Eulogy for Edward D. Freis, MD*

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It is a great honor for me to be able to say a few words about the life of Ed Freis. I knew him for close to 25 years and have a lot of fond memories from our association. I had the good fortune to know Edward Freis as a man, a physician, a scientist, and personally. Ed Freis was a good man, a great scientist, and a great philanthropist. He had a good life and a great career, and he died happy, fulfilled by his achievements and appreciated by his peers.

I could spend hours talking about his scientific work and the many contributions he made to medical research. Instead, I'll give you a little personal version, the view of an insider.

Ed Freis was a good man and a great scientist. Although he ventured briefly into the word of Hollywood and acting, pretty quickly and with help from his family, he realized that medicine was more suited to his personality and far more rewarding. He started his career and work in the field of hypertension in the early 1940s, treating high-risk patients with difficult-to-tolerate medications. He was the first to recognize the importance of treating hypertension and the first to investigate the efficacy and safety of diuretics. In 1956, he presented an abstract at the American Heart Association's annual meeting demonstrating the efficacy and safety of diuretics as monotherapy (in 10 patients) and in combination with other medications available at the time. That was his first major contribution.[1]

Up to that time, the prevailing scientific opinion was that hypertension should be left alone in patients with target organ damage, because treatment was considered detrimental. It was Ed Freis who first hypothesized that treating hypertension would save lives and prevent strokes and heart attacks, and he designed the first Veterans Administration cooperative studies to prove it. Those were the first multicenter studies done in cardiovascular disease. The 2 landmark reports he published in 1967 and 1971 changed the course of history.[2] The first proved that treating severe hypertension can have a dramatic impact on cardiovascular morbidity and mortality. The second proved that even in patients with mild to moderate hypertension, treatment can prevent most cardiovascular complications.[3]

Hypertension thus became a treatable disease, and the complications of hypertension became preventable. The nation and the world appreciated the results of those studies, and large-scale programs began for the treatment and control of high blood pressure. Dr. Freis deserves most of the credit. For his work, he was awarded the prestigious Albert Lasker Award, and he was nominated for the Nobel Prize twice.

Let me talk to you a little bit about Ed Freis the man. I first met him in 1981, when I walked into his office looking for a job. I was a research fellow, then at the National Institutes of Health, investigating the role of murine macrophages on immunoreactivity, but I had had enough and decided that I wanted to deal with patients. Having heard about Dr. Freis and his work, I called him up and got an appointment for an interview. It did not take long. After a brief conversation, he said "So, you are interested in clinical research? Ha, and what have you done so far?" When I told him about my experience working with mice, that my group had published 11 reports in 18 months, and that I was more interested in humans, he said "You've got the job, when can you start? And by the way, how much money do you make?" After I explained that I was making only $13,000 a year, he said, "We can do better than that: we'll pay you $18,000." We had a deal, and I started working with him.

Ed Freis was a fair and a generous man. He was fair to his science and supportive to those who worked for him. By the time I joined his group in June 1981, his landmark work had had a big impact on patient care and the medical community. The treatment of hypertension was widespread, and many other outcome trials were in press or in progress. His work was mostly focused on the treatment of hypertension using diuretic-based regimens. He always held the position that these regimens were safe and effective, but his competitors tried in many different ways to undermine his work.

Soon after I joined his group, Dr. Freis attended the American Heart Association's annual meeting, at which Dr. Bryand Holland presented data from a small study suggesting that diuretics cause arrhythmias and sudden death.[4] This became very controversial and dominated research on hypertension throughout the 1980s. No wonder Dr. Freis asked me to design a protocol to assess the effect of diuretic-induced hypokalemia on cardiac arrhythmias.

The initial study was designed and carried out in patients treated with high-dose diuretics who developed severe hypokalemia.[5] Yet our data indicated no harm from diuretics to our patient population. Even severe hypokalemia had no effect on arrhythmias. After that, we carried out several other studies in the clinic that repeatedly proved the safety of diuretics.[6–8] Ed Freis found great satisfaction in these results and continued commenting and writing about them

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for the next 2 decades. Our team and Marvin Moser were the lone defenders of diuretics in the 1980s and part of the 1990s.

Nevertheless, the issue remained controversial and culminated in the design of the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial,[9] which as we all know proved definitively that Ed Freis was correct: diuretics are effective in preventing cardiovascular complications, and diuretic-induced hypokalemia has no adverse effect on cardiovascular events.

Ed Freis was a kind man, devoted to medicine. He held a journal club almost every week and reviewed the charts of his most complex patients with the clinic staff regularly. Aldo Notargiacomo, Madelene Metcalf, and Barbara Gregory worked with him for >20 years. Research fellows were an integral part of the hypertension research clinic, and Ed Freis trained some of the most prominent researchers in cardiovascular disease, including Jay Cohn and Edward Frolich, to name just a few.

Ed Freis was a good man. One of the high points during each academic year was the trip to the annual meeting of the Council for High Blood Pressure Research, usually held in Cleveland. Participation was strictly by invitation only, but members of the council could bring colleagues or coworkers with them. Using that avenue, I was able to go to the meeting several times, until I became a member myself. The annual meeting of the council was where all the great minds in hypertension research gathered every year to discuss new developments. It was where one could meet with researchers such as Irving Page, Marvin Moser, Ray Gifford, Norman Kaplan, and others. And it was where one could realize the recognition and respect the medical community had for Ed Freis.

During an annual meeting of the council, Ed Freis was awarded the prestigious Ciba-Geigy Award, among the highest awards given for hypertension research. I remember that during the dinner after he received the award, John Laragh came to our table and discussed the lack of clinical presentations at the meeting and the need for another society with a clinical orientation. That is how the idea of forming the American Society of Hypertension began. The society is today among the most successful clinical societies in cardiovascular disease.

Ed enjoyed life tremendously. He prided himself on knowing every good restaurant in town, particularly every good deal in town. Confidentially, he told me that the best deal was a Greek restaurant called Abrosia, where one could dine on good food for $15. On numerous occasions, he commented on how much he enjoyed Greek food and in particular my wife's cooking.

Long after he retired, Ed continued coming to the clinic, and in fact we shared office space for another decade. He authored >400 original reports, editorials, book chapters, and reviews.

Ed practiced what he preached. He diagnosed himself with hypertension and treated himself aggressively, because he wholeheartedly believed that lower blood pressure was better. He controlled his systolic pressure to <120 mm Hg and his cholesterol to <150 mg/dl, he quit smoking, he exercised, and he kept his weight under control. Ed lived to be 92 years old, and he had no evidence of atherosclerotic heart disease.

Ed Freis had a good life and a brilliant career, and he passed away happy. My wife and I were grateful for the opportunity to spend time with him and his lifelong companion Mary Rose. He was proud and supportive of his family, and he loved his children, grandchildren, and great grandchildren.

Edward D. Freis died on February 1, 2005.

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