John P. Merrill: The Father of Nephrology as a Specialty

Murray Epstein

Department of Medicine, University of Miami School of Medicine, and South Florida VA Foundation for Research and Education, Miami, Florida

Clin J Am Soc Nephrol 4: 2–8, 2009. doi: 10.2215/CJN.04830908

"In the years I spent as a member of the Peter Bent Brigham Hospital house staff, I had the privilege of gaining some unique insights into both Merrill-the-physician and Merrill-the-man.

As a physician, history will accord Dr. Merrill a long sequence of outstanding scientific contributions in the field of nephrology. And history will say it was he who played an integral role in making renal transplantation a lifesaving tool. But I see Merrill-the-physician in a different light. I see him as a very courageous man. I say that because as a member of the Brigham house staff during the early days of transplantation, I know how open to criticism he was. I know, he knew, there were many whisperings in the scientific world about the audacity of his concepts. The easy way would have been to back down; after all, he was a world-leading nephrologist already . . . so what could be the personal gain?

But John Merrill persisted in pursuing his vision. And John Merrill won . . . mostly because he is courageous" (1).

John Putnam Merrill was one of the giants of the world of nephrology. He occupies a place in history as the leading pioneer in dialysis and kidney transplantation. As we approach the 25th anniversary of his tragic death, it is worth reviewing the enormous contributions of this gifted and charismatic pioneer.

Today, nephrology is perceived as a multidimensional specialty offering a home to eclectic interests including clinical nephrologists, experts in dialysis, transplantation medicine, immunology, and hypertension. Such a multifaceted specialty did not exist before 1950. Its evolution and development were rapid. Attendance at the first International Society of Nephrology Congress in Evian, France, in 1960 was a mere 100+. By November 2007, the number of attendees at the American Society of Nephrology meeting was 13,960 (Mark Kerlin, American Society of Nephrology, Washington, DC, September 2, 2008, personal communication). Merrill, more than any other physician and investigator, was responsible for fostering the development of the modern specialty of nephrology. He was not only brilliant and visionary but also eclectic in his wide-ranging clinical and investigative interests: Hemodialysis, peritoneal dialysis, hypertension, acute renal failure, chronic renal failure, pathophysiology of uremia, transplantation, glomerulonephritis, and fluid and electrolyte physiology and all of their interrelated medical problems. Addressing a gathering of Merrill's trainees at a Merrill Celebration Symposium, October 11 to 12, 1985, Nancy Boucot Cummings commented, "All of us here today, in our many different career paths, which are more varied than one might expect to see from training under one mentor, have been affected strongly by our years under Merrill's sway" (2).

Merrill was born in Hartford, CT, in 1917. He graduated Phi Beta Kappa from Dartmouth College in 1938 and attended the Harvard Medical School, from which he graduated in 1942. After graduation, he was an intern at the Peter Bent Brigham Hospital and then, during World War II, spent 4 yr in the Air Force. He spent 2 yr on Kwajalein Island in the Pacific with "Operation Crossroads" and had the notable assignment of serving as the flight surgeon to the crew of the Enola Gay, the aircraft that dropped the atomic bomb on Hiroshima in 1945.

In 1947, he returned to the Brigham Hospital as an assistant resident in medicine. Although his initial clinical interests were in cardiology, Dr. George Thorn recognized Merrill's attributes and assigned him to spearhead the efforts to develop the artificial kidney at the Brigham. Merrill began his studies with the artificial kidney dialysis machine, which, in collaboration with surgical colleagues, was modified from the original design of Dr. Wilhelm Kolff. The artificial kidney developed by Merrill and his associates (the Brigham-Kolff dialyzers) was highly successful, especially in the treatment of acute renal failure and subsequently in the management of chronic renal failure.

In 1954, Merrill led the multidisciplinary team that performed the first successful transplant in which the donor was an identical twin. There was no immunologic rejection of the donor kidney. Tragically, Merrill died on April 14, 1984, in a boating accident while vacationing in Hopetown, the Bahamas. He was 67 yr old. Had he lived, he certainly would have been awarded the Nobel Prize in Medicine.

Merrill was a gifted teacher and author of more than 400 publications and received many awards and honors and an honorary degree from the University of Paris. He was a member of many medical societies and was particularly active as president of the American Society for Clinical Investigation, the American Society of Artificial Internal Organs, and the Inter-

Published online ahead of print. Publication date available at www.cjasn.org.

Correspondence: Dr. Murray Epstein, Nephrology Section, VA Medical Center, University of Miami School of Medicine, 1201 NW 16th Street, Miami, FL 33125. Phone: 305-575-3103; Fax: 305-575-3378; E-mail: murraye@gate.net

ISSN: 1555-9041/401–0002

national Society of Nephrology. He was a prime mover in establishing the National Kidney Foundation, in promoting dialysis centers nationwide, and in persuading Congress to provide funding for patients requiring long-term dialysis and kidney transplantation.

Merrill's medical accomplishments were complemented by his multifaceted talents and interests. He enjoyed tennis, sailing, skiing, and music—playing the clarinet and composing music. As recounted by Nancy Boucot Cummings, he loved the unknown, the unchartered, the dangerous. He went big-game hunting in Africa, scuba diving off the Great Barrier Reef in Australia, and fishing among the crocodiles and piranha on the Orinoco River in Venezuela. "He wanted to experience everything that life had to offer at least once" (2).

The next few sections describe his seminal role in developing dialysis, transplantation, and other disciplines that comprise contemporary nephrology.

The Birth of Dialysis

"No man and no institution have done more for the propagation of dialysis in the United States than John P. Merrill and the Peter Bent Brigham Hospital" (3).

Wilhelm Kolff is considered by many to be the titular inventor of the artificial kidney. In addition to Kolff, much credit for the initial pioneering efforts in developing the artificial kidney must be given to Nils Alwall (4). In 1946, Alwall used hemodialysis to treat a critically ill patient with severe renal failure (4), using the artificial kidney that he had constructed himself just a few years earlier. Alwall also pioneered the technique of ultrafiltration and introduced the principle of hemofiltration. Regardless of who was first, informed opinion posits that Merrill was instrumental in both defining the role of hemodialysis in the management of both acute renal failure and end stage renal disease (ESRD) and its widespread adoption globally.

To appreciate fully Merrill's seminal contribution to the development of hemodialysis as a safe and efficient viable treatment for ESRD, one must be cognizant of the setting in which the Kolff-Brigham kidney was developed. At the time, dialysis was scorned by many in the medical establishment. It was stated that"dialysis was only good for the Peter Bent Brigham Hospital because the artificial kidney would never be something more than a deluxe toy for a smart and restricted elite and of no use in other institutions" (5).

A major figure in fostering Merrill's career and the development of the Kolff-Brigham kidney was his legendary chief, the brilliant and visionary George W. Thorn. He devoted his inaugural Shattuck Lecture in 1943, entitled "Physiologic Considerations in the Treatment of Nephritis," to focus on the management of chronic renal disease (6). Subsequently, Thorn heard of Kolff's dialyzer and invited Kolff to visit the Brigham. As a consequence, Carl Walter and Edward Olson built the "Kolff-Brigham Kidney," an improved stainless steel modification of the original Kolff kidney. Propitiously, Thorn assigned Merrill, who had recently returned from military service, to shepherd the development of dialysis at the Brigham Hospital. As Thorn wrote in a 1973 tribute to Merrill, "With our tradition of kidney disease research, we felt we should sponsor the so-called artificial kidney. But who could take on this complex—and risky—research project? My choice was John P. Merrill. With his excellent medical background . . . 4 yr as a flight surgeon . . . interest in cardiorenal disease . . . and the intellectual curiosity that characterizes a born researcher . . . he was ideally suited" (7).

Despite early successes by the Brigham team, many medical leaders expressed skepticism and indeed voiced their outright opposition (8). A 1949 editorial in the *British Medical Journal* condemned the artificial kidney as still an "ideal and not an accomplished fact. Its principle is simple enough, but its translation into practice brings difficulties to the doctor and real hazards to the patient" (9).

John P. Peters (1887–1955), the highly influential professor of medicine and chief of the "chemical division" at Yale University's School of Medicine, and Louis G. Welt (1913–1975), then one of Peters's fellows, also challenged the value of the kidney machine in a 1951 review (10). Peters and Welt and their progeny argued that with a physiologic approach (the so-called conservative treatment), anuric patients could survive in reasonable comfort for weeks, without dialysis, until the renal lesion healed and function returned (10). As a medical student at Columbia University, I vividly remember my professor of medicine, Stanley Bradley, scorning the use of "this device," and recommending that we rely on the mainstay of conservative treatment.

In the late 1950s, dialysis was accepted by many as a standard treatment modality for the management of acute renal failure. In the early 1960s, the American pioneers of chronic dialysis—Merrill, Belding Scribner, Schreiner, and Kolff—tentatively began chronic dialysis treatment. In contrast to its tentative acceptance in treating acute renal failure, there was reluctance and indeed frequent opposition to chronic maintenance dialysis. In a widely read review published in the *New England Journal of Medicine* in 1964, Norman Levinsky warned that "both chronic dialysis and transplantation . . . are properly considered clinical experiments rather than established modes of treatment at this time" (11). A year later, the influential Scientific Advisory Board of the National Kidney Foundation (chaired by Neal Bricker) wrote a skeptical position paper that opposed endorsement of expanding community dialysis centers (12). Merrill's major contribution to the establishment of dialysis as the mainstay of ESRD was based not only on his medical innovations but also on his relentless and courageous "staying the course" despite this chorus of opposition until dialysis was ultimately accepted as a safe and effective mainstay of renal replacement therapy (RRT).

Transplantation

"John Merrill made a tremendous contribution to the field of immunology. Few 'pure' immunologists can match it" (3).

From 1951 to 1953, David Hume together with Merrill and Thorn carried out a series of kidney transplants in patients with chronic renal failure. Although several of these grafted kidneys did function for several months, these investigators were forced to conclude that "at the present state of our knowledge, renal

homotransplants [later to be called "allograft"] do not appear to be justified in the treatment of human disease" (13).

A chance opportunity in December 1954 changed the course and revolutionized the outlook for renal transplantation (14,15). Richard Herrick, a 24-yr-old patient with chronic kidney disease and severe hypertension secondary to glomerulonephritis and an identical twin, was referred to the Brigham by his physician, David Miller. Merrill appreciated that the kidney machine could never be more than a stopgap measure, able to keep a patient alive for a period of time but never able to offer a cure. What he was really interested in was the possibility of kidney transplantation. Like other experts in his field, Merrill was convinced the transplants were not failing because of problems with the surgery or because an organ from one person simply could not function in another but rather because the transplanted organ was being rejected by the recipient's immune system. Merrill had argued for some time that human identical twins should be able to exchange organs and tissues without any fear of immunologic rejection, and that was what interested him about Richard Herrick. To ensure that the brothers were identical, not fraternal, twins, the Brigham team had both brothers fingerprinted by the Boston Police Department (15). As a preliminary test of his hypothesis, Merrill's team carried out an exchange of skin grafts between Richard and his twin brother that was successful.

Although it was widely known at the time that a healthy individual can live normally with a solitary kidney, the outcome of the contemplated operation was clearly uncertain, and it was appreciated that there was an implicit risk in undergoing any surgical procedure. Despite these qualms and initial hesitation, the transplant of a kidney from one twin (Ronald Herrick) to the other (Richard Herrick) occurred on December 23, 1954. The success of the first kidney transplant between identical twins attracted extraordinary coverage by the media and refocused the world's attention on the curative potential of kidney transplantation (Figure 1).

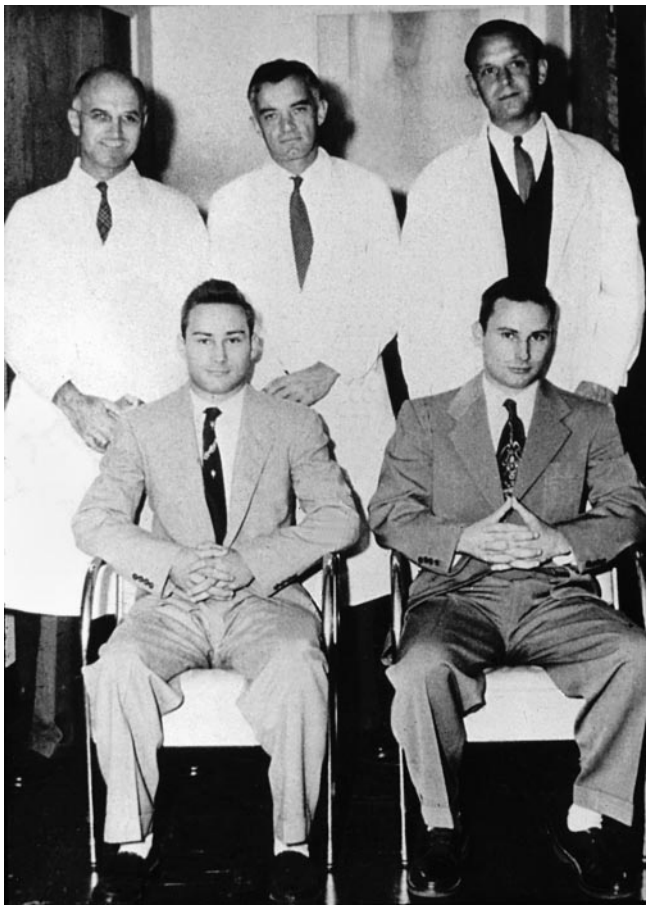

Figure 1. The participants in the world's first successful transplant. Seated (left to right) are Richard Herrick (the original transplant recipient) and his twin brother, Ronald (the kidney donor). Standing left to right, Drs. Joseph Murray, John P. Merrill, and J. Hartwell Harrison.

Richard Herrick, the recipient, had a remarkable clinical course. He married Clare Burta Herrick, the nursing supervisor in the recovery room who had volunteered on that Christmas weekend for care of Richard (Clare Herrick, August 28, 2008, personal communication). Richard and Clare had two daughters, one a nurse at a kidney dialysis unit. Herrick died of a myocardial infarction 8 yr after the transplant.

Subsequently, Murray and Merrill carried out six more renal transplants in identical twins (14,16,17) (Figure 2), and other transplant groups in both North American and European centers followed their example. Renal transplantation was a reality and a success. These initial transplant procedures in identical twins demonstrated the technical feasibility of the procedure.

Obviously, transplantation between identical twins is an infrequent event and not feasible for the overwhelming majority of patients with kidney failure. Consequently, Merrill began to dedicate his efforts to the problem of kidney transplantation in nonidentical twins, with the first such successful transplant performed at the Brigham in 1960 (18), followed in 1963 by the first successful cadaver kidney transplant, sustained by immunosuppressive therapy (19). His immunologic interests extended from those relevant to transplantation to include those related to glomerulonephritis. Here, he had the hope that ultimately glomerulonephritis could be prevented when the knowledge about its underlying immunologic mechanisms was expanded. The initial success of the Boston group prompted both the Boston group and Jean Hamburger's team in Paris to carry out transplants between fraternal (dizygotic) twins. For combating rejection, these transplant recipients were treated with steroids and irradiation.

Merrill himself "spent a research year (1955–1956) with Hamburger in Paris studying the effects of radiation on the immune system" and "hypothesized that a predetermined sublethal dose of x-ray could temporarily impair recipient responsiveness to a kidney allograft" (20). During the 1960s at the Peter Bent Brigham, one of the treatments of acute allograft rejection was local irradiation of the allograft. Dr. Bernard Carpenter also tested the feasibility of extracorporeal blood irradiation in human renal allograft recipients. Then "between April 1958 and March 1962 the physicians treated 11 individuals with total-body radiation before transplantation" (20).

Unfortunately, sepsis was the dominant cause of recipient

Figure 2. The "Team of Glory" at the Peter Bent Brigham Hospital. The photo was taken in 1965, when they received the gold medal of the New York Academy of Sciences for the world's first kidney transplant. On the left is J. Hartwell Harrison, chief of urology and the surgeon for the donor nephrectomy. Second from left is John Merrill, the leader of the team and chief of nephrology. Second from the right is David Hume, the surgical genius who spearheaded the early transplant initiatives at the Brigham Hospital and collaborated closely with Merrill. On the right is Joseph Murray, the surgeon who performed the Herrick transplant.

mortality in those times. Tilney captured the emotional turbulence created by these early failures. "Only Moore, Thorn, Murray and Merrill continued to push on, having faith that the situation would change" (20), and it did change when incremental radiation was prescribed rather than a single large dose. "Over the next 2 yr, kidneys were transplanted into other radiated recipients with and without coincident bone marrow infusion in France, the United States, and the United Kingdom" (20).

Merrill had a vision of kidney transplantation that he developed at every level. His amazing ability to attract talented young investigators in basic transplantation was exemplified by the work of Dr. Ronald Guttman and Dr. Bernard Carpenter. Recruiting and retaining Carpenter provided an immediate clinical and experimental expansion of investigations in alloimmunity as well as a legendary legacy for the training of numerous transplant nephrologists who went on to direct their own transplantation programs. They were the nidus of the early American Society of Transplant Physicians, later to become the American Society of Transplantation, and this transformative odyssey began with Merrill. Merrill helped add renal transplantation as a monumental new treatment for ESRD while at the same time contributing to improving dialysis techniques and an understanding of acute renal failure.

A consideration of the extraordinary magnitude of transplant recipients provides a gauge of the enormity of Merrill's contributions to transplantation. Although precise numbers are difficult to ascertain, a reasonable estimate is that, in 2007, approximately 1.3 million people were living around the world on some form of RRT (dialysis or renal transplants). Approximately 300,000 are transplant recipients, and approximately 1 million are maintained on dialysis (R. Glassock, The David Geffen School of Medicine at UCLA, Los Angeles, CA, July 1, 2008, personal communication). A reasonable approximation is that the total number (both living and dead) who have started some sort of an RRT program since the inception of chronic dialysis and transplantation in 1960 probably amounts to approximately five times the total now living (approximately 6.5 million: 1 million transplants and 5.5 million on dialysis).

Hypertension

To gauge Merrill's contribution to hypertension requires the reader to appreciate the nihilism and therapeutic wasteland that defined the "state of the art" of this disease. Hypertension in the 1950s was believed to be an essential natural adaptive reaction to pathology in either the kidneys (white hypertension) or the vasculature (red hypertension), which was necessary to drive and maintain perfusion to vital organs. The prominent cardiologist Paul Dudley White, responsible for the cardiovascular care of many American presidents and national leaders, stated in 1937 that "the treatment of hypertension itself is a difficult and almost hopeless task in the present state of knowledge, and in fact for aught we know . . . the hypertension may be an important compensation mechanism which should

not be tampered with, even were it certain that we could control it" (21).

Treatment was meager. As Paul Wood lamented, "It must be said at once that there is no satisfactory treatment for essential or for malignant hypertension" (22). In many cases, no treatment was given on the belief that the symptomatic patient would live for many years without complications. Salt intake was stringently restricted, and diets with <1 g/d salt, such as the Kempner rice diet, were popular, although one author stated, "The evils of rigid sodium restriction usually outweigh the benefit" (23).

In this nihilistic setting that was not conducive to either research on hypertension or treatment, Merrill boldly stepped forward and advocated the overriding importance of treating elevations of BP. He wrote, "Severe hypertension in uremic patients should be treated as in other individuals. In the past it has been suggested that lowering of BP in patients with renal disease may further impair renal hemodynamics. Drastic and excessive reductions in BP may decrease filtration rate and increase blood urea nitrogen levels. However, when BP is reduced to moderate levels and maintained there over long periods of time, further impairment of renal function does not occur" (24).

Merrill noted that "with increasing frequency we are discovering cases with so-called 'essential' hypertension, with normal urines and normal renal function" (25). Merrill proposed that "the genesis of hypertension in advanced renal failure is a melange of the same known and unknown factors. It is now well documented that patients with even advanced renal failure may have enough functioning renal tissue to produce large amounts of renin" (26). "When blood volume is increased, there appears to be a diminished response to ganglioplegic drugs suggesting the preponderance of volume over sympathetic tone in maintaining BP" (26).

Merrill conceived and initiated seminal studies that delineated the pathogenesis of renoprival hypertension and demonstrated the importance of sodium retention in its pathogenesis (27–32). Collectively, his studies helped to establish hypertension as an integral and substantive part of the multidimensional specialty of nephrology (29–32).

Acute Renal Failure

In addition to his successful application of the Kolff-Brigham artificial kidney to the dialysis of patients with acute renal failure, Merrill was instrumental in both characterizing the clinical feature of this syndrome and spearheading investigations that delineated its pathogenesis (33–36). With his strong support and guidance, a multipronged research initiative was launched. At a preclinical level, gifted research fellows including Thomas Biber, Gilbert Thiel, Franklin McDonald, Gerald DiBona, and Walter Flamenbaum conducted elegant studies in diverse rat models that contributed importantly to the elucidation of its pathogenesis. Concomitantly, Norman Hollenberg and I conducted a series of clinical studies to delineate the intrarenal hemodynamic alterations that underlie the clinical abnormalities of diverse acute renal failure syndromes (37,38). We used the 133 xenon method that entailed the direct injection into the renal artery of the gamma emitter xenon 133 with simultaneous selective renal arteriography. We were the first to demonstrate that the underlying renal hemodynamic abnormality in both acute renal failure and the acute renal dysfunction of the transplanted kidney comprised renal hypoperfusion with a selective renal cortical ischemia (37). We also demonstrated that the acute oliguric renal failure of liver disease (now termed the hepatorenal syndrome) was characterized by intense renal cortical ischemia that was more profound than that observed in classic acute renal failure (38). In concert, these investigations and the expertise gained by the in-depth Brigham clinical experience in submitting patients with acute renal failure to dialysis subserved a clinical platform that enhanced and modernized the treatment paradigm for the management of patients with this devastating renal disorder.

A Global Perspective

A mark of the man was Merrill's global perspective. He strove and succeeded in attracting fellows and trainees from all corners of the globe. More than 62 fellows and associates came from at least 29 countries to study under his tutelage, as well as more than 105 US fellows from at least 26 states. He was an international figure, a cosmopolitan man, fluent in Spanish and French, and an ambassador in the best sense of the word. Consequently, he was able to put this veritable United Nations of visitors at ease. His vision was broad and expansive. We all remember the constant procession of visitors to the Cardiorenal Laboratory to learn about the latest advances in nephrology and transplantation; to exchange experiences; and, indeed, to seek Merrill's recognition, support, and validation. As Gabriel Richet eloquently summed up in his eulogy, Merrill acted as a "kind fairy," hovering protectively over the growth of the International Society of Nephrology during its nascent years. He ignored national boundaries, realizing that "the roots of science are varied, differing from one country to the other, all of them deserving attention, none to be scorned" (5).

Merrill's leadership and organizational talents were extraordinary. He helped found and served as an officer of some of the most illustrious and learned societies in medicine. Merrill was visionary in his thinking and stalwart in his resolve. As he stated in his presidential address to the American Society for Clinical Investigation in April 1963, "Shortly after my election to this office, I asked one of the elder statesmen of the society whether he had any words of guidance for me. He did, and they were brief: 'Don't rock the boat,' he said. From the vantage point of a year of experience as president, I am not sure that this advice is correct. The winds of change are blowing; the boat can and should rock; the important thing is that it remain upright when the storm subsides" (39).

Merrill's Progeny: The Legacy Propagates from Generation to Generation

An example of great immediacy illustrates the vibrancy and growing impact of Merrill's legacy in many medical fields, especially transplantation and immunology 25 yr after his death. With the advent of kidney transplantation, Merrill inextricably linked immunology and nephrology. Notably, al-

though not often appreciated, physiology and biophysics dominate immunology just as they do nephrology. As a first-generation disciple of Merrill, I mentored Dr. Robert Sackstein during high school. He subsequently earned a medical degree and a doctoral degree in immunology. At age 13, Sackstein was introduced to the physiology and biophysics of transport processes in my laboratory, specifically the molecular effectors of water and solute transport in the kidney. Apparently, this understanding of fluid dynamics and irreversible thermodynamics was indelibly etched. As a second-generation disciple of Merrill, he focused his scientific career on tackling the central problem of organ transplantation that Merrill faced: graft rejection. At its core, transplant rejection is rooted in the physiology and biophysics of "transport," in this case, the highly efficient transport of alloreactive lymphocytes from the vasculature and into the graft. Sackstein has successfully applied the fundamental principles of fluid dynamics to elucidate the molecular effectors of tissue-specific cell migration (40,41). His studies have revealed how immune cell trafficking depends on hemodynamic shear stress and have led to the identification of several critical adhesion molecules regulating the binding of cells in blood flow to vascular endothelium at target tissue(s). Sackstein has also developed novel therapeutic agents to treat transplant rejection on the basis of disruption of lymphocyte migration to the graft. Thus, a legacy of immunology and nephrology lives in direct lineage, passed from "scientific" grandparent to grandson.

A Man of Many Interests and Universal Concerns

"John Merrill is a many-faceted man. And the thing I admire about him most is how each facet is unique and totally reflective of a bright, introspective, dedicated . . . let me say Renaissance type of man" (1).

Merrill's interests were wide ranging. He was a gifted writer and editor from his earliest days in prep school, edited the Dartmouth journal, and later edited the *Harvard Medical Alumni Bulletin*. In addition to his many medical papers, he wrote a landmark book: *The Treatment of Renal Failure.*

Merrill was a gifted musician who also composed musicals. In 1969, he composed the theme song for the International Society of Nephrology. Kolff recounted his attendance at a dinner party after the European Dialysis and Transplant Association meeting in Prague, when Merrill played a beautiful trumpet solo (3). Kolff noted that "John once considered becoming a professional musician. To the good fortune of hundreds of thousands of kidney patients, he did not do it" (3).

Merrill was also deeply concerned and engaged with a wide range of societal issues apart from the realm of medicine, including access to medical care for all strata of society globally and the threat of a nuclear holocaust. Kolff's recounting of his last conversation with Merrill: "Pim, from now on, I am going to spend a major part of my time trying to do whatever I can to help avoid a nuclear war. This is more important than anything else I can do" (3).

One of Victor Hugo's famous quotes is, "Concision in style, precision in thought, decision in life" (42). Clearly, Merrill eminently exemplified all three traits. Conciseness characterized his speeches and writings. Precision characterized his reasoning in didactic lectures, discourses, and writing of articles. Most important, Merrill was decisive. Whether weighing whether to conduct the first kidney transplant in an era when there was no precedent or whether to make a major commitment to proceed in developing hemodialysis as a major therapeutic modality, when the entrenched power elite were outspoken in their opposition, Merrill's career was marked by decisiveness. Clearly he was "comfortable in his own skin." Reflecting on Merrill's extraordinary accomplishments throughout a stellar career, one has the sense that he was "larger than life." Were he alive in 1990, there is certitude that he would have been a co-recipient, with Joseph Murray, of the Nobel Prize in Medicine. Today, hundreds of thousands of patients with ESRD in every corner of the globe are enjoying fulfilling lives as a result of Merrill's pioneering efforts in developing extracorporeal dialysis, transplantation, and transplant immunology. As Eli Friedman glowingly wrote, "Were there a book of distinguished synonyms, the listing under nephrology would first be Merrill, J.P., and *vice versa*" (43).

Acknowledgments

I acknowledge the excellent editorial support of Sally Baron in the preparation of the manuscript, to Nina Epstein for expert editorial review, and Monica Barrio-Aparicio for accessing many of the articles and archival materials and Steven Peitzman for many helpful suggestions. I also acknowledge many helpful discussions with the following fellow JPM trainees who provided additional personal perspectives and archival materials: Richard J. Glassock, Eli Friedman, Lee Henderson, Norman K. Hollenberg, William Braun, Edmund G. Lowrie, Constantine (Gus) Hampers, and J. Michael Lazarus.

Finally, it has been a privilege to be afforded the opportunity to interview the family of the original transplant recipient: His wife Clare Herrick; Ronald Herrick, the donor of the original transplant kidney and identical twin brother of Richard Herrick; and Richard Herrick's daughter, Margie Herrick-Hinrichs. They all were receptive, forthcoming, and supportive of this project, for which I am extremely grateful.

Disclosures

None.

References

1. Fuisz RE: *Essays in Medicine: The Brigham, John P. Merrill and the Evolution of Nephrology*, New York, Medcom Learning Systems, 1973
2. Cummings NB: John Putnam Merrill: An appreciation. *Artif Organs* 11: 438–441, 1987
3. Kolff WJ: About John P Merrill. *Artif Organs* 11: 442–444, 1987
4. Alwall N: Historical perspective on the development of the artificial kidney. *Artif Organs* 10: 86–99, 1986
5. Richet G: In Memoriam: John Putnam Merrill: 1917 to 1984. *Kidney Int* 26: 98, 1984
6. Thorn G: A 50th anniversary celebration. *Transplant Proc* 13[Suppl 1]: 24–28, 1981

7. Thorn G: *Essays in Medicine: Topics in Nephrology*, New York, Medcom Communications Group, 1973
8. Peitzman SJ: Chronic dialysis and dialysis doctors in the United States: A nephrologist-historian's perspective. *Semin Dial* 14: 200–208, 2001
9. Editorial: The artificial kidney. *BMJ* 2: 920–921, 1949
10. Welt L, Peters J: Acute renal failure: Lower nephron nephrosis. *Yale J Biol Med* 24: 220–230, 1951
11. Levinsky N: Management of chronic renal failure: Part 2. *N Engl J Med* 271: 458–463, 1964
12. Rettig RA: The policy debate on patient care financing for victims of end-stage renal disease. *Law Contemp Probl* 40: 196–230, 1976
13. Hume DM, Merrill JP, Miller BF, Thorn GW: Experience with renal homotransplantations in the human: Report of nine cases. *J Clin Invest* 34: 327–382, 1955
14. Peitzman SJ: Dropsy, dialysis, transplant: A short history of failing kidneys. In: John Hopkins Biographies of Disease, edited by Rosenberg CE, Baltimore, Johns Hopkins University Press, 145–153, 2007
15. Murray JE: Nobel Lecture, December 8, 1990. In: *Nobel lectures: Physiology or Medicine 1981–1990*, edited by Lindsten J, Singapore, World Scientific Publishing, 558–572, 1993
16. Merrill JP, Harrison JH, Murray J, Guild WR: Successful homotransplantations of the kidney in an identical twin. *Trans Am Clin Climatol Assoc* 67: 166–173, 1956
17. Merrill JP, Murray JE, Harrison JH, Guild WR: Successful homotransplantation of the human kidney between identical twins. *J Am Med Assoc* 160: 277–282, 1956
18. Murray JE, Merrill JP, Harrison JH, Wilson RE, Daminin GJ: Prolonged survival of human-kidney homografts by immunosuppressive drug therapy. *N Engl J Med* 268: 1315, 1963
19. Merrill JP, Murray JE, Takacs FJ, Hager EB, Wilson RE, Dammin GJ: Successful transplantation of kidney from a human cadaver. *JAMA* 185: 347–353, 1963
20. Tilney NL: *Transplant from Myth to Reality*. New Haven, Yale University Press, 2003
21. White PD: *Heart Disease*, 2nd Ed., New York, Macmillan, 1937, p 326
22. Wood P: *Diseases of the Heart and Circulation*, London, Eyre and Spottiswoode, 1950
23. Friedberg C: *Diseases of the Heart*, Philadelphia, W.B. Saunders, 1950
24. Merrill JP, Hampers CL: *Uremia: Progress in Pathophysiology and Treatment*, New York, Grune & Stratton, 1971, p 51
25. Merrill JP: *Treatment of Renal Failure*, 2nd Ed., New York, Grune & Stratton, 1965
26. Merrill JP, Hampers CL: *Uremia: Progress in Pathophysiology and Treatment*, New York, Grune & Stratton, 1971, p 23
27. Merrill JP, Giordano C, Heetderks DR: The role of the kidney in human hypertension: I—Failure of hypertension to develop in the renoprival subject. *Am J Med* 31: 931–940, 1961
28. Merrill JP: A possible mechanism for human renal hypertension. *Trans Am Clin Climatol Assoc* 70: 81–86, 1959
29. Hollenberg NK, Epstein M, Basch RI, Couch NP, Merrill JP, Hickler RB: Renin secretion in essential and accelerated hypertension. *Am J Med* 47: 856–859, 1969
30. Merrill JP: The role of the adrenal in hypertension. *Ann Intern Med* 37: 966–971, 1952
31. Hollenberg NK, Epstein M, Basch RI, Merrill JP, Hickler RB: Renin secretion in the patient with hypertension: Relationship to intrarenal blood flow distribution. *Circ Res* 24-25: I113–I121, 1969
32. Hollenberg NK, Epstein M, Basch RI, Merrill JP: "No Man's Land" of the renal vasculature: An arteriographic and hemodynamic assessment of the interlobar and arcuate arteries in essential and accelerated hypertension. *Am J Med* 47: 845–854, 1969
33. Finkenstaedt JT, Merrill JP: Renal function after recovery from acute renal failure. *N Engl J Med* 254: 1023–1026, 1956
34. Merrill JP: Clinical application of an artificial kidney. *Bull New Engl Med Cent* 11: 111–114, 1949
35. Merrill JP: *The Treatment of Acute Renal Failure*, New York, Grune & Stratton, 1955
36. Swann RC, Merrill JP: The clinical course of acute renal failure. *Medicine* 32: 215–292, 1953
37. Hollenberg NK, Epstein M, Basch RI, Oken DE, Merrill JP: Acute oliguric renal failure in man: Evidence for preferential renal cortical ischemia. *Medicine* 47: 455–474, 1968
38. Epstein M, Berk DP, Hollenberg NK, Adams DF, Chalmers TC, Abrams HL, Merrill JP: Renal failure in the patient with cirrhosis: The role of active vasoconstriction. *Am J Med* 49: 175–184, 1970
39. Merrill JP: Proceedings of the 55th annual meeting of the American Society for Clinical Investigation, Inc., held in Atlantic City, N.J., April 29, 1963. Presidential address. *J Clin Invest* 42: 906–911, 1963
40. Sackstein R, Merzaban JS, Cain DW, Dagia NM, Spencer JA, Lin CP, Wohlgemuth R: *Ex vivo* glycan engineering of CD44 programs human multipotent mesenchymal stromal cell trafficking to bone. *Nat Med* 14: 181–187, 2008
41. Schreiber TH, Shinder V, Cain DW, Alon R, Sackstein R: Shear flow-dependent integration of apical and subendothelial chemokines in T-cell transmigration: Implications for locomotion and the multistep paradigm. *Blood* 109: 1381–1386, 2007
42. Hugo V: Thoughts, Postscriptum de ma vie. In: *Victor Hugo's Intellectual Autobiography*, translated by O'Rourke L, New York, Funk and Wagnalls, 1907
43. Friedman EA: Merrill JP: The father of nephrology as a craft. *Nephron* 22: 6–8, 1978