ANNOUNCEMENT

David Kritchevsky, Ph.D. — A Tribute

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David Kritchevsky, Ph.D., one of the most influential researchers on diet and health of the 20th century and past president of the Society for Experimental Biology and Medicine, died of multiple organ failure on November 20, 2006. He was born on January 25, 1920 in Kharkov, Russia, the only child of Jacob and Leah Kritchevsky. The family immigrated to the United States in 1923 and settled in Chicago where Dave grew up. He received B.S. and M.S. degrees from the University of Chicago in 1939 and 1942, respectively, in chemistry and organic chemistry. In Dave's typical fashion, he described his need to get a job as a homozygous genetic problem—his father was poor and his mother was poor. He was a chemist at Ninol Laboratories in Chicago from 1940–46. After earning his Ph.D. in organic chemistry from Northwestern University in 1948, Dave and his wife, Evelyn, went to Zurich, Switzerland, where he had obtained a postdoctoral fellowship with Leopold Ruzicka, Nobel laureate in chemistry, at the Federal Institute of Technology. Melvin Calvin, another Nobel laureate in chemistry, offered him a position at the Radiation Lab at the University of California, Berkeley where he worked from 1950 until 1952, when he joined Lederle Laboratories in Pearl River, New York. There he met Hilary Koprowski, who would be named Director of the Wistar Institute in 1957. Dave joined the Wistar staff that same year and held many positions of increasing seniority, including Associate Director, and was Institute Professor and Caspar Wistar Scholar at the time of his death.

In addition to his position at Wistar, Dave held many titles at the University of Pennsylvania. He was Professor of Biochemistry in the School of Veterinary Medicine, Professor of Biochemistry in Surgery in the School of Medicine, and a member of the Graduate Group in Biochemistry in the Graduate School of Arts and Sciences. His term as Chairman of the latter lasted from 1972 until 1984. Dave was called before the Dean of Medicine early in his teaching career at Penn for teaching the citric acid cycle to the tune of "Tiptoe Through the Tulips" and for using other "teaching aids" while instructing on "serious subjects" such as cardiovascular disease. Dave's response was that you can do your job and present the facts dryly, or you can present the facts and enjoy it while having students remember even more of what was taught. If someone had taught us the Krebs cycle with music, we'd probably not need to look it up today. Dave was frequently invited to scientific meetings around the world to play the piano and perform songs he had written to the music of popular tunes. These included the "Cholesterol Biosynthesis Song," sung to the tune of "Jingle Bells," and "If I Had a Big Grant" to the tune of "If I Were a Rich Man" from the musical *Fiddler on the Roof.* All the more remarkable was that he did not read music and played by ear.

David Kritchevsky, Ph.D., 1920–2006.

Generic Drug Song by David Kritchevsky
Tune: Rags to Riches
I know I'll go from rags to riches

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This compound really cuts blood fats
It just has one small drawback which is
It's toxic to the rats.
The boss is jumping with elation
There is no other of its kind
There's just one consideration
It makes the bald mice blind.
So just take the nitrogen out of the ring
Sprinkle some halogens into the thing
Put a diethylaminophenol on the wing
The stockholders are feeling gay too
For this will really, really pay
If we can only find some way to
Bypass the FDA.

Dave joined many professional societies, served on numerous committees, and was recognized as a Fellow of the American Society for Nutrition, the American Oil Chemists Society, and the American Association for the Advancement of Science. He was elected president of the American Institute of Nutrition for 1979–80 and the Society for Experimental Biology and Medicine for 1984–86. Dave served on many study sections and committees for the National Institutes of Health, on the Food and Nutrition Board of the National Academy of Sciences (1976–80), and on the Dietary Guidelines Advisory Committee (1983–85). He served on numerous editorial boards of journals and book series. Some of the more notable book series include Advances in Experimental Medicine and Biology, Advances in Lipid Research, The Bile Acids, and Monographs in Atherosclerosis. He was Western Hemisphere Editor of *Atherosclerosis* (1977–89) and was Consulting Editor at the time of his death, along with service on nine other editorial boards during 2006.

Some of the more noted awards Dave received include the St. Ambrose Medal (1968) from the City of Milan, Italy; the Borden Award (1974) from the American Institute of Nutrition; the Philadelphia Award (1977) from the American Chemical Society; the Outstanding Achievement Award (1978) from the American College of Nutrition; a Professional Achievement Award (1979) from the University of Chicago; the Robert H. Herman Memorial Award (1992) from the American Society for Clinical Nutrition; the Auenbrugger Medal (1994) from the University of Graz, Austria; the Supelco-AOCS Research Award (1996) from the American Oil Chemists Society; a Special Recognition Award (1999) from the International Soybean Symposium; an honorary D.Sc. (2001) from Purdue University; the Lifetime Achievement Award (2005) from the International Whole Grains Symposium; the Alton E. Bailey Award (2006) from the American Oil Chemists Society; and the inaugural David Kritchevsky Career Achievement Award (2006) from the American Society for Nutrition, which will be awarded annually. Dave enjoyed receiving these honors but was actually uncomfortable being in the spotlight. He was always modest and gave full credit to those who worked with him.

Dave's interest in the physiologic and pathologic roles of cholesterol began while studying its synthesis at the Radiation Lab in Berkeley. He performed the first large-scale biosynthesis of radio-labeled cholesterol by feeding ^{14}C-acetate to hens, collecting the eggs, and isolating high specific activity cholesterol from the yolks (1), which was reported in *Proceedings of the Society for Experimental Biology and Medicine*. In his typical self-deprecating manner, he said he had the idea but the chickens did all the work. This reflected his love of research—he didn't really feel like he was working when he was in the lab. The labeled cholesterol was subsequently fed to animals and humans to trace the metabolic fate and estimate its absorption, plasma half-life, and deposition in the aorta in work with Max Biggs, a physician working for John Gofman, who had developed the ultracentrifugation technique of separating serum lipoproteins.

Dave published the first observation that unsaturated fat was less atherogenic for rabbits than saturated fat in 1954 (2); this observation became the basis for subsequent research on type of fat and risk for heart disease while most of the field was still focused on total fat rather than type of fat. In 1958, Dave published *Cholesterol*, the first book on that subject, which is now considered a classic. Fittingly, the week that the state of Pennsylvania increased the number of digits from six to seven on automobile license plates, Dave got a personalized tag that read C27H46O—the chemical formula for cholesterol. Dave was interested in how triglyceride structure affects atherogenesis and produced many papers in this area. In recent years, he became a leader in the study of conjugated linoleic acid with papers on its inhibition of cancer and atherosclerosis in animal models. Dave coauthored the first book on beta-sitosterol with O. J. Pollak in 1981.

Dave realized in the early 1960s that dietary saturated fat was atherogenic for rabbits when added to a purified diet but not when incorporated into a standard alfalfa and grain-based diet. This set the stage for his publication in 1968 of the discovery of the cholesterol-lowering property of dietary fiber, when it was still known as roughage (3). He told us getting this publication accepted was the most difficult of his career, in part because it challenged the dogma that fiber was inert material. This led to his decades of ascendancy in the dietary fiber field and friendships with the other leaders in this area. In 1988, he and Denis Burkitt were featured on the cover of *Cancer Research* for their advancement of the study of dietary fiber and colon cancer. Denis was well known for his discovery of Burkitt's lymphoma, but in later years drew considerable medical and popular attention to the lack of fiber in Western diets as a cause of various illnesses. Denis visited Dave whenever he was in the United States. At their first meeting, Denis, a very proper gentleman who spent 20 years as a medical missionary in Africa, said he had read so many of Dave's papers that he asked if he

could address him by his Christian name. Dave's response was, "It's my Jewish name, but go ahead." With George Vahouny of George Washington University, Dave was a co-organizer of a series of dietary fiber meetings that became the premier gatherings for the field and were published as a series of books on fiber. Work done by one of us with Dave on bile acid-binding by dietary fiber (4, 5) expanded on the observations of Martin Eastwood and led to new areas of research in relating these findings to cholesterol-lowering and colon cancer. It also stimulated Dave's conception of the ratio of primary to secondary bile acids being a risk factor for colon cancer.

In the early 1960s, Dave perfected the use of the cholesterol-free purified diet for studies of lipid metabolism and atherosclerosis in rabbits (6). While Dave gave credit to the few who had used such diets before him, Prof. Haqvin Malmros of University Hospital, Lund, Sweden, who was the first to feed such diets to rabbits, averred that it was Dave who deserved most of the credit for the diet's utility. This diet caused endogenous hypercholesterolemia when saturated fat and the correct types of protein (casein) and fiber (cellulose) were included. Observations with these diets led to Dave's emphasis on nutrient interactions, which many nutrition researchers are only now realizing may be as important as individual nutrient differences.

Dave published more than 1,000 papers, chapters, and books during his career; his 420 research papers have been cited by other authors in excess of 10,000 times. His first paper was in 1943 on the synthesis of a new compound, diethyl acetal of 3-methylbuten-3-al-1 (7). He is listed as one of the 250 most highly cited authors in the field of agricultural sciences by the Institute for Scientific Information. Remarkably, he published 41 papers in *Proceedings of the Society for Experimental Biology and Medicine*, forerunner to *Experimental Biology and Medicine*. His first paper in *Proc Soc*, as it was usually referred to then, was in 1951 on labeling the cholesterol in chicken eggs with ^{14}C (1). His last appeared in 1991, about how caloric restriction was highly effective in inhibiting mammary cancer in obese rats that remained obese, but smaller, on the diet (8). He continued actively contributing to science, though in the last several years he no longer ran a lab. By sharing ideas with colleagues, he was coauthor on four original research papers that appeared in 2006.

Reflecting Dave's interest in free exchange of scientific ideas, he was willing to share his thoughts with anyone in the field and was not worried about being preempted. He gave advice freely to people in academics, government, and industry. He had far more ideas than any group of scientists could pursue and most were worth further exploration. He was disappointed that most large meetings had become places to present work that was already published.

Over the years, Dave was awarded many grants to support his research from the government, nonprofits, and the food and pharmaceutical industries. He was adamant that industry support would not color his opinion of whatever was being studied and is to be admired for providing an example of how an ethical approach to science can coexist with private funding. Dave was the recipient of an NIH Research Career Award that began in 1961 and was still active at his death 45 years later (9).

Dave was one of the earliest investigators to study the health benefits of soy protein; it can be argued that his work and that of Ken Carroll paved the way for the current research interest in soy lowering risk of heart disease. In addition to his well-known work on soy and atherosclerosis, he also studied it in relation to gallstones. After a 1979 paper, written with one of us, on inhibition of cholelithiasis in hamsters appeared in the *American Journal of Clinical Nutrition* (10), he got a phone call from an irate individual who had read an article in the *National Enquirer* that stated doctors had the secret to curing gallstones but were keeping it to themselves in order to keep the medical business lucrative. Dave's response to the caller, "For a hamster, you speak English very well," put an abrupt end to their conversation.

After one of us and Dave published the first study demonstrating a benefit against atherosclerosis in rabbits from consumption of red wine (11), that not only opened a wider field of scientific inquiry by others but also proved to be fodder for his wit. Since the only modalities for raising HDL-cholesterol at the time were alcohol ingestion and exercise, Dave often recommended running from bar to bar.

During Dave's service on the Food and Nutrition Board of the National Academy of Sciences, he was part of a panel that authored a short report entitled "Toward Healthful Diets" (1980), which evoked tremendous controversy among scientists, the news media, and the general public. The report found no conclusive evidence that dietary modification could reduce serum cholesterol and heart disease; it pointed out that almost all the data were circumstantial—there was an absence of long-term safety information on low-fat, low-cholesterol diets and a lack of evidence relating diet with cancer. The report concluded that "Good food that provides appropriate proportions of nutrients should not be regarded as a poison, a medicine or a talisman. It should be eaten and enjoyed." Dave firmly believed this and enjoyed small portions of chocolate and ice cream throughout his life. The panel recommended eating a variety of foods, adjusting energy intake and expenditure to avoid obesity, reducing intake of nutrient poor foods if energy requirements are low, and moderating intake of sodium. The panel was excoriated for these conclusions by many. In the last few years, Dave had intended to revisit the recommendations of this report and write a review summarizing the current state of the science, which for the most part still supports the original conclusions.

When Dave served on another National Academy of Sciences committee that wrote the first report on Diet, Nutrition, and Cancer (1982), he described the process as deliberate regarding all nutrients except when it came to fat;

he said at that point the committee became a lynch mob. When literature from the 1940s was reviewed that demonstrated reduced food intake inhibited cancer growth in rodents, most of the committee dismissed those studies because they believed fat explained the observations and because not all required nutrients had been supplied in the rodent diets used at that time. He and one of us conducted a series of studies using carefully crafted diets that reawakened interest in caloric restriction as a cancer preventive and dissociated the effect of dietary energy from fat, which is highly correlated in human diets (12). We were also the first to implicate insulin-like growth factor I as a tumor growth factor responsive to chronic caloric deprivation, to show body fat was not driving the dietary fat effect, and to determine the degree of caloric restriction needed to inhibit tumorigenesis. We also proposed that the calorie-restricted animal was closer to normal than a freely fed, sedentary control, which should be viewed as the equivalent of a morbidly obese human (13).

Dave's 10 most highly cited papers reveal his ability to make significant contributions in a variety of scientific disciplines over an extended period of time (14). Each paper was cited more than 158 times. Publication dates ranged from 1952 to 1997, with the earliest a method for detecting steroids in paper chromatography and the latest on inhibition of atherosclerosis by conjugated linoleic acid being cited in excess of 500 times. Other topics in Dave's top 10 list include *in vitro* binding of bile acids by dietary fiber, effects of soy protein on serum lipids and atherosclerosis, and the inhibition of tumors by caloric restriction. But this list is just a sample of the different contributions Dave made to science. He was well known for research on a variety of factors affecting atherosclerosis: thyroid hormone, mitochondrial oxidation, and the lysine:arginine ratio of the diet. He tested many pharmaceutical agents for inhibition of atherosclerosis and published early studies that D-thyroxine, probucol, lovastatin, and other commonly used drugs were efficacious against atherogenesis. With George Rothblat, he conducted the first studies of cholesterol metabolism in cell culture that characterized cholesterol influx and efflux. Dave was a major figure in early studies of cholesterol metabolism and atherosclerosis in nonhuman primates; this work was carried out primarily in Africa over 20 years with NIH support.

One of Dave's defining characteristics was skepticism about scientific ideas. He wanted data to back up dietary recommendations to prevent chronic disease. He quoted the late playwright, Wilson Mizner, as saying, "I respect faith, but it is doubt that gets you an education." Another of Dave's characteristics was immense energy. He said that if hyperactivity had been a recognized condition when he was a child, he probably would have been labeled that way. Fortunately for those of us in science, he channeled his energy and intellect into research, a result he credited to his mother. He was more interested in getting the facts correct than in proving a hypothesis. Dave was fond of quoting the 19th-century biologist Thomas Huxley, who said, "The tragedy of science is the slaying of a beautiful hypothesis by an ugly fact." These attitudes explain, in part, why Dave did not prefer taking a problem and exploring it in greater and greater depth, but why he was more interested in understanding the big picture of nutrition and disease prevention. This also explains his frustration in simplistic answers to complex problems—one of the many reasons the news media called Dave for sound bites on the latest nutrition research.

An annual highlight in the lipid field was the December arrival of Dave's Christmas poem. For decades, he incorporated the names of many dozens of the best known scientists into rhyming verse that ran for several typed pages. Michael Brown, Nobel laureate in physiology or medicine, said, "You really know you've arrived when you make it into Dave's Christmas poem." Despite Dave's seeming ease in putting all those names into verse, he said he had repeated trouble with only one name even with the use of a rhyming dictionary—Kritchevsky. As a result, he ended each edition by finding a name that rhymed, ranging from obscure Russian poets to former University of Iowa football coach Forest Evashevski, and providing a footnote identifying the person. The poems always ended with, "Good luck, good health from Dave Kritchevsky."

Irving Berlin said, "Life is 10 percent of what you make it and 90 percent of how you take it." We could quibble with the percentages but it captures a spirit reflected in Dave's personality. He was always optimistic. Scientific disagreements never became personal; he respected colleagues even when he disagreed with them. Throughout this article, we have referred to Dr. Kritchevsky as Dave, in part because that's what we called him. But it reflects another lesson he taught us by his actions. In the 1970s, it was quite rare for students to call their mentor by first name. It was even less common for staff such as secretaries or janitors to do that. Dave never minded when this happened; he said it didn't bother him, didn't cost anything, and made relations at work better. He treated everyone with respect and tried to put them at ease. We are confident that he is the only scientist who ever was told in preparation for meeting the Dutch royal family that the prince was addressed as "Your Royal Highness" and not as "Claus, Baby." Dave was a mentor to many scientists, not just those who worked directly with him as we were privileged to do. We were lucky enough to get his wisdom and advice in more concentrated doses than most. He acted as a mentor to us, long before that word came into fashion, and both of us owe him much gratitude for his long-term advice and friendship. Together, we published more than 100 research papers with Dave but also spent countless hours discussing science, sending each other picture postcards from our travels, and maintaining the utmost respect for an exceptional person and scientist.

Dave was an extraordinary teller of stories and jokes. We have both had the experience of telling him a joke and

months later hearing a better version, barely recognizing it until he got to the same punch line. Some of our fondest memories are of Dave trading jokes and stories with colleagues in a hotel lobby or bar after a long day of scientific meetings. There are a number of one-liners Dave coined that are repeated at scientific meetings, such as "moderation, not martyrdom," "the data were tortured until they confessed," and "*in vivo* veritas."

We are better scientists for having known him and, more importantly, better people for having had him as our friend. David Kritchevsky is survived by his wife of 58 years, Evelyn, their children, Barbara, Janice, and Stephen, and six grandchildren.

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