A third-year medical student sat in the 17 W workstation at University Hospital in the spring of 1975 after meeting a patient with acute illness, taking a history, and performing a physical examination. This medical student had been very well prepared in the second-year course to understand clinical and pathologic concepts related to acute and chronic GN. Seeing a patient with acute GN, clearly diagnosed according to clinical parameters, he wondered whether this resolving injury might result in chronic disease. A bit confused by the nomenclature, and largely unacquainted with clinical matters, the medical student asked the attending, “Does acute glomerulonephritis go on to chronic glomerulonephritis? Are they the same thing?” The attending laughed, and with a twinkle in his eye replied, “I’m working on that.”

David S. Baldwin was born in Rochester, New York in 1921 and graduated from the University of Rochester School of Medicine in 1945. He came to the New York University (NYU) School of Medicine in 1947 to work with Homer Smith, then the University (NYU) School of Medicine in 1945. He came to the New York University (NYU) School of Medicine in 1947 to work with Homer Smith, then the acknowledged leader in the field of renal physiology.1 He finished a New York Heart Association Fellowship in Medicine and Physiology in 1950.2 NYU was uniquely suited to Baldwin’s plan as it allowed him to work closely with William Goldring and Herbert Chasis,2 who had applied physiologic principles and methods—established by Smith in fish, eels, and a variety of animals3—to the study of renal diseases in humans.4 The main focus of the Renal Laboratory in the Department of Medicine was to investigate the role of the kidney in the pathogenesis of essential hypertension. With evidence that renal artery stenosis was characterized by excessive sodium reabsorption,5,6 Baldwin and others in the laboratory sought to determine whether the abnormalities in the renal excretion of sodium might be a feature of essential hypertension.

Even as Baldwin was occupied with physiologic studies in hypertensive patients, he was called upon by physicians and house staff to consult on patients with renal diseases, many of whom had glomerular diseases. Baldwin learned the technique of percutaneous renal biopsy and evaluated patients on all three services (NYU, Columbia, and Cornell) in Bellevue Hospital. Soon, Baldwin initiated regular Saturday morning rounds with students and house staff, during which he would hear presentations, examine the patients, and almost always finish by writing a very concise, well-structured, logical note. All relevant data from the past history and present findings were entered onto a “Yellow Card” (Figure 1), a system of record-keeping developed by Goldring and Chasis in their studies of patients with hypertension2 and adapted by Baldwin to the study of patients with glomerular diseases. Baldwin applied the same careful data collection to patients he saw in private consultation. These meticulous observations served as the basis for much of his productive career as a student of the natural history of renal diseases.

In these early days, through the 1960s and 1970s, Baldwin’s clinical observations were supplemented by close collaboration with Robert McCluskey, a pioneering renal pathologist, and by the application of immunofluorescence microscopy for the evaluation of renal biopsy specimens. McCluskey and Baldwin met weekly to examine renal biopsy specimens and relate the histopathologic findings to the clinical data. This fruitful collaboration, conducted with Gloria Gallo, also gave birth to the very exciting weekly renal pathology teaching conferences that almost every participant recalls with memories of the brilliance of Baldwin’s clinical expertise.

At this time, Baldwin undertook a collaboration with Naomi Rothfield, the director of the Rheumatic Disease Section, that focused on systemic lupus erythematosus (SLE). Joint rounds and close follow-up of a large population of patients with SLE led to a presentation of the classification of lupus nephritis at the first meeting of the newly formed American Society of Nephrology. These efforts,7,8 along with those of other groups, helped form the foundation of the current histopathologic classification of glomerular disease in SLE.9

Baldwin’s contribution to an understanding of the natural history of glomerular diseases resulted from careful observation and meticulous scrutiny of clinical data. Nephrology today focuses on large data sets collected from many participating institutions, which will likely yield...
important information regarding pathogenesis and response to new therapies. Baldwin’s contribution was unique with regard to the careful observations and physiologic insights he brought to the data he collected. Rather than using data from randomized controlled trials, Baldwin inferred clinical responses from studies in which each patient served as her or his own control.

It is said that fortune favors the prepared mind. The puzzling finding of hypertension in a young boy on the Bellevue pediatric service opened a new area of Baldwin’s thinking. This boy had normal BUN and serum creatinine levels, negative urine, and all the appropriate tests to exclude consideration of curable forms of hypertension. Questioning the family, he learned the boy had been treated for poststreptococcal GN, documented by renal biopsy, at another hospital, 1 year earlier. Baldwin gave this case considerable thought before recommending a second renal biopsy. The unexpected finding of several totally sclerotic glomeruli and the absence of any residual inflammation led to the consideration that poststreptococcal GN could “heal,” leaving behind damaged glomeruli that might progress to sclerosis, hypertension, and possibly renal failure. Here, Baldwin’s collection of “Yellow Cards” was a virtual treasure trove. With the help of a fellow and a volunteer in the Renal Laboratory (now the Homer Smith Laboratory), many patients who had biopsy-proven poststreptococcal GN and were thought to be healed were contacted and invited to be seen in the Bellevue Renal Clinic during the late 1960s and 1970s. This investigation confirmed Baldwin’s suspicions: there was a much greater than expected incidence of hypertension, urinary abnormalities, impaired glomerular filtration, and “exaggerated
natriuresis” (markedly increased sodium excretion in response to saline infusion) in many patients thought to have recovered from poststreptococcal GN.10

The preeminent paradigm in those days, possibly supported by misinterpretation of studies by Finkenstaedt and Merrill11 and Lowe,12 was that complete recovery characterized the renal response after acute GN, perhaps analogous to the then-accepted benign long-term course of acute tubular necrosis or the ability of the liver to regenerate after injury. Sequelae of AKI in GN, such as abnormal urinary protein excretion, the presence of hematuria, hypertension, and diminution in GFR, were defined by the NYU group.10 The observations made in children after episodes of poststreptococcal GN decades ago are consistent with current concepts of the interdigation of AKI and CKD13,14 and have been confirmed over the ensuing years.15

The finding that GN might progress, silently, over many years, led Baldwin to examine the possible mechanisms for progression of glomerular disease. In studies carried out with a succession of renal fellows and young investigators in the Homer Smith Laboratory, he sought evidence of ongoing immunologic and nonimmunologic abnormalities that might result in progressive glomerular damage,16,17 building on elegant micropuncture studies performed by Barry Brenner and colleagues.18

Returning to his earlier interest in hypertension, Baldwin undertook, with a series of colleagues and junior faculty, physiologic studies of glomerular permeability and renal injury induced by hypertension and hyperfiltration in animal models of glomerular diseases.19–24 He went further, to establish the idea that nonimmunologic mechanisms play a key role underlying the progression and loss of function in immunologic kidney diseases.16 These concepts have evolved with time, yet they remain the basis for our current understanding of the mechanisms that contribute to progressive kidney injury. In careful animal studies, Baldwin and colleagues showed that factors patients and nephrologists have struggled with in the clinic for decades, including high-protein diets, dietary sodium load, and level of hypertension, were associated with maladaptive pathophysiology and progressive loss of renal function in animals.19,20 As in human studies, he worked closely with the nephropathologists Gloria Gallo and Helen Feiner.

These studies stand out today as examples of the way in which a clinical observation can provide the basis for deeper physiologic or molecular investigation of disease mechanisms.

Baldwin spearheaded three distinct areas of research that still have clinical and basic science implications today: the natural history and classification of glomerular diseases, including lupus nephritis, poststreptococcal GN, and the renal disease of subacute bacterial endocarditis; the relationship of hypertension to decrement in renal function and to progressive renal disease; and the identification of factors that promote or ameliorate progression of the chronic course of kidney disease.

The findings were identified and formulated before desktop computers were invented, developed, and disseminated; before large patient registries were established; and before large clinical databases were available. The scientific conclusions from this team, which have passed the test of time, continue to influence the course of nephrology research today.

Baldwin’s work on essential hypertension is now informed by changes in our nomenclature. We have moved from consideration of essential hypertension...
compared with malignant hypertension, to analyses of associations of hypertension with genetic susceptibilities to kidney injury in particular patients, as well as focusing on the interactions between genetic predisposition, environmental triggers and molecular agents of progression of renal disease. Nevertheless, the foundations of our current understanding of the pathobiology of hypertension are firmly rooted in these early observations and insights.

Baldwin’s life and research exemplify the interrelationship between basic and clinical sciences that is at the center of current notions regarding translational research. Baldwin proposed clinical hypotheses, considered their tenability during the clinical care of patients over decades, and evaluated concepts related to these hypotheses in laboratory studies. Baldwin, using clinical research methods, before the availability of molecular biologic techniques and the creation of knockout animals, established clinical principles that still hold today. His career illustrates how clinical research and multidisciplinary collaboration can both stimulate and benefit from basic research in general, and ultimately affect the care of patients.

The investigations of Dr. Baldwin emphasize the overriding importance of clinical observation. As specialists, we as nephrologists may have sometimes underemphasized the importance of the approach used by Baldwin that enabled his critical insights. Baldwin’s work, seeking out experts in pathology, rheumatology, and other fields, with whom effective collaborations were established, demonstrates the importance of “team science” in advancing biomedical research. At present, there is a true crisis in nephrology due to the declining recruitment of young physician-scientists to our discipline. The research contributions and the careers of physician investigators like Dr. David Baldwin can be effective in motivating, attracting, and mentoring medical students and residents to seek work over a lifetime in nephrology as a discipline.

Dr. Baldwin died in December 2013 at the age of 92. He was a careful researcher and a charismatic student of nephrology (Figure 2) who inspired younger students of nephrology in his wake. Baldwin’s students of the 1950s, 1960s, 1970s and 1980s were edified and stimulated by his teaching, and his astute clinical acumen, and many have become students and teachers of nephrology as well.

Figure 2. Dr. David S. Baldwin, 2004.