

Laboratory Hematology

Faculty coordinator M. Elaine Eyster, MD

Michael Bayerl, MD in Surgical Pathology (Bone marrows and flow cytometry), Keri Donaldson, MD in Clinical Pathology (Peripheral smears, automated CBCs and thrombosis testing), Melissa George DO (Blood component therapy and compatibility testing), Elaine Eyster MD (coagulation assays)

Goals:

The hematology fellow must become proficient in 1) morphologic evaluation of peripheral blood smears and bone marrow aspirates. 2) principles of flow cytometry and interpretation of leukemia, lymphoma, myeloma and PNH panels 3) interpretation of hematology and coagulation/thrombosis tests. 4) selection of appropriate hematology and coagulation/thrombosis tests. 5) technical evaluation of test methods in hematology and coagulation/thrombosis. 6) collection and preparation of bone marrow biopsies and aspirates, 7) Blood component therapy and the technical aspects and interpretation of red cell compatibility testing, antibody identification and recognition of transfusion reactions.

In addition, the hematology fellow must gain sufficient knowledge of laboratory hematology, coagulation/thrombosis, and transfusion medicine sufficient for satisfactory performance of the Hematology Board examination.

The above goals will be met by 2 one- month rotations focusing on the technical aspects of 1) general hematology tests and interpretation of peripheral smears and bone marrow aspirates/biopsies. 2) Assays and procedures typically performed in the Coagulation/Thrombosis and Special Hematology laboratories and the Blood Bank, 3) Clinical decision making utilizing test results..

Specific learning objectives:

- 1) The principles and methods of electronic blood cell counting, and the parameters measured.
- 2) The interpretation of bone marrow aspirates and peripheral blood smears.
- 3) The principles of flow cytometry and the interpretation of leukemia, lymphoma and PNH panels.
- 4) The PTT-based clotting assays and mixing studies.
- 5) The Xa –based assay and the indications for its use
- 6) The tests which are used to detect a lupus anticoagulant.
- 7) The prothrombin time, how the INR is calculated, and the reasons for its use.
- 8) The tests used to detect intravascular coagulation, and in particular, the principles and use of the D-dimer and FDP tests.
- 9) The tests used to evaluate thrombophilia
- 10) Sickle cell solubility testing
- 11) Hemoglobin electrophoresis
- 12) Immunofixation and measurement of quantitative immunoglobulins
- 13) P2Y₁₂ ADP receptor assay for clopidogrel inhibition

- 14) ABO and Rh typing, red cell compatibility testing and antibody identification
- 15) Workup of warm auto antibodies and positive Direct Antihuman Globulin Test (DAT)
- 16) Principles of blood component therapy

The fellow is responsible for attending bone marrow sign out rounds with Dr. Bayerl or his associate and for scheduling instruction for the following laboratory procedures at the following locations. He/she should gain an understanding of the technical aspects of each procedure. The fellow should observe each of the following procedures, and perform those marked with an *. He/she should become technically expert in the performance of bone marrow aspirations and biopsies, and in the preparation of peripheral blood and bone marrow aspirate smears.

Main clinical laboratory (section supervisor, Victoria Smalls)

- CBC by automated cell analyzer
- Platelet count (automated and manual)
- Reticulocyte count (automated and manual)
- Leukocyte differential (automated and manual)
- Prothrombin time (and INR), and partial thromboplastin time
- Fibrinogen level
- Coagulation factor assays
- Anti Xa heparin assay
- Antithrombin assay
- Protein C and S assays
- Activated Protein C Resistance assay
- Factor V Leiden and Prothrombin G202010A assays (Dr. Donaldson)
- D-Dimer assay
- Thromboelastograph
- Sickle solubility (prep)
- Hemoglobin electrophoresis (Dr. Castellani)
- Hemoglobin quantitation by HPLC (Dr. Castellani)
- Immunofixation and quantitation of immunoglobulins (Dr. Castellani)
- Red Cell Osmotic fragility assay (send out test)

The fellow observes each of the above procedures and should gain an understanding of the technical aspects of each.

Special Heme Lab (C6609) (section supervisor Jeff Sanders)

- Clotting factor inhibitor assays*
- Clotting factor inhibitor assays*
- Von Willebrand factor assays *
- PFA-100 closure time*
- Platelet aggregation*
- Preparation of peripheral smears and bone marrow aspirates (technical proficiency required)
- PNH flow cytometry

Educational challenges of the accuracy and usefulness of diagnostic tests in clinical decision making.

* hands-on performance

He/she should contact Dr. Donaldson (HG 150 x 5660, pager 3384) to arrange to be instructed in the interpretation of thrombophilia/thrombosis tests, and Dr. Eyster (room C6606) for interpretation of coagulation and platelet tests.

At the conclusion of the **first rotation**, he/she will be expected to complete

- 1). A practical examination by performing a factor VIII and IX assay on the STAGO instrument in the SHL
- 2). The case studies provided
- 3). The educational challenge of the accuracy and usefulness of diagnostic tests in clinical decision making.

At the conclusion of the **second rotation**, he/she will be expected to successfully complete the on line examinations

Clinical Hematology lab and Heme/Path Elective **Schedule**

Rotation #1

8:00– 11:00 SHL and Clin Heme lab regularly when procedures are performed, as needed to achieve goals and objectives.

11:00 –12:00 daily –CBC and slide review; coagulation and thrombosis discussions – Dr. Donaldson

2:00-5:00PM daily – Hemepath review with Dr. Bayerl in microscope room

Rotation #2

Mornings in the Blood Bank under supervision of Dr. Melissa George.

Afternoons in the SHL on special projects, flow cytometry core lab and Hemepath review with Dr. Bayerl

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Hematopathology

The faculty coordinator for this part of the rotation is Michael Bayeryl, MD

The fellow should attend daily bone marrow sign out sessions with review of morphology and flow cytometry in C 6618 from 2-5 PM daily with Dr. Michael Bayerl or his designee.

Medical Knowledge

Fellows are expected to review bone marrow biopsies and aspirates, and flow cytometry results daily and formulate a diagnosis which is to be written in pencil on the diagnosis sheet. Fellows will then review the cases with hematopathology attending and residents in the scope room from 2-5PM.

Patient Care

Fellows should examine charts of patients' whose bone marrows they are evaluating to incorporate clinical data into the diagnosis.

Fellows should recognize leukemia, dysplasia, fibrosis, infiltration on bone marrow biopsy

Fellows should recognize acute and chronic leukemia, hemolysis. TTP, sickle cell, megaloblastic anemia

Professionalism

Interact respectfully with pathology staff

Respect patient confidentiality

Communication

Fellows should communicate marrow and flow cytometry results to the treating physician.

Systems Based Learning

Understand the preparation of bone marrow biopsy specimens and special staining techniques. Understand the principles of flow cytometry

Practice Based Learning

References for hematopathology are attached. They have been purchased for use by the fellow on hematopathology and are available in Dr. Cream's office.

Major Reference: WHO Classification of Tumours. Pathology and Genetics. Tumours of Haematopoietic and Lymphoid Tissues. Jaffee ES, Harris NL, Stein H and Vardiman JW. IARC Press

Laboratory Hematology – Routine, Coagulation and Special tests

Faculty coordinators: M. Elaine Eyster, MD and Keri Donaldson, MD

Medical Knowledge

- Develop and maintain a knowledge base in automated hematology testing, peripheral blood analysis, flow cytometry analysis of blood and bone marrow aspirates as they relate to RBC disorders, platelet disorders, leukemias, lymphoproliferative disorders, inflammatory disorders, and disorders of coagulation and thrombosis.
- Effectively examine and interpret peripheral blood smears
- Effectively analyze and interpret coagulation and thrombosis testing.
- Develop and maintain a knowledge base in the basic and clinical sciences necessary for effective consultation in Laboratory Hematology that includes automated hematology testing, peripheral blood analysis, and disorders of coagulation and thrombosis.
- Understand the various levels of evidence in medicine and their translation into evidence-based practice.

Patient Care

Gather essential and accurate information about patients using all relevant available modalities and incorporate into pathologic interpretations.

- Effectively examine and interpret bone marrow biopsies and aspirates, incorporating flow cytometry and molecular/cytogenetic information.
- Understand and become proficient in the procedural aspects of bone marrow aspiration and biopsy.
- Effectively consult on interpretation of tests of disorders of coagulation and thrombosis.
- Effectively consult on interpretation or follow-up of unusual or unexpected hematologic test results.
- Effectively participate in laboratory hematology at multidisciplinary conferences.

Professionalism

- Demonstrate compassion: be understanding and respectful of patients, their families, and the staff and physicians caring for them.
- Interact with others without discriminating based on religious, ethnic, sexual, or educational differences.
- Demonstrate positive work habits, including punctuality, dependability, and professional appearance.
- Demonstrate responsiveness to the needs of patients and society that supersedes self-interest.

- Demonstrate principles of confidentiality with all information transmitted both during and outside a patient encounter.
- Demonstrate a commitment to excellence and ongoing professional development.
- Demonstrate interpersonal skills in functioning as a member of a multidisciplinary health care team.

Interpersonal and communication skills

- Demonstrate the ability to write an articulate, legible, and comprehensive yet concise consultation note; provide a clear and informative report, including when appropriate a precise diagnosis, a differential diagnosis, and recommended follow-up or additional studies.
- Effectively participate and present at multidisciplinary conferences in focused, clear, and concise fashion.
- Use effective modes and mechanisms of communication.

Systems-based practice

- Demonstrate the ability to design resource-effective diagnostic plans based on knowledge of best practices in collaboration with other clinicians.
- Demonstrate knowledge of the laboratory regulatory environment.
- Understand policies and systems to continually improve patient safety as they relate to
- hematology and coagulation/thrombosis testing.

Practice-based learning and improvement

- Demonstrate knowledge of evidence-based medicine and apply its principles in practice.
- Develop personally effective strategies for the identification and remediation of gaps in medical knowledge needed for effective practice.
- Use laboratory problems and clinical inquiries to identify process improvements to increase patient safety.

Specific Skills in Patient Care and Medical Knowledge Required to Achieve These Competencies

Red Blood Cells:

1. Describe the morphology and physiology of RBC production.
2. Understand the principles of laboratory methods used to measure and/or calculate RBC indices including: RBC count, Hb concentration, HCT, MCV, MCH, MCHC.

3. Be familiar with the normal ranges for Hb concentration and HCT, and how these vary with: age, gender, hydration status, local elevation, handling and storage of specimen, etc.
4. Accurately identify polychromatophilic RBC on a blood smear. Understand the principles of laboratory measurement of reticulocyte counting, physiologic corrections and interpretation of results.
5. Identify normal and abnormal RBC morphology on a blood smear and generate differential diagnoses based on common abnormalities such as: hypo/hyperchromatic cells, macro/microcytes, polychromasia, elliptocytes/ovalocytes, spherocytes, burr/spur cells, dacrocytes, target cells (leptocytes), schistocytes, sickle cells, Howell-Jolly bodies, Pappenheimer bodies, bite cells, normoblasts, etc.
6. Describe the laboratory methods, interpretation and limitations of measuring ESR.

Granulocytes:

1. Describe the morphology and physiology of myelopoiesis (neutrophilic, monocytic, eosinophilic and basophilic lineages). Describe the concept of the margined pool of neutrophils and its physiologic/pharmacologic regulation.
2. Describe the laboratory methods, limitations and interpretation of counting leukocytes in the blood and generating a leukocyte differential. Explain why our clinical laboratory does not report "bands."
3. Generate a differential diagnosis for quantitative leukocyte disorders..Specifically define neutropenia, degrees of severity and clinical consequences. Know the major hereditary neutropenic disorders.
4. Identify the major, qualitative, disorders of neutrophils. Correlate the clinical syndromes associated with these disorders.
5. Differentiate neoplastic from non-neoplastic myeloid disorders.

Lymphocytes:

1. Correctly request and interpret flow cytometric and immunoperoxidase immunophenotyping on bone marrow aspirates for diagnosis and prognosis as related to lymphoproliferative disorders.
2. Correctly request and interpret molecular and cytogenetic testing prognosis as related to lymphoproliferative disorders.
3. Apply 1. through 6. to differentiate physiologic from neoplastic lymphoid proliferations.
4. Recognize non-neoplastic lymphoid patterns with specific clinical correlates. Correctly classify lymphoid neoplasm based on the WHO 2001 classification, including clinical, morphologic, immunologic and molecular correlates.

Platelets:

1. Describe normal megakaryopoiesis, physiologic control and morphology.
2. Describe normal platelet functions.

3. Develop a differential diagnosis for thrombocytopenia and an algorithm for diagnosing specific etiologies.
4. Develop a differential diagnosis for thrombocytosis and an algorithm for diagnosing specific etiologies.
5. Describe the pathophysiology of specific platelet function disorders.
6. Describe the underlying principles, interpretation and limitations of specific platelet tests:
 1. Platelet / Megakaryocyte morphology
 - Platelet morphology in blood film
 - Platelet granules by EM
 2. Platelet counting
 - Visual platelet estimate
 - Hemocytometer phase contrast
 - Automated
 3. Platelet function testing
 4. PFA 100 Closure time
 5. Platelet aggregation and release
 6. Antiplatelet antibody testing

BLOOD BANK ROTATION: Melissa George DO>Specific Learning Objectives:

- To understand the role of the transfusion medicine service and how to appropriately utilize the resources of this service for optimal patient care.
- To be able to interpret basic blood bank testing.

Medical Knowledge

Fellows must demonstrate knowledge about established and evolving best practices in transfusion medicine and apply them to the practice of transfusion medicine services.

Fellows are expected to:

- Observe blood bank procedures at the bench and understand the immunohematologic principles behind the testing. The recommended procedures to observe are outlined in the checklist below:
 - Specimen handling
 - ABO/Rh typing
 - Antibody screens
 - Antibody identification (and special techniques to aid this process)
 - Workup of warm autoantibodies and positive DATs
 - Workup of transfusion reactions
 - Observation of apheresis procedures
 - Observe blood donor screening and collection (whole blood and apheresis components)

- Read recommended scientific literature and protocols provided in the blood bank rotation guide and discuss their content during regular, informal meetings with the medical director or attending of the day.

Patient Care

Fellows are expected to:

- Learn the scope and limitations of immunohematology tests and be able to discuss them with requesting and interpreting physician staff.
- Learn to interpret relevant lab results and integrate patient history into the diagnosis and make appropriate recommendations regarding the administration and selection of blood components and appropriateness of apheresis therapy.
- Learn to evaluate transfusion reactions and adverse blood donor and apheresis patient reactions.

Professionalism

Fellows must conduct themselves in a professional manner when interacting with patients, donors, laboratory personnel, nurses, and medical staff. They must be committed to fulfilling their professional responsibilities abiding by ethical principles and sensitivity to diverse patient populations. Fellows are expected to:

- Demonstrate a commitment to excellence and ongoing professional development
- Adhere to ethical principles pertaining to confidentiality of patient information, informed consent and business practices at all times
- Adhere to guidelines and regulations set forth by regulatory and accrediting agencies
- Demonstrate compassion and integrity in all interactions with patients, their families, faculty, other trainees, technologists, and other staff
- Practice positive work habits; punctuality, dependability, and professional appearance
- Attend all required conferences and actively participate in them to enhance individual and group learning
- Be respectful of patients, and those involved in their care
- Be an active listener
- Be able to identify deficiencies in peer performance and address them in a constructive manner to ensure appropriate patient care and safety
- Demonstrate sensitivity and responsiveness to ethnicity, diversity, age, gender, sexual orientation, and disabilities of patients, colleagues, and staff and interacting with them without discrimination
- Demonstrate responsiveness to the needs of patients that supersedes self-interest

Interpersonal and communication skills

Fellows must be able demonstrate interpersonal and communication skills that result in effective information exchange and learning with other health care professionals, patients and patients' family or other representatives. Fellows are expected to:

- Exhibit effective listening skills, follow verbal instructions and written standard operating procedures
- Interact with laboratory staff, departmental faculty, fellow house staff and other health care providers and administrators in an effective and professional manner
- Work effectively as a team member with other health care professionals and staff
- Answer questions pertaining to blood components, blood testing, apheresis procedures and to utilize appropriate resources to make appropriate recommendations to clinicians, including

Systems-based practice

Fellows must be aware of the importance of transfusion medicine in the larger context of the health care system and be able to call on system resources to help respond to needs as they emerge ensuring appropriate transfusion medicine services to provide optimal patient care. The fellow is expected to:

- Approach blood banking/transfusion medicine in the greater context of the particular patient's medical care and hematologic needs
- Understand the optimization of workflow in the laboratory and computer information systems and EMR as a means to efficiently and accurately obtain clinical information
- Demonstrate understanding of the role of the clinical laboratory in the health care system
- Demonstrate the ability to design resource-effective diagnostic plans based on knowledge of best practices in collaboration with other clinicians to provide cost-effective services without compromising patient care
- Demonstrate knowledge of the laboratory regulatory environment
- Understand policies and systems to continually improve patient safety as they relate to clinical laboratory testing at all levels acting as an advocate for quality patient care

Practice-based learning and improvement

Fellows must demonstrate the ability to evaluate and improve clinical practices based on new and evolving scientific evidence. Fellows are expected to:

- Use the current scientific literature and apply consensus recommendations to patients undergoing apheresis and blood component therapy

- Utilize library, web-based, and other education sources for self-study, troubleshooting and to help answer clinical/technical questions
- Participate in clinical conferences, be aware of new testing being introduced into the laboratory
- Serve as consultants to requesting physicians regarding applications of transfusion medicine to optimize patient outcomes
- Arrange for effective clinical care efficiently according to established protocols
- Utilize performance evaluations to improve practice
- Engage in “lifelong” learning through critical review and assimilation of scientific studies related to specific transfusion medicine challenges
- Facilitate learning of medical students, residents and fellows (within and outside the Pathology department), and other health care professionals with regard to blood banking and transfusion medicine services

Specific Topics and Reading Assignments

- **The basic core reading** for the rotation is **Transfusion Medicine and Hemostasis: Clinical and laboratory Aspects**. Hillyer CD, Shaz BH, Zimring JC and Abshire TC. Elsevier Press 2009.
- **Selected reading on erythrocytes, granulocytes, lymphocytes and platelets**
Henry, JB. Clinical Diagnosis and Management by Laboratory Methods (20th Ed.). Philadelphia: Saunders, 2001, Chapters 19, 24-28
- Klein HG, Anstee, DJ (Ed): *Mollison’s Blood Transfusion in Clinical Medicine* (11th Ed.), Blackwell, 2005.

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