Franklin H. Epstein:
Reminiscences of a Brilliant
Physician-Scientist and Master
Clinician

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Franklin Harold Epstein, MD, died on November 5, 2008. As the William Applebaum Professor of Medicine at the Harvard Medical School, he was 84 years old and actively engaged in research, teaching, and clinical care until a few weeks before his death. Frank exemplified the ideal physician: an investigator, a teacher, and a master clinician, and he encouraged this model in his trainees.

I first met Frank in New Haven in 1963 while interviewing for an internship in Paul Beeson’s Department of Medicine. I was attracted to Yale because of his research, and he invited me to lunch that day. He talked about his new studies on the effects of water diuresis on susceptibility to pyelonephritis and his previous articles in the Journal of Clinical Investigation on the mechanism of impaired concentrating ability in hypokalemia and hypercalcemia. I was struck by his clarity and intellectual rigor, his capacity to probe complex renal and electrolyte disorders, and his sheer brilliance. A few years later, we published together an in-depth analysis of the mechanism of lithium-induced diabetes insipidus in human and the rat. Frank was widely considered one of the giants of metabolism and nephrology. Among his more than 400 publications, he published 39 articles in the Journal of Clinical Investigation and 26 in the New England Journal of Medicine. He reveled in the discoveries and accomplishments of others, and his generosity with ideas inspired those who worked with him. He was a cheerful and enthusiastic man who laughed heartily and sang or whistled constantly, always on pitch.

Frank entered Brooklyn College at the age of 16 and graduated summa cum laude in 1944. His father was a school principal and his mother a teacher who taught him elocution, at which he excelled. He then entered the Yale University School of Medicine, graduating cum laude in 1947. During his internship and residency at Yale-New Haven Hospital, he came under the influence of John P. Peters, the leading American physician-scientist of that time, who was exploring the pathophysiology of water and electrolytes in human disease. Eventually, Frank succeeded Peters as chief of the Division of Metabolism at Yale.

After a fellowship at Boston University Medical School and service in the United States Army at Walter Reed Army Hospital and the First General Dispensary at Fort Richardson, AK, Frank returned to Yale, where he was rapidly promoted to full professor. In 1972, he moved to Boston to head the Thorndike Memorial Laboratory and the Harvard Medical Unit of Boston City Hospital. One year later, he moved to the Beth Israel Hospital as chairman and physician-in-chief of its Department of Medicine, and he remained at the Beth Israel, now the Beth Israel-Deaconess Medical Center, thereafter.

Frank received many national and international honors for his accomplishments in nephrology, including the John P. Peters Award of the American Society of Nephrology in 1985, the David Hume Award of the National Kidney Foundation in 2003, the Bywaters Award from the International Society of Nephrology, and honorary degrees from Oxford University and the Medical Academy of Gdansk, Poland. His research encompassed the physiology of the renal medulla; disorders of urinary concentrating ability; mechanisms of acute renal failure; disorders of water, sodium, and potassium; the movement of ions across marine epithelia; and medical complications of pregnancy, including preeclampsia. He was a longstanding editor of Harrison’s textbook, Principles of Internal Medicine, and the New England Journal of Medicine. His last article in the Journal of Clinical Investigation in 2008 recalled the glory days of the trisociety meetings of academic internal medicine in Atlantic City.

Frank had the highest expectations of himself and others. Although on medical rounds he asked exacting and sometimes intimidating questions, his trainees revered him as a gentle and kind person.

“My debt to him is beyond measure,” said Dr. Ananth Karumanchi of Beth Israel-Deaconess Medical Center. Frank recently encouraged Karumanchi’s acclaimed research unraveling the protein puzzles behind preeclampsia. “My career was really jump-started by him. I knew he was a legend in his own right, yet I could call him anytime. He was a medical encyclopedia. I didn’t have to go to the library. He knew every paper published in this field,” Karumanchi said.

In the summer of 1970, Patricio Silva, Alan Cohen, and I began fellowships with Frank and joined his laboratory at the Mount Desert Island Biologic Laboratory (MDIBL). He had begun working there two years earlier on the comparative physiology of salt and water homeostasis in lower vertebrates. This past summer, he celebrated his 40th year as a...
seasonal investigator at MDIBL (Figure 1). His impact on the laboratory was extraordinary, an influence not seen since the days of Homer Smith, some 50 years earlier. He served as a trustee for 38 years and was chairman of the Scientific Advisory Committee and Long Range Planning Committee before becoming president of MDIBL from 1986 through 1995. In 1998, at our centennial, he wrote, “A Laboratory by the Sea,” the definitive history of MDIBL.9

He attracted dozens of investigators to MDIBL and patiently trained multitudes of high school students, undergraduates, medical students, and fellows at the bench, many of whom recall him as dramatically influencing their lives. Alex Peters, an undergraduate at Princeton, wrote, “He engaged all students at MDIBL warmly and never overlooked a question, as simple as it might have been. Although he may not have realized it, his unfailing tendency to ask a thoughtful, interesting, and challenging question at the end of every presentation—be it in Maren Auditorium, on Monday mornings at Star Point, at brown bag lunches, or at any other opportunity—inspired the curiosity of all those around him.”

Lewis Landsberg, who moved with Frank from Yale to Harvard, was his vice chairman at the Beth Israel Hospital, and then served as chairman of medicine and dean at Northwestern, recalled, “In the fall of 1960, I was a first-year medical student at Yale attending ground rounds on Saturday mornings in the Fitkin amphitheater at the old Grace-New Haven Hospital. We students sat in awe of his lucid analysis of complex cases covering a broad range of topics and diagnoses. He seemed so smart! He was so clear in his explanations of complicated subjects that we wished he could teach us all of our subjects, even anatomy. His kindness to patients and colleagues was coupled with a penetrating intelligence. He taught me that you cannot be a good clinician without understanding the pathophysiology of disease, and no one understood pathophysiology like Frank. At the Beth Israel Hospital, he created an environment where young investigators and clinicians thrived. Right up until his death, he remained involved in figuring out the molecular pathogenesis of toxemia of pregnancy.”

Lloyd Cantley, a trainee with Frank at the Beth Israel Hospital and now a professor of medicine at Yale wrote, “My first day of nephrology fellowship began at MDIBL, when I met Frank at 8 a.m. and was not sure what to expect. His thirst for knowledge and love of learning were apparent. ‘Listen to what the patient is telling you,’ he said, ‘and let the course of their disease guide and focus your research.’ At the end of the hour, I understood for the first time that a career in research could be a life-long passion rather than a job, and I was hooked.”

What were the characteristics of this remarkable person? First was his pure brilliance. For many, Frank was the smartest person they ever met; for me, he was the individual I most respected. Second was his intense curiosity, about both things medical and the larger world. He was a reader of science, biography, politics, and history, a breadth of interest suitable to Benjamin Franklin, for whom he was named. Third, he had an eloquent style of speaking that could hold audiences spellbound. This past summer, addressing the MDIBL Corporation at the dedication of our new year-round green laboratory building, Frank’s delivery and facility with words captured everyone’s attention. These characteristics were blended in that brief moment at the end of practically every lecture or presentation when Frank would ask the penetrating question for which he was so well known.

For years, in the open air by the seaside on Frenchman’s Bay, Frank led our Monday morning seminars, a quintessential MDIBL experience. He brimmed with intellectual curiosity and a passion to link knowledge from the laboratory directly to the patient.

Throughout his career, Frank wrote passionately about the physician’s role in the preservation of life.10 He wrote recently,11 “In the modern hospital and in the present climate of the increased concern over medical cost, it has become fashionable to question the traditional duty of the physician to preserve life. I believe there are practical as well as legal and moral reasons to adhere to the ancient Hippocratic dictum: When efficacious treatment is possible, the physician’s duty is to the patient and to no one else—not to the family nor to the community—to prevent suffering and preserve life as long as you can. Life cannot be prolonged indefinitely and death comes at last, but the little we can do has an importance that transcends the patient for it carries a message to all our patients and to the world: Human beings are important.”
His exuberance for life was expressed years ago when Frank left Yale to move to the Boston City Hospital. The Department of Medicine was without a chairman, and the Medical School and the University were between deans and presidents. There was no formal recognition of Frank’s contributions to the school. We, his fellows, gathered in the upstairs dining room at the tables down at Mory’s for a farewell dinner. After a few speeches, Frank rose and recited, from memory, the poem “Ulysses,” by Alfred Lord Tennyson, which concludes with,

“We are not now that strength which in old days
Moved earth and heaven, that which we are, we are—
One equal temper of heroic hearts,
Made weak by time and fate, but strong in will
To strive, to seek, to find, and not to yield.”

After his death, his family found Tennyson’s poem on his desk with the final lines underlined.

All of nephrology and medicine mourn the loss of Franklin Epstein.

DISCLOSURES
None.

REFERENCES