D. Mark Hegsted

1914–2009

BIOGRAPHICAL *Memoirs*

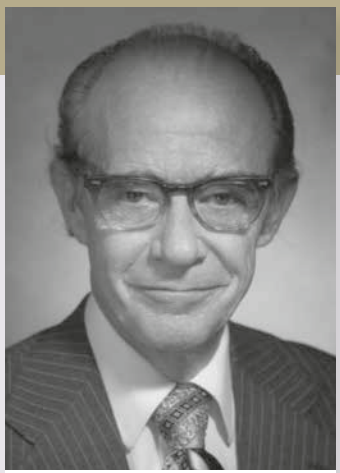
A Biographical Memoir by
Nevin S. Scrimshaw

NATIONAL ACADEMY OF SCIENCES

DAVID MARK **HEGSTED**

March 25, 1914–June 16, 2009

Elected to the NAS, 1973



By Nevin S. Scrimshaw

David Mark Hegsted was one of the most productive and influential nutrition scientists of his time. He was notable for his critical and questioning approach to nutrition issues and spoke out strongly against concepts, whether new or established, that he believed were not supported by sufficient evidence. He also made numerous positive contributions to various aspects of nutrition that have stood the test of time. Never using his first name, he was known to all as "Mark."

A career spent mostly at Harvard

Mark was born on a small farm near Rexburg, Idaho, on March 25, 1914, and he died on June 16, 2009, in Wellesley, Massachusetts, a suburb of Boston. In an unpublished autobiography he stated that he "was not involved in the operation of the farm because it was managed by Japanese tenants, and my father served as county clerk and auditor." But "I suppose that my interests in biology were encouraged by life on the farm. In addition to the usual few cows, [there were] a team of horses, sheep, and hogs [and] whatever else my brother and I could collect, including pigeons, pheasants, wild ducks, badgers, and chipmunks."

Mark was a good student and received a Smith-Hughes Agricultural Scholarship to the University of Idaho. "It would have been impossible to get to a university otherwise," he recalled, "since my father died in 1934, leaving my mother with little in the middle of the Depression and five little kids to raise." He graduated from the university in 1936 with a bachelor's degree in agricultural chemistry.

Mark then accepted a research fellowship at the University of Wisconsin, as the faculty of Wisconsin's Department of Nutrition at that time was, he later wrote, a "Who's Who in nutrition." The department was "a wonderful place to be in those days," he said, as "the nutrition field was breaking wide open during the late 1930s. We expected to hear some

Mark stated in his unpublished autobiography that "Harvard's Department of Nutrition was a beehive of experimental, clinical, and community-based scientific activity in he 1960s. ..."

major development at each annual meeting of FASEB [Federation of American Societies for Experimental Biology]. None of us had any money, so we worked from about seven in the morning to 11 at night and were expected to. There were 30 to 40 graduate students and someone was working on practically every current topic in nutrition. We learned more from bull sessions than in all our classes."

His first research assignment involved the nutritional value of alfalfa silage for dairy cattle, but after two years Mark concluded there was little new to be learned on this topic. He then became part of an attempt to identify essential but previously undiscovered nutrients, with his own work being to study growth factors for the chick.
For this research he was directly responsible to the department head, Conrad Elvehjem. The topic helped him earn an M.S. degree in 1938 and a Ph.D. in 1940. However, at that time there were few positions available in his field, so he stayed on for an additional year of research.

Mark then accepted a job as a research chemist at Abbott Laboratories in North Chicago and married his childhood sweetheart, Maxine Scow. After a year he was recruited by Fredrick Stare, the designated head of a new Department of Nutrition in the Harvard School of Public Health. Stare also recruited four of Mark's fellow alumni of the University of Wisconsin's nutrition program.

Mark spent the rest of his career researching and teaching at the Harvard School of Public Health, with the exception of the years 1978 to 1982, when he was on leave in Washington, D.C., to administer a new program in human nutrition at the U.S. Department of Agriculture. Mark came to Harvard in 1943 and became a full professor in 1962. From 1982 to 1986 he served concurrently as associate director for research at the Harvard Medical School's New England Regional Primate Research Center. He conducted research in that center for many more years both before and after that service.

Mark stated in his unpublished autobiography that "Harvard's Department of Nutrition was a beehive of experimental, clinical, and community-based scientific activity in the 1960s. It ranged from *in vitro* and animal studies to the effects of artificial blood and the nutritional requirements of cats." He noted in particular that "The basic science researchers collaborated happily with cardiologist Bernard Lown, M.D., (later a winner

of the Nobel Peace Prize) and his medical fellows who were treating patients with heart disease. …On the two floors above Lown's offices, the other professors' offices and laboratories lined the hall, followed by a few small rooms filled with graduate student desks and the spacious, luxurious rooms housing the nonhuman primate colony, reminding the graduate students of their place in the natural order of things."

One of Mark's first research projects at Harvard was a study, supported by the American Meat Institute, of animals' protein requirements. He disappointed the sponsor by finding that these requirements were lower than previously assumed. His early work led to the conclusion that the whole literature on animal-protein requirements was "a statistical fluke inherent in the calculation of balance." Thus began, however, his lifelong interest in studies of protein nutrition.

Influential in research and policy

Mark supervised a large and productive research laboratory and soon became widely recognized for his investigations of some of the most pressing nutrition problems of his time. Moreover, his work on nutrition policy influenced overall health policy and helped to integrate the two.

D. Mark Hegsted, mid-career.

Mark's intellectual rigor and independence were reflected in his studies of dietary requirements for protein, calcium, and iron. This work contributed to the reassessment and updating of recommendations concerning intakes of these nutrients and of several others.

His research included not only determining the nutrient requirements of nonhuman primates but also investigating certain human nutritional diseases, such as protein-energy malnutrition, for which the animals were models. He collaborated with other members of the department who were conducting obesity-prevention studies in a nearby community and also conducting a large intervention study in developing countries on amino-acid supplementation of various staple cereal grains.

In the early 1950s Mark received an invitation to develop a laboratory, in the Institute of Nutrition in Lima, Peru, whose primary aim was to develop and apply analytical methods for food analysis and to conduct dietary surveys. This effort eventually resulted in a published food-composition table used in the country's dietary surveys.

Another research issue to which he made an important contribution was the relationship between milk and calcium metabolism. In the United States, milk was promoted as an important source of calcium. But if milk was so important, then people who consumed little milk could be expected to be calcium-deficient if their diets contained no other significant source of calcium. Mark obtained permission to study calcium requirements of prisoners in Peru's National Penitentiary, and he hired a dietitian recently trained in that country and another trained in the United States. The director of the Institute of Nutrition selected 10 volunteers, and a small test kitchen was set up "in the bowels of the prison."

The basic design of the experiment was to use the foods in the prison diet, eliminate what little milk and high-calcium foods the prisoners were eating, and determine calcium balance on this adjusted diet as well as on the same diet with graded amounts of milk added. An advantage for the prisoners was that the food was much better prepared than what they usually received.

The resulting data indicated that the average calcium requirement for the subjects was about 300 mg a day, compared with the nearly 700 mg per day suggested by calcium balance studies in the United States. This finding explained why people all over the world developed healthy bones on low intakes of calcium, though it was frustrating to many nutritionists in the developed countries who believed higher intakes were essential.

Studying a wide range of nutrients

One of Mark's studies with rats indicated that energy deficiency was corrected more efficiently on a high-fat diet than when energy was provided in the form of carbohydrate or protein. Even when the total energy intake from fat was inadequate to allow normal growth, the test animals were fatter than those fed comparable energy from carbohydrate or protein. In other words, Mark said, "Fat makes you fat more readily."

Another of his research activities concerned fluoride, which had been shown to provide protection against dental caries. He obtained X-rays of all available subjects over the age of 45 in the state of North Dakota and confirmed that high fluoride intakes protected

against osteoporosis and fractures. Mark was unable to get funding to continue these studies, but he maintained that the levels of fluoride commonly used to fluoridate water supplies for preventing dental caries probably have little or no effect on bone density or strength.

A serious problem in many developing countries was iron deficiency, but an exception was a population of South African natives who suffered from excessive iron intakes. Mark and his colleagues demonstrated that the local beer was very high in iron because it was fermented in large iron pots. The absorption of excess iron in the diet is normally blocked at the intestinal wall and iron overload is thus prevented. However, the work in South Africa showed that this mechanism could be overwhelmed under some conditions and also that it could be protected by the addition of phosphates to the diet.

This work established the respective effects of saturated, polyunsaturated, and monounsaturated fatty acids on blood cholesterol. It was evident that saturated fatty acids elevated blood cholesterol, that polyunsaturated fatty acids actively lowered it, and that monounsaturated fatty acids had no significant effect.

Mark was perhaps best known for his investigations of the relationship between dietary fats and blood cholesterol. One set of experiments was conducted on nearly two-dozen men in a prison in Danvers, Massachusetts, who were studied for four-week periods on diets with the same caloric intake from various combinations of fats. The results obtained with 36 fats showed marked differences in their effects on blood-cholesterol levels.

This work established the respective effects of saturated, polyunsaturated, and monounsaturated fatty acids on blood cholesterol. It was evident that saturated fatty acids elevated blood cholesterol, that polyunsaturated fatty acids actively lowered it, and that monounsaturated fatty acids had no significant effect. The results of these studies were closely similar to those of Ancel Keys and his group at the University of Minnesota, and the two groups developed similar equations for calculating the effects of various fats on levels of blood cholesterol (though Mark's equation is the one most commonly used today). These findings soon led the Food and Nutrition Board of the National Research Council and the American Heart Association to update their recommendations for dietary fat.

Mark was a key advisor to the Multiple Risk Factor Intervention Program in a large cohort of middle-aged men throughout the United States—a study, sponsored by the

Centers for Disease Control and Prevention, that provided data on the effects of diets low in saturated fat and cholesterol on the morbidity and mortality rates of coronary heart disease. The study confirmed the benefits of a low-fat diet.

A remarkable record of service

Mark strongly emphasized that experiments that provided hard data were essential to policy recommendations and decisions. When definitive evidence was lacking, it was time to get on with the task of doing an experiment. When a colleague once complained that a particular clinical study would be too difficult, Mark replied that this was all the more reason to get started.

He was vocal on the nutrition issues of his time. Sometimes he took a view diametrically opposed to the conventional wisdom, and further study often proved him right. Other times, Mark's questioning of the strength of the evidence for a concept stimulated investigators to obtain the additional evidence needed to prove it. An example was his commentary when the author gave a seminar at Harvard in the 1950s on the "Interactions of Nutrition and Infection," based on work in Guatemala. He said that my hypothesis was plausible but that the evidence for it was insufficient. My ultimate response was a World Health Organization monograph on the topic with 900 supporting references and a great deal of additional original data, which together provided overwhelming evidence for a synergistic interaction between nutrition and infection. Similarly, Mark's questioning of the evidence that kwashiorkor in developing countries was due to protein deficiency had a comparable result worldwide.

In addition to his election to the National Academy of Sciences in 1973, Mark received many other honors and awards. They included the Osborn and Mendel Award (1965) and the Conrad A. Elvehjem Award (1978) of the American Institute of Nutrition and the Eleanor Naylor Dana Award (1980) of the U.S. Department of Agriculture for "helping to strengthen the critical analysis of nutrition research, particularly in its application to disease prevention." He was elected to the Alumni Hall of Fame of the University of Idaho (1976) and was a Fellow of the American Institute of Nutrition and of the American College of Nutrition.

Mark was also an honorary member of the Chilean Nutrition Society, the South African Nutrition Society, the Peruvian Public Health Association, and the Latin American Nutrition Society.

He served on the editorial boards of *Nutrition and Cancer* (1979-1994), the *Journal of Chronic Diseases* (1978-1982), and the *Journal of Lipid Research* (1964-1965). He edited *Nutrition Reviews* from 1968 to 1978 and was associate editor of the *American Journal of Clinical Nutrition* (1950-1952) and the *Journal of Nutrition* 1968-1978).

Mark was an author or coauthor of more than 400 scientific publications. And his professional activities included a remarkable record of public service, both foreign and domestic. Among his foreign activities was nutrition consulting to the government of Colombia and to Peru's Institute of Inter-American Affairs. He was a long-time member of the World Health Organization's Advisory Panel on Nutrition and he served as a member of the technical advisory committees of the Institute of Nutrition of Central America and Panama and of the United Nations' Food and Agriculture Organization.

Mark's experimental work covered nearly all of the major nutrition questions of diet and health of the late 20th century.

Mark's record of national service was even more extensive. A partial list includes membership in the Nutrition Study section of the National Institutes of Health, the Council on Food and Nutrition of the American Medical Association, the Nutrition Advisory Committee of the Centers for Disease Control and Prevention, and the Advisory Board on Military Research Supplies. He was a member of the National Research Council's (NRC's) Food and Nutrition Board and served on its committees on amino acids, dietary allowances, geographic nutrition, and military personnel supplies. He was chairman of the Food and Nutrition Board from 1968 to 1972. Mark was also a member of the Panel on Nutrition and Feeding of the NRC's Space Science Board and served a term as chairman of the Nutrition Sciences Training Committee of the National Institutes of Health.

Mark's experimental work covered nearly all of the major nutrition questions of diet and health of the late 20th century. As an educator and research scientist for nearly five decades at the Harvard School of Public Health, he influenced hundreds of students and colleagues. With his death in 2009 a unique and important leader of nutrition training, research, and policy was lost to the field, and along with it his persistent demand for reliable data on which to base nutrition decisions.

At the time of Mark's death he was survived by a son, Eric, his son's wife, Ann Macaire, and their sons, Charles and William Hegsted, all of White Horse, Yukon, Canada. A granddaughter, Sarah Hespe, and a great-granddaughter, Camilla Franck, live in New York City. Mark was widowed in 1998 by the death of his wife, Maxine, after 52 years of marriage.

ACKNOWLEDGEMENTS

The author is indebted to two excellent shorter obituaries published in the *Journal of Nutrition* (140:1402-1403) by J. T. Dwyer, L. Ausman, and E. Kennedy, and in the *American Journal of Clinical Nutrition* (90:887-889) by A. H. Lichtenstein. He was also fortunate in finding an unpublished and undated autobiography of 18 single-spaced pages. All of Mark's quotations come from this source.

SELECTED BIBLIOGRAPHY

1939 With F. W. Quackenbush and W. H. Peterson. A comparison of alfalfa silages prepared by the A. I. V. and molasses methods. *J. Dairy Sci.* 22:489-500.

1940 With J. J. Oleson, C. A. Elvehjem, and E. B. Hart. The essential nature of a new growth factor and vitamin B6 for chicks. *Poult. Sci.* 19:167-176.

1941 With R. C. Mills, C. A. Elvehjem, and E. B. Hart. Choline in the nutrition of chicks. *J. Biol. Chem.* 138:459-466.

1944 The amino acid requirements of Lactobacillus arabinosus 17-5. *J. Biol. Chem.* 152:193-200.

1945 The specificity of the leucine, isoleucine, and valine requirements of Lactobacillus arabinosus 17-5. *J. Biol. Chem.* 157:741-746.

1946 With A. Williamson, J. M. McKibbin, and F. J. Stare. Protein requirements of adults. *J. Lab. Clin. Med.* 31:261-284.

1947 With J. Worcester. A study of the relation between protein efficiency and gain in weight on diets of constant protein content. *J. Nutr.* 33:685-702.

1948 The determination of minimum vitamin requirements for growth. *J. Nutr.* 35:399-409.

1949 With V. K. Haffenreffer. Calorie intakes in relation to the quantity and quality of protein in the diet. *Am. J. Physiol.* 157:141-148.

1950 With F. C. Charalampous. Effect of age and diet on development of cataracts in the diabetic rat. *Am. J. Physiol.* 161:540-544.

1952 With C. A. Finch and T. D. Kinney. The influence of diet on iron absorption. *J. Exp. Med.* 96:115-119.

1953 With J. P. Milner, D. Wilson, and P. Ginna. Studies on effect of salt intakes on changes in muscle composition induced by protein depletion in the rat. *Am. J. Physiol.* 172:19-22.

1954 With M. Trulson and F. J. Stare. The role of wheat and wheat products in human nutrition. *Physiol. Rev.* 34:221-258.

1956 Nutrition and atherosclerosis. *Proc. 8th Research Conference*, pp. 11-14. Chicago: American Meat Institute, Council on Research.

1957 Calcium requirements. *Nutr. Rev.* 15:257-258.

With A. Gotsis and F. J. Stare. The effect of various fats upon experimental hypercholesterolemia in the rat. *J. Nutr.* 63:377-391.

1959 With A. Gotsis, F. J. Stare, and J. Worcester. Interrelations between the kind and amount of dietary fat and dietary cholesterol in experimental hypercholesterolemia. *Am. J. Clin. Nutr.* 7:5-12.

1961 Some consequences of overnutrition with minerals. *Am J. Clin. Nutr.* 9:548-552

1963 Variation in requirements of nutrients—amino acids. *Fed. Proc.* 22:1424-1430.

1965 With R. B. McGandy, M. L. Myers, and F. J. Stare. Quantitative effects of dietary fat on serum cholesterol levels in man. *Am. J. Clin. Nutr.* 17:281-295.

1967 Osteoporosis and fluoride deficiency. *Postgrad Med.* 41:A49-53.

Mineral intake and bone loss. *Fed. Proc.* 26:1747-1754.

1968 Minimum protein requirements of adults. *Am. J. Clin. Nutr.* 21:352-357.

Amino acid fortification and the protein problem. *Am. J. Clin. Nutr.* 21:688-692.

1969 Bone density, aortic calcification, and fluoride. In *Proc. Western Hemisphere Nutrition Congress*, vol. II, pp. 64-69. Chicago: American Medical Association.

Published since 1877, *Biographical Memoirs* are brief biographies of deceased National Academy of Sciences members, written by those who knew them or their work. These biographies provide personal and scholarly views of America's most distinguished researchers and a biographical history of U.S. science. *Biographical Memoirs* are freely available online at www.nasonline.org/memoirs.