



Hamish N. Munro

1915–1994

BIOGRAPHICAL

Memoirs

*A Biographical Memoir by
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and Nevin S. Scrimshaw*

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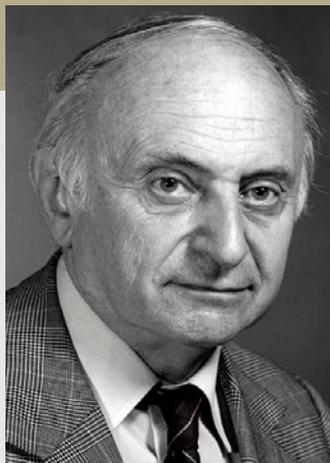
NATIONAL ACADEMY OF SCIENCES

HAMISH NISBET MUNRO

July 3, 1915–October 22, 1994

Elected to the NAS, 1974

Hamish Nisbet Munro was by far his generation's most illustrious and productive expert on mammalian protein metabolism. His four-volume series on this subject, the first two with James B. Allison as coauthor, were remarkably comprehensive and a key resource for several pioneering decades. The number and diversity of his research approaches during the period of rapid development of the field of protein metabolism were unequaled. The new scientific knowledge derived from his research has benefited the health of humankind.



Photograph courtesy of USDA

Hamish N. Munro

By Robert M. Russell
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From Village School to Glasgow University

Hamish was born on July 3, 1915, in Edinburgh, Scotland, and died in Glasgow in 1994 after a long illness. He began his education at a private day school in Edinburgh (George Watson's Boys School), but when his father was transferred by the bank for which he worked to a remote village in northern Scotland, Hamish found himself in another world. The village lacked electricity and telephones, and the main occupation of the area was farming. He was proud that his father was the only educated man in the village.

The new school in which Hamish found himself drew children from the village and a nearby gypsy encampment, as well as a number of foster children who were sent to the village from cities in southern Scotland because their parents were in prison or otherwise unable to make a home for them. Hamish recalled that his work was done on a slate with a slate pencil, and it was only when he reached the university that he bought a copybook and learned to write in a normal way. An accomplished pianist, he also had a good ear for languages. His interest in linguistic studies included Anglo-Saxon and Middle English. Hamish also became proficient in Latin, and throughout his later life he was able to give seminars in French, German, or Italian.

Hamish's village-school class initially had 25 children in it, but once they reached the age of 14, class size decreased to six. (In Scotland, schooling was compulsory up to 14 years of age.) Of these six, Hamish was the only student to ultimately obtain a university degree. At age 16 Hamish left the village school and spent the spring and summer of 1932 reading pharmacy and chemistry in Edinburgh in order to pass the university entrance examination.

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He began his advanced studies at Glasgow University, where he delved into the subject of physiology (which included biochemistry) under the direction of Edward P. Cathcart and David Cuthbertson. In 1934, when Hamish was 19 years old, he started to assist Cuthbertson, later Sir David, on a project to determine whether boiled-milk proteins were as

well digested and metabolized as raw-milk proteins. He was fortunate that Cuthbertson was one of the leading nutritionists of his time and internationally respected.

The following year Hamish began research with Cuthbertson and completed his bachelor of science degree with first-class honors in physiology (metabolism). His research project was to determine the effects of various sources and levels of energy intake on body-protein metabolism, as measured by nitrogen

balance. This work resulted in his first series of publications, in which he showed that one could pass from body-protein loss to gain simply by changing dietary energy intake.

Following completion of his B.Sc. courses he entered the medical program. During the three years needed to qualify for bachelor of medicine and bachelor of surgery degrees, he continued to pursue research on the effect of energy intake on protein metabolism.

In 1940, after training as a medical resident, Hamish was offered the position of clinical tutor of medicine at the Victoria Infirmary, Glasgow. Because World War II had started, he accumulated a series of additional responsibilities, including running a venereal-disease clinic, operating a blood-transfusion service, and directing the hospital's pathology service. At this time, Hamish also pursued an interest in vitamin C and published several papers on capillary fragility caused by a deficiency of this vitamin.

Hamish met Dr. Edith Little while doing this latter work—when she provided several cases of scurvy for him to study. They were married on April 5, 1946, a union that produced one daughter and three sons.

Also in 1946, Hamish received his first grant from the British National Research Council and set up a research unit at Glasgow University to study metabolic responses to injury. He then accepted a position as assistant professor in the Physiology Department at Glasgow University and transferred to the Biochemistry Section, where he remained for 20 years, during which time he rose to the rank of professor.

Throughout this period, Hamish continued his studies on protein metabolism and also ventured into the investigation of nucleic acids and protein metabolism. Toward the end of this time, he completed his first two volumes of *Mammalian Protein Metabolism*, coauthored with James B. Allison. Two subsequent volumes, authored by Hamish alone, appeared in 1969 and 1970. These four volumes included virtually all that was then known about protein and amino-acid metabolism and were very well written. They were an important factor in his growing national and international reputation.

In the 1950s Hamish began using isotopically labeled amino acids to study the uptake of glycemic acid in protein under various conditions. He also began to examine the synthesis of RNA and the influence of dietary conditions on the aggregation of RNA. This was the starting point for a shift in Hamish's main research interest from the whole animal to the regulation of protein metabolism at the molecular level. This was the line that he pursued when he moved to the Massachusetts Institute of Technology.

A U.S. citizen, an academy member

At the beginning of 1966 one of us (NSS) traveled to Glasgow to interview and recruit Hamish as professor of nutritional biochemistry and metabolism in MIT's new Department of Nutrition and Food Science. It was not difficult to recruit him because he was dissatisfied with his treatment in the Glasgow department and by the English medical establishment. One complaint, for example, was that only the department head had a key to the elevator.

When he came to the United States, his wife Edith continued her work in London and visited him from time to time in Cambridge, Massachusetts, where he lived alone in a modest apartment. Hamish was proud of her professional expertise and independence. He spent vacation time in London, and for a time had a houseboat there on the Thames River (and complained bitterly about the cost of its maintenance). In 1969 he bought a house in Needham, a suburb of Boston, and was joined by his wife and youngest son, who attended the local high school. Edith returned to England in 1974 and Hamish sold

the house soon afterward. When Edith died after a short illness in 1987, he was devastated and retreated further into his laboratory.

Hamish flourished in the freedom and support of the MIT environment. He was not only an outstanding researcher but also a superb teacher and mentor to the new department's graduate students and postdoctoral fellows. Throughout his career at MIT he continued to teach the basic required course in "Nutritional Biochemistry and Metabolism," which became legendary. He soon completed the last two volumes of *Mammalian Protein Metabolism* and produced a long series of seminal papers on a wide range of topics in this field.

Though proud of his British roots, Hamish applied for and received U.S. citizenship in order to be eligible for activities of the U.S. government, the National Research Council, and other nongovernmental agencies. Years later this status was critical to his appointment as director of Tufts University's Human Nutrition Research Center, sponsored by the U.S. Department of Agriculture.

Hamish's research achievements made him an obvious choice for membership in the National Academy of Sciences (NAS). He was nominated and elected in 1974. His membership led to many effective contributions to the work of the Academy. For example, he chaired an important study that examined the nutritional needs of developing countries. When his interests eventually turned to nutrition and aging, he was selected to be chairman of an NAS committee on this topic. Its report, with Hamish as senior editor, became the first source book on this subject.

Serving MIT, Tufts, and other entities

Hamish attracted high-caliber graduate students and postdoctoral fellows even though, or because, he demanded excellence and productivity. All of his research was done in collaboration with them, except for the joint work with Vernon Young and one project with Richard Wurtman. During his career, he was the principal thesis advisor of 37 Ph.D. candidates (mostly at MIT) and supervised the work of more than 40 postdoctoral fellows, many of whom are now prominent academics in universities around the world. He also interacted with hundreds of other students.

His laboratory was incredibly productive, and Hamish was author or a coauthor of more than 700 scientific publications that concentrated mainly on the regulation of intermediary metabolism. Hamish didn't require much leisure and spent most of his time in

the laboratory, though he did manage to see an occasional movie. He had no interest in competitive sports, although he was apparently quite good at golf early on. He said that he would try to “go for a round” but got too bored to finish.

In 1977 he was invited to join a task force studying the feasibility of building a national center for research in nutrition and aging on the Boston campus of Tufts University. The U.S. Department of Agriculture accepted the plans for this institute, and groundbreaking took place in 1979, the year in which he was appointed its first scientific director. During this time he maintained his laboratory at MIT and continued to supervise his graduate students and postdoctoral fellows.



Groundbreaking for the Human Nutrition Research Center. (Photograph courtesy of Digital Collections and Archives, Tufts University.)

During the initial years of directing the center (now called the Human Nutrition Research Center on Aging), Hamish assembled a group of first-rate scientists to study the proposition that nutrition may modulate the age-related loss of function of various organs and the accumulation of chronic disabilities. He felt that nutrition scientists

should know more about the needs of adults of all ages, especially the elderly. The Tufts center has become a global leader in this field, now has some 50 scientists and over 300 employees, and is without question the largest facility of its kind in the world. Hamish envisioned the center as having an important public health impact over the long run, and this goal is now a reality.

Hamish was the recipient of many awards, including the Osborne and Mendel Award (1969) and the Borden Award (1978) from the American Institute of Nutrition; the Bristol-Myers Award for distinguished achievement in nutrition (1981); the Rank Prize for work toward man’s understanding of the biochemical effects of nutritional change (1982); the Bellton Medal from the University of Glasgow (1984); and the Corson Medal from the Franklin Institute (1987). In addition he became a fellow of the Royal College of Physicians, London. As noted above, he was a member of the U.S. National

Academy of Sciences and a fellow of the Academy of Arts and Sciences. In 1988 he was inducted into the U.S. Agriculture Research Service Hall of Fame.

Hamish served as president of the American Institute of Nutrition and was a member of numerous other American and British professional nutrition societies. He was chairman of the Nutrition Study section of the National Institutes of Health and was a member the Food and Nutrition Board of the National Research Council (NRC) from 1975 to 1980. Hamish was also chairman of the NRC Committee on Biochemical Nomenclature. He served on a number of U.N. Food and Agricultural Organization/World Health Organization committees and working groups that set global nutrition policy—most notably those on energy and protein requirements in 1963, 1971, and 1981, to which he made important original contributions. At the 1971 meeting it was he who proposed the factorial method of estimating protein requirements, thereby stimulating a whole new area of investigation for obtaining the required data. He also chaired a small task force on energy nomenclature for the International Union of Nutrition Sciences.

A sampling of his research

Hamish's own scientific research dealt in large part with processes to provide the needed amino acids for the synthesis of ferritin (a cellular protein that stores and releases iron), with 50 publications and communications from his laboratory on this topic. His laboratory early on cloned mRNA for one of the two subunits of ferritin, which led to studies on the regulation of the expression of this protein. In contrast to albumin, ferritin is made by the polyribosomes, suggesting the generalization that secreted proteins are synthesized by membrane-bound ribosomes and that retained proteins are synthesized by free ribosomes.

He showed that the induction of protein synthesis was a remarkable example of translational control. In the non-induced state there is a substantial pool of free mRNA for both heavy and light chains of ferritin, which on stimulation by Fe are taken up in the polyribosomes and become translatable. In the unstimulated state a repressor protein is bound to a highly conserved sequence in the untranslated region of ferritin mRNA. On the administration of Fe, this protein is released and translation of stored mRNA can go forward.

In 1968 with postdoctoral fellow Sampson Jacob, Hamish guided the differentiation of the RNA polymerase family in eukaryotes; their work was the first identifier of amanitin as a specific inhibitor of RNA polymerase. These findings led to research on the

secondary structure of the regions in mRNA that are important for the binding of the regulatory protein.

In the late 1960s Hamish began studying the effects of protein deficiency on the developing rat placenta and found the RNA content severely affected, with a parallel reduction in the capacity of the placenta to secrete lactogen. In the course of these studies his group also demonstrated that the changing patterns of serotonin affected the capacity of the placenta to secrete two of the major peptide hormones, chorionic gonadotrophin and lactogen. Their production was determined by the relative amounts of mRNAs in the placenta at different stages of its development.

In 1970, Hamish became interested in the problem of measuring turnover of muscle protein. While listening to a lecture on the problems of such measurements, it occurred to him that some of the modified amino acids found in proteins would not undergo recycling and might be excreted in the urine following their release by protein breakdown. In collaboration with Vernon Young he set out to examine 3-methylhistidine, found in highest concentration in muscle protein. Methylhistidine soon came to be widely used to follow muscle-protein breakdown under a variety of nutritional, hormonal, and pathological conditions. Although the specific origin of methylhistidine from skeletal muscle has been challenged, it has a prominent place among the parameters for measurement of protein metabolism.

During the 1970s, Hamish collaborated with Richard Wurtman on a project to examine the action mechanisms of aromatic amino acids that are precursors of serotonin and norepinephrine. They wrote a series of papers showing that excess precursors could lead to inhibition of brain protein synthesis, a response that could be averted by blockers of brain receptors for these two neurotransmitters.

In the 1980s, Hamish continued to collaborate with Vernon Young. They examined the synthesis of serum albumin in young and older adults manifesting different levels of protein intake. This work showed that the elderly were less responsive to protein supplements.

Sources of pride

Hamish retired from MIT on September 30, 1990, at the age of 75. Throughout his life he never lost sight of the practical problems of human nutrition and the need for basic science to contribute to the improvement of human nutritional health. He believed that studies at the molecular level were required to improve understanding of how metabolic processes are integrated in the body.

Hamish was very proud of his Scottish heritage and often told of a remote ancestor who was flag bearer to the Chief of the MacDonell clan of Glengarry. His ancestor carried the flag in the last great battle in Scotland on Culloden Moor in 1746. With Hamish's characteristic humor and a twinkle in his eye, he chuckled that his ancestor fled from this disastrous affair and hid the flag in his house, where it resided under the floorboards for many years. The flag is now several centuries old and appears to be the only one—out of more than 100 Scottish clan flags of early times—to survive.

ACKNOWLEDGEMENTS

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