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Nephrology: As It Was Then, But Is Not Now

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Diseases of the kidney are old, but the discipline dedicated to their study, nephrology, is barely more than 50 years old. As recounted in this recollection of those events, the rudiments of what would become nephrology emerged in the time between the 2 World Wars from basic studies of normal kidney function and flourished after the integration of their methodologies into clinical medicine thereafter. Although shaped by studies of kidney function in the 1960s, it was the subsequent advent of dialysis that fueled the growth of nephrology well into the 21st century. Although to some extent this growth was a product of technical developments (micropuncture, dialysis, biopsy, etc), it was the paradigm shifts they engendered that brought about the revolutionary changes that stimulated the growth of nephrology from its formative years in the 1960s. Notable among those was the classification of chronic kidney disease on the basis of kidney function, calculated from serum creatinine level as estimated glomerular filtration rate, that has expanded nephrology's interaction with and integration into other disciplines and begat the recent outpouring of epidemiologic and interventional studies, thereby establishing it as a leading discipline dedicated to improving outcomes for individuals with kidney disease worldwide.
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> He who sees everything grow from the beginning will have the best view of them.
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> Homer Smith, *Man and His Gods*[1]

The title of this personal reminiscence of the changes in nephrology over the past 50 years is borrowed from *As It Was… But Not Now: A Memoir* by Joseph Merrill (born 1923), a past vice-president of Baylor College of Medicine, of his 60-year journey through medicine.[2] That is just about the lifespan of nephrology. For although diseases of the kidney are ancient, the discipline dedicated to their study is relatively new. It was in 1960 when the inaugural International Congress of Nephrology convened with the consequent establishment of the International Society of Nephrology in 1961.[3] It was then that "nephrology" entered the parlance of medicine. That was just 5 years before I embarked on my career in nephrology in 1966, the year in which the American Society of Nephrology was founded, although nephrology would not become a certifiable specialty until 1972.

THE TERRAIN

The 1960s were heady times in the progress of medicine in general and of nephrology in particular. It was then that the quantitative methods of the basic sciences were integrated into clinical medicine, a process that would propel the empirical practice of medicine theretofore into a hypotheses-driven scientific discipline, which lend to quantification and experimental verification, as we know it now.[4] To a great extent, what catalyzed this change was the targeted research effort of World War II (WWII), which was goal directed and encouraged multidisciplinary investigation by applying the tools and methodologies of the basic sciences to resolving the clinical problems encountered in the battlefields.[5] In the decades preceding WWII, studies of the kidney had been done by a growing number of physiologists, pathologists, and internists, often working independently, who may have been "nephrophiles," but none considered themselves nephrologists, and several of whom were recruited to contribute to the war effort.[6] One especially relevant example of this course of events is Alfred N. Richards (1876-1966), who between 1924 and 1941 developed a micropuncture technique of the renal glomerulus and made one of the most significant contributions to the understanding of kidney

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function by isolating and demonstrating the protein-free glomerular filtrate and its electrolyte composition,[7] work that he abandoned during the war to chair the Committee on Medical Research, one of the divisions of the Office of Scientific Research and Development chaired by the electrical engineer Vannevar Bush (1896-1974). What carried the interface between basic research and clinical medicine into the postwar era was the visionary leadership of the likes of Vannevar Bush and Alfred Richards, who convinced the federal government that targeted scientific research was a national asset deserving of financial support. This was a fundamental change that in the postwar period fostered academic departments dedicated to clinical investigation, where laboratories as well as physiology and chemistry methods were adopted and incorporated into the study of clinical disorders, a merging that would transform the conjectural art of medicine into an evidence-based rigorous science.[4]

Serendipitously but propitiously for nephrology, the war effort's targeted research on shock, hemorrhage, crush injury, blood transfusion, and fluid replacement and elimination were directly relevant to the elucidation of kidney function, whereas that of the independent development of dialysis machines in the early 1940s by Willem Kolff (1911-2009) in Holland, Nils Alwall (1904-1986) in Sweden, and Gordon Murray (1894-1976) in Canada would prove central to the treatment of kidney failure.[8,9] Essentially, the seeds of nephrology were planted during WWII and then nurtured in the favorable environment of the immediate postwar "golden years" of research funding. As summed in 1951 by Homer W. Smith (1895-1962) in his landmark book *The Kidney: Structure and Function in Health and Disease,* this was when the kidney had a revolutionary metamorphosis from a "mere servant" of nutrition to a "master chemist" fundamental to the very process of life.[10]

FORMATIVE YEARS

It is in this environment and in one of the beneficiaries of these developments, the Department of Medicine, established in 1951 by Donald W. Seldin (born 1920) at the University of Texas Southwestern Medical School in Dallas, TX, that I began my training in kidney and electrolyte metabolism (viz not nephrology) in 1964. By then, clearance studies refined by Homer Smith were well established,[10] micropuncture techniques introduced by Alfred Richards were being revived and refined,[11,12] and samples analyzed by the chemical methods were compiled, developed, and perfected by John P. Peters (1887-1955) and Donald Van Slyke (1883-1981) in the several revisions of their benchmark 2-volume *Quantitative Clinical Chemistry*, first published in 1931.[13]

It was to learn micropuncture and electrolyte transport that I elected training in Dallas. How Floyd Rector (born 1929), then in charge of the laboratory, could foretell the limitations of my patience and dexterity to master micropuncture and assigned me to clearance studies remains a mystery, but is another measure of Floyd's ingenuity. The clearance studies I was assigned to perform were directed at the elucidation of segmental tubular function in support of the results obtained from micropuncture studies, using the clearance of free water during volume expansion, diuretic administration, and urinary tract obstruction. That being 1964, the determination of electrolytes depended on a flame photometer, and of osmolalities, on a freezing point depression osmometer, laborious procedures that added several hours of tedious work at the end of the day's experiment before one could leave the laboratory.[14,15]

Although clearance and micropuncture studies are now a relic of the past, 2 transforming technical developments that continue to affect the progress of nephrology occurred during my training. The first was the autoanalyzer, an early model of which was acquired by the laboratory. It was a major time saver that would periodically dysfunction, necessitating our reluctant fall back on the old standby flame photometer. At the practical level, autoanalyzers created a new need for nephrologists to interpret and manage the now easily detectable electrolyte abnormalities being reported by clinical laboratories.[15] The second technical development was the availability of a noisy and clumsy punch card calculator that reduced the time spent on tedious calculations to less than an hour. Unfortunately, it provided only partial relief, limited by the number of punch cards allotted to each trainee, the huge demand for time on the machine necessitating scheduling for access to it, and ultimately the return of the machine to the manufacturer after the 2-month trial period. The role of subsequent generations of machines in facilitating calculations and that of the new programmable computer-based statistical analyses was beyond my imagination then. The impact of calculators on research in nephrology is self-evident in the extensive statistical validation of data that appear in the literature nowadays, even when little or none may be needed, and particularly in the "fast and furious" proliferating number of published epidemiologic and interventional studies based on analysis of information compiled by an increasing number of data banks.