

## RETROSPECTIVE

**Victor A. McKusick (1921–2008)**

Francis S. Collins

It is the rare scientist who is universally recognized as the founder of a field. Even rarer is the one who witnesses his vision evolve from a solitary pursuit into a major discipline. But such was the life of the father of medical genetics, Victor Almon McKusick, who died 22 July after more than a half-century of pioneering research, mentorship, and leadership.

McKusick was the driving force for moving genetics beyond the tidy realm of flies and mice in the research lab into the messier realm of the medical clinic. In 1957, he established a medical genetics clinic at Johns Hopkins, the model for what would become more than 100 such clinics nationwide, and unleashed a flood of discoveries that demonstrated connections between genes and disease. Today, thanks largely to McKusick's creative and tireless contributions, the field of medical genetics is at the center of medicine.

While the influence of some scientific leaders wanes with their passing, McKusick's will only grow with time. His work created a dynamic legacy that lives on in the thousands of physician-researchers he mentored, and the marvelous, updatable resources he created. Nearly every medical geneticist, including myself, can trace his or her scientific lineage back to McKusick.

The first of my many sips from McKusick's seemingly bottomless well of knowledge came in 1981. As a medical genetics fellow at Yale, I was confronted with a puzzling infant with a congenital intestinal obstruction. The child had a sibling with an identical condition. I was stumped about the diagnosis, as was my attending physician, Uta Francke. So, we consulted McKusick's landmark text, *Mendelian Inheritance in Man*, and came upon entry "\*243600, Familial apple peel jejunal atresia," a perfect description of the child's condition. Whereupon, Uta said, "This is wonderful. Victor should win the Nobel Prize!"

Scientific prizes probably were not on anyone's mind when McKusick and his identical twin, Vincent, were born 21 October 1921 on a dairy farm in Parkman, Maine. In fact, McKusick considered becoming a min-

ister until age 15, when he developed a serious streptococcal infection and came away inspired by the physicians who saved his life. After spending 3 years as an undergraduate at Tufts, McKusick enrolled in 1943 in the Johns Hopkins School of Medicine, from which he graduated in 1946 and where he held a series of distinguished professorships up until his death.

While he authored many seminal papers and books on genetics, McKusick also delighted in sharing the story of his first encounter with the world of scientific publishing. As a medical student, he and his brother Robert (who became a dairy farmer) wrote a paper on the inheritance pattern of coat color in Jersey cattle, describing how the apparently dominant fawn color was actually a recessive trait. They eagerly sent their genetics paper off to the *Journal of Heredity*, but never got a response. Fortunately, both for McKusick and the scientific community, future journal editors would display better judgment.

Among his key publications was a 1966 paper describing the first mapping of a human autosomal gene, the Duffy blood group locus. He also clinically defined a series of connective tissue disorders, the most famous of which is the Marfan syndrome. The tour de force of McKusick's publications, however, remains his constantly updated *Mendelian Inheritance in Man*, a catalog of human genes and genetic disorders. This classic reference first appeared in print in 1966 and contained about 1500 entries. Today, an electronic version features nearly 19,000 entries.

No description of McKusick's impact on science is complete without mentioning his prescient call for mapping the human genome. In August 1969, at the International Conference on Birth Defects in The Hague, McKusick proposed that mapping all human genes would be useful for understanding basic derangements in birth defects. "The proposal reflected the exuberant mindset that followed the first Moon landing by Apollo 11," he recalled in a 2006 article. But the idea met with perplexed silence, in part because

The founder of medical genetics was a driving force behind current progress in applying genetic information to medicine.

no one—not even McKusick—was clear on what methods could be used to achieve such an ambitious goal. Thankfully, McKusick was not one to give up easily, and was a strong advocate for The Human Genome Project, stepping forward in the mid-1980s to serve as the founding president of the Human Genome Organisation.

During a career that spanned an impressive 60 years, McKusick received many accolades, including election to the National Academy of Sciences in 1973, the Albert Lasker Award for Special Achievement in Medical Science in 1997, the National Medal of Science in

2001, and the Japan Prize in Medical Genetics and Genomics in 2008.

Medals and proclamations aside, I suspect that one achievement that McKusick would most want to be remembered for is his role in establishing the legendary "Short Course in Medical and Experimental Mammalian Genetics." This 2-week event, held each summer at The Jackson Laboratory in Bar Harbor, Maine,

has had a profound influence on medical genetics. Since it began in 1960, more than 5000 clinical specialists, educators, and others have had the privilege of learning about the latest advances from some of the best minds in the field. In fact, according to Anne, McKusick's physician wife of 59 years, hours before her husband died peacefully of cancer at their home outside Baltimore, Maryland, he had enjoyed watching the live streaming video of this summer's "Short Course."

More than a century ago, the father of modern medicine, Sir William Osler, wrote: "To wrest from nature the secrets which have perplexed philosophers in all ages, to track to their sources the causes of disease, to correlate the vast stores of knowledge, that they may be quickly available for the prevention and cure of disease—these are our ambitions." Victor McKusick, who appropriately held the Osler Professorship for many years at Johns Hopkins, lived that vision better than any other physician of the last half-century.





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