Victor A. McKusick 1921–2008

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Victor A. McKusick died on July 22, 2008 at the age of 86. He was a University Professor of Medical Genetics at Johns Hopkins University, where he spent his entire medical career. He was revered as the 'Father of Genetic Medicine' and was a master clinician, scientist, medical historian, writer, teacher and mentor. Victor was first and foremost a physician and followed the Oslerian tradition of paying close attention to his patients, seeking insight into the cause and management of their disease.

Having trained in cardiology, he encountered families with Marfan syndrome and conceived that understanding the pleiotropic effects of a single gene affecting one element of connective tissue would reveal the basic defect. He became interested in the clinical and genetic aspects of the various heritable disorders of connective tissue and published his first book, *Heritable Disorders of Connective Tissue*, in 1956.

McKusick excelled in the clinical nosology of genetic disorders. Some viewed his research as medical stamp collecting and wondered if it was even science. But Victor perceived that the future of medicine—and insight into the molecular mechanisms that underlie disease—would be through medical genetics. He did not limit himself to descriptive studies. Collaborating with basic scientists, he helped define the biochemical and molecular defects in many disorders. He was especially effective in working across specialties and across basic science and clinical lines. His ultimate goal may have been reached in Marfan syndrome, with Hal Dietz, the first McKusick Professor at Johns Hopkins, finding a potential pharmacologic therapy for the aortic disease—clinical genetics at its best.

In 1957, McKusick started a comprehensive division of medical genetics within the Department of Medicine and brought genetics into the mainstream of clinical medicine. His was perhaps the earliest clinical cytogenetics laboratory in any large general hospital. Pharmacogenetics also started there, with the study of the genetics of metabolism of the antituberculosis drug isoniazid, or INH.

McKusick studied the Amish community and illustrated a number of genetic principles, such as consanguinity and founder effect, serving as a model for studies in other isolated populations. He uncovered about a dozen previously unrecognized inherited disorders, and his description of dwarfing conditions in the Amish catalyzed a long-standing relationship with Little People of America. This work led to the definition of the basic defect in many of these disorders.

McKusick and his colleagues made the pioneering observations that *G6PD* and color vision are closely linked on the X chromosome and that the Duffy blood group is located on chromosome 1. His determination to identify and catalog genes and chromosomes associated with genetic syndromes led to the publication of his classic "Mendelian Inheritance in Man," long considered the bible of medical genetics, a catalog of genetic diseases and the genes that cause them. He computerized it in 1964, and the printout became one of the first computer-generated medical texts. The continuously updated online version, OMIM, was one of the first medical uses of the web.

In 1969, at the International Birth Defects meeting in The Hague, McKusick suggested that mapping the human genome would unravel the mysteries of birth defects and genetic diseases:

"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 of proteins and the location of each on the chromosomes of man."

In 1973, with Frank Ruddle, he began the International Workshops on Gene Mapping in Man and pioneered the use of computers for linkage work. He approached the genome as an organ and wrote about the morbid and functional anatomy of the human genome. As a leading advocate and advisor of the Human Genome Project, he was named founding president of the International Human Genome Organization (HUGO). Thus, Victor was a true cartographer, whose efforts not only led to the mapping of the human genome, but also put genetics on the medical map.

Over the years, McKusick trained numerous fellows from around the world in medical genetics, many of whom became international leaders in the field. Through fellowship training, courses, meetings and writings, Victor was an extremely effective teacher and salesman for medical genetics. His genetics course at Bar Harbor, Maine, given annually since 1960, is widely credited with training generations of genetic medicine practitioners and scholars. A major objective was to upgrade the teaching of genetics by teaching the teachers. He co-founded the annual European School of Medical Genetics in Italy, which has now educated hundreds of individuals from Europe and the Middle East. These courses led to an incursion of genetics into medicine and clinical medicine into basic science. McKusick also created the annual Clinical Delineation of Birth Defects meetings about nosology in clinical genetics, bringing together clinicians and scientists to discuss the classification and pathogenesis of numerous genetic syndromes.

McKusick was always decades ahead of his time: creating a division of medical genetics, inventing spectrophonocardiography, predicting the usefulness of linkage and gene mapping, and pioneering the use of computers in publishing and the medical use of the internet. He made major contributions to biochemical, molecular and population genetics without formal training in the laboratory, mathematical genetics or computer technology. He considered his lab to be the clinic and the library.

He was the recipient of numerous awards, including the Allan Award of the American Society of Human Genetics, the Gairdner Award, the Lasker Award, the National Medal of Science and the Japan Prize.

His enormous energy, rigorous work ethic, effective time management, ability to foresee the use of multiple new technologies and rapid response to new findings, coupled with the personality of a sympathetic doctor, devoted teacher and good friend, made for a remarkable individual who has inspired thousands of students, doctors and scientists around the world. Almost every physician will directly or indirectly benefit from McKusick's research, teaching and persistent and successful championing of medical genetics and the Human Genome Project. ■

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