The University of Texas at El Paso
College of Health Sciences

Clinical Laboratory Science Program

CLSC 3364 Hematology II

Course Outline

Spring
What do you see? What is in your Head?

Video or audio recordings will not be permitted.
Instructor
M. Lorraine Torres, Ed. D, MT (ASCP)
College of Health Sciences Room 423
Phone: 747-7282
E-Mail: lorit@utep.edu

Office Hours
TR 3:00 – 4:00 p.m., Friday 2 – 3 p.m. or by appointment

Class Schedule
Monday and Wednesday 11:00 – 12:30 A.M. HSCI 135

Course Description
This course is a sequel to Hematology I. It will include but is not limited to the study of the white blood cells with emphasis on white cell formation and function and the etiology and treatment of white blood cell disorders. This course will also encompass an introduction to hemostasis and laboratory determination of hemostatic disorders. Prerequisite; CLSC 3356 & CLSC 3257.

Topical Outline
1. Maturation series and biology of white blood cells
2. Disorders of neutrophils
3. Reactive lymphocytes and Infectious Mononucleosis
4. Acute and chronic leukemias
5. Myelodysplastic syndromes
6. Myeloproliferative disorders
7. Multiple Myeloma and related plasma cell disorders
8. Lymphomas
9. Lipid (lysosomal) storage diseased and histiosytosis
10. Hemostatic mechanisms, platelet biology
11. Coagulation pathways
12. Quantitative and qualitative vascular and platelet disorders (congenital and acquired)
13. Disorders of plasma clotting factors
14. Interaction of the fibrinolytic, coagulation and kinin systems
15. Laboratory methods

REQUIRED TEXTBOOKS: same books used for Hematology I

Louisiana State University Health sciences Center foundation. New Orleans.

OPTIONAL: A color atlas or your choice but recommend
HEALTHY PEOPLE 2020
This course aligns with the Healthy People 2020 initiative and discusses Blood Disorders and Blood Safety.

UNANNOUNCED QUIZZES AND ASSIGNMENTS:
Tickets to Class and unannounced quizzes will be given throughout the course and will constitute 10% of the final grade. There are no make-up exams or quizzes. **Assignments turned in late will not be accepted.**

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.

**Venipuncture:** The student must perform 10 venipunctures during the semester.

**Differentials:** The student must perform 100 differentials on their own time.

ALL STUDENTS MUST INFORM MS. DOLORES LICERIO WHEN YOU ARE GOING INTO THE LAB AS THE LAB DOORS WILL BE LOCKED.

Dolores Licerio CHS room 418, 747-8396

The lab will be open for you to perform differentials on Thursday from 8:30 a.m.– 12:00 p.m. Friday the lab will be open from 9:00 A.M. – 3:30 P.M.. If you plan to use this time you must inform Ms. Dolores Licerio that you will be in the lab. There is plenty of time to perform 6-8 differentials per week (ONE LOG SHEET). When you make your schedule be sure to mark the time you will be performing differentials per week.

Each Friday the student is required to turn in ONE LOG SHEET. The student will receive a zero for the week if the differential log is not turned in by the due dates stated below. **DO NOT TURN IN MORE THAN ONE LOG SHEET PER WEEK!**

Jan 25
Feb 1, 8, 15, 22;
March 1, 8, 15, 28 (This is a Thursday)
April 5, 12, 19, 26;
May 3, 10.
Hematology, for educational purposes, has been divided into two components, Hematology I (CLSC 3356) which encompassed the study of the Red Blood Cell and Hematology II (CLSC 3264) which will entail the study of the White Blood Cells and Hemostasis. The Student is expected to recall the information presented in Hematology I and relate the information to Hematology II so as to “complete the picture”. Make it a habit to keep up with the readings and be aware that unexcused absences will not be tolerated. All students should attend all classes scheduled during the semester, and they should be on time. All exams will be comprehensive. NO MAKE UP EXAMS WILL BE GIVEN! At the instructors discretion an exam may be taken late with an automatic deduction of 10 points.

% Grade Scale

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>100 – 90</td>
<td>A</td>
<td>Exams</td>
</tr>
<tr>
<td>89.9 – 80</td>
<td>B</td>
<td>Quizzes &amp; Ticket to class</td>
</tr>
<tr>
<td>79.9 – 75</td>
<td>C</td>
<td>Differentials</td>
</tr>
<tr>
<td>74.9 – 70</td>
<td>D</td>
<td>Venipuncture</td>
</tr>
<tr>
<td>69.9 – 60</td>
<td>F</td>
<td><strong>Comprehensive final including last semester</strong></td>
</tr>
</tbody>
</table>

Instructional Strategies/Attendance:

All exams will be comprehensive. NO MAKE UP EXAMS WILL BE GIVEN! At the instructors discretion an exam may be taken late with an automatic deduction of 10 points.

The student is expected to attend all classes. It is 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/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. If the student misses an exam and he/she does not have appropriate justification a grade of 0 (zero) will be given.

University Policy on examinations and quizzes:

When examinations are administered, students are to place book bags, papers and other personal belongings at the front of the room. Students will spread around the room when seating themselves. **No hats, caps, or bulky clothing may be worn.** 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, 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 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.

**Academic dishonesty:**

Academic dishonesty is prohibited and is considered a violation of the UTEP Handbook of Operating Procedures. It includes, but is not limited to, cheating, plagiarism, and collusion.
Cheating may involve copying from or providing information to another student, possessing unauthorized materials during a test, or falsifying research data on laboratory reports. Plagiarism occurs when someone intentionally or knowingly represents the words or ideas of another person's as one's own. And, collusion involves collaborating with another person to commit any academically dishonest act. Any act of academic dishonesty attempted by a UTEP student is unacceptable and will not be tolerated. Violations will be taken seriously and will be referred to the Dean of Students Office for possible disciplinary action. Students may be suspended or expelled from UTEP for such actions.

Academic dishonesty is an assault upon the basic integrity and meaning of a University. Cheating, plagiarism, and collusion in dishonest activities are serious acts which erode the University’s educational and research roles and cheapen the learning experience not only for the perpetrators, but also for the entire community. It is expected that UTEP students will understand and subscribe to the ideal of academic integrity and that they will be willing to bear individual responsibility for their work. Materials (written or otherwise) submitted to fulfill academic requirements must represent a student’s own efforts. Any act of academic dishonesty attempted by a UTEP student is unacceptable and will not be tolerated. Violations will be referred to the Dean of Students Office for possible disciplinary action. Students may be suspended or expelled from UTEP for such actions.

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.

Please read material on academic integrity [http://sa.utep.edu/osccr/academic-integrity/](http://sa.utep.edu/osccr/academic-integrity/)

**Students with Disabilities:**
If you have or suspect a disability and need accommodations, you should contact The Center for Accommodations and Support Services (CASS) at 747-5148. You can also email the office at cass@utep.edu or go by the Union Building East, Room 106. For additional information, visit the CASS website at [http://sa.utep.edu/cass/](http://sa.utep.edu/cass/) it is the responsibility of the student to notify the instructor that CASS accommodation guidelines are needed.

**Cell Phones:** All cell phones should be TURNED OFF during class period. Use of cell phone is not allowed during lecture.

**Lap Tops:** Surfing the internet or e-mail during lecture is strictly forbidden. If the student is found using his/her computer other than for taking notes and updating class materials, she or he will be asked to leave the classroom and won’t be allowed to bring the computer again.

**Lecture Materials:** All lecture power points, additional cases, study questions and supplemented
materials will be posted in blackboard. It is responsibility of the student to download the materials. It is highly recommended that the students print power points to supplement them with additional information given in lecture.

**STATEMENT ON HARRASSMENT**

**Harassment:**
Please be aware that harassment is unacceptable in the classroom. No jokes, comments of sexual nature as well as racists will be tolerated. The student that uses harassment will be sent to the Dean of students for disciplinary action.

**NON-DISCRIMINATION STATEMENT**

**Title IX Statement:**
Title IX of the Education Amendments of 1972 (Title IX), prohibit discrimination on the basis of sex in education programs or activities operated by recipients of Federal financial assistance. Sexual harassment of students, which includes acts of sexual violence, is a form of sex discrimination prohibited by Title IX. Sexual violence refers to physical sexual acts perpetrated against a person's will or where a person is incapable of giving consent due to the victim's use of drugs or alcohol. An individual also may be unable to give consent due to an intellectual or other disability. A number of different acts fall into the category of sexual violence, including rape, sexual assault, sexual battery, sexual coercion, stalking, and relationship violence. All such acts of sexual violence are forms of sexual harassment covered under Title IX.

In accordance with Title IX of the Education Amendments of 1972, UTEP does not discriminate on the basis of sex in the operation of its educational programs and activities. This commitment to non-discrimination applies to both employment in and admission to such programs and activities. [Link to full text at http://admin.utep.edu/Default.aspx?tabid=68750]

**Inquiries regarding Title IX should be referred to the University's Title IX Coordinator(s):**

- Sandy Vasquez, Title IX Coordinator (Investigation of concerns related to Faculty and Staff)  
  **915.747.5662** svasquez@utep.edu

- Dr. Ryan C. Holmes, Deputy Title IX Coordinator (Investigation of concerns related to Students)  
  **915.747.8694** rholmes@utep.edu

- Dr. Catie McCorry-Andalis, Deputy Title IX Coordinator (Education, Training and Outreach)  
  **915.747.5648** cmandalis@utep.edu

**Related Resources**
- Center Against Family Violence Hopelines: **915.593.7300 or 1.800.727.0511**
- El Paso Police Department (911) or UTEP Police Department (747-5611).
- For suspected harm of children or older persons, Child/Adult Protective Services **1-800-252-5400**.
- National Domestic Violence Hotline **1-800-799-SAFE (7233)**.

**STUDENT SUPPORT SERVICES STATEMENT**
Student Support Services:
All students experience stress and emotional challenges. The following resources can help those feeling stressed, experiencing loss, and considering ending their life.
- UTEP’s Counseling Center offers free counseling to all students with the same number leading to an after-hours crisis line: (915) 747-5302
- Mental Health Crisis Line (915) 779-1800
- National Suicide Prevention Hotline 1-800-273-8255 and Veterans Crisis Line 1-800-273-8255
- NAMI of El Paso (National Alliance Against Mental Illness) (915) 534-5478

Course Objectives:
Successful completion of the course will require that the student be able to

1. Describe normal and abnormal white cell biology according to the various white cell and FAB classifications and its manifestation seen in bone marrow and peripheral smears.

2. Demonstrate the ability to differentiate between normal and abnormal white cell reactions to various stimuli and relate these reactions to the appropriate disease and or neoplastic states along with the patient’s clinical picture and correlating laboratory exams.

3. Describe platelet development and biology and its role in hemostasis.

4. Recognize and describe normal and abnormal coagulation pathways and relate them to various hemostatic disorders along with the corresponding laboratory exams.

No one cares how much you know until they know how much you care!
Affective Objectives

Goals / Purpose: Clinical laboratory science students are expected to show growth in professional behaviors appropriate to a laboratory setting and to maintain those behaviors possessed at time of entry.

Objectives: To show the appropriate responsible behaviors, students will demonstrate:

1. A positive attitude by being prepared for lecture and laboratory sessions, completing assigned tasks on time, and displaying self-motivation and initiative.
2. Organization by utilizing time efficiently, sequencing and prioritizing tasks for completion with time constraints, & maintaining a neat & clean work area.
3. Attention to detail by diligently pursuing accuracy and documenting data accurately and legibly.
4. Problem solving ability by explaining the purpose of each step in a diagnosis, interpretation, procedure, or instrument operation, recognizing discrepancies in techniques or procedures, and repeating lab tests when necessary.
5. Dependability by following directions, working independently, after being given directions, and being present and on time with only excused absences.
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 the 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.

TIME NEEDED TO STUDY!
For each hour you spend in class, you should spend 2-3 hours outside of class studying.
VERY TENTATIVE COURSE SCHEDULE AND BOOK CHAPTERS

LEUKOCYTES: (Chapters 7, 12, 29 – 36)

JAN 23  Cell biology, granulocytic and monocytic series (7, 12)
JAN 28  Non-malignant Leukocyte disorders (29)
JAN 30  Lipid (lysosomal) Storage Diseases and Histiocytosis (29)
FEB 4  Non-malignant Lymphocytic disorders (Reactive lymphocytes & IM) 29
FEB 6  EXAM I (7, 12, 29)
FEB 11  Introduction to leukemias and acute leukemia (Acute Vs. Chronic)
FEB 13  Cytogenetics (30) Molecular Diagnostics (31)
FEB 18  Flow cytometry (32)
FEB 20  Myeloproliferative Neoplasms: CMPD: CML, PV, ET, MF (33)
FEB 25  Myeloproliferative Neoplasms CMPD: CML, PV, ET, MF) (33)
FEB 27  EXAM II (23, )
MAR 4  Myelodysplastic Syndromes (34)
MAR 6  Acute Leukemias (35)
MAR 11  Mature Lymphoid Neoplasms (36)
MAR 13  Lymphoma, Multiple Myeloma, and related plasma cell disorders
MAR 18, 20  SPRING BREAK
MAR 25  EXAM III (34- 36)

HEMOSTASIS: NOTE: I do a lot of drawing on the board and limited power points (Chapters 13, 37- 44)

MAR 27  INTRO: Mechanism of blood coagulation
APR 1  Platelet structure and function
APR 3  Coagulation Cascade Theory
APR 8  Quantitative and qualitative vascular & platelet disorders
APR 10  Laboratory Assessment of Blood coagulation factors
APR 15  Protective agents against thrombosis
APR 17  EXAM IV (13, and from my notes)
APR 22  Vascular disorders / Abnormal Platelet Morphology
APR 24  Qualitative Platelet Disorders
APR 29  Qualitative Characteristics of Platelets
MAY 1  Bleeding disorders related to blood clotting/Hypercoagulable states
MAY 6  Bleeding disorders related to blood clotting/Hypercoagulable states
MAY 8  COAGULATION EXAM V (37 – 44)

MAY 17  COMPREHENSIVE FINAL (including Heme I) 9A.M. – 12: P.M.

As a reminder, the final exam in Hematology II will be comprehensive including information covered in Hematology I
MLS Hematology cognitive objective covered in Hematology I, Hematology I Laboratory and Hematology II
Upon completion of this course, the student should be able to: Define, discuss, explain, identify and perform …

Normal hematopoietic system (Hematology I)
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 (Hematology I)
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
- 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

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 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 (Hematology I)**

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 Level 1
- Embden-Meyerhof/glycolytic
Erthrocytic Hemoglobin (Hematology I)
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 (Hematology I)
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
- Biliverdin
- Bilirubin (unconjugated/conjugated)
- Urobilinogen
- Urobilin
- Hemoglobin dimers
- Haptoglobin
- Hemopexin
- Hemoglobinemia
- Hemoglobinuria
- Hemosiderinuria
Erythrocyte Evaluation (Hematology I)

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  
Level 2
blood cell morphology

Distinguish between normal and abnormal red blood cell morphology  
(List 2)

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

Correlate automated hemogram parameters and calculated indices with each other and with peripheral smear exam results  
(List 3)

Calibrate and perform preventive maintenance on instruments used to evaluate erythrocytes and their physical properties  
(List 2)

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

Take corrective action to resolve unexpected results and/or events on instruments used to evaluate erythrocytes  
(List 3)

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

Leukopoiesis (Hematology II)

State reference values that reflect variations in gender and age for the leukocyte counts in peripheral blood  
(List 1)

Total leukocyte count
Relative and absolute values for neutrophil, lymphocyte, eosinophil, basophil and monocyte counts

Identify factors that alter leukocyte values  
(List 1)

Physiologic variation
Pathologic abnormalities

Enumerate and/or calculate leukocyte counts  
(List 2)

Relative values
Absolute values

List morphologic features used to differentiate developing leukocytes  
(List 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

Leukopoiesis: Granulocytes (Hematology I and II)
- 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)

Leukopoiesis: Monocytes and Lymphocytes (Hematology II)
- 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
Leukocyte Evaluation (Hematology I and II)

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

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

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

Correlate and verify automated cell counts and differentials with established criteria

Estimate the total white blood count from a smear

Correct leukocyte counts for the presence of nucleated red cells

Determine differential cell counting using automated methods

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

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

Correlate and verify automated cell counts and differentials with established criteria

Estimate the total white blood count from a smear

Correct leukocyte counts for the presence of nucleated red cells

Calibrate and perform preventive maintenance on instruments used to evaluate 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

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

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

Nonmalignant Leukocyte Disorders (Hematology II)

Explain the classification of nonmalignant leukocytic disorders

Quantitative changes

Qualitative changes
Compare and contrast absolute values with relative values
   Neutrophilia
   Neutropenia
   Eosinophilia
   Eosinopenia
   Basophilia

Associate quantitative and qualitative leukocyte disorders with expected results
   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
   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

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  
Level 1

Compare lymphocyte absolute values with relative values  
Level 2

Compare and contrast morphologic features of reactive lymphocytes and normal lymphocytes  
Level 3
- Size
- Nucleus
- 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 (Hematology I)

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, Myelophthisic)
- 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
- 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
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) (Hematology I)
Polycythemia vera is in Hematology II

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 (Hematology I)

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

Red Blood Cell Disorders: Megaloblastic Anemias (Hematology I)

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 B₁₂
- 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

Red Blood Cell Disorders: Hypoproliferative Anemias: Congenital and Acquired (Hematology I)

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 (Hematology I)

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  
Perform /observe the procedure  
Apply appropriate quality control procedures  
Evaluate results

Red Blood Cell Disorders: Hemoglobinopathies (Hematology I)

Define hemoglobinopathy  
Distinguish between qualitative and quantitative hemoglobin defects  
Describe clinical and laboratory findings of hemoglobinopathies

- 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

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

Describe the hemoglobin gene defect in alpha and beta thalassemia  
Define the hemoglobin defect in thalassemia

Describe the terminology associated with thalassemias

- 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

Describe the pathophysiology of thalassemias

- 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

Discuss the principles of hemoglobin electrophoresis (cellulose acetate, alkaline pH vs. citrate agar, acid pH) Level 1

Discuss the principles of hemoglobin quantification (HbA, HbA2, HbF) Level 1

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) Level 2

Hb F, Hb A, Hb S, Hb C, Hb D, Hb E, Hb A2

Hemolytic Anemias (Hematology I)

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 Level 1
Autoimmune hemolytic anemias
  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** *(Hematology I)*
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** *(Hematology I)*
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 (Hematology II)

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
Hypossegmentation
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

- 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** (Hematology II)

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
  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
  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) (Hematology II)

Define and describe cellular features that characterize the MDS

- 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)
- 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

- 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

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

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

**Chronic Myeloproliferative Neoplasms (Hematology II)**

Classify Chronic Myeloproliferative Neoplasms by cell type
- 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
- 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
- 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 (Hematology II)**

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

List diagnostic features CLL
- 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
- 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
- Modified Rai
- Binet

Discuss the diagnostic features of PLL
- 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
- 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
- Splenectomy
- Other drugs
- Describe laboratory findings seen in the variant form of HCL

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

Apply diagnostic criteria to blood and bone marrow findings for the differential identification of Adult T-cell leukemia
- 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

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

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

**Lymphoma** (Hematology II)

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

Outline a multidisciplinary workup and list laboratory findings used to diagnose 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 presence of lymphoma cells

**Plasma Cell Disorders** (Hematology II)

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

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

Level 3

Compare and contrast the following for plasma cell disorders
  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
  Flaming plasma cell
  Mott cells
  Rouleaux formation of red blood cells

**Thrombopoiesis/megakaryopoiesis** *(Hematology II)*

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
  Thrombocytopenia
  Thrombocytosis

Level 3

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
  State the principles of method analysis and histogram/scatterplot review
  Compare absolute count with those estimated from blood smear exam

Level 1

Level 3

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 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 (Hematology II)**

- 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 (Hematology II)**

- 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 (Hematology II)**

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 luminaggregometry  
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 (Hematology II)

Define the coagulation factors
- Roman numerals
- Common names
- Synonyms

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

Discuss characteristics of the coagulation factors
- Contact group
- Prothrombin group
- Fibrinogen group

List the vitamin K-dependent factors

Compare and contrast the plasma-based (in vitro) and cell-based (in vivo) mechanisms of coagulation (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

Summarize the interaction of the coagulation system with the vascular and platelet systems to form a hemostatic plug

Describe the physiologic controls of hemostasis
- Blood flow
- Feedback inhibition
- Liver clearance

Identify the inhibitors of hemostasis
- 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 analysis of plasma samples.
subsequent handling of specimens for coagulation testing

- 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

- 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

Discuss the principle and clinical significance of Factor assays
Perform the procedure (performed in preceptorship)
Describe the procedure
Describe appropriate quality control procedures and sources of error
Interpret results
Describe interferences and sources of error

Identify technical conditions that cause false coagulation testing results

**Fibrinolytic system (Hematology II)**

Define fibrinolysis
Discuss the physiological role of the fibrinolytic system
Identify the major components of the fibrinolytic system
Discuss the mechanisms of the activation of plasminogen
  - Intrinsic activators
  - Extrinsic activators
  - Exogenous activators
List the major fragments of fibrinogen degradation
Explain the role and clinical significance of physiologic controls
  - Alpha-2-antiplasmin
  - Alpha-2-macroglobulin
  - Plasminogen activator inhibitors (PAI)
Identify and describe laboratory procedures that are used to evaluate the fibrinolytic system

Discuss the principle and clinical significance of the FDP assay
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 the D-Dimer Assay
Perform the procedure (performed in preceptorship)
Describe the procedure
Describe appropriate quality control procedures and sources of error
Interpret results

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

**Disorders of primary hemostasis  (Hematology II)**

Differentiate between disorders of the vasculature
Acquired purpura
Henoch-Schölein purpura
Hereditary hemorrhagic telangiectasia
Ehlers-Danlos syndrome
Pseudoxanthoma elasticum

Define the following terms associated with hemostasis disorders
- Thrombocytopenia
- Thrombocytosis
- Thrombocythemia

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

Describe the inheritance pattern, pathophysiology, clinical features, and laboratory findings of disorders of secondary hemostasis (Hematology II)
- 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
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
Interpret results

Discuss the principle and clinical significance of the Dilute Russell viper venom time (DRVVT)
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 the Low-phospholipid (LA-sensitive) vs. high-phospholipid APTT
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 the Platelet neutralization procedure

Perform the procedure (performed in preceptorship)

Describe the procedure

Describe appropriate quality control procedures and sources of error

Interpret results

Outline a protocol to follow when investigating a patient with an unknown bleeding disorder

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 (Hematology II)

Differentiate between primary and secondary fibrinolysis

Define disseminated intravascular coagulation (DIC)

Identify mechanisms by which clotting is initiated during DIC

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)

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

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

**Anticoagulant therapy** (Hematology II)

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** (Hematology I)

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 maintenance and troubleshooting Level 1
- Perform maintenance/corrective action (performed in preceptorship) Level 2

Identify basic concepts of quality assurance for automated hematology cell counting 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 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
Troubleshoot and corrective action Level 2

Discuss 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