Issues About Tissues, Part I: The Objectives of Histopathology

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Abstract

This work was presented at the 30th National Society for Histotechnology Symposium at Toronto in 2004, where it described the importance and recognition of histopathology as a valuable diagnostic tool. Histopathology is a stimulating and demanding science, and it is the interpretation of biopsies and smears that remains one of the principal systems for predicting the biological behavior of disease and for controlling patient management. This work not only considers the diagnosis but describes, through the adoption of strict laboratory guidelines, how diagnostic fallibility can be minimized. Despite its demise, the value of the autopsy in clinicopathological correlation, biopsy technique, and education of anatomy also is described. (*The J Histotechnol* 28:63, 2005)

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Introduction

The principal role of the histopathologist is to provide an efficient and reliable diagnostic service. Through biopsy interpretation and assessment of surgical resections and autopsies, diagnostic testing is able to differentiate between normal and abnormal states. Making a diagnosis is a powerful cognitive process involving both knowledge and judgement (1). Knowledge is defined as the acquisition of information and may comprise a taught and a read element. Judgement (and intuition) are the skills linked to practice and it is this which enables the pathologist to recognize and classify diseases (2). Both the clinician and the histopathologist must accurately record what they observe and subsequently make a diagnosis. These diagnostic skills are linked to the thought process (critical thinking), which in 1956 was classified into six categories by the educational psychologist Benjamin Bloom (3). The relationship of these areas to the fields of pathology and medicine are described as follows:

1. *Knowledge:* to have a good working knowledge of symptoms and disease
2. *Comprehension:* to understand the tissue and organ systems that may be involved
3. *Application:* to be able to identify pathological processes that may occur
4. *Analysis:* to have the ability to discriminate one pathological process from another
5. *Synthesis:* to decide on the most likely causes from epidemiological data
6. *Evaluation:* to decide on the likely diagnosis.

The progress that has been made in biopsy methods have led to a more detailed understanding of many disease processes. With diagnosis being made on the basis of tiny fragments of tissue, a compromise has to be found between the amount of tissue required for reliable interpretation and that which can be removed safely (1). Generally, selecting a technique often will be determined by patient status, location of the lesion, the equipment available, and personal experience.

The procurement and interpretation of an accurate biopsy specimen is one of the most important steps in the management of patients, and this step may be afforded by the participation of pathologists in clinical teams. This participation is achieved through multidisciplinary meetings during which the clinical pictures and biopsy interpretations are presented and discussed with other hospital specialists. Biopsies provide a diagnosis that determines the extent of a particular lesion and can help predict biological behavior (1). This subsequently aids in determining both the type (e.g., surgery, radiation, chemotherapy) and extent of treatment (e.g., conservative, aggressive).

This is well illustrated by the use of quadrant biopsies in patients with Barrett's esophagus, where the method of surveillance is intended to monitor the increased risk of cancer development (4). The aim of endoscopic surveillance is to detect dysplasia, a change that is unequivocally neoplastic. Dysplasia is characterized by nuclear changes and generally is reported using a standard five-tier system of negative, indefinite, low-grade, high-grade, and carcinoma. Using these guidelines, a negative biopsy would require repeated

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endoscopy every few years, whereas more frequent endoscopy would be required for low grade dysplasia.

The approach to high-grade dysplasia in Barrett's esophagus provides three options: surgery, continued surveillance, or ablation therapy (4). Surgery would provide diagnostic certainty that would eliminate further surveillance. However, surgery not only requires expertise but carries a significant increase in mortality, particularly in elderly patients. Although continued surveillance would limit surgery to the diagnosis of cancer only, there is a need for more frequent endoscopy which would require expert gastrointestinal knowledge. Finally, ablation therapy is minimally invasive and avoids the problems associated with surgery, although it would still require the continuation of surveillance.

The response of patients to treatment may be followed in biopsies where findings may support or disprove clinical assessment of the effectiveness of therapy (1). The presence of villous regrowth and lymphocyte reduction in jejunal biopsies of celiac patients treated by a gluten-free diet is a prime example. Prevention, diagnosis, and treatment of disease originates from the application of research in both pathology and medicine (5). Many advances in medical knowledge directly result from the application of cellular pathology to disease. However, the development and improvement of diagnostic methods generally is gained from other disciplines, such as molecular biology, radiology, and pharmacology.

Because diseases have unique biological signals, their detection (and progression) also can be made through simple blood tests, such as the prostate-specific antigen (PSA) test for detecting prostatic diseases. Each year, millions of men have a PSA test, but it is those who test positive that will invariably have a biopsy, even though a high number of these turn out not to have cancer. One recent study has shown that as many as 15% of patients with a PSA within normal ranges will test positive on biopsy, suggesting that the detection of prostate cancer would be compromised by cutting down the number of unnecessary biopsies (6).

Table 1. The Epidemiology of Nonmalignant Diseases

Agents	*Causes*	*Effects*
Genetic	Chromosome abnormality	Down's syndrome
	Autosomal dominant (one parent)	Achondroplasia
	Autosomal recessive (both parents)	Cystic fibrosis
Acquired	Deficiency (e.g., vitamin D)	Osteomalacia
	Physical agents (e.g., cold, heat)	Frostbite, burns
	Chemicals (e.g., cyanide)	Poisoning
	Drugs (e.g., analgesics)	Liver disease
	Bacteria	Tuberculosis
	Viruses	Influenza
	Parasites	Schistosomiasis
	Hypersensitivity (e.g., allergy)	Hay fever
	Autoimmunity	Thyroiditis
	Psychogenic (acquired)	Schizophrenia
	Psychogenic (addiction)	Alcoholism

Table 2. The Epidemiology of Malignant Diseases

Agents	*Causes*	*Effects*
Chemical	Arsenic	Skin cancer
	Asbestos	Mesothelioma
	Azo dyes	Bladder cancer
	Benzene	Leukaemia
	Betel nut	Mouth and throat cancer
	Soot	Cancer of scrotum
Environmental	Agent orange (dioxin)	Lymphoma
	Radiation	Thyroid cancer
	Smoking	Lung cancer
	Sunlight	Skin cancer
Oncogenic	Human papillomavirus	Cervical cancer
	Epstein-Barr virus	Burkitt's lymphoma
	Hepatitis B virus	Liver cancer

Disease, Diagnosis, and Competence

Studies of the incidence and prevalence of disease as it affects groups of people is termed epidemiology. Originally, epidemiology dealt with epidemics of infectious diseases (such as smallpox) and outbreaks of infections (such as gastroenteritis). Nowadays, it is applied to widespread noninfectious diseases, such as cancer and heart disease (Tables 1 and 2). The incidence of a disease describes the extent or frequency of its occurrence, whereas prevalence indicates how widespread a particular disease is (prevalence = incidence × duration). In other words, each incidence of a particular disease joins an already-existing list (the prevalence pool) and if that pool remains static, then the number of new cases of disease will equal the number of old cases.

Because of the large volume of tissue samples examined, histopathologists ideally are placed to study epidemiology (1). Classification of diseases with uniformly consistent nomenclature also makes it easier to collect and investigate patients with the same disease. The identification and determination of cancerous and precancerous lesions also may involve screening asymptomatic populations, as seen with breast and cervical smear testing. Histopathologists require a broad-based knowledge and understanding of the pathological and clinical aspects of disease. They must be self-motivated, have the ability to work alone and as part of a team, regularly make critical decisions, have problem-solving skills, and have good visual pattern recognition (1). Histopathologists regularly interact with surgeons, oncologists, and radiologists during clinicopathological meetings, during which the diagnosis and clinical management of patients is discussed. Often, histopathologists develop a subspecialty interest in which they become expert in fields, such as renal and respiratory pathology.

Making a diagnosis is the act of recognizing a disease and

giving it a name. Diseases are recognized from disorders in the structure and function of tissues, and it is these disturbances that are the hallmarks of a disease. Recognition of disease is accomplished by comparing the patient or lesion with what is regarded as the normal state. Normality is not a discrete single locus but rather a bell-shaped curve of a normal distribution (7).

Although the art and skill of laboratory diagnosis generally lies within the realm of microscopy, tentative diagnoses can be achieved by the skilled pathologist and histotechnologist from the macroscopic appearance of certain tissues in the dissection room. Benign conditions, such as lipomas, fibroid uteri, and dermoid cysts, can quite easily be recognized. Similarly, carcinomas of the breast, bowel, and ovary, for example, can be readily identified.

A diagnosis is never made on macroscopic appearances alone but is always supported by microscopic examination, where the pathological process is assigned a name (e.g., papilloma, carcinoma) and tissue type (e.g., squamous, glandular). In tumor pathology, the degree of differentiation (grading) and depth of invasion (staging) also are major prognostic factors. Grading usually is classified as low-grade (grade 0 or 1) or high-grade (grade 3 or 4). There are various staging systems in current use, such as the TNM system, where T is the extent of the primary tumor, N indicates the absence or presence and extent of regional lymph node metastases, and M indicates the absence or presence of distant metastases (8).

Although the histopathological diagnosis plays a major role in the treatment of cancers and other diseases, errors do occur (1). Errors can take place at any level of diagnosis, and it is up to the clinician in charge of the case to interpret the full meaning of the biopsy result. Diagnostic fallibility is an expression of error, and it is these inaccuracies in histology reports that can critically affect patient care (9). Errors are categorized as oversights, in which significant pathology is missed, or misinterpretations, in which pathological changes are wrongly interpreted. These errors generally are classified as category 1, where the error would have a definite influence on clinical management and possible outcome; category 2, where misinterpretation or oversight has the potential to affect clinical management or outcome; and category 3, where a minor discrepancy of disease classification would likely to be of little clinical significance. Although fallibility is the expression of error, credibility is the extent to which a diagnostic opinion can be believed. Plausibility, however, does not question how valid a particular diagnosis is but rather questions the consistency that exists between the diagnosis and the clinical picture where substantial error rates have been reported (1,9).

Unfortunately, diagnostic errors are not peculiar to histopathology because they are well documented in the interpretation of radiographs, electrocardiographs, and clinical assessments of various disorders. Comparing individual pathologists is a difficult task because most pathologists have specialist areas of interest. Individual histology samples may have differing degrees of challenge and uncertainty and, as a result, an audit will only have a limited role in assessing the competence of individual histopathologists (9). As part of their risk-management strategy, cellular pathology departments should hold regular audits to minimize the chances of an incorrect diagnosis. There are several options available to improve standards, and these include clinicopathological meetings to maintain clinical liaison, peer review auditing using selected samples, and specialist referral of difficult cases (9,10). The adoption of standard histological criteria and reporting guidelines will contribute to the quality standards and help to reduce the variations in interpretation of single samples by the same observer (1).

Errors can give rise to damage liability; therefore, it is essential that all procedures and circumstances surrounding a litigation event be documented sufficiently and that includes reception of samples, gross descriptions, and microscopic interpretation (1). The signature on the final report endorses the diagnosis and all the statements in that report. The differences between what constitutes an error of judgement and that which is regarded as negligence or incompetence are clearly defined. For a mishap to be attributable to an error of judgement, it must be shown that the pathologist was exercising the same levels of competence and knowledge that would be shown by others of similar experience. Failure to apply those same general levels will expose him to the risk of successful litigation through negligence and incompetence (1,9). Human error and excessive workload are major contributory factors for potential in altering patient management.

The Role of the Autopsy

For hundreds of years, dissection of the dead has been central to medical education. More recently, medical students were expected to participate in complete body dissections and to attend hospital autopsies as a means of teaching pathological concepts, clinicopathological correlations, and anatomy. Even today, autopsies have a vital role in auditing medical care and perioperative deaths (11,12). Because many disorders are unrecognizable before death, comparing histological diagnoses with those from subsequent autopsies will help improve diagnostic methods and the degree of errors that occur in biopsy sampling (13). Discordance between primary clinical diagnosis and that obtained from autopsy has been found to be high, particularly if tumors are malignant (9,14). In fact, in many patients, an undiagnosed tumor often is found to be the immediate cause of death. The decline of the autopsy in medical education has meant that fewer medical students are aware of its role in the teaching of medical fallibility and ethical practices in bereavement. During the past 40 years, the autopsy rate for patients dying in hospital has dropped steeply in the United States, New Zealand, and the United Kingdom. Indeed, fewer than half of the Australian medical schools require attendance at autopsy, and most students graduate without attending a single session (15).

Generally, it is these graduates that request autopsies if other techniques have failed to show a clear cause of death. One of the main reasons for the decline in the number of autopsies is an increased confidence in more modern methods of diagnosis, such as radiological imaging techniques, computerization, plastination, and other audiovisual teaching methods. Fear of malpractice, general apathy, and controversies surrounding organ retention also play a role (16). Even when autopsies are performed, the information often is underused, with delays in reporting and lack of participation from clinicians. Autopsies should be the subject of external audit processes and clinicians should be involved in evalu-

ating the quality of reports and the basis of conclusions and that includes the cause of death (12).

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