Profiles in Cardiology

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Herbert N. Hultgren

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Herbert N. Hultgren, M.D., Professor of Medicine (Cardiovascular) Emeritus, at Stanford University School of Medicine died on October 18, 1997, at his home on the Stanford University campus. His career epitomized the growth and development of academic cardiology during the last half of the twentieth century that saw a remarkable development of cardiology and cardiac surgery.

Herbert Nils Hultgren was born on August 29, 1917, in Santa Rosa, California, a small city in the northern part of the San Francisco Bay area. His parents were of Swedish origin. He attended Santa Rosa Junior College for two years and then transferred to Stanford University, from which he was graduated in 1939. He then attended Stanford University School of Medicine, whose clinical facilities were located in San Francisco, with the preclinical years on the main university campus 38 miles south in Palo Alto. He received the M.D. degree in 1943, stayed at Stanford for a residency in internal medicine, and then served in the U.S. Army in Europe from 1944 to 1945. His period of military service was notable for his experience at the end of the war with starved prisoners in German concentration camps. He later published careful and systematic observations on severe starvation, using simple methodology; the account displayed a scientific style that remained characteristic throughout his career.¹

He returned to San Francisco in 1946 for a year of residency in pathology, and then went to Boston for a year of training in cardiology at the Thorndike Memorial Laboratory of the Harvard Medical School at Boston City Hospital, under the direction of Dr. Laurence B. Ellis. He arrived in the midst of the beginnings of a new era in cardiology, in which cardiac catheterization was being introduced into clinical practice and the surgical treatment of mitral stenosis was beginning.

Dr. Hultgren joined the faculty of the Stanford University School of Medicine in San Francisco in 1948, founding the Division of Cardiology and establishing the first cardiac catheterization laboratory in northern California. Over the next 11 years he teamed with the cardiac surgeon, Dr. Frank Gerbode, in guiding Stanford to a place among the world's leading institutions in the new fields of hemodynamically oriented cardiology and cardiac surgery. Pathophysiologic and diagnostic aspects of valvular and congenital heart disease were his central research interests in this period, as they were with many of the young leaders of academic cardiology in the 1950s. Memorable contributions from this period included the description of the respiratory variation in the systolic ejection click of pulmonary valve stenosis,² the venous pistol shot sound in severe tricuspid regurgitation,³ the clinical and physiologic picture of patent ductus arteriosus with severe pulmonary hypertension,⁴ and the syndrome of reopened ventricular septal defect after attempted total correction of tetralogy of Fallot.⁵ He continued his interest in this area throughout his career, continuing to employ simple clinical and hemodynamic methods even as ever more elaborate and technological methods of study developed. Thirty years later, in the 1980s, he explored the assessment of left bundle-branch block and of aortic stenosis by means of phonocardiograms and indirect carotid arterial pulse recordings, techniques long since abandoned by the cardiological mainstream.^{6,7}

An outgrowth of his interest in the pathophysiology of congenital heart disease in the 1950s was a focus on the problem of arterial hypoxemia and its relation to the physiology of the pulmonary circulation. He linked this academic interest to his lifelong interest in mountain climbing. On a trip to Peru in 1959 he encountered the entity of high altitude pulmonary

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FIG. 1 Herbert N. Hultgren, M.D., 1917–1997

edema, previously known to relatively few and not described in the U. S. medical literature. An account published in the *Stanford Medical Bulletin* in 1960 noted 41 cases from the Chulec General Hospital, located at an altitude of 12,000 feet in the Peruvian Andes mountains.⁸ In 1961, with several colleagues, he described these cases in detail, along with 15 cases in U.S. mountaineers, in the first definitive U. S. presentation of this entity.⁹

High altitude medicine in general, and high altitude pulmonary edema in particular, remained his most avid academic interests for the rest of his career. His many subsequent studies documented increased reactivity of the pulmonary vascular bed to hypoxia in high altitude residents and the frequent occurrence of pulmonary hypertension, particularly in those subject to high altitude pulmonary edema. He developed a theory of the mechanism of this condition, holding that pulmonary vasoconstriction in response to acute hypoxia may be nonuniform in the lung, resulting in diversion of the blood flow to less constricted areas, overperfusion of these areas, and extravasation of fluid through the capillary walls of overperfused areas. An analogy was made with the pulmonary edema occasionally seen in acute pulmonary embolism in humans. Experimental work supported this theory, which remains viable although controversial. Dr. Hultgren collected his many years of work on hypoxemia and high altitude medicine into a comprehensive book, published a few months before his death.¹⁰

In 1959, the Stanford University School of Medicine reorganized, moving all its activities from San Francisco to the main campus in Palo Alto, where a new comprehensive academic medical center was built. Only a small nucleus of full-time faculty members in the clinical departments made the move, since most of the clinical faculty were primarily based in practice in San Francisco. The new school featured a true full-time faculty and a redirection toward research. As the head of the Division of Cardiology, working with a young and relatively unknown cardiac surgeon, Dr. Norman E. Shumway, Dr. Hultgren faced a major rebuilding program. The program was brilliantly successful, greatly supported by Dr. Hultgren's widely recognized excellence in the field of valvular and congenital heart disease. Dr. Shumway quickly demonstrated excellence in the new field of open heart surgery, and the program blossomed, culminating in a signal event—the first adult human heart transplant in the U. S. in 1968.

In 1967, Dr. Hultgren moved across the campus to the Palo Veterans Administration Medical Center, where he remained the head of the Cardiology Division for the next two decades. Here he developed a third area of research interest—the clinical results of coronary artery bypass graft surgery. In the early 1960s, he had already shifted his primary cardiological interest to coronary artery disease. The Veterans Administration Cooperative Study of Coronary Artery Surgery, in which he played a leadership role for many years, was a pacesetter in the use of large, randomized, controlled clinical trials of the type that later assumed vast influence with the advent of thrombolytic therapy for acute myocardial infarction. Dr. Hultgren brought his clinical acumen and his analytic abilities to bear on this field, becoming the chief spokesman for the study. He ably defended the study against the critics who found its conclusions not always to their liking. The superiority of surgical over medical therapy in left main coronary artery disease was shown, but for other patients the differences in mortality were not striking. His summary after many years of follow-up has stood the test of time:

Patients who have high-risk left main disease should have prompt surgery irrespective of the severity of symptoms . . . Survival is improved by surgery in the subgroup of patients with three-vessel disease and impaired LV function. However, it should be pointed out that the most significant improvement . . . was had only in the presence of multiple clinical risk factors such as resting ST depression, history of MI, and history of hypertension . . . There is no evidence that survival is significantly improved by surgery in subgroups of patients without left main disease who have a good prognosis on medical therapy, i.e., patients with single- or double-vessel disease, those without multiple clinical risk factors, and those with normal LV function.¹¹

Dr. Hultgren was one of a small group of founding members of the Association of University Cardiologists in the early 1960s. He was active in the Association, becoming its President later in the 1960s and arranging for the move of its

annual meeting from January in Chicago to Arizona and later to other sunbelt sites. He was a member of the Cardiovascular Subspecialty Board of the American Board of Internal Medicine, becoming its Chairman in the 1970s, and overseeing the conversion of its examination from the oral to the written format. He was an active and respected voice at the national level in policy statements regarding training and manpower in cardiology. As in his research, his thoroughness, balanced approach, and emphasis on proven fundamentals won him respect in the policy area.

Dr. Hultgren continued his research and teaching after his retirement in the late 1980s. He also continued his avid outdoorsmanship and mountaineering until the last year of his life.

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