

NATIONAL ACADEMY OF SCIENCES

VERNON R. YOUNG
1937—2004

A Biographical Memoir by
NEVIN S. SCRIMSHAW, ARNOLD L. DEMAIN,
AND NAOMI K. FUKAGAWA

*Any opinions expressed in this memoir are those of the authors
and do not necessarily reflect the views of the
National Academy of Sciences.*

Biographical Memoir

COPYRIGHT 2008
NATIONAL ACADEMY OF SCIENCES
WASHINGTON, D.C.



Vern R. Young Jr.

VERNON ROBERT YOUNG

November 15, 1937–March 30, 2004

BY NEVIN S. SCRIMSHAW, ARNOLD L. DEMAIN,
AND NAOMI K. FUKAGAWA

VERNON ROBERT YOUNG WAS THE world's leading expert on human protein and amino acid requirements and metabolism at the time of his death of complications of renal cancer at the age of 66. He was a key investigator in the series of studies that revealed the inadequacy of the 1973 Food and Agriculture Organization/World Health Organization Recommended Allowance for human protein requirements and the research that corrected this serious error. Later his innovative use of stable isotopes showed that the estimated essential amino acid requirement levels universally accepted since the 1940s were much too low. These erroneous values had been endorsed by a series of FAO/WHO committees, including one that met as late as 1985.

With confirmation in Indian subjects from his collaborator Anura Kurpad in Bangalore, Young proposed a new "MIT" pattern that was adopted, with minor changes, by the 2003 FAO/WHO/UNU Expert Consultation. It recognized that adult essential amino acid requirement estimates per gram of protein needed to be increased by a factor of 2 to 3, depending on the specific amino acid. He reported this work and a great deal of other groundbreaking research in over 600 full-length articles and book chapters, approximately

one per month for 42 years. His contributions to human nutritional science were exceptional.

Vernon Young was born in Rhyl, North Wales, in 1937 but lived in Cardiff from an early age. His interest in agriculture developed from visits to an uncle's farm in Nottinghamshire. He obtained his B.Sc. from the University of Reading in 1959 and a postgraduate diploma from Cambridge University in 1960. He then moved to the University of California, Davis, and obtained his Ph.D. in 1965 with a thesis on calcium and phosphorus homeostasis in sheep. He came to the Department of Nutrition and Food Science of the Massachusetts Institute of Technology as a postdoctoral fellow in the same year and was promoted to assistant professor the following year. He rose rapidly through the ranks and became a full professor in 1977.

Soon after arriving at MIT he met his future wife, Janice Harrington, of Wellesley, Massachusetts, a suburb of Boston, who was then executive secretary of the department. They were married in 1966 and settled permanently in Wellesley. Vernon Young's life was dedicated to his research at MIT and with many collaborators in other institutions and countries, but he was also devoted to his wife, his four sons—Christopher, Andrew, Michael, and Richard—and his daughter, Patricia. They were a happy and devoted family. Vernon did much of his writing at his home in Wellesley when he was not in his MIT office or traveling. A twin sister, Sylvia Young Price, lives in Council Bluffs, Iowa.

ADDITIONAL ACADEMIC APPOINTMENTS

In addition to his professorship at MIT Young served as associate program director of the MIT Clinical Research Center, 1985-1987, and director of research for the Shriners Burns Institute, 1987-1990. Additional appointments in Boston at the time of his death included lecturer in sur-

gery, Harvard University, and senior visiting scientist, U.S. Department of Agriculture Human Center on Aging, Tufts University, 1988-2004.

Young also held appointments as visiting professor at the University of California, Los Angeles, 1983; University of Southern California Medical School, March 1984; University of Illinois, Urbana, March 1986; University of Michigan, Ann Arbor, March 1986; University of Iowa, Iowa City, May 1986; University of Florida, Gainesville, December 1987; Dartmouth Medical School, Hanover, January 1988; Case Western Reserve School of Medicine, Cleveland, September 1988. He served as visiting research fellow, Merton College, Oxford, U.K., April-June 1994; visiting scholar, University of Texas Health Sciences Center at San Antonio 1996; and visiting professor, the Universities of Wageningen and Maastrich, The Netherlands, 2000; and visiting research fellow, University of Ulster, Coleraine, Northern Ireland, 2002.

NATIONAL AND INTERNATIONAL LECTURESHIPS AND COMMITTEES

Young's named lectureships included the Vickers Lecture of the British Neonatal Health Science Center, San Antonio, 1986; the American Society for Nutritional Sciences McCollum Award Lecture, 1987; Burns Lecture, Royal College of Physicians and Surgeons, Scotland, 1990; Brackenridge Lecture, University of Texas Health Science Center, San Antonio, 1996; Bruce and Virginia Street Lecture in Preventive Nutrition, University of North Texas, Fort Worth, 1996; Ninth Annual Malcolm Trout Lecture, Michigan State University, 1997; Rudolf Schonheimer Centenary Lecture, Nutrition Society of U.K., 1998; first David Murdock Lecture in Nutrition, Mayo Clinic, Rochester, 1998; Jonathan Roads Lecture, American Society for Parenteral and Enteral Nutrition, 1999; Hans Fischer Lecture, Rutgers University, New Brunswick, 1999; and W. O. Atwater Lecture and Award, USDA Agricultural

Research Service, 2001. Editorial boards on which he served included the *American Journal of Clinical Nutrition*, 1976-1978; *Nutrition Research*, 1980-1984; *Advances in Nutrition Research*, 1976-2004; *Pediatric Gastroenterology and Nutrition*, 1981-1985; *Age*, 1977-1982; *Growth*, 1986-1990; *Journal of the Nutrition Society of Nigeria*, 1990-1994; and *Nutrition Today*, 1997-2004.

The preceding description of Young's positions, honors, named lectures, and editorial boards does not capture the extent of his influence in Boston, nationally and throughout the world. Within MIT he served as a member of the important Committee on the Use of Humans as Experimental Subjects from 1978 to 1984 and the Committee on Radiation Safety. Within the Department of Nutrition and Food Science he served as an undergraduate and graduate adviser and on the Curriculum Committee, the Nutrition and Metabolism Doctoral Committee, Doctoral Examination Committee, and Executive Committee. Nationally he served as a member of the Food and Nutrition Board of the Institute of Medicine, 1992-1998. He chaired the Nutrition Implementation Committee, National Cancer Institute Division of Cancer Prevention from 1998 until 2004.

Among the many national committees to which Young contributed were the Food and Drug Administration Board of Inquiry on aspartame, 1978; the National Institutes of Health Nutrition Study Section, 1981-1985, and numerous ad hoc study sections; the NIH Consensus Panel on Health Risks, the Children's Nutrition Research Center at Baylor University, Houston, 1985; National Academy of Sciences Committee on Diet and Health, 1986-1987; USDA Council of Scientific Advisors, Houston; Scientific Advisory Committee, Pennington Medical Center, Baton Rouge, 1991-1998; National Dairy Council, 1994-1998; and the Basic Science Implementation Subcommittee, National Cancer Institute Division of Cancer Prevention, 1998-2004. Internationally he

was a member of the Committee on Human Protein-Energy Requirements, International Union of Nutrition Sciences, 1991-1997; FAO/WHO/UNU Expert Group on Protein and Energy Requirements, 1981; Visiting Group of the Rowett Research Institute, Aberdeen, 1992; Scientific Advisory Committee, Deutsches Institut für Ernährungsforschung, 1995-1998. In honor of his nutrition expertise he was elected in 2001 to the Board of the Nestle Company, Vevey, Switzerland.

INITIAL RESEARCH AT MIT

Brilliance and exceptional scientific intuition characterized his research career from the beginning. Young published several papers on the effects of dietary protein, infection, and hormones on the translation step of protein synthesis by muscle ribosomes with special attention to initiation and elongation. This led to work on *in vivo* protein degradation, specifically targeted to certain muscle proteins containing methylated amino acids such as 3-methylhistidine occurring in actin and various types of heavy chain myosin. Stimulated by studies of Hamish Munro in rats, Young was the first to demonstrate in humans that urinary 3-methyl histidine is a direct indicator of muscle proteolysis and hence muscle mass. The discovery was of such great interest that the paper describing this finding became a Citation Classic in 1992. He also prepared and examined ribosomal fractions from skeletal muscle with respect to their capacity for protein synthesis in response to insulin and other factors.

HUMAN OBLIGATORY NITROGEN LOSSES AND PROTEIN REQUIREMENTS

Together with Nevin Scrimshaw and their many graduate students, Young guided a series of studies that measured the variations in adult obligatory nitrogen losses as the basis for predicting adult protein requirements. This work, complemented by that of Doris Calloway at the University of Cali-

fornia, Berkeley, became the basis for the 1973 FAO/WHO report. Unfortunately this committee failed to take into account the lower utilization of protein at requirement levels and arrived at an erroneously low recommendation that was later corrected by Young and Scrimshaw as described below.

PROTEIN QUALITY STUDIES

An extended series of studies explored nitrogen absorption and retention in human subjects and yielded improved procedures for the use of nitrogen balance in the assessment of the quality of dietary proteins. The initial work on cereal proteins demonstrated the progressively higher percent retention of absorbed nitrogen as protein intake decreased below requirement levels. This led to extensive studies of the protein value of soy protein isolate. These demonstrated that this soy protein as a sole source for human feeding had a protein utilization comparable to that of animal protein.

Based on the internationally accepted essential amino acid pattern at the time, it should have been possible to "dilute" good quality protein with inexpensive nonessential amino acids without lowering its protein quality. Nitrogen balance studies with milk protein fed to adult subjects failed to confirm this expectation, suggesting that the accepted reference pattern was too low in the proportion of essential amino per gram of nitrogen. There was then no methodology available to explore this further.

PROTEIN REQUIREMENT STUDIES

Young and Scrimshaw's graduate student Cutberto Garza showed in three successive nitrogen balance studies with MIT students that the level of protein intake recommended by the 1973 FAO/WHO Expert Group resulted in loss of lean body mass, lower serum albumin, and in some subjects,

signs of liver pathology. They developed a unique 15-day day multilevel N balance approach to determining protein quality and applied it in a United Nations University-sponsored uniform field trial in 15 countries. On the basis of the data obtained they proposed a recommended protein intake one-third higher than the 1973 international Recommended Protein Allowance. This level proved adequate when fed to subjects for 50-90 days in six countries. With minor adjustment the value that they proposed was adopted by the 1985 FAO/WHO/UNU Joint Expert Consultation on Protein-Energy Requirements with a profound effect on estimates of protein deficiency in developing countries and on nutrition, agriculture, and health policy.

REVISION OF HUMAN AMINO ACID REQUIREMENTS

Young's most recent and most important work was to pioneer the use of stable isotopes in studies of human nutrition, leading to the development of methods to build on and replace nitrogen balance as the approach for the assessment of protein and amino acid requirements. In a very productive collaboration with Dennis Bier at Washington University, St. Louis, Young showed that whole-body amino acid flux, protein synthesis, breakdown, and amino acid oxidation in humans respond to the content of meals and that these responses are modulated by the protein, amino acid, and energy components of the diet. At the beginning of these studies his graduate students went to Bier's laboratory in St. Louis to analyze their samples, using a mass spectrometer available there. His output was increased when Young established mass spectrometry facilities, including isotope ratio and gas chromatography mass spectrometry and later liquid chromatography mass spectrometry at MIT. The pace of the work accelerated because students used both facilities.

The qualitative importance of both protein synthesis and breakdown in premature infants was first demonstrated in Young's studies using ^{15}N as a tracer. Using ^{15}N -labeled amino acids in adults, he reported a redistribution in the pattern of whole-body protein metabolism with advancing age.

The various ^{15}N tracer studies of amino acid (N) and protein metabolism changed our fundamental understanding of mammalian protein and amino acid nutriture. This was further extended to demonstrate enhanced rates of protein synthesis and breakdown in children suffering from burns that provided a metabolic explanation for the greatly increased protein requirement of a burned patient.

Using different stable isotope probes, Young and his colleagues elucidated the age- and disease-related changes in amino acid, glucose, and fatty acid metabolism. Using a novel approach, Young developed a stable isotope method using ^{15}N glycine tracers to explore changes in albumin synthesis with advancing age. His findings indicated that albumin synthesis is regulated by amino acid intake at a lower set-point in the elderly than in young adults.

Together with one of his last students, Naomi Fukagawa, Young demonstrated for the first time in humans using stable isotope tracers and the euglycemic insulin clamp technique that insulin's primary role was to inhibit proteolysis and that stimulation of protein synthesis necessitated amino acid availability. He also played a major role with M. Janghorbani in developing and applying new stable isotope techniques for studying the metabolism of trace minerals such as zinc, copper, iron, selenium, and calcium in human subjects. This involved their analyses in blood, urine, and feces during metabolic studies. He was the first to compare intrinsic and extrinsic probes for measurement of dietary zinc and selenium bioavailability in humans.

Using the facilities of the MIT Clinical Research Center, Young introduced stable isotope studies of amino acid oxidation as an index of amino acid balance. His work on ^{13}C -labeled amino acids, especially leucine, valine, lysine, and threonine, replaced nitrogen balance techniques and led to a new approach for estimating amino acid requirements. This involved infusing a ^{13}C -labeled test amino acid over several hours after intakes of the amino acid were varied over a wide range to determine the intake level associated with increased oxidation, measured as $^{13}\text{CO}_2$ content in expired breath.

With his students Young successfully quantified the requirements for leucine, lysine, threonine, methionine, and cystine using this approach. Later he very ingeniously reversed the procedure by measuring the level of intake of a specific amino acid at which oxidation of another labeled essential amino acid (e.g., leucine) was reduced. Using this approach over a 24-hour period during the postabsorptive or fed states, he was able to determine the requirement of amino acids and the levels of intake that would achieve amino acid balance. He is credited with developing the 24-hour indicator amino acid balance approach widely used today to determine amino acid requirements in health and disease.

Using stable isotope approaches, Young also explored the metabolism of dispensable amino acids, such as glycine, and developed a new approach for quantifying the whole-body synthesis rate of dispensable amino acids, particularly alanine, glycine, proline, and arginine. This was the first time this approach had been used, and it enabled him to demonstrate the sensitivity of whole-body alanine synthesis to changes in the availability of carbon, hydrogen, and nitrogen moieties. Young deftly adopted compartmental and noncompartmental models to further expand his use of stable isotope probes and later included multiple tracers to permit the dissection of complex metabolic processes *in vivo* in humans.

Young's last completed work was a series of elegant multitracer studies using both isotopomers and isotopologues of arginine and related urea cycle intermediates (arginine, ornithine, and citrulline) together with a labeled essential amino acid, such as leucine, to explore the nutritional significance of arginine and its role in metabolism and nitric oxide synthesis. He suggested that arginine homeostasis is achieved by a balance between intake and breakdown with *de novo* arginine synthesis playing only a minor role. Young was also at the forefront of using short-lived isotopes (^{11}C) and PET scanning in experimental nutrition studies.

True to his visionary spirit Young embraced the advances made in molecular biology and saw opportunity in the postgenome era to explore the dynamics of nutrient-gene interactions. However, he always reminded one of the importance of probing at a higher level of biological complexity and that integrative science or systems biology would be key to advancing nutritional science together with modern technology in the 21st century.

FINAL COMMENTS

Vernon Young was recognized as a major force in human nutrition. He was elected to the National Academy of Sciences in 1990 and the Institute of Medicine in 1993. Other awards and honors include the 1973 Mead Johnson Award and the 1983 Borden Award from the American Institute of Nutrition; the 1987 McCollum Award for Distinguished Achievement in Nutrition Research from the American Society for Clinical Nutrition; the 1997 Rank Prize in Nutrition, U.K.; the 1991 Gopalan Oration and Gold Medal, Nutrition Society of India; the 1995 the Bristol-Myers Squibb Award for Distinguished Achievement, U.S.; the 1996 Roger Williams Award in Preventive Nutrition; the 1997 Danone International Prize for Nutrition (France); the W. O. Atwater Award

(U.S.); the 1998 International Award for Modern Nutrition, Switzerland; the 1999 Jonathan E. Rhoads Award, American Society for Parenteral and Enteral Nutrition; the 2001 W. O. Atwater Lecture and Award, USDA Agricultural Research Service; and the 2003 Conrad Elvehjem Award, American Society for Nutritional Sciences. In 1997 he received a doctor of medicine *honoris causa* from Uppsala University, Sweden, and the 1999 Award of Excellence from the Alumni Association of the University of California, Davis.

Since its founding in 1982, Young was a board member and officer of the International Nutrition Foundation, which has extensive international fellowship programs and publishes the *Food and Nutrition Bulletin* on behalf of the United Nations University. He served as vice president from 1989 to 1991 and president from 1991 to 1992 of the American Institute of Nutrition. During 1996-1998 he served as the first chairman of the Food and Nutrition Board Committee, responsible for the new and greatly expanded Recommended Dietary Allowances (RDAs) and skillfully guided the group to a consensus. He served as a director of the American Board of Nutrition, 1979-1990.

While words can describe his scientific achievements and his national and international reputation, they cannot adequately convey his ebullient Welsh personality, sly humor, and unusual charisma. Young would tease outrageously anyone at any level of society, and they loved it. He was widely and greatly admired as a teacher, researcher, colleague, and exceptional human being. He was brilliant, completely dedicated, and exceptionally considerate of others at all professional and social levels. He was an outstanding mentor whose infectious curiosity stimulated inquiry and new discoveries. There are few persons who have been so universally liked throughout the world or who have contributed as much to nutritional science. In one of his last lectures

he quoted Arthur M. Sackler, who established the *Medical Tribune* newspaper: “Art is a passion pursued with discipline and science is a discipline pursued with passion. Passion is the engine that drives creativity.” This latter well describes Vernon.

SELECTED BIBLIOGRAPHY

1966

With G. P. Lofgreen and J. R. Luick. The effects of phosphorus depletion, and of calcium and phosphorus intake, on the endogenous excretion of these elements by sheep. *Br. J. Nutr.* 20:795-805.

1968

With S. C. Chen and P. M. Newberne. Effect of infection on skeletal muscle ribosomes in rats fed adequate or low protein. *J. Nutr.* 94:361-368.

1969

With P. C. Huang. In vivo uptake of [^{14}C]leucine by skeletal muscle ribosomes after injury in rats fed two levels of protein. *Br. J. Nutr.* 23:271-280.

1971

With S. C. Stothers and G. Vilaire. Synthesis and degradation of mixed proteins, and composition changes in skeletal muscle of malnourished and refed rats. *J. Nutr.* 101:1379-1390.

With M. A. Hussein, E. Murray, and N. S. Scrimshaw. Plasma tryptophan response curve and its relation to tryptophan requirements in young adult men. *J. Nutr.* 101:45-59.

1972

With K. Tontisirin, I. Ozalp, F. Lakshmanan, and N. S. Scrimshaw. Plasma amino acid response curve and amino acid requirements in young men: Valine and lysine. *J. Nutr.* 102:1159-1169.

1973

With Y. S. Taylor, W. M. Rand, and N. S. Scrimshaw. Protein requirements of man: Efficiency of egg protein utilization at maintenance and submaintenance levels in young men. *J. Nutr.* 103:1164-1174.

1976

An overview of protein synthesis, degradation and the regulation of protein content in skeletal muscle. *Environ. Qual. Saf. Suppl.*, pp. 20-42.

1978

Nutrition and aging. *Adv. Exp. Med. Biol.* 97:85-110.

1981

Dynamics of human whole body amino acid metabolism: Use of stable isotope probes and relevance to nutritional requirements. *J. Nutr. Sci. Vitaminol.* (Tokyo) 27:395-413.

1984

With M. Puig, E. Queiroz, N. S. Scrimshaw, and W. M. Rand. Evaluation of the protein quality of an isolated soy protein in young men: Relative nitrogen requirements and effect of methionine supplementation. *Am. J. Clin. Nutr.* 39:16-24.

1986

Nutritional balance studies: Indicators of human requirements or of adaptive mechanisms? *J. Nutr.* 116:700-703.

With N. Fukagawa, D. M. Bier, and D. Matthews. Some aspects of in vivo human protein and amino acid metabolism, with particular reference to nutritional modulation. *Verh. Dtsch. Ges. Inn. Med.* 92:640-65.

1987

Kinetics of human amino acid metabolism: Nutritional implications and some lessons, 1987 McCollum Award Lecture. *Am. J. Clin. Nutr.* 46:709-725.

With D. M. Bier. A kinetic approach to the determination of human amino acid requirements. *Nutr. Rev.* 45:289-298.

1989

With D. M. Bier and P. L. Pellett. A theoretical basis for increasing current estimates of the amino acid requirements in adult man, with experimental support. *Am. J. Clin. Nutr.* 50:80-92.

1990

With J. S. Marchini. Mechanisms and nutritional significance of metabolic responses to altered intakes of protein and amino acids, with reference to nutritional adaptation in humans. *Am. J. Clin. Nutr.* 51:270-289.

1991

With D. A. Wagner, R. Burini, and K. J. Storch. Methionine kinetics and balance at the 1985 FAO/WHO/UNU intake requirement in adult men studied with L-[2H3-methyl-1-13C]methionine as a tracer. *Am. J. Clin. Nutr.* 54:377-385.

With Y. M. Yu and N. K. Fukagawa. Protein and energy interactions throughout life. Metabolic basis and nutritional implications. *Acta Paediatr. Scand.* 373(suppl.):5-24.

1992

With A. el-Khoury. Protein requirements of adults from an evolutionary perspective. *Am. J. Clin. Nutr.* 56:1070-1071.

1994

Adult amino acid requirements: The case for a major revision in current recommendations. *J. Nutr.* 124(suppl.):1517S-1523S.

1999

With A. M. Ajami. Isotopic metaprobes, nutrition, and the roads ahead, 1999 Jonathan E. Rhoads Lecture. *J. Parenter. Enter. Nutr.* 23:175-194.

2000

With S. Borgonha. Nitrogen and amino acid requirements: The Massachusetts Institute of Technology amino acid requirement pattern. *J. Nutr.* 130:1841S-1849S.

2002

Human nutrient requirements: The challenge of the post-genome era. 2001 W. O. Atwater Memorial Lecture and the 2001 ASNS President's Lecture. *J. Nutr.* 132:621-629.

2003

A vision of the nutritional sciences in the third millennium. *Forum Nutr.* 56:24-29.