

A tribute to Franklin H. Epstein

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Obituary

Franklin Harold Epstein, William Applebaum Professor of Medicine at Harvard Medical School, died on November 5, 2008. He was 84 years old and actively engaged in research, teaching, and clinical care until a few weeks before his death from a brain tumor. Frank Epstein 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 the fall of 1963, after interviewing for an internship in the Department of Medicine of Yale University. I was attracted to Yale partly because of Frank's research, and he invited me to lunch at a nearby restaurant that day. He talked about his new studies on the effects of water diuresis on susceptibility to pyelonephritis (1) and his previous JCI papers on the mechanism of impaired concentrating ability in hypokalemia and hypercalcemia (2, 3). I was struck by Frank's clarity and intellectual rigor, his capacity to probe complex renal and electrolyte disorders, and his sheer brilliance. A few years later we published an in-depth analysis of the mechanism of lithium-induced diabetes insipidus in humans and rats (4). Frank was widely considered to be one of the giants of metabolism and nephrology. Among his more than 400 publications, he published 39 papers in the JCI and 26 in the [...]

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Frank was widely considered to be one of the giants of metabolism and nephrology. Among his more than 400 publications, he published 39 papers in the *JCI* 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.

A gifted student, 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 was a teacher, who taught him elocution at which he excelled. He then entered the Yale University School of Medicine, graduating cum laude in 1947. He completed his internship and residency at Yale–New Haven Hospital, where he came under the influence of John P. Peters, the leading American physician-scientist of that time, who explored the pathophysiology of water and electrolytes in human disease.

After a fellowship at Boston University Medical School and service in the United States Army, first at Walter Reed Army Hospital and then at the First General Dispensary at Fort Richardson, Alaska, Frank returned to Yale, eventually becoming the head of the Division of Metabolism. There he was promoted to full professor before coming to Boston in 1972 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 Beth Israel thereafter (Figure 1).

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 M. 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. His research encompassed the physiology of the renal medulla; disorders of urinary concen-

trating 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 long-standing editor of *Harrison's principles of internal medicine* textbook and of the *New England Journal of Medicine*.

Frank had the highest expectations of himself and others. Although on medical rounds he asked intimidating and exacting questions, his trainees revered him as a gentle and kind person. "My debt to him is beyond measure," said Ananth Karumanchi of Beth Israel Deaconess Medical Center. Frank recently encouraged Karumanchi's acclaimed research unraveling the protein puzzles behind preeclampsia (5, 6). "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, I began a fellowship with Frank and joined his laboratory at the Mount Desert Island Biological Laboratory (MDIBL). Frank had begun working there two years earlier on the comparative physiology of salt and water homeostasis in lower vertebrates (7). This past summer he celebrated his fortieth year as a seasonal investigator at MDIBL. His impact on the lab was enormous, an influence not seen since the days of Homer Smith 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 1986–1995. In 1998, the centennial of MDIBL, he wrote *A laboratory by the sea*, the definitive history of MDIBL (8).

He attracted dozens of investigators to MDIBL and patiently trained multitudes of high school students, undergraduates, medical students, and fellows, most of who recall him as dramatically influencing their lives. Alex Peters, an undergraduate at Princeton, wrote that "He engaged all students at MDIBL warmly, and never overlooked a question, as simple as it might have been. Though he may not have realized it, his unflinching tendency to ask a thoughtful, interesting, and challenging question of every speaker inspired the curiosity of all those around him." Patricio



Figure 1
Franklin H. Epstein, speaking at the dedication of the new year-round laboratory building at MDIBL, July 2008.



Silva, Section Chief of Nephrology at Temple, whose friendship with Frank spanned almost four decades, commented that “Dr. Epstein was the most significant influence in my career. I was in awe of him. He had the capacity to cut to the chase effortlessly, but he never showed off.”

What were the distinguishing characteristics of this remarkable person? First was his pure brilliance. For many, Frank was the smartest person they ever met; for me, he became the individual I most respected. Second was his intense curiosity, both about 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.

His exuberance for life was expressed years ago when Frank Epstein 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, completely from memory, the poem “Ulysses”, by Alfred Lord Tennyson, which concludes with the following lines:

*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.*

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

All of medicine mourns the loss of Franklin Epstein.

John N. Forrest Jr.

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1. Andriole, V.T., and Epstein, F.H. 1965. Prevention of pyelonephritis by water diuresis. Evidence for the role of medullary hypertonicity in promoting renal infection. *J. Clin. Invest.* **44**:73–79.
2. Manitius, A., Levitin, H., Beck, D., and Epstein, F.H. 1960. On the mechanism of impairment of renal concentrating ability in potassium deficiency. *J. Clin. Invest.* **39**:684–692.
3. Manitius, A., Levitin, H., Beck, D., and Epstein, F.H. 1960. On the mechanism of impairment of renal concentrating ability in hypercalcemia. *J. Clin. Invest.* **39**:693–697.
4. Forrest, J.N., Jr., Cohen, A.D., Torretti, J., Himmelhoch, J.M., and Epstein, F.H. 1974. On the mechanism of lithium-induced diabetes insipidus in man and the rat. *J. Clin. Invest.* **53**:1115–1123.
5. Venkatesha, S., et al. 2006. Soluble endoglin contributes to the pathogenesis of preeclampsia. *Nat. Med.* **12**:642–649.
6. Levine, R.J., et al. 2006. Soluble endoglin and other circulating antiangiogenic factors in preeclampsia. *N. Engl. J. Med.* **355**:992–1005.
7. Epstein, F.H., Katz, A.I., and Pickford, G.E. 1967. Sodium- and potassium-activated adenosine triphosphatase of gills: role in adaptation of teleosts to salt water. *Science.* **156**:1245–1247.
8. Epstein, F.H. 1998. *A laboratory by the sea: The Mount Desert Island Biological Laboratory 1898–1998.* The River Press. Rhinebeck, New York, USA. 365 pp.