss the absorption and metabolism of vitamin B₁₂ and folate  
Describe clinical features of megaloblastic anemia  
Identify the hematologic abnormalities present in megaloblastic anemia  
- Peripheral blood changes  
- Bone marrow-morphological changes  

Compare and contrast pernicious anemia to the other types of vitamin B₁₂ deficiency  

Outline a sequential approach to the differential diagnosis of megaloblastic anemia using the following laboratory procedures  
- Mean corpuscular volume (MCV)  
- Blood and bone marrow smear evaluation
Serum B\textsubscript{12}  
Serum folate  
Red cell folate  
Anti-intrinsic factor antibodies  
Anti-parietal cell antibodies  
Methylmalonic acid  
Homocysteine

Differentiate nonmegaloblastic macrocytosis from megaloblastic anemia

Peripheral blood and bone marrow characteristics

Serum vitamin B\textsubscript{12} level

Serum folate level

Red cell folate level

Reticulocyte findings


Define aplastic anemia

Identify common factors associated with the development

Describe the clinical features and pathophysiology

Acquired aplastic anemia  
Fanconi’s anemia

Congenital pure red blood cell aplasia

Anemia caused by myelophthisis

Describe the laboratory findings

Peripheral blood changes

Bone marrow changes

Other laboratory findings

Define Fanconi’s anemia

Describe the genetics and possible pathophysiology

Describe the laboratory findings

Peripheral blood changes

Bone marrow changes

Other laboratory findings

Define pure red cell aplasia (Diamond-Blackfan anemia)

Describe the clinical features and pathophysiology
Describe the laboratory findings
  Peripheral blood changes
  Bone marrow changes
  Other laboratory findings

Define and differentiate Congenital dyserythropoietic anemias (types I, II, and III)

Describe the clinical features

Describe the laboratory findings

Define myelophthisis

Describe the clinical features

Describe the laboratory findings
  Peripheral blood changes
  Bone marrow changes
  Other laboratory findings

**Red Blood Cell Disorders: Hemolytic Anemias**

Describe the etiology, pathophysiology, clinical features, and laboratory findings of red cell membrane defects
  Hereditary spherocytosis
  Hereditary elliptocytosis
  Paroxysmal nocturnal hemoglobinuria (PNH)
  Hereditary pyropoikilocytosis
  Hereditary acanthocytosis
  Hereditary stomatocytosis (hydrocytosis)
  Hereditary xerocytosis

Identify and correlate data from laboratory tests that are used to detect increased RBC destruction and production due to RBC membrane abnormalities

Discuss the principle of the Osmotic fragility test
  Describe the clinical features
  Describe the laboratory findings
  Perform /observe the procedure
  Apply appropriate quality control procedures
  Evaluate results
Describe the utility of flow cytometry in assessing red cell membrane defects  Level 2

Describe the etiology, pathophysiology, and clinical features of red cell enzyme abnormalities
- Glucose-6-phosphate dehydrogenase (G6PD) deficiency
- Pyruvate kinase (PK) deficiency
- Methemoglobin reductase

Discuss the principles of G6PD assay, pyruvate kinase assay and staining for Heinz Bodies  Level 1

Identify laboratory test results based upon
- Describe the laboratory findings  Level 1
- Perform /observe the procedure  Level 2
- Apply appropriate quality control procedures  Level 2
- Evaluate results  Level 3

Red Blood Cell Disorders: Hemoglobinopathies

Define hemoglobinopathy  Level 1

Distinguish between qualitative and quantitative hemoglobin defects  Level 1

Describe clinical and laboratory findings of hemoglobinopathies  Level 1
- Hb SS
- Hb AS
- Hb CC
- Hb AC
- Hb DD
- Hb EE
- Hb SC

Identify the amino acid substitutions associated with sickle cell anemia and hemoglobin C disease  Level 1

Describe the physiologic abnormality associated with hemoglobin variants with altered oxygen affinity (Unstable hemoglobins, Methemoglobinemia)  Level 1

Describe the hemoglobin gene defect in alpha and beta thalassemia  Level 1

Define the hemoglobin defect in thalassemia  Level 1

Describe the terminology associated with thalassemias  Level 1
Alpha thalassemia
- 4 gene deletion
- 3 gene deletion (Hb H disease)
- 2 gene deletion
- 1 gene deletion

Beta thalassemia
- Beta-thalassemia major
- Beta-thalassemia intermedia
- Beta-thalassemia minor

Describe the clinical features associated with different gene combinations in alpha and beta thalassemia Level 1

Describe the pathophysiology of thalassemias Level 1
- Hemoglobin Lepore
- Delta-beta thalassemia
- Hb H
- Bart’s hemoglobin
- Hereditary persistence of fetal hemoglobin
- Hb Constant Spring

Identify the characteristic clinical and laboratory findings associated with thalassemia Level 1

Describe the peripheral blood morphology associated with different gene combinations in alpha and beta thalassemia Level 1

Discuss the principle of the solubility test for sickling hemoglobin Level 1
- Describe the laboratory findings Level 1
- Perform /observe the procedure Level 2
- Apply appropriate quality control procedures Level 2
- Evaluate results Level 3

Discuss the principles of hemoglobin electrophoresis (cellulose acetate, alkaline pH vs. citrate agar, acid pH) Level 1
- Describe the laboratory findings Level 1
- Perform /observe the procedure Level 2
- Apply appropriate quality control procedures Level 2
- Evaluate results Level 3

Describe the separation of hemoglobin by capillary electrophoresis Level 1
Discuss the principles of hemoglobin quantification (HbA, HbA2, HbF)  
- Describe the laboratory findings  
- Perform /observe the procedure  
- Apply appropriate quality control procedures  
- Evaluate results  

Describe acid elution test (Kleihauer-Betke) or flow cytometry in regards to Hemoglobinopathies  

Correlate screening test for sickling hemoglobin with peripheral blood morphology and electrophoretic patterns of hemoglobin  

Identify the electrophoretic patterns (cellulose acetate, alkaline pH vs. citrate agar, acid pH) Hb F, Hb A, Hb S, Hb C, Hb D, Hb E, Hb A2  

**Hemolytic Anemias**

Identify mechanisms of immune hemolytic anemias  

Define and describe the etiology and clinical features and laboratory findings of  
   - Alloimmune hemolytic anemias  
     - Acute hemolytic transfusion reaction  
     - Delayed hemolytic transfusion reaction  
     - Hemolytic disease of the newborn (HDN)  
   - Autoimmune hemolytic anemias  
     - Warm autoimmune hemolytic anemia (WAIHA)  
     - Cold autoimmune hemolytic anemia  
     - Cold agglutinin syndrome (Idiopathic, Secondary)  
     - Paroxysmal cold hemoglobinuria  

Identify mechanisms of drug-induced immune hemolytic anemia  

Identify the etiology of nonimmune hemolytic anemia  
   - Infectious organisms  
   - Mechanical agents  
   - Chemicals  

Describe the hematologic findings associated with nonimmune hemolytic anemias  
   - Malaria  
   - Babesiosis  
   - Bartonellosis
Clostridium perfringens (welchii) infection
Cardiac prosthetic devices
Microangiopathic hemolytic anemia
Chemicals and venoms
Thermal injury
Disseminated intravascular coagulation

**Acute Blood Loss**

Describe the etiology of anemia of acute blood loss  
List the clinical symptoms of acute blood loss  
Identify the laboratory findings of acute blood loss

**Anemias associated with systemic disorders**

Describe the clinical features and laboratory findings associated with nonhematologic disorders
- Chronic disorders and inflammation
- Connective tissue disorders
- Malignant diseases
- Renal disease
- Liver disease
- Alcoholism
- Endocrine disease

**Neoplastic Disorders**

Define and list categories associated with Neoplastic Disorders of Leukocytes  
- Leukemias
- Myelodysplastic syndromes
- Myeloproliferative disorders
- Lymphoproliferative disorders

Identify major systems used to classify neoplastic disorders of leukocytes
- French, American-British (FAB) Cooperative Group
- World Health Organization (WHO)

Observe and/or perform procedures, apply appropriate quality control procedures, Level 2 and interpret laboratory findings for laboratory procedures used in the identification, classification and differentiation of neoplastic disorders
- Complete blood count
Hemograms
Scatterplots and histograms

Review the criteria used to classify nonmalignant leukocytic disorders  
Quantitative changes  
Qualitative changes (inherited, acquired)

Identify on Romanowsky stained smears, photographs, electronic images or other visual means of representation of morphologic changes in neutrophils that may accompany nonmalignant neutrophilic disorders  
Shift to the left  
Toxic granulation  
Döhle bodies  
Vacuolization  
Leukemoid reaction  
Leukoerythroblastic reaction  
Agranulation, hypogranulation  
Hypossegmentation  
Hypersegmentation  
Intracellular microorganisms

Compare and contrast the principles of various cytochemical stains and the cell lineages they react with  
Myeloperoxidase  
Sudan black B (SBB)  
Esterases (specific substrate/non-specific substrate)  
Periodic-acid Schiff (PAS)  
Leukocyte alkaline phosphatase (LAP)  
Tartrate resistant acid phosphatase (TRAP)  
Iron staining

Describe the use of various diagnostic techniques used to assess neoplastic disorders of blood and bone marrow cells  
Immunophenotyping  
Terminal deoxynucleotidyl transferase (TdT)  
Monoclonal antibodies  
Myeloid from lymphoid  
T and B cell immunophenotypes  
Acute myelocytic leukemia (AML) subgroups cell lineages  
Cytogenetics  
Molecular genetics
Apply knowledge and skills in interpreting laboratory results and recognizing clinical syndromes that are unique to the neoplasm  

Read case studies of neoplastic disorders and apply knowledge and skills in interpreting laboratory results  

**Acute Leukemias**

Apply general criteria to classify leukemias  
Cell maturity (Acute/Chronic)  
Cell lineage (Myeloid / nonlymphoid)  
Lymphoid  

Describe the clinical findings and laboratory results for leukemia  

Compare the FAB with the WHO acute myeloid leukemia subgroups and apply diagnostic blood and bone marrow findings to the differential identification  

FAB classification  
M0 -- acute myeloid leukemia with minimal differentiation  
M1 -- acute myeloid leukemia without maturation  
M2 -- acute myeloid leukemia with maturation  
M3 -- acute promyelocytic leukemia  
M4 -- acute myelomonocytic leukemia  
M5 -- acute monoblastic leukemia  
M6 -- acute erythroleukemia  
M7 -- acute megakaryoblastic leukemia  

WHO classification  
AML with recurrent genetic abnormalities  
AML with myelodysplasia-related changes  
Therapy-related myeloid neoplasms  

List the WHO acute leukemia subgroups  
AML with recurrent genetic abnormalities  
AML with myelodysplasia-related changes  
Therapy-related myeloid neoplasms  
AML, not otherwise specified  

Interpret findings from immunophenotypic, cytogenetic and molecular findings and apply to criteria used by WHO  

Describe for each leukemia  
Clinical findings and symptoms
Incidence and epidemiology
Risk factors associated with the development of leukemia
Hereditary abnormalities
Environmental
Viral infections
Immunologic disorders

Identify the pathophysiology of leukemia
   Stem cell clonality
   Oncogene and tumor suppressor gene development

Describe the survival rates and prognosis

Describe the treatment options and correlation with hematologic complications
   Level 1
   Chemotherapy
   Bone marrow/stem cell transplant

Identify diagnostic findings on permanently stained blood and bone marrow smears, photographs, kodachromes, or electronic images by which the FAB cooperative group and WHO classify acute leukemia. Morphology, number, and differentiation of blast and immature cells
   Greater than 30%
   Predominant cell type
   Auer rods

Define the reactivity of leukemic cells with cytochemical stains

Apply diagnostic blood and bone marrow findings to the differential identification
   Level 3
   Acute myeloid leukemia (AML)
   Acute nonlymphocytic leukemia (ANLL)
   M0--acute myelogenous with minimal differentiation
   M1--acute myelogenous without maturation
   M2--acute myelogenous with maturation
   M3--acute promyelocytic leukemia
   M3m--acute promyelocytic leukemia variant
   M4--acute myelomonocytic leukemia
   M4Eo--acute myelomonocytic leukemia variant
   M5--acute monocytic leukemia
   M5a--poorly differentiated
   M5b--well differentiated
M6—acute erythroleukemia
M7—acute megakaryocytic leukemia
Acute lymphocytic leukemia (ALL): L1, L2, L3—Burkitt's

List the subgroups (WHO) and apply diagnostic blood, bone marrow, immunophenotype, cytogenetics and molecular findings to the differential identification
B lymphoblastic leukemia/lymphoma, not otherwise specified
T lymphoblastic leukemia/lymphoma

Interpret findings from an immunologic workup to formulate an immunophenotypic classification for ALL apply to criteria used by WHO
B lineage
Early B precursors
“Common” CALLA (CD10) positive
Pre-B
T-cell lineage and early T precursor (pro-T, pre-T, cortical-T, medullary-T)
Precursor lymphoid neoplasms

List cytogenetic and molecular abnormalities commonly associated with the major acute leukemic subtypes

Myelodysplastic Syndromes (MDS)
Define and describe cellular features that characterize the MDS
Dyserythropoiesis
Dysgranulopoiesis
Dysmegakaryocytopenia

List subgroups recognized by the World Health Organization (WHO) Cooperative Groups for the MDS classification and discuss the rationale for revisions to the classification
Refractory cytopenia with unilineage dysplasia (RCUD)
Refractory anemia (RA)
Refractory neutropenia (RN)
Refractory thrombocytopenia (RT)
Refractory anemia with ringed sideroblasts (RARS)
Refractory cytopenia with multilineage dysplasia (RCMD)
Refractory anemia with excess blasts (RAEB)
RAEB-1
RAEB-2
Myelodysplastic syndrome, unclassifiable (MDS-U)
Myelodysplastic syndrome with isolated del (5q)
List subgroups recognized by the French, American, and British (FAB) Cooperative Level 1 Group for the MDS classification

- Refractory anemia (RA)
- Refractory anemia with ringed sideroblast (RARS)
- Refractory anemia with excess blast (RAEB)
- Chronic myelomonocytic leukemia (CMML)
- Refractory anemia with excess blasts in transition (RAEB-t)

Identify key morphologic features on permanently stained blood and bone marrow smears, photographs, electronic images or other visual means of representation Level 2

Correlate the diagnostic blood and bone marrow findings to the differential identification Level 3

Describe characteristics of MDS Level 2
- Median age of onset
- Epidemiology
- Chromosomal association with pathogenesis
- Clinical course with associated hematologic changes
- Treatment options
- Prognosis

**Chronic Myeloproliferative Neoplasms**

Classify Chronic Myeloproliferative Neoplasms by cell type Level 1
- Granulocytes—Chronic myelogenous/granulocytic leukemia (CML/CGL)
- Erythrocytes—polycythemia vera (PV)
- Megakaryocytes—essential thrombocytopenia (ET)
- Fibroblasts—agnogenic myeloid metaplasia (AMM)

List Chronic Myeloproliferative Neoplasms subtypes Level 1
- Chronic myelogenous leukemia (CML) BCR/ABL1 positive
- Essential thrombocytopenia (ET)
- Primary myelofibrosis (PMF)
- Chronic neutrophilic leukemia (CNL)
- Chronic eosinophilic leukemia not otherwise specified (CEL, NOS)
- Mastocytosis

List subgroups recognized by WHO for the myelodysplastic/myeloproliferative classification and discuss the rationale for the classification Level 2
- Chronic myelomonocytic leukemia (CMML)
- CMML-1
CMML-2
Atypical chronic myeloid leukemia (aCML), BCR-ABL1 negative
Juvenile myelomonocytic leukemia (JMML)
MDS/MPN, unclassifiable

Discuss and compare features commonly shared by Chronic Myeloproliferative Neoplasms

Clinical manifestations
Pathophysiologic mechanisms
Blood and bone marrow findings
Transitional forms between stages
Disease evolution with potential for blastic transformation

Identify key morphologic features on permanently stained blood and bone marrow smears, photographs, kodachromes, or electronic images

Correlate diagnostic criteria to these findings for the differential identification

Chronic myelogenous leukemia (CML)
Leukocytosis with absolute neutrophilia and left shift maturation
Absolute basophilia and eosinophilia
Thrombocytosis
Bone marrow hypercellularity with granulocytic proliferation
Cytogenetic (karyotype): t(9;22)(q34;q11)
Molecular products: BCR/ABL fusion gene, fusion mRNA

Polycythemia vera (PV)
Increased red blood cell (RBC) mass
Leukocytosis with mild left shift maturation and basophilia
Thrombocytosis
Bone marrow hypercellularity with all cell lines increased
Molecular studies (JAK2)
Red cell morphology (Initial phase, “Spent” phase)

Essential thrombocythemia (ET)
Marked thrombocytosis with platelet aggregates and abnormal forms
Megakaryocytic hyperplasia of bone marrow
Molecular studies

Primary myelofibrosis (PMF)
Leukoerythroblastosis with teardrop-shaped red cells
Leukocytosis with left shift maturation to occasional immature myeloid cell
Bone marrow fibrosis and relationship to megakaryocytic hyperplasia
Molecular studies
Identify treatment options and recognize effects on peripheral blood white cells, Level 3
Chemotherapy
Splenic irradiation/splenectomy
Phlebotomy
Bone marrow or stem cell transplant
Targeted molecular therapy

**Chronic Lymphoproliferative Disorders**
Name and classify the chronic lymphoid leukemias by T and B cell lineage, Level 1
Chronic lymphocytic leukemia (CLL)
B-cell prolymphocytic leukemia (PLL)
Plasma cell neoplasms
Hairy cell leukemia (HCL)
Adult T-cell leukemia
Sézary syndrome
Extranodal marginal zone lymphoma or mucosa-associated lymphoid tissue (MALT lymphoma)
Follicular lymphoma
Mantle cell lymphoma
Diffuse large B-cell lymphoma, not otherwise specified
Burkitt lymphoma

Identify key morphologic features on permanently stained blood and bone marrow smears, photographs, kodachromes, or electronic images, Level 2
List diagnostic features CLL, Level 1
Median age of onset
Symptoms and clinical findings
Blood and bone marrow findings
Peripheral blood absolute lymphocytosis
Leukemic cell line of mature, small lymphocytes with monotonous morphology and smudge/basket cells
Immunophenotypic cell surface markers and clonality
Bone marrow lymphocytosis

Recognize and describe features associated with aggressive forms of the disease, Level 1
Autoimmune hemolytic anemia (AIHA)
Chromosome and/or molecular abnormalities
Richter’s syndrome
Immunophenotypic cell surface markers

Name and compare systems used to stage disease severity and progress, Level 2
Modified Rai
Binet

Discuss the diagnostic features of PLL
Level 2
Median age of onset and gender
Clinical finding of severe splenomegaly
Blood and bone marrow findings
Markedly elevated white count with absolute lymphocytosis
White cell differential predominantly of prolymphocytes (greater than 55%)
Immunophenotypic profile
Chromosome and/or molecular

Discuss the diagnostic features of HCL
Level 2
Median age of onset and gender
Clinical finding of severe splenomegaly
Blood and bone marrow findings
Pancytopenia
Morphology: leukemic cell line of “hairy” cells
Immunophenotypic B-cell profile
“Dry” tap; marrow fibrosis and infiltrates

Discuss treatment options
Level 2
Splenectomy
Other drugs
Describe laboratory findings seen in the variant form of HCL
Level 1

List diagnostic features of Adult T-cell leukemia
Level 1
T-cell large granular lymphocytic leukemia (LGL)
Human T-cell lymphotropic virus-1 (HTLV-1)
Endemic areas

Apply diagnostic criteria to blood and bone marrow findings for the differential identification of Adult T-cell leukemia
Level 2
Lymphoid cell line of small to large cells with cloverleaf/knotty nucleus
Immunophenotypic T cell associated profile

Identify key morphologic features on permanently stained blood and bone marrow smears, photographs, electronic images or other means of visual representation
Level 2

List diagnostic features of Sézary syndrome
Level 1
Relationship to mycosis fungoides
Clinical findings--skin involvement

Review blood and bone marrow findings of Sézary syndrome Level 2
Absolute lymphocytosis
Morphology: lymphoid cell line of medium cells with cerebriform nucleus
Immunophenotypic T cell associated profile

Lymphoma
Define lymphoma and generally classify using key terminology Level 1
Hodgkin
Reed-Sternberg cells
Rye modified cells
Non-Hodgkin

Outline a multidisciplinary workup and list laboratory findings used to diagnose Level 2 and stage Hodgkin lymphoma
Complete blood count (CBC)
Liver function tests
Renal function tests
Blood and bone marrow findings of Hodgkin's lymphoma
Radiologic studies
Physical examination
Lymph node biopsy
Recognize key morphologic features and correlate with diagnostic criteria for the Level 3 presence of lymphoma cells

Plasma Cell Disorders
Name disorders based on proliferation of plasma cells and abnormal Level 1 production of immunoglobulins

Discuss classification based on proliferation of plasma cells and abnormal Level 2 production of immunoglobulins
Multiple myeloma
Waldenstrom’s macroglobulinemia
Plasma cell leukemia (PCL)
Heavy-chain disease
Monoclonal gammopathy of undetermined significance (MGUS)

Compare and contrast classification based on proliferation of plasma cells Level 3 and abnormal production of immunoglobulins
Compare and contrast the following for plasma cell disorders

**Level 3**

**Pathophysiology**

**Clinical findings**

**Laboratory findings**

- Complete blood count (CBC) and peripheral smear review
- Bone marrow biopsy including immunophenotypic cell markers
- Blood and urine protein electrophoresis and immunoelectrophoresis
- Quantitative immunoglobulins
- Chemistry panels—blood urea nitrogen, creatinine, calcium, lactic dehydrogenase
- Serum viscosity
- Beta-2-microglobulin
- Radiologic studies of bones

Identify key morphologic features for plasma cell disorders on permanently stained blood and bone marrow smears, photographs, electronic images or other visual means of representation

**Level 2**

- Flaming plasma cell
- Mott cells
- Rouleaux formation of red blood cells

**Thrombopoiesis/megakaryopoiesis**

List the maturation sequence for stages of developing megakaryocytes and platelets

**Level 1**

Cite reference values for absolute platelet counts in the peripheral blood

Correlate quantitative variations with disease manifestations

- Thrombocytopenia
- Thrombocytosis

Correlate functional or qualitative variations of platelets with disease manifestations

**Level 3**

Perform absolute platelet counts on patient and control specimens using manual and automated methods in accord with prescribed criteria for accuracy and precision

**Level 2**

State the principles of method analysis and histogram/scatterplot review

Compare absolute count with those estimated from blood smear exam

Identify platelets and platelet morphologic variations on a properly prepared
Romanowsky stained blood smear and/or recognize factors that alter hemogram results
  Platelet satellitism
  Platelet aggregates
  Giant platelets
  Cell fragments
  Extreme microcytosis

Evaluate platelet histograms and scatterplots for diagnostic and quality control purposes
  Platelet satellitism
  Platelet aggregates
  Giant platelets
  Cell fragments
  Extreme microcytosis
  Agranular and hypogranular platelets

Recognize and troubleshoot pre-analytical (pre-examination), analytical (examination) and post-analytical (post-examination) causes for problems or unexpected results

Make decisions to recommend appropriate follow-up to prevent unexpected results and/or events from reoccurring

Calibrate and perform preventive maintenance on instruments used to evaluate platelets

**Hemostasis/ Coagulation**

Define hemostasis

Explain the general interaction of systems involved in maintaining hemostasis

Of systems involved in maintaining hemostasis describe how changes in one effect the other
  Vasculature
  Platelets
  Plasma coagulation factors
  Fibrinolysis

Differentiate between primary and secondary hemostasis

**Vascular**

Explain the functions of the vascular system in maintaining hemostasis
Describe metabolic functions of the endothelium and substances contributing to the thromboresistance properties of endothelium

- Heparan sulfate
- Thrombomodulin
- Tissue plasminogen activator
- Prostacyclin (PGI2)
- Tissue factor pathway inhibitor

**Platelets**

Discuss the production of platelets

State the average time in circulation, normal peripheral count, and total body distribution of platelets

Describe the ultrastructural components of a platelet

- Alpha granules
- Dense bodies
- Lysomes
- Microtubules
- Open canalicular system
- Platelet membrane
- Glycocalyx

Discuss the physiological role of platelets in hemostasis

- Platelet plug formation
- Maintaining normal vascular integrity

Describe the series of morphologic changes that occur in platelets following physiologic stimulation

- Adhesion
- Aggregation
- Activation

Discuss the effect of aspirin on platelet function

- Biochemical mechanism
- Duration of the effect

Discuss principle for platelet aggregometry and platelet function analyzers

Interpret results of platelet function assay tests

- Significance in terms of platelet function
Associated abnormal conditions
Sources of error

Discuss the principle and clinical significance of platelet aggregation
Level 1

Describe the principle of light transmittance, whole blood impedance and
lumiaggregometry
Level 1

Perform the procedure
Level 2

Describe the procedure
Level 2

Describe appropriate quality control procedures and sources of error
Level 1

Interpret results and clinical significance
Level 3

Plasma coagulation factors

Define the coagulation factors
Level 1
Roman numerals
Common names
Synonyms

Discuss the physiological role of the coagulation phase within the
hemostatic process
Level 1

Discuss characteristics of the coagulation factors
Level 1
Contact group
Prothrombin group
Fibrinogen group

List the vitamin K-dependent factors
Level 1

Compare and contrast the plasma-based (in vitro) and cell-based (in vivo)
mechanisms of coagulation
Level 3
Level 3
Plasma-based (in vitro) mechanism
Intrinsic
Extrinsic
Common
Cell-based (physiologic, in vivo) mechanism
Initiation
Amplification
Propagation

Identify substances that are contact activators \textit{in vitro} \hspace{1cm} \text{Level 1}

Summarize the interaction of the coagulation system with the vascular and platelet systems to form a hemostatic plug \hspace{1cm} \text{Level 2}

Describe the physiologic controls of hemostasis \hspace{1cm} \text{Level 1}
- Blood flow
- Feedback inhibition
- Liver clearance

Identify the inhibitors of hemostasis \hspace{1cm} \text{Level 2}
- Antithrombin III
- Heparin cofactor II
- Tissue factor pathway inhibitor (TFPI)
- Protein C
- Protein S
- Alpha-2-macroglobulin
- Alpha-1-antitrypsin
- C1 inactivator
- Z-dependent protease inhibitor (ZPI)

Identify the special precautions that must be taken in the collection and subsequent handling of specimens for coagulation testing \hspace{1cm} \text{Level 1}
- Anticoagulant
- Ratio of blood to anticoagulant
- Patient hematocrit values
- Centrifugation
- Storage conditions including temperature
- Transport
- Phlebotomy procedure
  (e.g., time tourniquet is on arm, needle gauge, probing, etc.)

Identify and describe tests that are used to monitor the coagulation phase of Hemostasis \hspace{1cm} \text{Level 1}

Discuss the principle and clinical significance of the Prothrombin time test \hspace{1cm} \text{Level 1}
- Perform the procedure \hspace{1cm} \text{(performed in preceptorship)}
- Describe the procedure \hspace{1cm} \text{Level 2}
- Describe appropriate quality control procedures and sources of error \hspace{1cm} \text{Level 1}
Interpret results Level 3
Describe the International Normalized Ratio (INR) Level 1
Calculate an INR given the international sensitivity index of the thromboplastin Level 2
Describe interferences and sources of error Level 1

Discuss the principle and clinical significance of the Activated partial thromboplastin time Level 1
Perform the procedure (performed in preceptorship) Level 2
Describe the procedure Level 2
Describe appropriate quality control procedures and sources of error Level 1
Interpret results Level 3
Describe interferences and sources of error Level 1

Discuss the principle and clinical significance of the Activated clotting time Level 1
Perform the procedure (performed in preceptorship) Level 2
Describe the procedure Level 2
Describe appropriate quality control procedures and sources of error Level 1
Interpret results Level 3
Describe interferences and sources of error Level 1

Discuss the principle and clinical significance of the Thrombin clotting time Level 1
Perform the procedure (performed in preceptorship) Level 2
Describe the procedure Level 2
Describe appropriate quality control procedures and sources of error Level 1
Interpret results Level 3
Describe interferences and sources of error Level 1

Discuss the principle and clinical significance of the Fibrinogen assay Level 1
Perform the procedure (performed in preceptorship) Level 2
Describe the procedure Level 2
Describe appropriate quality control procedures and sources of error Level 1
Interpret results Level 3
Describe interferences and sources of error Level 1

Discuss the principle and clinical significance of Factor assays Level 1
Perform the procedure (performed in preceptorship) Level 2
Describe the procedure Level 2
Describe appropriate quality control procedures and sources of error Level 1
Interpret results Level 3
Describe interferences and sources of error Level 1
Identify technical conditions that cause false coagulation testing results  Level 1

**Fibrinolytic system**

Define fibrinolysis  Level 1

Discuss the physiological role of the fibrinolytic system  Level 1

Identify the major components of the fibrinolytic system  Level 1

Discuss the mechanisms of the activation of plasminogen  Level 1

- Intrinsic activators
- Extrinsic activators
- Exogenous activators

List the major fragments of fibrinogen degradation  Level 1

Explain the role and clinical significance of physiologic controls  Level 1

- Alpha-2-antiplasmin
- Alpha-2-macroglobulin
- Plasminogen activator inhibitors (PAI)

Identify and describe laboratory procedures that are used to evaluate the fibrinolytic system  Level 1

Discuss the principle and clinical significance of the FDP assay  Level 1

- Perform the procedure  (performed in preceptorship)  Level 2
- Describe the procedure  Level 2
- Describe appropriate quality control procedures and sources of error  Level 1
- Interpret results  Level 3

Discuss the principle and clinical significance of the D-Dimer Assay  Level 1

- Perform the procedure  (performed in preceptorship)  Level 2
- Describe the procedure  Level 2
- Describe appropriate quality control procedures and sources of error  Level 1
- Interpret results  Level 3

Identify technical conditions that cause false coagulation testing results with or without established protocol  Level 1

**Disorders of primary hemostasis**

Differentiate between disorders of the vasculature  Level 2

- Acquired purpura
- Henoch-Schölein purpura
- Hereditary hemorrhagic telangiectasia
- Ehlers-Danlos syndrome
Pseudoxanthoma elasticum

Define the following terms associated with hemostasis disorders Level 1
Thrombocytopenia
Thrombocytosis
Thrombocythemia

Describe the etiology, pathophysiology, clinical features, and laboratory findings of quantitative defects of platelets Level 3
Idiopathic thrombocytopenic purpura
Autoimmune thrombotic thrombocytopenic purpura
Post-transfusion purpura
Disseminated intravascular coagulation
Hemolytic uremic syndrome
MYH9 inherited thrombocytopenias, e.g. May-Hegglin anomaly
Wiscott Aldrich anomaly
Neonatal alloimmune thrombocytopenia
HELLP syndrome
Heparin-induced thrombocytopenia
Drug-induced immune thrombocytopenia
Myeloproliferative disorders
Secondary (reactive) conditions

Describe the etiology, pathophysiology, clinical features, and laboratory findings of qualitative defects of platelets Level 3
von Willebrand’s disease
Bernard-Soulier syndrome
Glanzmann’s thrombasthenia
Storage pool deficiencies
Acquired platelet function disorders

Disorders of secondary hemostasis
Describe the inheritance pattern, pathophysiology, clinical features, and laboratory findings Level 1
Factor I deficiency
Factor II deficiency
Factor V deficiency
Factor V Leiden
Factor VII deficiency
Factor VIII deficiency (Hemophilia A)
Factor IX deficiency (Hemophilia B)
Factor X deficiency
Factor XI deficiency
Factor XII deficiency
Factor XIII deficiency
Prekallikrein deficiency
High-molecular-weight kininogen deficiency
von Willebrand’s disease
Alpha-2-antiplasmin deficiency
Antithrombin III deficiency
Heparin co-factor II deficiency
Protein C deficiency
Protein S deficiency
Plasminogen deficiency
Homocystinemia/homocystinuria

Describe clinical features and laboratory findings of acquired coagulation Level 1 disorders
Vitamin K deficiency
Liver disease
Renal disease

Describe the significance and clinical implications of the development of circulating anticoagulants
Specific factor inhibitors
Nonspecific factor inhibitors
Global inhibitors

Identify and describe laboratory procedures that are used to evaluate circulating anticoagulants or inhibitors

Discuss the principle and clinical significance of Correction study using normal plasma
Perform the procedure (performed in preceptorship)
Describe the procedure
Describe appropriate quality control procedures and sources of error
Interpret results

Discuss the principle and clinical significance of APTT screening with moderate-high LA responsive reagent (LA-sensitive, low phospholipid)
Perform the procedure (performed in preceptorship)
Describe the procedure
Describe appropriate quality control procedures and sources of error  Level 1
Interpret results  Level 3

Discuss the principle and clinical significance of the Dilute Russell viper venom time (DRVVT)  Level 1
Perform the procedure  (performed in preceptorship)  Level 2
Describe the procedure  Level 2
Describe appropriate quality control procedures and sources of error  Level 1
Interpret results  Level 3

Discuss the principle and clinical significance of the Low-phospholipid (LA-sensitive) vs. high-phospholipid APTT  Level 1
Perform the procedure  (performed in preceptorship)  Level 2
Describe the procedure  Level 2
Describe appropriate quality control procedures and sources of error  Level 1
Interpret results  Level 3

Discuss the principle and clinical significance of the Platelet neutralization procedure  Level 1
Perform the procedure  (performed in preceptorship)  Level 2
Describe the procedure  Level 2
Describe appropriate quality control procedures and sources of error  Level 1
Interpret results  Level 3

Outline a protocol to follow when investigating a patient with an unknown bleeding disorder  Level 2
Factor assays with dilutions for detection of nonparallel results
Bethesda titer for factor VIII or IX inhibitors
Describe interferences and sources of error

**Disorders of fibrinolysis**

Differentiate between primary and secondary fibrinolysis  Level 1

Define disseminated intravascular coagulation (DIC)  Level 1

Identify mechanisms by which clotting is initiated during DIC  Level 1
Describe the effect of DIC on laboratory procedures

Prothrombin time
Activated partial thromboplastin time
Thrombin clotting time
Platelet count
Fibrinogen
Fibrin/fibrinogen degradation products (FDP)
D-dimer
Blood smear

Describe conditions that are predisposing to recurrent thrombosis

Antithrombin III deficiency
Heparin cofactor II deficiency
Primary antiphospholipid antibody syndrome
Protein C deficiency
Protein S deficiency
Activated Protein C resistance
Prothrombin gene mutation (G20210A)
Hypermomocystinemia
Acquired risk factors to thrombophilia (e.g., age, malignancies, including leukemias, chronic inflammation, surgery, immobilization, obesity, pregnancy, hormone replacement therapy, oral contraceptives, PNH, autoimmune disorders)

Describe laboratory tests for antithrombin III, protein C, and protein S comparing activity vs. antigen techniques

Perform the procedure (performed in preceptorship)

Describe the procedure

Describe appropriate quality control procedures and sources of error

Interpret results

Anticoagulant therapy

Explain the action of anticoagulant therapy

Vitamin K Reductase inhibitors
Direct acting oral anticoagulants
Heparin high/low molecular weight
Antiplatelet agents

Identify laboratory tests used to monitor anticoagulant therapy, indicate therapeutic intervals and sources of error and discuss emerging assays

Oral anticoagulant therapy (warfarin)Vitamin K Reductase inhibitors
Direct acting oral anticoagulants
Oral direct Xa inhibitors; anti-Xa
Heparin high/ low molecular weight
  Low molecular weight heparin; chromogenic anti-Xa
  Unfractionated heparin; PTT and chromogenic anti-Xa
  Pentasaccharide, e.g., fondaparinux sodium (chromogenic anti-Xa)
  Direct thrombin inhibitors; APTT, ecarin clotting time, dilute thrombin assay
Antiplatelet agents; platelet aggregometry
  Aspirin
  Thienopyridines: Clopidogrel, prasugrel
  Glycoprotein IIbIIIa inhibitors

Instrumentation
Identify basic concepts of electrical impedance, optical detection, radio frequency, Level 1 and of light scatter plus cytochemical stain systems
  Discuss the principle
  List components
  Describe operation
  Perform Analysis (performed in preceptorship)
  Describe maintance and troubleshooting
  Perform maintance/ corrective action (performed in preceptorship)Level 2
Identify basic concepts of quality assurance for automated hematology cell counting systems
  Describe acceptable practices
  Perform basic quality assurance (performed in preceptorship)
  Assess data to ensure quality.
  Monitor quality assurance program
  Describe the limitations and list interfering substances

Identify and describe hemogram parameters
  Evaluate patient data
  Describe the flagging system
  Correlate scatter plots, histograms and data plots with the peripheral smear
  Describe the mathematical calculations used to monitor instruments
  Recognize unexpected results
  Troubleshoot and corrective action

Discuss the principle of Automated reticulocyte counting
  Describe acceptable practices
  Perform basic quality assurance (performed in preceptorship)
  Assess data to ensure quality
Monitor quality assurance program Level 3
Describe the limitations and list interfering substances Level 1

Identify basic concepts of electromechanical and photo-optical systems Level 1
Describe acceptable practices Level 1
Perform basic quality assurance (performed in preceptorship) Level 2
Assess data to ensure quality. Level 3
Monitor quality assurance program Level 3
Describe the limitations and list interfering substances Level 1

Identify basic concepts of quality assurance for automated coagulation systems Level 1
Describe acceptable practices Level 1
Perform basic quality assurance (performed in preceptorship) Level 2
Assess data to ensure quality. Level 3
Monitor quality assurance program Level 3
Describe the limitations and list interfering substances Level 1

Identify basic concepts of spectrophotometric, chromogenic substrate assays Level 1
Describe acceptable practices Level 1
Perform basic quality assurance (performed in preceptorship) Level 2
Assess data to ensure quality. Level 3
Monitor quality assurance program Level 3
Describe the limitations and list interfering substances Level 1

Identify basic concepts of overall laboratory quality assurance Level 1
Describe acceptable practices Level 1
Perform basic quality assurance (performed in preceptorship) Level 2
Assess data to ensure quality. Level 3
Monitor quality assurance program Level 3