The Evolution of Heart Failure Therapy in the Past Sixty Years: One Man's Journey

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The editor has asked me to write about my recollections of the changes that have occurred in heart failure therapy over the past 60 years. I wondered why he charged me with this topic but I quickly realized that there are only a few octogenarians still around to tell the story. Fortunately, there will be fewer still who will challenge my memory. I will try to provide the dimension of changes that occurred as viewed through my somewhat distorted vision. A multitude of basic and clinical investigators, some of whom were colleagues and friends, participated in this exciting adventure. I will refer to a few of the publications to chart the course that we all followed over the past half-century. Behind each reference, however, lay many groundbreaking observations that I will not touch upon. There have been many blind alleys that had to be pursued before we found the scientific truths that we now understand. Thinking back to that early period, it is obvious that I was present during a remarkable period of discovery.

Early Years

To appreciate the changes, I must paint a picture of cardiac therapy as it was in the mid-twentieth century when I was began my medical career. The patients with heart failure that I saw in 1955 when I became an intern at New York Hospital were younger by contemporary standards. The image of those patients remains indelible in my mind. Most had severe dyspnea and profound edema that encompassed a cachectic and cyanotic body. Many had rheumatic valvular disease as a result of childhood rheumatic fever which was just becoming extinct in America with the introduction of antibiotic therapy in the previous decade. Patients with severe hypertension and end-stage ischemic heart disease also populated the general medical ward. There were no designated wards assigned to cardiac patients. Patients with acute transmural myocardial infarctions were identified with the use of electrocardiographic (ECG) criteria together with hematologic evidence of acute inflammation. The nuance of transient ischemia had to wait another 10 years for the development of coronary angiography and 30 years for the introduction of biomarkers of ischemia. Of course angina pectoris was common, but the ECG changes associated with ischemia were poorly understood and stress testing was not routinely performed. The primitive nature of our world at that time can be exemplified by the excitement associated with the arrival of a portable hot-stylus paper ECG recorder on the medical ward which enabled us to record QRS and ST-segment abnormalities in addition to arrhythmias at the bedside. Before that, ECGs were recorded on photographic paper which required a darkroom and time-consuming developing process.

But let's go back to where it all began in 1929 in a small town in eastern Germany where Werner Forssmann was beginning his surgical training. Either by curiosity or imagination he passed a rubber catheter of questionable sterility into his right ventricle through the left antecubital vein and took a picture of it on the hospital x-ray machine. That episode and experience was the beginning of the exploration of the heart chambers and their functional anatomy. Almost a decade later Andre Cournand and Dickinson Richards, in a laboratory at Bellevue Hospital in New York, began measuring Fick cardiac output and, using specially designed catheters, recorded the first intracardiac pressure measurements of the functioning heart. For their breakthrough observations all 3 received the Nobel Prize in 1956.

When I first saw patients with valvular heart disease, I was limited by the primitive knowledge of the hemodynamics of valvular disease which prevailed in 1955. Finger fracture of the mitral valve through the left atrial appendage was just becoming possible. Cardiac catheterization laboratories were being developed with rudimentary imaging techniques requiring dark adaptation for 3−4 minutes with red glasses. The selection of the ideal patient for mitral valvuloplasty depended on the pressure characteristics and the difference between the pulmonary capillary wedge pressure and the assumed left ventricular pressure. Image amplification fluoroscopy became available a few years later and we were able for the first time to visualize the

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heart in a lighted room. We waited another 20 years before echocardiography provided us with even more accessible imaging of the heart. Open-heart valve repair and bypass surgery with pump support became widely available in the mid 1960s.

Few drugs were available for the treatment of patients with heart disease. Digitalis was the only drug available for heart failure treatment and for the slowing of atrial fibrillation and flutter. Some of the leading physicians at that time advocated 1 year of bed rest as the best treatment for heart failure. Two drugs, quinidine and procaine amide, together with digitalis were used to slow atrial fibrillation and flutter and to convert to normal sinus rhythm. Intramuscular mercurial drugs were the only diuretics available and could be used only intermittently because of metabolic alkalosis. Thiazide diuretics were just being developed, and loop diuretics became available within a few years. Rotating tourniquets, intravenous morphine, and, as a last resort phlebotomy, were the standard and only treatment for acute heart failure and pulmonary edema. I recall using Southey tubes, inserted subcutaneously in the thigh, to drain subcutaneous interstitial fluid in patients with anasarca.

There were no drugs available for the treatment of hypertension. Low-salt diets were the only proposed treatment. It was not unusual to see patients with systolic pressure >200 mm Hg and diastolic pressure >110 mm Hg. Only 10 years earlier, in 1945, President Franklin Roosevelt, who had a history of severe hypertension with systolic pressures >250 mm Hg for many years before his death, died at 63 years of age owing to a stroke preceded by congestive heart failure.[1]

In 1959 I returned to New York Hospital−Cornell Medical Center, after serving my obligatory 2 years as an Army doctor, as an assistant resident and later as a Cardiology Fellow with Tom Killip, supported by a grant from the American Heart Association. Killip had just returned to New York Hospital as Chief of Cardiology. I spent one-half of my time with Killip and one-half in the catheterization laboratory with Dan Lukas, who taught me how to read and think. Working with Killip we embarked on a study of the effect of the modification of the sympathetic nervous system with the use of a drug that depleted cardiac sympathetic receptor on cardiac function in patients with thyrotoxic heart disease. That study introduced me to the excitement of measuring the effect of a pharmacologic intervention on clinical heart disease at the bedside, and the experience runs through much of what I have accomplished in cardiology since then. It resulted in my first publication and a presentation at the American Heart Association meeting in Cleveland in 1963.

When I finished my cardiology training, I took a position at the Rochester General Hospital as director of the Cardiac Catheterization Laboratory and as an Assistant Clinical Professor of Medicine at the University of Rochester (UR). That position gave me the opportunity to develop a cardiology fellowship program and to participate in the development of a cardiosurgical program. It also gave me the opportunity to hire 3 additional staff cardiologists who were wonderful associates and superb doctors to whom I owe a great deal for their support. About this time UR was selected to participate in the Myocardial Infarction Research Unit (MIRU) program with a grant from the National Institutes of Health (NIH). Directed largely to the study of events occurring in the Coronary Care Unit (CCU), Arthur Moss and I, together with psychiatrist Bill Green and with MIRU support, explored the prehospital events that preceded the infarction, particularly the prodromal symptoms. Studying a large industrial plant in Rochester, we observed that although many patients were admitted to the hospital with the acute event, the number of sudden deaths that occurred before hospitalization was remarkably high. Years later, in Detroit, this observation served as the genesis of my research into out-of-hospital sudden death. About this time I became an Associate Professor at UR and was granted a sabbatical to spend a year at the Thoraxcenter in Rotterdam working with Paul Hugenholtz, who was then the director of that institute. I wanted to satiate my desire to do animal research and embarked on an animal study of the metabolic and physiologic changes that occurred in regional myocardial ischemia. Although productive of a number of papers, it did not hold the thrill of doing clinical research at the bedside. It did, however, open the door to the European world of cardiology, which stood me in good stead in the future.

When I returned from Rotterdam I accepted the position of Division Head of Cardiology at the Henry Ford Hospital. That institution provided a unique environment to continue my clinical research and to expand a training program and staff. Also at the time, the institution was given a large grant from the Ford Foundation to support and expand its research program within which cardiology would play a large role. The creation of a basic research laboratory that could identify new drugs which then could be applied to clinical research in a busy CCU seemed to a perfect fit. Over the next 40 years, with the leadership of Hani Sabbah, that laboratory focused its efforts on identifying and developing new drugs and devices for heart failure therapy. That laboratory has explored a variety of important dysfunctional mechanisms leading to heart failure progression, including the role of neuroendocrine overexpression, apoptosis, and mitochondrial function.

In the 1970s and 1980s, being a division head in cardiology was an exciting and creative role. The ability to focus on patient care, educate medical students, house staff and trainees, and direct new clinical research was wonderfully rewarding. However in the 1990s, as academic medicine became ‘‘bottom-line’’ oriented, the job lost its charm and it became clear to me this it was a role that I no longer enjoyed. It was clear to me that it was a role I no longer enjoyed.