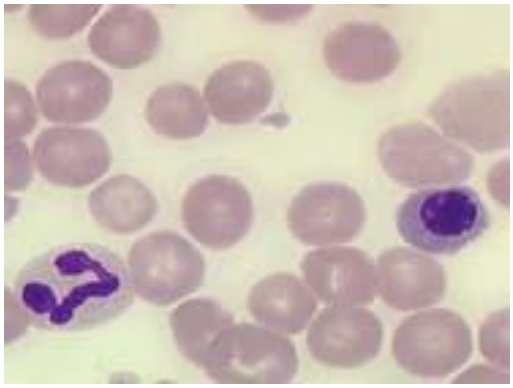
UTEP
Clinical Laboratory Science

CLSC 3356
Restricted for CLSCUD majors only
Hematology I
Course Outline

What do you see? What is in your Head?



hues http://www.xrite.com/online-color-test-challenge

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

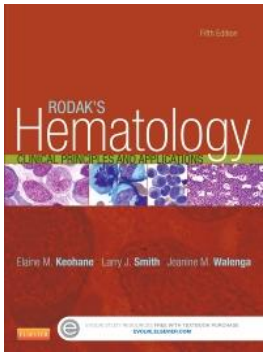
MW 8 - 9:20; College of Health Sciences 135

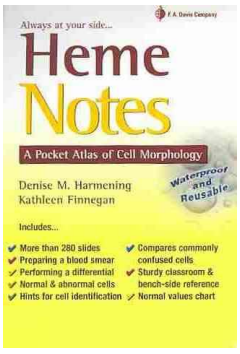
REQUIRED TEXTBOOKS:

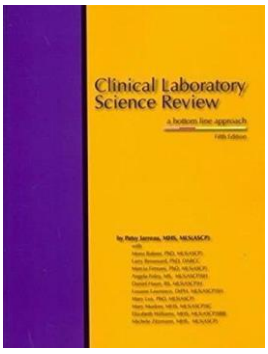
Keohane, E.M., Smith, L.J. and Walenga, J.M. 2016. *Rodak's Hematology: Clinical Principles and applications.* 5th ed. Elsevier.

Harmening, DM and Finnegan, K. 2014. *Heme Notes a pocket atlas of cell morphology*. F.A. Davis. Philadelphia, PA.

Jarreau, P. 2015. *Clinical Laboratory Science Review a Bottom Line Approach (5thed.).* Louisiana State University Health sciences Center foundation. New Orleans.







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 diagnose 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 lecute 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:

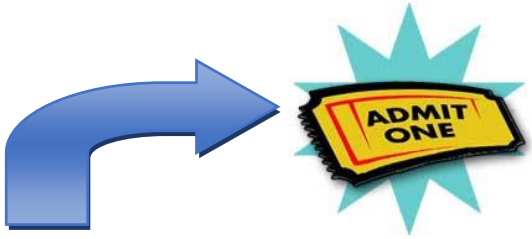
A 100 - 90%
B 89 - 80%
C 79 - 75 %
D 74.9 – 70%
F 69 or below

FINAL GRADE CALCULATION:

Exams	40%
Quizzes/ homework	20%
Final	40%

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

DATE	Topic to be covered
Aug 27	Overview of Hematology & Hematopoiesis
Aug 29	Bone Marrow / Red Blood Cell Structure & Function
Sep 3	**Labor Day NO CLASS**
Sept 5	Erythrocyte structure & function, hemoglobin
Sept 10	Erythrocyte structure & function
Sep 12	Anemia: Diagnosis and Clinical Considerations (19)
Sep 17	Evaluation of Cell Morphology / corpuscular constants
Sep 19	**EXAM 1 (Chapters 6–10, 14, 17, & 19)**
Sep 24	Iron Metabolism
Sept 26	Hypochromic anemias / Fe deficiency
Oct 1	Hypochromic anemias
Oct 3	Megaloblastic anemia
Oct 8	Megaloblastic anemia
Oct 10	**EXAM 2 (chapters 6 - 11, 14, 17, 19- 21)**

Chapter 6 review from general Bio.

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 — Level 2
Type I
Type II
Type III

Perform differential count on normal bone marrow specimens — Level 2

Distinguish between normal and abnormal hematopoietic elements found within the peripheral blood — Level 2

Correlate bone marrow findings with peripheral blood evaluation — Level 3

Prepare peripheral blood for routine hematologic procedure and smear analysis — Level 2

Determine specimen acceptability — Level 2

List appropriate anticoagulants and mechanism of anticoagulation — Level 1

Identify acceptable ratio of anticoagulant to blood for specimens obtained from venipuncture and skin puncture — Level 1

List reasons for rejecting specimens — Level 1

Stain smears using Romanowsky dyes and techniques according to established procedures — Level 2
Manual, Automated

List and define components of stain and explain the principle — Level 2

Judge the acceptability of blood smears through microscopic evaluation and established criteria — Level 3
Random distribution of cells
Good stain quality
Absence of artifact

Troubleshoot staining problems — Level 3

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 (B_{12} / 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 — Level 1
- Embden-Meyerhof/glycolytic
- Hexose monophosphate shunt
- Methemoglobin reductase
- Luebering-Rapoport

Erthrocytic Hemoglobin

Summarize the mechanisms by which normal hemoglobin is structured and synthesized in the developing red cell — Level 1

- 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 A_2)

Describe normal hemoglobin-oxygen function using the oxygen dissociation curve (ODC) — Level 1

Identify the effect various conditions can have on the oxygen dissociation curve — Level 3
- pH (Bohr effect)
- Temperature
- CO_2
- 2,3-DPG (2,3-BPG)
- Hb S,F and other variants

Interpret the effect of various factors on the concentration of hemoglobin — Level 3
- Age and gender
- Pregnancy
- Altitude
- Smoking
- Associated disease
- Altered hemoglobin derivatives (carboxyhemoglobin/methemoglobin/sulfhemoglobn)

Erythrocytic Catabolism

Summarize the mechanism by which red cells are catabolized — Level 2
- Identify phases (extravascular, intravascular) — Level 1
- Trace the basic steps associated with each phase — Level 1
- Define terms associated with red cell destruction — Level 1

Biliverdin
Bilirubin (unconjugated/conjugated)
Urobilinogen
Urobilin
Hemoglobin dimers
Haptoglobin
Hemopexin
Hemoglobinemia
Hemoglobinuria
Hemosiderinuria
Methemalbumin

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 Level 2
- Supravital smear method with Miller disc
- Supravital smear method without Miller disc
- Automated methods

Perform and interpret calculations associated with reticulocyte assays Level 3
- 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 Level 2

Distinguish between normal and abnormal red blood cell morphology Level 2

List red blood cell count and indices reference values that account for variations in gender and age Level 1

Correlate automated hemogram parameters and calculated indices with each other and with peripheral smear exam results Level 3

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

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 erythrocytes Level 3

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

Leukopoiesis

State reference values that reflect variations in gender and age for the leukocyte counts in peripheral blood Level 1
- Total leukocyte count
- Relative and absolute values for neutrophil, lymphocyte, eosinophil,

basophil and monocyte counts

Identify factors that alter leukocyte values — Level 1
- Physiologic variation
- Pathologic abnormalities

Enumerate and/or calculate leukocyte counts — Level 2
- Relative values
- Absolute values

List morphologic features used to differentiate developing leukocytes — Level 2
- 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

Leukopoeisis: Granulocytes

List the maturation sequence of neutrophils, eosinophils, and basophils — Level 1

Differentiate distinguishing morphology for stages of developing blood granulocytes — Level 2

Explain mechanisms that regulate and modulate granulopoiesis — Level 2
- Regulatory growth factors and inhibitors
- Kinetics (life span, circulation)
- Biochemistry (granule content and surface membrane receptors, energy metabolism)

Explain the functions associated with granulocytes — Level 2
- 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 — Level 2

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

List the maturation sequence of monocytes and macrophages — Level 1

List the maturation sequence of lymphocytes — Level 1

Summarize structural and functional features that characterize lymphopoiesis — Level 2

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 — Level 1

Recognize morphology of developing lymphocytes — Level 1

Describe the use of monoclonal antibodies to differentiate lymphocytes by immunophenotype — Level 2

- 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 — Level 2

State the principles and clinical utility of histogram/scatterplot review — Level 1

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 — Level 2

Calibrate and perform preventive maintenance on instruments used to evaluate white cells — Level 2

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 leukocytes and their physical properties Level 2

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 qualitiative 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 neutrophilic disorders — Level 2
Shift to the left
Toxic granulation
Dohle bodies
Vacuolization
Leukemoid reaction
Leukoerythroblastic reaction
Agranulocytosis
Hyposegmentation
Hypersegmentation

State characteristic abnormalities and clinical features for the qualitative/functional disorders of neutrophils — Level 1
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 — Level 1

Define monocytosis — Level 1

Compare absolute monocyte values with relative values — Level 1

Identify causes of monocytosis — Level 1

Identify abnormal lipid accumulations within monocytes and macrophages — Level 1

Identify causes of non-neoplastic disorders of lymphocytes and plasma cells — Level 1

Define lymphopenia/ lymphocytosis — Level 1

Compare lymphocyte absolute values with relative values — Level 2

Compare and contrast morphologic features of reactive lymphocytes and normal lymphocytes
Size

Nucleus Level 3
Cytoplasm
Heterogeneity

Differentiate between reactive and resting lymphocytes on Romanowsky stained smears Level 2

Identify the causes of reactive lymphocytosis Level 2

Red Blood Cell Disorders: Anemia

Define anemia Level 1

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 Level 1

Describe the expected laboratory results seen in the various pathophysiologic classifications of anemias Level 2
- Decreased red cell production (Bone marrow failure, ineffective hematopoiesis, Myelophthsic)
- Increased red cell destruction, hemolytic processes
- Loss of red blood cells

Discuss the clinical utility of the RBC indices as relates to physiologic conditions Level 3

Explain sources of error of the red cell indices Level 2

Use the RBC indices as a quality control mechanism for assessing the validity of the erythrocyte count, hemoglobin, and hematocrit values Level 2

Define common terms used to describe red cell morphology Level 1
- Anisocytosis
- Poikliocytosis
- 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 Level 2
Basophilic stippling
Cabot rings
Heinz bodies
Howell-Jolly bodies
Malarial and other blood parasites
Pappenheimer bodies/siderotic granules
Hemoglobin crystals (C, S, SC, H inclusion bodies)

Red Blood Cell Disorders: Erythrocytosis (Polycythemia)

Define polycythemia Level 1

Differentiate between absolute polycythemia and relative polycythemia Level 2

Compare and contrast secondary polycythemia, and relative erythrocytosis Level 3
Etiology
Clinical features
Laboratory findings
Prognosis

Describe changes in the bone marrow and peripheral blood with polycythemia vera Level 2

Red Blood Cell Disorders: Hypochromic Anemias

Define hypochromic anemia — Level 1

List the causes of hypochromic anemias — Level 1

Discuss the etiology and pathophysiology of hypochromic anemias — Level 2
- 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 — Level 2
- 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 — Level 3

Red Blood Cell Disorders: Megaloblastic Anemias

Discuss the absorption and metabolism of vitamin B_{12} and folate — Level 2

Describe clinical features of megaloblastic anemia — Level 1

Identify the hematologic abnormalities present in megaloblastic anemia — Level 2
- Peripheral blood changes
- Bone marrow-morphological changes

Compare and contrast pernicious anemia to the other types of vitamin B_{12} deficiency — Level 3

Outline a sequential approach to the differential diagnosis of megaloblastic anemia using the following laboratory procedures — Level 3
- Mean corpuscular volume (MCV)
- Blood and bone marrow smear evaluation

Serum B_{12}
Serum folate
Red cell folate
Anti-intrinsic factor antibodies
Anti-parietal cell antibodies
Methylmalonic acid
Homocysteine

Differentiate nonmegaloblastic macrocytosis from megaloblastic anemia — Level 3
Peripheral blood and bone marrow characteristics
Serum vitamin B_{12} level
Serum folate level
Red cell folate level
Reticulocyte findings

Red Blood Cell Disorders: Hypoproliferative Anemias: Congenital and Acquired

Define aplastic anemia — Level 1

Identify common factors associated with the development — Level 1

Describe the clinical features and pathophysiology — Level 2
Acquired aplastic anemia
Fanconi's anemia
Congenital pure red blood cell aplasia
Anemia caused by myelophthisis

Describe the laboratory findings — Level 1
Peripheral blood changes
Bone marrow changes
Other laboratory findings

Define Fanconi's anemia — Level 1

Describe the genetics and possible pathophysiology — Level 2

Describe the laboratory findings — Level 1
Peripheral blood changes
Bone marrow changes
Other laboratory findings

Define pure red cell aplasia(Diamond-Blackfan anemia) — Level 1

Describe the clinical features and pathophysiology — Level 2

Describe the laboratory findings Level 1
- Peripheral blood changes
- Bone marrow changes
- Other laboratory findings

Define and differentiate Congenital dyserythropoietic anemias (types I, II, and III) Level 2

Describe the clinical features Level 1

Describe the laboratory findings Level 1

Define myelophthisis Level 1

Describe the clinical features Level 1

Describe the laboratory findings Level 1
- 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 Level 1
- 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 Level 2

Discuss the principle of the Osmotic fragility test Level 1
- Describe the clinical features 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 utility of flow cytometry in assessing red cell membrane defects	Level 2
Describe the etiology, pathophysiology, and clinical features of red cell enzyme abnormalities	Level 1
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	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

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) 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 acid elution test (Kleihauer-Betke) or flow cytometry in regards to Hemoglobinopathies Level 1

Correlate screening test for sickling hemoglobin with peripheral blood morphology and electrophoretic patterns of hemoglobin Level 3

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 A_2 Level 2

Hemolytic Anemias

Identify mechanisms of immune hemolytic anemias Level 1

Define and describe the etiology and clinical features and laboratory findings of Alloimmune hemolytic anemias Level 1
- Acute hemolytic transfusion reaction
- Delayed hemolytic transfusion reaction
- Hemolytic disease of the newborn (HDN)

Define and describe the etiology and clinical features and laboratory findings of Autoimmune hemolytic anemias Level 1
- Warm autoimmune hemolytic anemia (WAIHA)
- Cold autoimmune hemolytic anemia
- Cold agglutinin syndrome (Idiopatic, Secondary)
- Paroxysmal cold hemoglobinuria

Identify mechanisms of drug-induced immune hemolytic anemia Level 1

Identify the etiology of nonimmune hemolytic anemia Level 1
- Infectious organisms
- Mechanical agents
- Chemicals

Describe the hematologic findings associated with nonimmune hemolytic anemias Level 1
- 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 — Level 1

List the clinical symptoms of acute blood loss — Level 1

Identify the laboratory findings of acute blood loss — Level 1

Anemias associated with systemic disorders

Describe the clinical features and laboratory findings associated with nonhematologic disorders — Level 1

- 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 — Level 1

- Leukemias
- Myelodysplastic syndromes
- Myeloproliferative disorders
- Lymphoproliferative disorders

Identify major systems used to classify neoplastic disorders of leukocytes — Level 1

- French, American-British (FAB) Cooperative Group
- World Health Organization (WHO)

Observe and/or perform procedures, apply appropriate quality control procedures, and interpret laboratory findings for laboratory procedures used in the identification, classification and differentiation of neoplastic disorders — Level 2

- Complete blood count

Hemograms
Scatterplots and histograms

Review the criteria used to classify nonmalignant leukocytic disorders Level 1
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 Level 2
Shift to the left
Toxic granulation
Döhle bodies
Vacuolization
Leukemoid reaction
Leukoerythroblastic reaction
Agranulation, hypogranulation
Hyposegmentation
Hypersegmentation
Intracellular microorganisms

Compare and contrast the principles of various cytochemical stains and the cell lineages they react with Level 2
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 Level 1
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 — Level 3

Read case studies of neoplastic disorders and apply knowledge and skills in interpreting laboratory results — Level 3

Acute Leukemias

Apply general criteria to classify leukemias — Level 1
- Cell maturity (Acute/Chronic)
- Cell lineage (Myeloid /nonlymphoid)
- Lymphoid

Describe the clinical findings and laboratory results for leukemia — Level 1

Compare the FAB with the WHO acute myeloid leukemia subgroups and apply diagnostic blood and bone marrow findings to the differential identification — Level 3
- 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 — Level 1
- 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 — Level 3

Describe for each leukemia — Level 1
- 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 Level 2
Stem cell clonality
Oncogene and tumor suppressor gene development

Describe the survival rates and prognosis Level 2

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 Level 2
Greater than 30%
Predominant cell type
Auer rods

Define the reactivity of leukemic cells with cytochemical stains Level 1

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 Level 2

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 Level 3

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 Level 1

Myelodysplastic Syndromes (MDS)

Define and describe cellular features that characterize the MDS Level 2

Dyserythropoiesis
Dysgranulopoiesis
Dysmegakaryocytopoiesis

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) Level 2
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 Group for the MDS classification — Level 1

- 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 thrombocythemia (ET)
- Fibroblasts--agnogenic myeloid metaplasia (AMM)

List Chronic Myeloproliferative Neoplasms subtypes — Level 1

- Chronic myelogenous leukemia (CML) BCR/ABL1 positive
- Essential thrombocythemia (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 — Level 3
- 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 — Level 2

Correlate diagnostic criteria to these findings for the differential identification — Level 3
- 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
- Mantel 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 and stage Hodgkin lymphoma Level 2
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 presence of lymphoma cells Level 3

Plasma Cell Disorders

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

Discuss classification based on proliferation of plasma cells and abnormal production of immunoglobulins Level 2
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 and abnormal production of immunoglobulins Level 3

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 Level 1

Correlate quantitative variations with disease manifestations Level 3
- 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 Level 1

Compare absolute count with those estimated from blood smear exam Level 3

Identify platelets and platelet morphologic variations on a properly prepared Level 2

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 — Level 3
- 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 — Level 3

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

Calibrate and perform preventive maintenance on instruments used to evaluate platelets — Level 2

Hemostasis/ Coagulation

Define hemostasis — Level 1

Explain the general interaction of systems involved in maintaining hemostasis — Level 1

Of systems involved in maintaining hemostasis describe how changes in one effect the other — Level 2
- Vasculature
- Platelets
- Plasma coagulation factors
- Fibrinolysis

Differentiate between primary and secondary hemostasis — Level 3

Vascular

Explain the functions of the vascular system in maintaining hemostasis — Level 1

Describe metabolic functions of the endothelium and substances contributing to the thromboresistance properties of endothelium — Level 1
- Heparan sulfate
- Thrombomodulin
- Tissue plasminogen activator
- Prostacyclin (PGI2)
- Tissue factor pathway inhibitor

Platelets

Discuss the production of platelets — Level 1

State the average time in circulation, normal peripheral count, and total body distribution of platelets — Level 1

Describe the ultrastructural components of a platelet — Level 1
- Alpha granules
- Dense bodies
- Lysomes
- Microtubules
- Open canalicular system
- Platelet membrane
- Glycocalyx

Discuss the physiological role of platelets in hemostasis — Level 1
- Platelet plug formation
- Maintaining normal vascular integrity

Describe the series of morphologic changes that occur in platelets following physiologic stimulation — Level 1
- Adhesion
- Aggregation
- Activation

Discuss the effect of aspirin on platelet function — Level 1
- Biochemical mechanism
- Duration of the effect

Discuss principle for platelet aggregometry and platelet function analyzers — Level 2

Interpret results of platelet function assay tests — Level 3
- 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 *in vitro*	Level 1
Summarize the interaction of the coagulation system with the vascular and platelet systems to form a hemostatic plug	Level 2
Describe the physiologic controls of hemostasis	Level 1
Blood flow	
Feedback inhibition	
Liver clearance	
Identify the inhibitors of hemostasis	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	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	Level 1
Discuss the principle and clinical significance of the Prothrombin time test	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 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 assciated 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 disorders Level 1
Vitamin K deficiency
Liver disease
Renal disease

Describe the significance and clinical implications of the development of circulating anticoagulants Level 1
Specific factor inhibitors
Nonspecific factor inhibitors
Global inhibitors

Identify and describe laboratory procedures that are used to evaluate circulating anticoagulants or inhibitors Level 1

Discuss the principle and clinical significance of Correction study using normal plasma 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 APTT screening with moderate-high LA responsive reagent (LA-sensitive, low phospholipid) 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 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 — Level 1
- 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 — Level 1
- 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)
- Hyperhomocystinemia
- 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 — 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

Anticoagulant therapy

Explain the action of anticoagulant therapy — Level 1
- 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 — Level 2
- 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, and of light scatter plus cytochemical stain systems	Level 1
Discuss the principle	Level 1
List components	Level 1
Describe operation	Level 1
Perform Analysis (performed in preceptorship)	Level 2
Describe maintance and troubleshooting	Level 1
Perform maintance/ corrective action (performed in preceptorship)	Level 2
Identify basic concepts of quality assurance for automated hematology cell counting systems	Level 1
Desccribe 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 and describe hemogram parameters	Level 1
Evaluate patient data	Level 3
Describe the flagging system	Level 1
Correlate scatter plots, histograms and data plots with the peripheral smear	Level 3
Describe the mathematical calculations used to monitor instruments	Level 3
Recognize unexpected results	Level 1
Trohubleshoot and corrective action	Level 2
Discus the principle of Automated reticulocyte counting	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 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