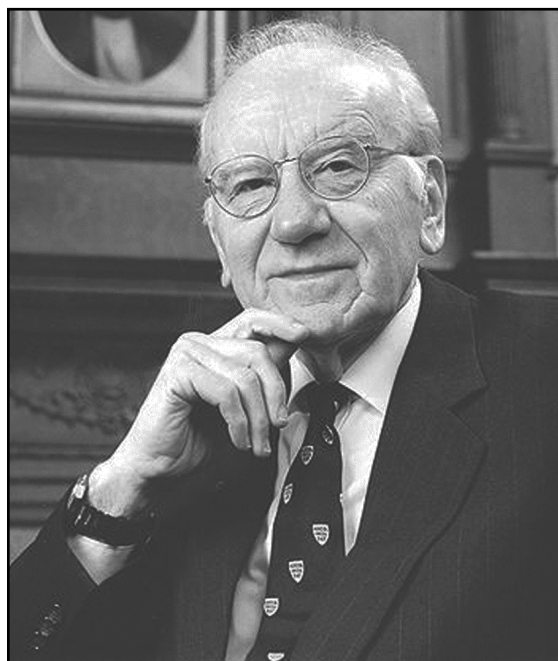

VICTOR A. MCKUSICK



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VICTOR MCKUSICK was the quintessential twentieth-century physician-scientist. Victor; his twin brother, Vincent; and their wives, Anne and Nancy, made up one of the Society's most distinguished, most faithful, and best loved families.

Victor is widely acknowledged as the father of genetic medicine. Initially a cardiologist, he developed an interest in the inherited components of disease. He founded a Division of Medical Genetics at Johns Hopkins and then became Physician-in-Chief there. He led the world in searching for identifying and mapping genes responsible for inherited conditions such as Marfan syndrome and dwarfism. In 1969, he was the first to propose mapping the human genome.

Victor and his identical twin, Vincent (later Chief Justice of Maine's Supreme Court), were born on 21 October 1921. Their father was a high school principal before deciding to become a dairy farmer. Their mother was an elementary school teacher. Victor and his five siblings grew up on a dairy farm in Parkman, Maine. Victor attended grammar school in a one room school house where he had the same teacher for 7 of 8 years.

At age 15, Victor developed a severe microaerophilic streptococcal infection in his left axilla and right elbow. Over the course of a 10-week hospitalization, he was treated successfully with the new sulfa drugs. The experience left Victor aspiring to a career in medicine.

After high school, Victor spent 2 years at Tufts University never receiving a bachelor's degree instead choosing early entry to medical school at Johns Hopkins. He graduated with his MD after only 3 years since the curriculum was abbreviated during World War II. He remained at Hopkins for internship, residency in internal medicine, and training in cardiology. In 1949, he married Anne Bishop, a rheumatologist at Johns Hopkins.

After initiating a successful practice in cardiology and inventing spectrophono cardiography for studying heart murmurs, Victor became interested in inherited disorders, an interest that began with his encounter of an unusually tall patient who had a detached retina and evidence of weakening of the wall of his aorta. He made his first breakthrough by discovering that the complex group of Marfan defects were from the pleiotropic effects of a single gene on an element of connective tissue. He then became interested in the clinical and genetic aspects of other heritable disorders of connective tissue and in 1956 published his first book, *Heritable Disorders of Connective Tissue*.

According to David L. Rimoin, some viewed his fascination with genetic disorders as medical stamp collecting, but Victor perceived that

the future of medicine would be through genetics and understanding the molecular mechanisms underlying disease.

In 1957, he established a division of medical genetics and a medical genetics clinic at Hopkins. This and a similar one started by Arno Motulsky at the University of Washington were the first such clinics in the United States. It is a tribute to these pioneers that there are now more than 100 accredited clinical genetics units in the United States. Victor's cytogenetics laboratory was also where pharmacogenetics began with the study of genetics of metabolism of the antituberculosis drug isoniazid.

Victor's study of genetics among the Amish may be his best known research. It illustrated a number of genetic principles, including consanguinity and founder effect. Initial study led to the identification of two recessive conditions named Ellis-vonCreveld syndrome and metaphysical chonorodysplasia, McKusick type. All told he discovered a dozen previously unrecognized inherited disorders and defined the basic genetic defect in many of them. This work served as a model for studies in other isolated populations leading other investigators to recognize hereditary related diseases.

In the 1950s, intrigued by genetic maps of the fruit fly, Victor envisioned a genetic map for humans. In studying links between inheritance and disease, he began mapping genes on human chromosomes. In 1969 at the International Birth Defects meeting in The Hague, he proposed mapping the human chromosome saying:

I propose that detailed exploration of the genetic constitution of man is ripe for an all-out attack. What we should know in full detail are the structure and geography of the chromosomes of man: the full nucleotide sequence of all genes determining the amino acid sequence and the location of each on the chromosomes of man.

Victor later said that this proposal reflected the exuberant mindset that followed the first moon landing.

In 1973 with Frank Ruddle, Victor began the International Workshops for Gene Mapping in Man, pioneering the use of computers for linkage works. As a leading advisor of the Human Genome Project, he became founding president of HUGO, the International Human Genome Organization.

From a pragmatic standpoint, one of Victor's most important contributions was his *Mendelian Inheritance in Man*. It began as a print edition in 1966 and since then has been continuously updated online as a searchable database. It remains the principal source of information on inherited diseases for clinical geneticists. It is derived from published

biomedical literature and updated daily. In addition to descriptions of the Mendelian disorders and the genes associated with disease phenotypes, extensive references are continuously updated. By the time of Victor's death in 2008, the 12th edition contained 18,961 full-text entries describing phenotypes and genes; 2,239 gene mutations causing disease; and 3,770 diseases with a molecular basis. Approximately 20 new entries were being added per month and 200 entries updated.

Early in his career, Victor recognized the value of the mouse model in understanding human disease. In 1960, he cofounded the Short Course in Medical and Experimental Mammalian Genetics. It was held in collaboration with the Jackson Laboratory at Bar Harbor, Maine. With a faculty from Hopkins, the Jackson Lab, and other institutions from around the world, the Short Course deserves the credit for the training of more than 4,000 medical geneticists. The day before his death, Victor watched a live stream of the course he had founded and directed annually for 40 years.

Throughout his life, Victor trained scores of fellows from around the world, many of whom became international leaders in the field of medical genetics. He was a highly committed and effective teacher. Additional examples of this were his cofounding of the European School of Medical Genetics in Italy, which trained hundreds of individuals from Europe and the Middle East. He also created the annual Clinical Delineation of Birth Defects meetings, which brought together clinicians and basic scientists to discuss the classification and pathogenesis of genetic syndromes.

Victor wrote extensively about the history of medicine and medical genetics. He told his students:

If you want to really get on top of some topic, you need to know how it got from where it was to how it is now. I was always strong in eponyms too—like Marfan syndrome, Freeman-Sheldon syndrome, Down syndrome, Tay Sachs disease, etc. On rounds . . . I would always ask so who is so and so for whom the disease was named.

Victor was one of the most honored physicians of his time. A few of his awards include 20 honorary degrees, the Lasker Award, the National Medal of Science, the Gardner Award, the Japan Prize, the Alan Award, and the Kober Medal.

Victor McKusick was one of the Society's most active and most loyal members. He served on the Committee on Development; the Library Committee; the Lashley Award Committee; the Daland Prize and Fellowship Committee, which he chaired; the Class 2 Membership Committee; and the Nomination of Officers Committee. He was on the Council from 1979–82, and from 1996–2002, he was Vice President.

In 1996, he was awarded the Society's Benjamin Franklin Medal for Distinguished Achievement in the Sciences. The citation read "in recognition of a great pioneer in the study of genetic diseases and the development of human genetics as a clinical specialty, the author of many influential books and founding editor in chief of *Genomics*, and a distinguished leader of the human genome project."

The Society continues to miss the gentle humor of this self-effacing giant of American medicine.

Elected 1975

CLYDE F. BARKER

President, American Philosophical Society

Donald Guthrie Professor of Surgery, Hospital of the University of Pennsylvania

Author's Note

This memoir also appears in *Biographical Memoirs of Members of the American Philosophical Society: Physicians, Volume III, Elected 1962–2006*, published by the American Philosophical Society in 2015.