VIEWPOINT

Why I became a haematopathologist

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The Editor has suggested that the Journal's readers would be interested to know how I came to follow my particular career pathway. Why this interest? Is it because it is an unusual career to have chosen? Has my career has been unusually long or unusually productive? Naturally, I like to think it is because of the latter but it is probably a mixture of all three. In any event, it was not the career I chose but the career that chose me.

Perhaps I should first explain why I chose to become a pathologist at all. I entered medical school, at the University of Cape Town, without the slightest knowledge of what was entailed in studying medicine. A year of general science was followed by the grind of anatomy and physiology, interesting in their own right but hardly the exciting stuff of medicine. The third year of medical school was an eye opener. We were still not exposed to patients and most of the year was devoted to pathology (histopathology, haematology, chemical pathology, and microbiology), at 592 hours by far the longest course of the entire curriculum. The pathology course comprised a mixture of lectures (unillustrated), a daily necropsy, comprehensive practical classes, and small group tutorials. Most of what we did would today be considered a colossal waste of time but the enthusiasm of our teachers was infectious and at last I realised what medicine was all about. What attracted me most to pathology was its logical, evidenced based nature, something distinctly lacking in other ingredients of the curriculum at that time. Not surprisingly, I chose to become a pathologist.

After starting my postgraduate training in pathology in the USA, I soon realised that surgical pathology was quite different from the pathology taught to me at medical school. The "evidence" for disease processes provided by data from animal experiments, tissue culture, and so on was largely irrelevant to the interpretation of surgical biopsies. The excitement of surgical pathology lay in other directions—the interface with clinical medicine and the gradual flowering of skills in pattern recognition, more art than science. Surgical pathology had emerged in the 1850s following Virchow's seminal publication on the cellular theory of disease, and gradually diverged from the science of pathology, branching out to become a largely different although still related discipline. Since the 1850s, advances in surgical pathology principally comprised technical improvements allowing more detailed and reproducible morphological observations of diseased tissue. This culminated in the 1950s with ultrastructural images obtained with the electron microscope. Surgical pathologists were concerned with correlating microscopic morphology with specific diseases

and not really interested in mechanisms; thus, true hypothesis driven research was not something commonly undertaken by them. The choice for the aspiring pathologist lay between so called academic pathology, which largely involved laboratory experiments, and human diagnostics; I had chosen the latter and at the end of my training embarked on lucrative private practice.

Despite the attractions of life in metropolitan Boston, I continued to miss the intellectual excitement that I had felt during my year of pathology in medical school. Interesting questions were, indeed, continuously thrown up by my surgical pathology cases but the means of answering them were not obviously apparent. The research techniques current in academic pathology departments at that time seemed remote from the clinic, too complex and anyway inaccessible to a diagnostic pathologist. Curiously, however, it was an academic experimental pathologist who provided the means to revolutionise diagnostic surgical pathology. Searching for a marker to attach to proteins so their migration in inflamed tissues could be traced, Professor Morris Karnovsky of Harvard Medical School lighted on the small molecule, horseradish peroxidase. This enzyme, as every surgical pathologist now knows, oxidises colourless diaminobenzidine to form an insoluble brown precipitate. By conjugating peroxidase to antibodies and using diaminobenzidine as a developing agent, the pathologist is potentially able to view any protein to which an antibody is available in the context of the structure of the tissue. At a stroke the number of "special stains" available to the surgical pathologist exploded from a handful to an almost infinite number. Immunohistochemistry finally enabled the pathologist to observe not only the structure of cells and tissues but also their function.

The advent of immunohistochemistry was the catalyst that caused me to abandon the private practice of pathology and embark on a career as an "academic" surgical pathologist in Britain. Throughout my career I had been fortunate in working with remarkable pathologists who were broadminded and encouraged free thinking. In joining Professor Dennis Wright's department in Southampton I encountered this same atmosphere. Although grantless, I was given the time and resources to pursue my original and as it turned out naive idea of using the immunoperoxidase technique to detect carcinoembryonic antigen in colonic biopsies with a view to developing a "special stain" for detecting colon carcinoma. After working for a few years on this and other gastrointestinal pathology projects, a single case changed my focus. In 1976, I received a small bowel resection specimen from a patient with refractory coeliac disease and so called

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idiopathic ulcerative jejunitis. Unwilling to accept the designation “idiopathic” for the ulcers, I doggedly sectioned ulcer after ulcer, all of which showed non-specific inflammatory changes until, in the base of one ulcer, I observed a minute focus of malignant lymphoma. Together with Professor Wright, who, conveniently, was already an internationally renowned haematopathologist, I set about using the new technique of immunohistochemistry, and later molecular biology, to study the association of lymphoma with coeliac disease and later to challenge and change long held concepts of intestinal and subsequently other lymphomas. I had become a haematopathologist.

It is difficult to describe the intellectual excitement that I have experienced from a career in the “new” post 1960s discipline of surgical pathology, and particularly haematopathology.

The nature of the surgical pathologist’s work permits privileged insights into human disease and provides unparalleled opportunities for formulating and testing new hypotheses. All he or she needs is the time (and relatively few resources) to take advantage of this privilege. But there lies the rub. The time is no longer available. Surgical pathology training has changed, become more formalised, shorter, more focused and examination centred. The deadly division between the surgical and academic pathologist has been resurrected. A few selected trainee pathologists may have the opportunity of embarking on an “academic” career which now means answering a question posed by his or her PhD supervisor, but the opportunity of asking their own questions and formulating and testing their own hypotheses seems to have been lost. I doubt that I could have pursued my career today.

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