Presentation of the 1999 Jean Hamburger Award to Robert H. Heptinstall

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It is a particular pleasure to me to be invited to present Robert H. Heptinstall for one of this year’s Jean Hamburger Awards, since I have had the great fortune to work with both men at different points in my career. Jean Hamburger was truly a giant among men. He started the first true Service of Nephrology at the Hôpital Necker-Enfants Malades in Paris in 1953. (Indeed, he coined the term “nephrology.”) He was a pioneer in transplantation, clinical nephrology, and dialysis, and under his direction Necker grew to be one of the premier nephrology units in the world, certainly the only one with its own annual meeting, the Actualités Néphrologiques, at which state of the art lectures are presented. He was in fact one of the driving forces in the founding of this organization, which held its first meeting at Evian in 1960. In his honor, the ISN has established the Jean Hamburger Award, whose prior recipients include Willem Koff, Frank Dixon, Gabriel Richet, Hugh de Wardener, Donald Sedlin, Renée Habib, and Priscilla Kincaid-Smith. Drs. Heptinstall and Brenner are worthy additions to this circle of illustrious figures in nephrology.

However, before proceeding, I should make a brief side comment. There are certain people whose nicknames are so intimately attached to their image and personality that it seems utterly pompous to refer to them by their given names, particularly if they are held in great affection. Such is the case with Robert Hodgson Heptinstall, known universally simply as “Heppy,” and that is how I will refer to him.

Heppy was born and raised in Cumberland, and on the eve of World War II came down to London to start medical school at the Charing Cross Hospital Medical School of London University. He graduated in 1943 and, after a brief six-month training period as House Surgeon to prepare for military service, went off to the Army and was sent to the Far East. He served there for three years as a Regimental Medical Officer, returning to London only in 1947. There he resumed his medical training, but this time in Pathology at St. Mary’s Hospital in Paddington, rather than in Surgery, and the surgeons have been the poorer for it ever since.

This period was marked by three life-moulding events. First, he met and married Ann Porter and began building a marriage and family, which ultimately grew to six children, the source of much happiness and some sadness, that would enrich his future life. Second, under Wilfrid Newcomb and others at St. Mary’s, he received the rigorous training in what was then known as Morbid Anatomy, which would make him a “compleat” pathologist. This training stood him in good stead throughout his career, not only in putting his research efforts into the proper clinical perspective, but later as Director of the Department of Pathology in constructing a department that was equally balanced between excellent diagnostic pathology and a focused research program.

Third, after a brief stint with Alexander Fleming, he came under the influence of George Pickering, one of the giants of British medicine, at the time the Chief of Medicine at St. Mary’s. Pickering recognized in Heppy a bright and promising young man, and tried to entice him into the world of hypertension and renal disease by proposing a collaborative study of the vascular lesions of malignant hypertension. Pickering succeeded. The entire course of Heppy’s life was determined by this experience. He put aside an early interest in thyroid disease, which had produced several good studies, and henceforth directed virtually all of his research efforts to renal disease, hypertension, atherosclerosis, and their interactions.

After his training, Heppy stayed on at St. Mary’s, where among other activities, he and Kendrick Porter on the pathology side and Marc Jockes on the clinical side developed one of the first true renal biopsy services in Britain. Renal biopsies were in their infancy at the time, performed in only a very few centers. Renal biopsies offered the first real opportunity to study renal diseases in their earlier stages, rather than from autopsy material with the biases that implies. As always with new techniques, there was much skepticism as to whether one could learn anything of value about the whole kidney from such a tiny slice of it. However, this skepticism was quelled once and for all with the landmark CIBA
Symposium on Renal Biopsies in 1961. Heppy and Joekes were important contributors, and indeed provided much of the motivating forces in putting the seminar together. In this early period, Heppy, Joekes and Porter made contributions on nephrotic syndrome, focal glomerulonephritis, and renal amyloid, all on the basis of their biopsy material.

In the meantime, he was actively involved in bench research, working with other collaborators on the relationships between increasing serum cholesterol, blood pressure and the extent of atheroma formation in the rabbit. Heppy made his first visit to the U.S. in 1954–55 as an Eli Lilly fellow of the British Medical Research Council in the Department of Pathology at Johns Hopkins in Baltimore under the aegis of Arnold Rich. There he met and first worked with Fred Germuth on immune-complex induced vascular and glomerular disease, and they were in fact the first to demonstrate by immunofluorescence techniques the presence of immune complexes in the tissues. He returned to England after this very productive year and continued his research on atherosclerosis and renal disease. In 1959 he spent a very happy two months with Harry Goldblatt in Cleveland, and in 1960 he came permanently to the U.S. to be a Visiting Professor at Washington University in St. Louis, and in his second year there he was invited back to Johns Hopkins, where he remains active to this day.

In Baltimore, he continued what would be an extended series of studies on pyelonephritis, which he had begun in England. This work, together with that of the British radiologist, John Hodson, with whom he collaborated, forms the basis of our thinking on this entity today. Pyelonephritis at the beginning of the 1960s was a very poorly understood entity. As it turns out, it was greatly overdiagnosed, and at the time was felt to be responsible for the bulk of end-stage renal disease in the U.S. Heppy on the pathologic side and Hodson on the radiologic side established strict criteria for diagnosis of pyelonephritis, and gradually were able to hold people to them. The result was that the majority of cases fell away, leaving a much smaller, but important group of patients with pyelonephritis, usually on the basis of ureteral reflux. On the experimental side, Heppy worked out the mechanisms of bacterial localization in the kidney, the differences between blood-borne and ascending infection, and the relationship between chronic infection and hypertension. It was at this point in early 1963 that I entered his lab as a sophomore medical student, and with his guidance, we performed a microangiographic study that established the primacy of tubulointerstitial, rather than vascular, lesions in the development of chronic pyelonephritis.

Heppy’s interests were turning increasingly toward hypertension and the juxtaglomerular (JG) apparatus. Together, we performed another microangiographic study on steroid-induced hypertension that produced some of the first evidence for glomerular damage being related to hyperperfusion at increased pressure, an idea that later became important in our thinking about glomerular lesions and proteinuria.

The year 1966 produced two pivotal events that together thrust Heppy, who had been quietly gathering a reputation as a solid researcher, toward center stage in national and international circles. First, Ivan Bennett, the Director of the Department of Pathology at Hopkins was summoned to Washington to act as a scientific advisor to then-President Lyndon Johnson, and Heppy was named the Acting Director, a post he held until 1969 when Bennett resigned definitively and Heppy was named his permanent replacement. He held the Directorship until his ostensible retirement in 1988, but in fact he still is very active, both with the renal biopsy service and the teaching of residents, as well as with writing. Those of us in the department during his Directorship remember this as a halcyon time, with excellent clinical training and service, and an active and flourishing research program, in a truly collegial atmosphere. Despite his increasing involvement with medical school and national commitments, he remained always an active participant in resident teaching, and was extremely supportive of his senior staff and researchers as well, always seeming to be able to come up with startup funds for budding researchers. His tenure produced many of the leaders in American pathology. He was also, not surprisingly, a guiding force in the development of a cadre of renal pathologists, starting with myself as his earliest fellow at Hopkins, and including Jean Olson, Kim Solez, Lorraine Racusen, and later Tibor Nadasdy. All in all, it was an exceedingly fruitful reign.

The second major event in 1966, one much more directly related to the Hamburger Award, was the publication of Pathology of the Kidney, surely his most lasting legacy. There had been books on the pathology of the kidney before, of course, but they were vastly out of date, and based purely on observations made at autopsy. Heppy felt, presciently, that the time was ripe for a new book consolidating what was known about renal pathology in a single place. The book produced was written almost entirely by him, and was a monumental effort taking over two years. This effort was crowned with instant success. The book was, for medical texts, a best seller, a must for everyone who wished to call himself a nephrologist or a renal pathologist. Because the 1960s produced a veritable explosion of new information, with immunofluorescence and electron microscopy being introduced on a wide scale, and new diseases being described almost monthly, it was necessary to produce a second edition in 1974. This book had, if anything, even wider distribution worldwide, even being translated into Spanish. When I came to the Hôpital Necker in Paris in
1975, copies were to be found in virtually every office, including Prof. Hamburger’s, and it was quoted in the same reverent terms that one would ordinarily use for a passage from the Gospel of St. Matthew.

Third and fourth editions followed, with Heppy still writing much or most of the text and editing the remainder, but with new authors included to make the task manageable, since the number of pages was increasing exponentially. Finally, with the fifth edition the task of even editing the book became so Herculean that Heppy ceded this task to a team of four editors, and he, himself wrote only the chapter in which he was most interested, that on urinary tract infections and pyelonephritis, the interests he had brought to the field so many years previously. However, now the book has been retitled Hephinstall’s Pathology of the Kidney. This action has, I suspect, several motivations: first, to truly honor Heppy, much as the Hamburger Award will, but secondly to establish the lineage of the book and to imply to the potential purchaser that the high quality of the previous editions will be continued in this one. Long may it continue!

With the increased visibility that the book and the departmental chairmanship brought, Heppy found himself involved in a variety of activities on the national and international levels. He was on the editorial board of a number of journals, including Kidney International and the American Journal of Pathology, and was the Editor for several years of Laboratory Investigation, the leading journal of pathology research. Similarly, he was on numerous NIH and WHO committees relating to renal disease.

At least as important were his activities with the American Society of Nephrology and the International Society of Nephrology. He was a part of the American Society of Nephrology from its infancy, and his activities on the ASN Council, sometimes as the lone voice for Pathology, resulted in his election to the Presidency of the ASN in 1972, one of the only two times that a pathologist has held this position. Similarly, he was Vice President of the International Society of Nephrology from 1981–84.

In recent years, all of Heppy’s work in these various arenas has been recognized by a number of major awards. First, in 1983 he was invited to give the Maude Abbott Lecture at the International Academy of Pathology, the highest recognition that pathologists can bestow on one another. In 1986 he won the David M. Hume Memorial Award of the National Kidney Foundation, and in 1992 the John P. Peters Award of the American Society of Nephrology. Thus, it might be said that being honored now with the Hamburger Award by the International Society of Nephrology completes the ‘hat trick’ of receiving all of the major awards that our respective organizations have to offer.

It is with great pleasure, then, that I present Robert H. Heptinstall for the Jean Hamburger Award of 1999.