

HEMATOPATHOLOGY (SHANDS HOSPITAL AT THE UNIVERSITY OF FLORIDA): Rotation Director: Ying Li, M.D., Ph.D., Assistant Professor

I. Description of the rotation: During this rotation, the resident will gain experience in morphology as well as *flow cytometry, immunohistology, molecular genetics and cytogenetics* (ACGME competencies #1: Pt. Care; #2: Medical Knowledge). *Integration* of laboratory results with clinical findings is the primary aim of this rotation (ACGME competency #2: Medical Knowledge). Procedures during this rotation include the following:

- 1) Bone marrow (>400/year): The bone marrow comprehensive studies are performed on bone marrow biopsy and aspirates including morphology and usually immunohistochemistry and/or flow cytometry. If necessary, cytochemical, molecular genetic and/or cytogenetic analysis may be performed.
- 2) Peripheral blood: Comprehensive studies are performed to detect or characterize acute leukemia and lymphoproliferative disorders. The studies include morphology and flow immunophenotype. If necessary, *molecular genetic analysis* may be performed.
- 3) Peripheral blood comprehensive studies to detect or characterize dysplastic and myeloproliferative syndromes, or acute leukemias; includes morphology, flow immunophenotype and cytogenetic analysis. If necessary, cytochemical or molecular genetic analysis may be performed. Rarely, *electron microscopy* is also used.
- 4) Lymph node/extranodal lymphoid masses. Slides and/or paraffin blocks for histology, with or without immunohistology, or fresh tissue for comprehensive studies including histology, cytology on touch imprints and cytopins, flow immunophenotype; if necessary, immunohistology and *molecular genetics are performed to evaluate reactive process and hematopoietic malignancy.*
- 5) Serosal fluids for comprehensive studies to diagnose and/or classify lymphoproliferative disorders and acute leukemias; includes cytology on cytopins, flow immunophenotype and, if necessary, molecular genetic analysis.
- 6) The resident should become familiar with the *bone marrow aspirate and biopsy techniques* and the mechanisms for establishing the adequacy of these techniques. If the resident wants to perform bone marrow aspirates or biopsies, arrangements will be made to do so. At the beginning of the rotation, the resident can contact the Hematology/Oncology physician assistants who perform most *bone marrow aspirations and biopsies* to arrange notification when a *bone marrow* is to be performed. Initially, the resident may perform bone marrow biopsies on anesthetized patients and progress to conscious patients (*graduated responsibilities*).

As appropriate to the individual case or consultation under review, the ethical, socioeconomic, medicolegal, and cost-containment issues are reviewed and discussed (ACGME competency #6: Systems-Based Practice). As well, research design, statistics, and critical review of the literature are discussed (ACGME competency #3: Practice-Based Learning). By use of the literature, Medline, and textbooks, the resident is trained to become a lifelong learner (ACGME competency #3: Practice-Based Learning).

II. Goals of the rotation: The resident will learn grossing of specimens, determining and prioritizing diagnostic procedures, analyzing results, gathering pertinent clinical information and additional laboratory data, and case presentation. *Management* issues (e.g. personnel and budget), medical/legal issues and socioeconomic issues (cost containment and test utilization) should be discussed as they pertain to individual cases. The resident is trained to become a lifelong learner by using the medical literature, Medline, and textbooks.

III. Duration of the Rotation: Three 4-week rotations over 4 years.

IV. Duties and Responsibilities of residents: The resident assumes increasing responsibility with increased experience (*graduated responsibility*). Residents receive intense training and demonstrations during the initial rotations and are assigned *increasing responsibilities* during subsequent rotations. The resident is involved in weekly conferences and in interactions with technical laboratory personnel (ACGME competency #4: Communication; #5: Professionalism). The resident and fellow keeps a log of bone marrow aspirations and biopsies performed/observed. This information is kept in the resident's or fellow's file for completing the application for Pathology Boards.

V. Teaching staff for the rotation: Ying Li, M.D., Ph.D.; Li-Jun Yang, M.D., Ph.D.; Samer Al-Quran, M.D.; Robert Allan, M.D.; Fellows; and Hematopathology staff.

VI. Resident supervision and evaluation:

1) **Resident supervision:** The residents are supervised by fellows and attending physicians. Cases are reviewed on a daily basis. Reports are generated in concert with the attending faculty and signed out by the attending faculty.

2) **Resident Evaluation:** Written monthly evaluation. Revised 2-19-2009

VII. CORE CURRICULUM FOR HEMATOPATHOLOGY (revised 2-19-2009)

Residents rotating through Hematopathology are encouraged and expected to improve their knowledge of this field of pathology in a step-wise fashion by not only increasing areas/subjects of knowledge, but also by graduated responsibility. By the time a resident has completed their final rotation, it is expected that he or she will be comfortable in full case management, formulation, and execution of diagnosis for the majority of hematopathology cases. The goals to be achieved by the end of each rotation are as follows:

Rotation 1.

General Knowledge

- a) Knowledge of basic hematopoietic cell morphology.
- b) Rotate through flow cytometry laboratory
- c) Observe and perform bone marrow biopsies (optional).

Morphology

- a) Morphologically recognize common peripheral blood/bone marrow abnormalities (leukopenia, anemia, thrombocytopenia, leukocytosis, lymphocytosis or leukoerythroblastic picture) and be able to assess iron stains performed on bone marrow aspirate smears.
- b) Perform accurate differential counts on standardized bone marrow aspirate smears. The residents are expected to be able to recognize blasts and normal granulocytic and erythroid precursor cells and perform at least five differential counts on bone marrow aspirate smears at the end of the first rotation.
- c) Accurately assess bone marrow core biopsy cellularity and basic infiltrative processes- lymphoma, acute leukemia, metastases, fibrosis, granulomata and be able to assess iron stains iron and reticulin stains.

- d) Approach basic lymph node diagnosis - reactive vs. neoplastic, classical Hodgkin lymphoma, diffuse large B-cell lymphoma, follicular lymphoma, CLL/SLL, mantle cell lymphoma and plasma cell neoplasm. The residents are expected to be able to assess results of common immunohistochemistry studies (CD3, CD20, CD5, CD23 cyclin D1 and Bcl-2).

Flow cytometry

- a) Observe the technical aspects of sample preparation and performance of flow cytometry.
- b) Obtain hands-on experience performing a basic flow cytometric panel (4 antibodies) and analyzing the resulting data.
- c) Begin basic flow cytometric analysis.
- d) Recognize basic immunophenotypic abnormalities such as B-cell clonality or acute leukemia.
- e) Recognize immunophenotypes of common B-cell lymphoma (follicular lymphoma, chronic lymphocytic leukemia and mantle cell lymphoma) as well as plasma cell neoplasms.

In addition, residents are strongly encouraged to read page 16-24 of Color Atlas of clinical hematology by A Victor Hoffbrand and John E Pettit for and Parts I and II of Joachim's Lymph Node Pathology by Harry L. Joachim, Howard Ratch to acquire basic knowledge of structures and cell populations of normal bone marrow and lymph nodes as well as principles of bone marrow and lymph node pathology.

Rotation 2

General Knowledge

- a) Understand classification of common hematologic processes according to the WHO classification scheme
- b) Triage of specimen- deciding which blocks/immunostains are needed.
- c) Formulate and record initial diagnoses before discussion with attending hematopathologists.

Morphology

- a) Morphologically recognize common peripheral blood/bone marrow diseases-acute leukemia, myelodysplasia, and myeloproliferative disorders (CML).
- b) Understand the morphological and immunophenotypic features of subtypes of low-grade lymphoproliferative disorders (follicular lymphoma, chronic lymphocytic leukemia, mantle cell lymphoma and marginal zone B cell lymphoma, etc). The residents are expected to understand the differential diagnosis of common non-Hodgkin lymphoma (B-cell), including follicular lymphoma, small lymphocytic lymphoma, mantle cell lymphoma, large B cell lymphoma, Burkitt lymphoma, and marginal zone lymphoma etc.
- c) Understand differential diagnosis of Hodgkin lymphoma and be able to assess results of common immunohistochemistry studies (CD30, CD15, CD20, CD45 and CD3).

- d) Recognize more uncommon types of lymphoma including anaplastic large cell lymphoma, peripheral T cell lymphoma and lymphoblastic lymphoma.

Flow cytometry

- a) Render more specific flow cytometric diagnosis and distinctions, such as main subtypes of acute leukemia (M3 vs non-M3) and immunophenotypic differential diagnosis of subtypes of B cell lymphoproliferative processes).
- b) Continue gaining hands-on experience with the analysis software and understand the maturational-related immunophenotypic changes (B cells, T cells, erythroid and granulocytic precursors).

Rotation 3

General Knowledge

- a) The residents are expected to understand main criteria of classification of common hematopoietic malignancy (FAB and WHO) and their associated molecular and/or chromosomal abnormalities.
- Acute myeloid leukemia with t(8;21), t(15;17) and inv(16)(p13q22) or t(16;16)(p13;q22),
 - Acute myelomonocytic leukemia
 - Acute monocytic leukemia
 - AML with myelodysplasia-related changes
 - Therapy-related myeloid neoplasm
 - Chronic myelogenous leukemia (t(9;22))
 - Chronic myelomonocytic leukemia
 - Classification of myeloproliferative disorders (Chronic myelogenous leukemia (CML), Polycythemia Vera (PV), Essential thrombocythemia (ET), Idiopathic myelofibrosis (IM))
 - Classification of myelodysplastic syndromes
 - Diffuse large B cell lymphoma
 - Burkitt lymphoma, t(8;15), t(2;8) or t(8;22)
 - Low grade B cell lymphoma,
 - Follicular lymphoma, t(14;18)
 - Chronic lymphocytic leukemia, trisomy 12
 - Mantle cell lymphoma, t(11;14)
 - Marginal zone B cell lymphoma, trisomy 3, t(11;18)
 - Hodgkin lymphoma
 - Common peripheral T cell lymphoma, including anaplastic large cell lymphoma and T/NK cell lymphoma.
- a) The resident should be able to manage common cases, from beginning (triage) to end with full write up, including integration of clinical, morphologic, flow cytometric, cytogenetic and molecular data.
- b) Triage of specimen- deciding which blocks/immunostains are needed and beginning to formulate which markers should be used in a limited panel to detect a potentially abnormal population.
- c) Communicate to or request from the clinician, pertinent information needed for case resolution or optimal patient care.

Morphology

- a) Ability to recognize a spectrum of common hematologic processes, including formulation of relevant differential diagnosis and increased understanding of processes that fall outside of the spectrum of pre-defined classification schema.

Flow cytometry

- a) Render specific flow cytometric diagnoses in most cases of hematopoietic malignancy and show increased understanding of more challenging distinctions (eg. Myelodysplasia, clonal T cell processes etc.)

VIII. HEMATOPATHOLOGY LECTURE AND EXAMINATION (revised 2-19-2009).

The residents and fellows will be given a series of lectures (including case discussion) every two years. The hematopathology lecture series include 18 lectures/case discussions, one examination and two lectures for discussing results of the examination. The results of examination will be used to evaluate the residents' or fellows' knowledge of hematopathology as well as to identify the weakness of hematopathology training so that we can improve the hematopathology training process.

IX. Reading List

Topics that are recommended as initial reading to provide basic background knowledge are denoted by an asterisk (*). The resident should make an effort to read about topics as they arise during the rotation and make an effort to complete this list by the end of their rotation schedule.

- Anemia- *hypochromic microcytic anemias, *megaloblastic anemias, anemia of chronic disease, aplastic/hypoplastic anemias, hemolytic anemias
- Reactive granulocytic/monocytic disorders- neutrophilia, eosinophilia, basophilia, monocytosis, neutropenia, functional defects in granulocytic, granulocytic disorders with abnormal morphology
- Reactive lymphocytic disorders- *infectious mononucleosis, etc.
- *Acute leukemias- including new WHO classification
- *Myelodysplastic syndromes- including WHO classification, cytogenetic abnormalities
- *Myeloproliferative disorders- Chronic myeloid leukemia, polycythemia Vera, essential thrombocythemia, idiopathic myelofibrosis, etc.
- *Chronic lymphoid leukemias- chronic lymphocytic leukemia, hairy cell leukemia
- Reactive lymph node disorders- eg. *infectious mononucleosis, HIV infection, *cat-scratch disease, *toxoplasmosis, *Kikuchi's disease, Castleman's disease, sarcoidosis, sinus histiocytosis with massive lymphadenopathy (Rosai-Dorfman disease), etc.
- Lymphomas- *Small lymphocytic lymphoma/leukemia, *follicular lymphoma, *mantle cell lymphoma, marginal zone lymphomas, *diffuse large cell lymphoma, *Burkitt's lymphoma, *lymphoblastic lymphoma, *Hodgkin's lymphomas, T-cell lymphomas, *anaplastic large cell lymphoma, angioimmunoblastic lymphadenopathy.
- Immunosecretory disorders- *multiple myeloma, monoclonal gammopathy of undetermined significance (MGUS), post-transplantation lymphoproliferative disorders

- Granulocytic Sarcoma (Extramedullary myeloid cell tumor)
- Mast cell Diseases- cutaneous vs. systemic mast cell disease
- Histiocytic and Dendritic Cell Neoplasms- Langerhans cell histiocytosis, follicular dendritic cell sarcoma/tumor, histiocytic sarcoma

IX. SUGGESTED REFERENCES:

- WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. Swerdlow SH, et al: Lyon, FR. IARC, 2008.
- Practical Diagnosis of Hematologic Disorders. Kjeldsberg (ed): Chicago, IL. ASCP Press, 2006
- Bone Marrow Pathology. Foucar K (ed): Chicago, IL, ASCP Press, 2001.
- Ioachim's Lymph Node Pathology by Harry L. Ioachim, Howard Ratach
- Color Atlas of clinical hematology by A Victor Hoffbrand and John E Pettit
- Atlas of Lymphoid Hyperplasia and Lymphoma. Ferry JA, Harris NL (eds): Philadelphia, PA, W.B. Saunders Company, 1997.