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ScienceDirect
Annals of Diagnostic Pathology 11 (2007) 137–141
Annals of DIAGNOSTIC PATHOLOGY

Technical Note

Histology: a unique area of the medical laboratory

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Abstract Fundamental differences in samples, procedures, nature of results, automation, productivity, staffing levels, and background decision making along work flow and turnaround times characterize histology as a unique area within the medical laboratory. For histology laboratories to function successfully, individual and collective training, well-defined goals, and implemented accountabilities with effective supervision are required. The pathologist, as immediate client of the histology laboratory, has to be involved in the whole operation to assure optimal patient care.

Keywords: Decision making; Training; Accountability; Pathologist involvement

1. Introduction

The histology laboratory (HL) represents one of the most crucial components in the chain leading to histopathologic diagnosis. Although traditionally staffed and managed by certified and experienced histotechnologists and technicians, the pathologist plays a critical role in guiding the way in which the work is done, in quality assurance, and in making sure that the final product meets adequate standards. Pathologists should therefore become aware of the fundamental differences between the HL and other areas of the medical laboratory (ML) in departments of pathology.

2. Peculiar characteristics of the HL

Understanding the uniqueness of the HL requires a comparison with the others areas of the ML. Comparisons can be made using generalizations that will apply in at least 90% of cases for any given laboratory, leaving the remaining 10% for the ever-present exceptions.

The generalizations include the basic work flow, from the source and characteristics of the samples, the nature and diversity of the testing methods, their automation and results, to the personnel composition and its origin.

The fundamental differences between the HL and other areas of the ML are summarized in Table 1.

2.1. Samples

Although some blood and urine samples are difficult to duplicate and constitute a unique snapshot of a patient's condition at the time the sample was taken, any single microliter of blood/serum is essentially identical to any other from the same sample and will provide the same results consistently.

Most histology specimens, on the other hand, are discrete, solid, heterogeneous, and essentially unique. Once obtained, they cannot be replaced and may be lost forever along with all of its intrinsic information.

Each histology section is also unique; any tissue section not used when the block is trimmed initially or during any subsequent processing reduces the sample's original information. The blocks saved after sectioning are the "leftovers" of the original specimen, usually with less diagnostic value.

2.2. Procedures

Marketing pressures determine testing diversity in chemistry and other areas of the ML, with a total of less than 400 current procedures [1].

Although the technical horizons and scope of esoteric tests in histology are constantly expanding, the "formalin-fixed paraffin-embedded" tissue sections followed by the "hematoxylin and eosin" routine stains remain its "bread and butter," followed in frequency by histochemical (HC) and immunohistochemical (IHC) tests.

The recognized procedures that a specimen can undergo to prepare a finished slide are in excess of 4500. Ninety-five

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doi:10.1016/j.anndiagpath.2007.01.002

Table 1
Summary of fundamental differences between histology and other areas of the ML

Aspect	Other areas of the ML	Histology area
Samples	Liquid, homogeneous, abundant, and usually *recollectable*	Solid, heterogeneous, unique, discrete, and *irreplaceable*
Procedures	Less than 400; diversified because of marketing pressures.	More than 4,500; diversified because of personal preferences and use
Results	Essentially quantitative and easy to qualify	Essentially qualitative and difficult to quantify.
Instrumentation	High productivity automation of ca 80% of all tasks	Less than 30% of all tasks are automated, and not in all laboratories
Work flow	Batches can be finished continuously in high-volume laboratories	Batches are finished intermittently in most laboratories.
Decision making	Only few tasks require a low level of decision	Each step of the work flow requires some type of decision impacting the finished slide
Productivity and workload	Automated and more productive instruments are used to compensate workload increments	Workload increments are compensated by increasing the staffing because of physiological limits of the fundamental manual tasks
Turnaround time	Except for some cultures, from seconds to minutes per test	Minutes to hours per test
Personnel	Less than 25% grandfathered for licensure after training on the job	About 50% (currently) grandfathered for licensure after training on the job

percent of them were published between 1841 and 1950 and developed empirically, with little chemical understanding of the underlying principles, so much so that even today, the mechanisms governing some HC procedures are deemed to be unknown. Personal preferences may also explain why any "general" method varies between laboratories even when applied to IHC, where each laboratory uses a preferred dilution ratio for the same antibodies [2-5].

There are no general standardized procedures, only some procedural consistency within any HL but not between laboratories. Each histotechnologist holds on to the "known methods" because they have proven to be reliable for the fundamental task of manual sectioning, and anything that threatens to interfere with it is rejected a priori.

2.3. Results

Results in the ML are usually clear-cut: a quantified amount, a frequency histogram or scatter diagram, pathogen identifications based on their physiology, something tangible and incontrovertible requiring little intervention from the pathologist other than verification or interpretation. When in doubt, the test can be repeated with an identical fraction of the same sample along with quantitative controls. Only the interpretation of quantitative results may be open to discussion, but not the actual values.

That is not the case in histology, where results are essentially qualitative, with only few attempts at quantification, usually limited by the quality of sections [5]. Histology is the realm of the "preferred diagnosis," where the interpretation of microscopic details can be the subject of discussion and "second opinions." This is so much so that in the markers program sponsored by the College of American Pathologists (CAP), the final results for the cases are offered as a "preferred interpretation" even when IHC has been applied.

2.4. Instrumentation/equipment

Microscopy is an old art initially developed as a hobby by some individuals who were awestricken by the beauty and appearance of nature under the microscope.

Table 2
Technical innovations and their impact on the histology work [6-9]

Year	Technical innovation
1868	Sliding microtome, more useful after the introduction of the paraffin process in 1869
1881	"L" molds to cast paraffin blocks, further improved with reusable metal molds in 1950
1884	Microtome with automatic block advance after each backward stroke
1886	Naples clamp for block orientation into any needed position
1887	Rotary automatic microtome
1888	Heated bath for simultaneous paraffin embedding of several specimens
1890	Heated water bath to handle paraffin sections ribbons
1894	Racks to stain up to 30 slides simultaneously
1899	Block trimmer to standardize block size and parallel orientation to the blade etch
1909	Basic automated clock-controlled tissue processor with a basket moving between stations
1924	Automated sharpening of microtome steel knives
1935	Adaptor to section with disposable 2-edge shaving blades
1945	Commercially available tissue processors developed from the basic 1909 design
1959	Disposable blades and holders, improved in the 1970s to present standards
1964	Embedding center with cold and hot areas
1980 to 2005	Tissue processors with vacuum, pressure, agitation, and temperature controls; microwave ovens; automated stainers for routine and special procedures: coverslippers; cassette writers; slides etchers; and even an automated embedding system

In those early days of the 17th and 18th centuries, the observer prepared the slides with mostly either plant materials sectioned "free hand" with razor blades or entire microscopic plants or animals.

"Histology" was not born until microscopy became a branch of medicine seeking explanations to known pathologies based on their microscopic appearance. At that moment, by the middle of the 19th century, some individuals were assigned the task of preparing histologic glass slides; and the trade of histotechnology emerged using basic procedures, many of which have survived to the present day after some technical innovations (Table 2).

In those early days, except for some "bacteriology" pioneering research and the microscopic observation of blood smears and urine sediments, the rest of the ML did not even exist!

2.5. Work flow

Although some types of samples in the ML are manually and individually processed (blood units, microbiology cultures, organisms staining), the norm is to batch them for processing, intermittently in small laboratories or continuously in high-volume settings.

In histology, only frozen sections are handled individually in a single continuous process; the rest of the samples are batched at every step. Some automated stainers, coverslippers, cassette labelers, and slides etchers, and the new throughput microwave tissue processor technology allow continuous flow within some steps; but all other instruments complete each step intermittently [10].

2.6. Decision making

Decision making during the processing of the samples is the fundamental difference between the HL work and that of the rest of the ML, and it can have a significant impact on the final diagnosis.

The medical technologist in the clinical laboratories is not involved in much decision making during sample processing other than detecting the need to rerun a test or for the evaluation of some specimens and culture results.

This is not the case in histology, where mistaken decisions by the histotechnologist are difficult to detect, impossible to undo, and can be made at every step along the work flow. Each small tissue sample is like a treasure trove of diagnostic information that can be lost or damaged forever because of a wrong decision.

The most important decisions are made while grossing, where selecting one part of the specimen over another to be processed into a tissue block is done by tactile or macroscopic appearance. Grossing is a "high complexity test" as defined by the Clinical Laboratory Improvement Amendments and should be reserved only for pathologists, pathology residents, or specially trained and certified pathology assistants, but never to histotechnologists, no matter how experienced the latter [11].

Unless the specimen is a "gross only," even when a specimen is "entirely submitted," it may be subjected to many decisions. The histotechnologists get to decide macroscopically how much tissue to allow per cassette for optimum processing, when a decalcification has been completed, how to embed the specimen if it is not inked or does not have a guiding notch, how deep to go into the block before cutting the final sections, which sections to discard in the water bath (forever!), and which to keep for staining.

Before staining, the histotechnologists are also charged with deciding when the sections are dry enough before heating to avoid artifacts, if the end point of the HC procedure was reached, or if the IHC controls reacted as expected before deciding to repeat the test or not [12].

2.7. Productivity/work load

As expected, the most productive area of the ML is chemistry, with an annual average of 49,000 billable tests per full-time employee (FTE), followed by microbiology with 10,000 tests per FTE. Cytology averages 7,000 accessioned cases per screener; and transfusion medicine, 4,000 type screenings and crossmatches per FTE [6,13].

Histotechnologists average 9,000 blocks per year, but measuring productivity as an individual event is the wrong approach and does not allow the optimization of each step of the work flow. Optimal productivity for histotechnologists would be about 7 blocks every hour, from specimen reception to slides ready for the pathologist [14].

In the ML as a whole, productivity increases with the workload; but in histology, it does not because there are physiological limits to any manual work. Hiring additional histotechnologists is generally the only solution to compensate workload increments [13,14].

2.8. Turnaround time

In the ML, the turnaround time can be from a few seconds for the most simple and automated chemistry test, to the many days needed to detect growth of some microorganism. The time required for the clinicians to receive the results adds to the total turnaround time.

Histology tests occupy some sort of intermediate position, from a few minutes to stain some smears or a frozen section to be completed, to several hours from the reception of the sample to the slides ready for the pathologist. Issuing the final report can take up to several days in very busy or understaffed laboratories.

Generally, the routine diagnosis is ready within 24 hours of specimen reception, which has been qualified as satisfactory by 96% of submitting surgeons [15].

2.9. Personnel/staffing

This is perhaps the most controversial aspect of the HL and the cause of salary disparities between histology and other areas of the ML, some of which have been corrected only recently. This has also added to a feeling by some histotechnologists of being "looked down on" [16].

The problem stems from the early days of the ML, approximately 50 to 60 years ago, when there were no licensure requirements and automation was almost nonexistent.

Who were the initial laboratory employees working in chemistry, microbiology, and hematology? They were chemical engineers, chemists, pharmacists, physicians, college graduates in several disciplines, bacteriologists, and graduates from other disciplines. Less than 25% were undergraduates, with their knowledge limited only to on-the-job training, who were grandfathered into licensed status when licensure became a requirement.

Who were the initial histotechnologists? They were medical students, nurses, and some college graduates in disciplines unrelated to medicine or even biology. They could also be anybody with manual dexterity willing to put up with toxic fumes and unsafe environments, including orderlies, janitors, or secretaries hoping to improve their lot, as well as high school graduates and even family members and friends of the pathologists. They were all trained on the job, and about 50% of the current histology personnel in the United States were grandfathered when licensing became mandatory.

Nowadays, all technical personnel in the ML, histology included, have to undergo specialized training; but that was not the case in the early days. Therefore, today, histotechnologists who are 50 years and older were essentially trained on the job regardless of their academic level. Histology schools have never been abundant and are even scarcer today, with only 23 "online" programs added to 11 college-level schools in 9 states (http://www.NSH.org) to cover all of the national needs and to fill the positions of many retiring histotechnologists.

The new histology esoteric tests require advanced academic preparation. The histotechnologists assigned to do the more esoteric tests, however, are usually not involved with the day-to-day manual operation involved in routine histology. The latter is still being handled by the most seasoned and usually less academically trained histotechnologists, who are the ones that will make every imaginable decision based only on experience.

3. How to assure quality in the HL

So far, I have presented the complex and unique characteristics of the HL and underscored the fact that all along the work flow there are decisions to be made that can affect the final product, that is, the quality of the slides the pathologists are going to base their diagnoses on.

How can we assure the best quality for the whole work flow? There are essentially 3 ways to accomplish that goal: training, accountability, and supervision.

3.1. Training

Training has to be individual and collective, and should include the whole personnel involved: residents, pathology assistants, and histotechnologists.

All HLs should be enrolled in the National Society for Histotechnology/CAP Histo QIP Program (http://www.NSH.org) and send slides for peer review. This will allow them to benefit from the final critique and find out if their quality level is at par with other laboratories.

The CAP inspections should not be viewed as the sporadic exercise of going through a checklist, but as a daily work guide once all required control systems are implemented. Every HL should participate in all available programs providing procedural peer review; the cost is worth it because it will be reverted into better training.

The internal critique is also fundamental and should be done by the pathologists, not by filling forms pointing out defects, but by actively identifying slides of substandard quality and sending them to be reviewed by the histology supervisor. The histology supervisor should then analyze and correct the problems and develop strong individual and collective performance improvement programs analyzing also the effect that workload, staffing, and scheduling may have on quality [5].

3.2. Accountability

Standards of performance and competency requirements for each step in the work flow in histology are required including specific safeguards to avoid block waste by assuring their optimal use, including norms on the initial number of sections to stain and retention of unstained slides for future tests.

The standard operation procedures manual has to be maintained, updated, and followed as a guide for performance quality. If procedural changes are needed, an experiment with blind comparisons and statistical validation has to be designed.

Accountabilities should be well defined, implemented, and documented!

3.3. Supervision

Histology laboratories with 29,000 cases per year or more have supervisors, but smaller laboratories usually only have lead technologists who are also in charge of complex bench tasks. Laboratories with less than 10,000 cases have 1 to 3 histotechnologists to do all the tasks [17]. Therefore, who is to supervise the 24% of all laboratories without a dedicated supervisor?

Like it or not, that is a task that should be carried out by the pathologist, after delegating some daily operations. They should remember their residence days and get involved! It is a waste of time, resources, and above all specimen integrity to have to ask for recuts because the tissue was incorrectly processed, sectioned, or stained.

It is also necessary to point out that when a supervisor is appointed to a busy laboratory, it should be on a full-time basis; supervisors with bench duties are going to end up as low productive histotechnologists and be inefficient supervisors, effective at neither task.

The pathologists also should interact with the histotechnologists in more ways than just to request a procedure or to complain about a slide of poor quality. They should let the histotechnologists know when their work is adequate or superior; the histotechnologists need to know their work is appreciated! [18].

Training, accountability, and supervision constitute the necessary triad to assure the successful operation and continued development of this unique section of the ML called the histology laboratory!

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