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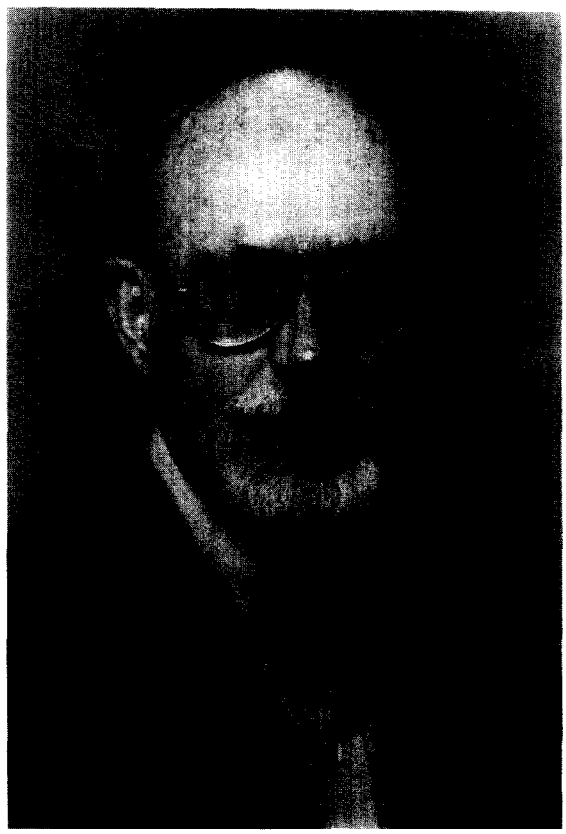
ATHEROSCLEROSIS

In Memoriam

David H. Blankenhorn, M.D. 1924–1993



It is hard to imagine that as recently as only six years ago, human atherosclerosis was generally believed to be irreversible. Armed with a vision of the future and support from the National Heart, Lung, and Blood institute (NHLBI), Dr. David H. Blankenhorn embarked on a scientific journey which would span some 40 years and leave in its path a lifetime of accomplishments. This journey would forge new friendships and enduring collaborations, integrate divergent scientific fields, and generate new technology and its applications. It would forever change our perspective on the reversibility of human atherosclerosis and how we could successfully effect it.

Recognizing that sequential quantitation of human atherosclerosis during the course of a therapeutic trial would be essential to proving reversibility of atherosclerosis, David envisioned early an application

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of computer image processing to angiograms. Computer image processing had recently been developed at the California Institute of Technology's Jet Propulsion Laboratory (JPL) to remove noise encountered during transmission of photographs from planetary spacecraft. In collaboration with Robert H. Selzer at JPL, David's pioneering work to apply image processing to femoral angiograms led to the development of the first computerized procedures for quantitative angiographic measurements of atherosclerotic lesions in 1974. This initial work led to a 25-year collaboration and friendship with Robert. Autopsy calibration studies, performed between 1974 and 1977 with Dr. Donald W. Crawford and other colleagues, demonstrated that there was a high correlation between arterial wall cholesterol content in femoral arteries and angiographic representation of atherosclerosis as evaluated by computer processing. In a clinical pilot study of femoral angiography in hyperlipoproteinemic patients completed in 1977, David and coworkers demonstrated angiographic evidence of regression by computer image processing and by visual inspection. This report received attention, but also skepticism, and atherosclerosis reversibility, especially coronary, was still doubted.

The computer procedure was extended to coronary angiograms in 1977, the same year that David, Dr. Miguel E. Sanmarco, and colleagues modified the angiographic panel reading procedure developed for the NHLBI Type II Coronary Intervention Study. David's goal was to use it as a safety surveillance procedure in a pilot study of coronary angiography which they were conducting. They found that use of individualized diagrams for each subject and the conduct of reading sessions under conditions which reduce reader fatigue led to improved precision. He used this refined panel reading procedure for the Cholesterol Lowering Atherosclerosis Study (CLAS) and later for his second coronary angiographic trial, the Monitored Atherosclerosis Regression Study (MARS).

David and coworkers completed pilot studies leading to the first published sample size projections for angiographic trials in 1981. In 1987, the CLAS study conclusively demonstrated that coronary atherosclerosis regression could be effected with drug therapy. These results were later confirmed by quantitative computerized analysis of the angiograms. Based on this landmark work by David, Dr. Linda C. Hemphill, Dr. Stanley P. Azen, Ms. Ruth Johnson, and the CLAS Investigators, a second generation of imaging trials have helped to change the consensus, and it is now generally believed that stabilization and reversal of human atherosclerosis is possible. It was with completion of the MARS trial by David and MARS Investigators — including many of whom participated in CLAS, as well as Dr. Dieter M. Kramsch, Dr. Wendy J. Mack, Dr. Petar Alaupovic, and myself — that he began to formulate new concepts about lesion progression and regression. It is this work we carry forward today.

David's most recent interest was in computerized measurement of non-invasive B-mode ultrasound detected atherosclerosis to be used for diagnosis and treatment of atherosclerosis at a very early stage of disease. He had used ultrasound scanning techniques in his clinical trials since 1982. These studies included both atherosclerosis evaluation and vascular physiology in human and animal models and were accompanied by development of new methods. Most recently, David had collaborated with JPL to develop a new, fully automated computerized edge detection method of ultrasound image analysis for measurement of carotid arterial wall intima-media thickness (IMT). It is similar to image filtering techniques used in angiographic image processing and has improved precision and accuracy of IMT measurements several-fold greater than currently available manual methods. Utilizing this new methodology for the first time in controlled clinical trials (CLAS and MARS), David and colleagues demonstrated that carotid IMT could be reduced with lipid-lowering therapy and that carotid IMT correlates with angiographic evidence of coronary and carotid atherosclerosis measured by fully automated computerized edge detection methods.

David received his medical degree from the University of Cincinnati in 1947. He was a research associate from 1952 to 1954 at the Rockefeller Institute for Medical Research and studied fat and cholesterol metabolism with Dr. Edward H. Ahrens, Jr. It was here where David's interest in the field of atherosclerosis and lipid metabolism was sparked. He joined the faculty of the University of Southern California in 1957 and

served as the Chief of Cardiology from 1963 to 1980. In 1980, he became Program Director of Atherosclerosis Research, and, in 1987, he became Director of the newly formed Atherosclerosis Research Institute.

David's enthusiasm and dedication to medicine and science is personified by those who he has trained as well as by his participation in professional societies and journal editorial boards, including *Atherosclerosis*. David's many contributions to research are highly regarded and recognized by his peers. He was the recipient of many prestigious awards including a Commonwealth Fellowship, an Honorary Doctorate from the University of Uppsala, the Daniel Drake Medal for achievement in medicine and science from his alma mater, University of Cincinnati College of Medicine; most recently he presented the George Lyman Duff Memorial Lecture at the American Heart Association Scientific Session in November of 1992.

David's research accomplishments have had profound implications for us as a society as well as for us as healers and researchers. Additionally, those of us who had the opportunity to study under and work closely with David, like myself, will always be grateful to him for his teaching, support, inspiration, insight, and most of all, his friendship.

David died Sunday, 9 May 1993 from cancer. Anne Blankenhorn, David's wife for 45 years, and Jo Darnall, his administrative assistant for more than 30 years, deserve our appreciation for their continual dedication and support of David, which allowed him to dedicate his life to his research pursuits. David is also survived by four children, David, Mary, Susan and John, and four grandchildren, David, Laurel, Michael and Keith.

It is with great sadness and personal loss that I submit this remembrance for the many students, colleagues, and friends of this remarkable man who has, and will touch so many lives.

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