Resident Training in Laboratory Hematology
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The Academy of Clinical Laboratory Physicians and Scientists (ACLPS) has published a template to serve as a guideline for designing a clinical pathology (CP) or laboratory medicine curriculum [1]. The document provides a broad overview of how CP training can be organized and how competencies can be assessed for residents undertaking CP training. When preparing the document, the authors took into consideration the Graylyn conference recommendations [2], which discussed changes that needed to be implemented to conform to the Accreditation Council for Graduate Medical Education (ACGME) guidelines for residency training, and the reduction in the duration of residency training in pathology from 5 to 4 years for combined anatomic pathology and clinical pathology candidates and 3 years for CP-only or AP-only candidates. According to these guidelines, laboratory hematology training includes training in the analysis of hematologic specimens (including morphologic inspection of peripheral blood smears, bone marrow specimens, and lymph nodes), body fluids, urinalysis, special hematology (including specialized studies of red cells and platelets), coagulation, and flow cytometry. In the current article, the authors attempt to summarize the principles that should apply when implementing a program that effectively trains residents to be competent pathologists in the various settings that they may encounter once they complete training.

When designing a training program, two (not necessarily divergent) perspectives have to be taken into account: those of the trainer and of the trainee. From their past experience the trainers formulate priorities and decide what knowledge is essential for a trainee to have for practice as a pathologist. The trainee, at the same time, begins every training with the

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question, “Why do I need to learn this?” To put this into perspective, one needs to refer to the recommendations of the Graylyn conference. According to these recommendations, a resident trained in CP should be capable of directing and managing clinical laboratory services and be able to serve as a consultant to physicians. It needs to be emphasized that 80% of the pathologists trained in the US practice in a community hospital [3], and 61% of these practice in a group of 6 or less pathologists. Accordingly, a resident pathologist coming out of training needs to have a very broad knowledge base to be able to serve as a consultant and to recognize when the case needs to be passed on to someone with more specialized knowledge. These recommendations are further emphasized in a recent report on expectations and essentials for the community practice of pathology [4].

Hematology comprises a very broad segment of laboratory medicine and pathology. For a wide variety of local and historic reasons, the various components of hematology have been divided into different divisions and subdivisions of the clinical laboratories. The most striking example of this phenomenon is the distinction between “dry” and “wet” hematology. In many institutions, the interpretation of “dry” material (including lymph node biopsies and bone marrow biopsies) is performed in anatomic pathology separately from “wet” specimens, including the interpretation not just of peripheral blood smears but also of bone marrow aspirates, which are in turn performed by a clinical pathologist or sometimes even by a clinical hematologist, without the involvement of a pathologist. Flow cytometric, immunohistochemical, molecular, and cytogenetic approaches to the study of hematologic disorders may have homes not only within the different subdivisions of laboratory medicine and pathology, but even in separate departments all together.

Even within the parameters of what most pathologists would agree is “wet” hematology, the responsibility for specific testing is handled quite differently from institution to institution. For example, many institutions have a dedicated laboratory for hemostasis and thrombosis. At other institutions, however, routine coagulation may be bundled into a core hematology lab, while advanced studies in hemostasis and thrombosis are performed in a separate laboratory. Similarly, hemoglobinopathy/thalassemia testing may be an integral part of the main hematology laboratory, or may be bundled with coagulation testing into a special hematology section. In yet other institutions, hemoglobinopathy/thalassemia testing has found an entirely new home within a clinical chemistry laboratory setting.

Given such heterogeneity in how laboratory hematology is actually practiced in different institutions, it should come as no surprise that there is also a great deal of heterogeneity in how residents are trained. There can be appreciable differences in the hematologic curriculum from one institution to another, particularly for residents who are training in AP-only or CP-only. For example, a CP-only resident in one institution may be exposed to a considerable amount of bone marrow and lymph node pathology.
whereas a resident training at another institution may have significantly less exposure to these subject areas. Moreover, even within a given institution, resident training may vary considerably with respect to the breadth and depth of hematology that they ultimately explore.

It is not the purpose of this article to advocate for one or another of the many possible ways that laboratory hematology can be organized within a particular institution. Nevertheless, it is important to emphasize that one of the most critical components of diagnostic laboratory hematology is the integration of laboratory data, generated from various sources, to formulate the final diagnosis. Despite the considerable variability in how the components of hematology testing are organized in an individual institution, there are certain underlying principles that should apply; these principles include active learning, an increasing assumption of the role of a clinical consultant, and an appreciation of the critical application of basic science to clinical medicine. These principles transcend the issue of which specific laboratory section within the clinical laboratories performs a particular test.

Additionally, the training must be organized in such a fashion that the resident makes progress within the set of ACGME competencies; these are patient care, medical knowledge, practice-based learning and improvement, interpersonal and communications skills, professionalism, and systems-based practice. Finally, every possible attempt should be made to ensure that a rotation or a component thereof does not end up being only an exercise in reading critically. While in-depth reading is of critical importance, it is not a substitute for the deeper learning that arises from a thorough evaluation of actual patient cases.

As mentioned earlier, training in laboratory hematology encompasses very diverse components of laboratory medicine. As such, training in the microscopic recognition of entities is an important part of training in diagnostic neoplastic hematopathology. On the other hand, laboratory hematology requires proficiency in various techniques used in the laboratory as well as familiarity with automation, sophisticated instrumentation, and the quality control issues involved therein. Therefore, a somewhat different approach needs to be used when designing a training program for these various components. For this reason alone, the authors have divided the subsequent discussion under the following headings: routine hematology and medical microscopy, erythrocyte abnormalities, hematopathology, and coagulation and platelet studies; however, this is by no means, a recommendation for splitting hematology training into such sections.

**Routine hematology and medical microscopy (including body fluids and urinalysis)**

Routine hematology and medical microscopy provide excellent examples of the crucial function that the pathologist performs in directing the management plan of an individual patient and in communicating that plan to
the primary care physician. A complete blood count and leukocyte differential are often among the first laboratory tests ordered on a patient presenting to a physician. The additional laboratory work-up and the management of the patient are influenced by what these tests show. In addition, body fluid specimens (cerebrospinal fluid [CSF], joint fluids, thoracocentesis fluids, and so forth) are also important, because the abnormal specimens provide additional opportunity for residents to consult with and learn from the clinical staff. It is therefore very important that residents be trained to understand the medical significance of the results generated by these tests; to formulate differential diagnoses based on the findings in the blood counts, the peripheral smear, or the body fluid examination; to communicate this to clinical colleagues; and to provide a plan for further laboratory work-up, if needed. This can be accomplished if the resident is the “go-to” person and is physically present in the laboratory to answer questions from the technical staff as well as from the clinicians. It is also important that the residents be trained to understand the influence of age on the various parameters being analyzed. There are at least two implications of this aspect: (1) the normal values for infant and pediatric patients may differ from the established adult normal values, and (2) laboratory results in infants and pediatric patients may provide clues about various congenital disorders.

Routine hematology relies heavily on automated instruments operated by the technical staff in the laboratory. Therefore, in addition to the medical implications of the results generated, the residents need to be trained in the basic principles that are applicable to the instruments, and in issues about informatics involved in interfacing the instrument with other laboratory information systems used in the hospital. An awareness of specimen requirements, quality assurance (QA)/quality control (QC) issues is important, as is the understanding of limitations and possible sources of errors in the information generated from an automated instrument. A classic example is the accuracy of mean corpuscular volume (MCV) and other red cell indices in a patient who has obvious red cell agglutination on the peripheral smear. It is therefore imperative that the resident be trained to interpret these values in the context of what is microscopically visible on the peripheral smear or the body fluid smear made from the specimen, and proceed to some of the more specialized approaches discussed below.

Hemoglobinopathies/thalassemias and other erythrocyte abnormalities

The study of qualitatively or quantitatively abnormal, individual hemoglobin species has a rich history within hematology. Morphologic clues to diagnosis can be either subtle or, in the case of a sickling crisis, extremely helpful in narrowing the differential diagnosis. The hematology laboratory has traditionally employed one or another environmental challenges to living erythrocytes to assess deviations from normality in the response. The Sickledex and sodium bisulfite test are examples of these challenges,
applicable to the evaluation of sickle hemoglobin. Virtually all of the enzymes involved in erythrocyte metabolism can also be analyzed [5]. Biochemical separation techniques, such as electrophoretic and chromatographic procedures, have also been invaluable in the identification of specific hemoglobin abnormalities [5]. Moreover, in some instances, only actual DNA sequence determinations permit a definitive diagnosis [5].

Resident involvement with hemoglobinopathies involves not only the initial diagnosis of a patient, but potentially extends also to patient management. A poignant example of this involvement is decision-making for the institution or continuation of red cell exchange in patients who have sickling disorders. Whether the actual Hemoglobin S (Hgb S) quantitative testing resides within one or another section of the hematology laboratories, or within a chemistry laboratory, the resident covering the transfusion medicine’s red cell exchange service needs to be able to interpret these values with regard to how they may contribute to clinical decision-making.

Hematopathology

As the authors alluded to in the introduction, a very important aspect of diagnostic hematology is the morphologic interpretation of pathologic entities by microscopy. This includes the interpretation of bone marrows and lymph nodes for neoplastic as well as nonneoplastic conditions, such as congenital disorders in infants and children. However, unlike most areas of anatomic pathology, the final diagnosis requires the integration of ancillary data generated from other parts of the laboratory. Thus, diagnosis of acute leukemia requires not just an interpretation of a bone marrow biopsy, but also an incorporation of the automated complete blood count with differential, flow cytometry, and genetic and molecular studies. Similarly, the diagnosis of a lymphoma requires incorporating immunophenotypic, cytogenetic, and molecular information into the morphologic interpretation of the specimen. The essential aspect of making an accurate and correct diagnosis is to obtain adequate diagnostic material and to process it such that all information necessary to make the diagnosis becomes available. Thus, a resident rotating through hematopathology is expected to learn how to obtain an adequate bone marrow biopsy and be a part of the decision-making process about what special tests (eg, cytochemistry, flow cytometry) need to be performed on any given specimen. Similarly, in a patient who has a suspected diagnosis of lymphoma, the residents participate in the decisions about how to process and divide fresh tissue for appropriate ancillary testing, including flow cytometry, cytogenetics, and molecular studies. The residents are also trained on how to recognize the technical limitations of a poor specimen and ways to correct the deficiencies in the specimen, if possible.

As far as improving the residents’ medical knowledge base is concerned, the authors have found it useful to use a two-pronged approach. On the one hand, resident involvement in the preview of specimens leads to the resident
becoming familiar with the relatively common diagnostic questions posed in hematopathology, including the diagnosis and evaluation of the response to therapy. This is complemented, in turn, by a systematic, didactic curriculum to cover both the common and not-so-common entities, in the format of a small, prepared, but informal talk given by the resident, and a review of slides from the archival teaching sets. The authors have found that this two-fold approach helps to familiarize the residents with the less common entities that they may or may not encounter during the limited time they spend rotating in the section of hematopathology. The authors have also found it useful to increase the resident responsibility in the sign-out process in a progressive manner. This maximizes their understanding of the issues involved without overwhelming them. Thus, at the beginning of the rotation, the resident involvement in the cases is limited to reviewing the case with the attending pathologist. This participation progressively increases to the preparation of reports, and the interpretation and integration of flow cytometry and other diagnostic processes. Competency in the medical knowledge base is assessed at the end of the rotation by an integrated quiz that includes morphologic interpretation. In addition, as a means of improving medical knowledge, the residents are also trained to understand the limitations of the clinical information provided and to take the initiative to obtain additional information when appropriate.

As a means to encourage practice-based learning and improvement, the residents are strongly encouraged to read and incorporate references from the literature when preparing reports on unusual or novel entities. The authors also find it useful to have residents assume the responsibility of discussing and communicating new diagnoses, as well as clinical issues, with the clinical colleagues. This achieves the two-fold objective of improving the resident’s communication skills and also preparing them for the role of the consultant, which they are expected to assume by the end of their training. Every attempt is made to train the residents to take into account laboratory costs when initiating a diagnostic work-up. Familiarity with a systems-based approach to practicing hematology is inculcated by familiarizing the residents with all laboratory information systems. The residents also learn how to use a multidisciplinary approach for the care of patients who have hematologic disorders. For example, the diagnosis of polycythemia vera requires taking into account specific red cell parameters obtained from either the routine hematology laboratory or from the section of nuclear imaging, erythropoietin levels from the clinical chemistry laboratory, and Janus Activated Kinase 2 (JAK2) mutation status from a molecular diagnostic laboratory, along with the microscopic interpretation of bone marrow morphology.

**Coagulation and platelet studies**

Resident rotations in a laboratory dedicated to coagulation and platelet studies should provide an introduction to the principles and practice of
laboratory hemostasis and thrombosis. Depending upon level of complexity of the testing offered, the rotation can potentially offer experience in all aspects of this field, including the evaluation of patients suspected of having increased bleeding or thrombotic tendencies, as well as patients who present with a variety of abnormal laboratory findings in primary hemostasis, secondary hemostasis, or fibrinolysis. Choosing the appropriate testing in hemostasis/thrombosis and properly interpreting the results of these tests constitutes a major challenge to the great majority of clinicians in the medical and surgical disciplines. A well-trained pathologist has the potential to facilitate this challenge significantly. Such a rotation should accordingly strive—above all else—to help train pathology residents to acquire the knowledge and experience needed to provide consultative assistance to clinicians in the area of hemostasis/thrombosis.

Learning which tests are most appropriate and efficient to diagnose and manage disorders of bleeding and thrombosis is fundamental. The resident must additionally learn the correct choice of anticoagulants, blood processing, and other preanalytic aspects critical to the proper specimen procurement for laboratory testing. It is important to provide opportunities for the resident to work effectively with technical staff. Typically, it is the technical staff who impart a great deal of practical knowledge, such as the ability to recognize technically poor patient specimens and take steps to obtain better specimens as appropriate. On the other hand, it is typically through interactions with faculty that the resident learns to recognize the limitations of the clinical history provided and takes the initiative to obtain additional information if necessary. Over time, the resident must learn to communicate effectively and take ownership of specific problems or queries from clinicians and ancillary medical personnel (eg, nurses, technologists) regarding laboratory procedures and results. Gradually, with appropriate mentorship, the resident learns to provide informative, accurate consultation to clinical staff and ancillary personnel regarding a wide range of diagnostic and management issues.

A resident should develop a basic knowledge of diagnostic and prognostic aspects of common bleeding and thrombotic diseases. These include vitamin K deficiency, warfarin anticoagulation, heparin anticoagulation, and direct thrombin inhibitor anticoagulation. Either through evaluation of current cases or evaluation of cases previously encountered by the laboratory, it is important for the resident to be exposed to cases of inherited coagulation factor deficiencies (typically with emphasis on hemophilia A), von Willebrand disease, consumptive coagulopathies (DIC), immunologic thrombocytopenic purpura (ITP), thrombotic thrombocytopenic purpura (TTP), and heparin-induced thrombocytopenia (HIT). The choice of which tests to employ, the potential pitfalls of testing, and the interpretation and communication of test results are all critical to learn. Even if some part of the testing must be sent out to a reference laboratory, it is important to provide just as rigorous an evaluation of such testing as if it were performed in-house.
Variability in the testing approaches among laboratories is at least as great in the evaluation of thrombotic risk factors, as in the case of bleeding disorders. It is important for the resident in training to be exposed to a diversity of approaches beyond the algorithms that have been adopted in a particular institution’s own laboratory. Clearly, the assignment of readings on a topical basis, as well as a subsequent discussion of these articles with faculty, is an excellent way to achieve this goal. It is also important for the resident to become aware of published guidelines by professional societies where they exist. Examples of these published guidelines include the evaluation of Platelet Function Analyzer 100 (PFA 100) testing on behalf of the International Society on Thrombosis and Haemostasis (ISTH) [6], as well as widely accepted recommendations pertaining to testing for heparin-induced thrombocytopenia and related disorders [7].

Platelet function testing is presently almost unique in the clinical laboratory, to the extent that it provides the resident an example of putting human cells through their physiological paces ex vivo, virtually in front of the resident’s eyes. As such, it may have educational value as a paradigm to be potentially emulated in other areas of the clinical laboratories. Perhaps more than any other aspect of testing within the coagulation laboratory, the interpretation of platelet aggregation (with or without concomitant secretion studies) possesses a subjective component. As in the case of histologic examinations of tissue, there is often richly textured information contained within the study. In addition to the actual total extent of aggregation achieved with particular platelet stimuli at defined concentrations, considerations of rate of aggregation, lag of aggregation or secretion responses, reversibility of aggregation, platelet shape change, and so forth, all contribute to the emerging picture. In some cases, careful examination of the platelet aggregation curves can provide the first suggestion that a circulating inhibitor of one or another platelet receptor may be present. Due to the rareness of certain disorders, it is almost always necessary to supplement present case material with additional studies, performed either in-house or reported in the literature. Important patterns to recognize are those caused by aspirin inhibition, clopidogrel inhibition, disorders of platelet signaling, platelet storage pool disease, inherited or acquired Glanzmann thrombasthenia, inherited or acquired Bernard-Soulier syndrome, and the different forms of von Willebrand disease.

To the extent that the work of the service permits, it is very beneficial to the resident in training to learn how to write clear, concise reports of hemostatic and thrombotic evaluations, and to present conferences to clinical colleagues and technical staff. The authors would also strongly suggest that residents develop and maintain a portfolio of all the clinical cases that they have been involved with, even if no formal written report results from a particular involvement. Regardless of the structure of the laboratory, ample opportunity must be provided for the resident to gain an in-depth
understanding of test validations and all ongoing measures related to quality assurance and management.

**Summary**

The actual duration of time spent in laboratory hematology depends on the way different laboratory sections are organized in an institution. However, a broad recommendation can be 5 to 6 months, including the time spent in laboratories performing more specific testing such as hemoglobin evaluation and platelet studies. It is equally important to reinforce the knowledge acquired throughout residency after the resident has finished the specific hematology rotations. This can be accomplished by means of “on-call” responsibilities, teaching conferences, and participation in tumor boards and other interdepartmental conferences.

As discussed by Genzen and Krasowski in their article on clinical chemistry elsewhere in this issue, and in previously published literature, a resident practicing in the community hospital, while primarily functioning as a surgical pathologist, might assume the role of a medical director of a clinical laboratory, including hematology. Similarly, even in the setting of a large institution such as an academic teaching hospital, the resident may eventually assume the role of laboratory director at some point in time after finishing training. It is therefore important to include the management issues in the training of residents. The authors find that the philosophy of “do and learn” is more effective than the philosophy of “watch and learn.” Resident participation in laboratory rounds to discuss technical, informatics, and personnel issues that come up in the laboratory is a way of achieving this target. To the extent possible, the residents should be asked to participate in quality assurance and quality control issues, including answering College of American Pathologists questionnaires, participating in mock College of American Pathologists inspections, and validating and implementing new tests and equipment.

In conclusion, hematology truly bridges the disciplines of laboratory medicine and anatomic pathology, and the training must span the spectrum from knowledge of laboratory instrumentation and management to analysis of fine details of cytology and tissues. It is likely that these aspects are split in different ways in different institutions. However, it is important to remember that, irrespective of the specifics of the training organization, certain principles need to be kept in mind. These can be summarized as follows:

- The residents need to be able to formulate a plan of action and communicate it to the clinicians, based on the evaluation of common laboratory tests such as a complete blood cell count
The resident needs to be able to integrate data from various laboratories
The resident needs to be familiar with management issues

Accomplishing these goals goes a long way to help not only residents with a special interest in hematology, but truly for all residents moving into careers in the broader area of laboratory medicine and pathology.

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References