Victor McKusick was legendary for his prodigious appetite for work. It was said that he was capable of writing two papers in a single day and an entire book over a weekend. Although transcribing his dictation, his secretary sometimes heard the sound of songbirds in the background testifying to McKusick's lifelong habit of beginning work before dawn. Fortunately
for humanity, McKusick found the perfect outlet for his exceptional capacity for hard work in the field of medical genetics. The reminiscences of some 20 or so colleagues and family members that are compiled in Victor McKusick and the History of Medical Genetics present a fascinating portrait of a man on fire with the idea of gaining and disseminating information about human genetics.

After graduating from Johns Hopkins School of Medicine, McKusick had intended to return home to Maine to practice general medicine, but he found the temptations of an internship on the prestigious Osler Medical service irresistible and, except for a two-year stint at the U.S. Marine Hospital in Baltimore, he would spend his entire career at Hopkins. His early work was in cardiology, but he had always had a lively interest in genetics, which he attributed in part to his being an identical twin. Already as a teenager, he had helped one of his brothers compose a paper on coat color inheritance in the Jersey cows on his parents' dairy farm. When in 1957 the Chairman of the Department of Medicine appointed McKusick to head the chronic disease clinic at Johns Hopkins Hospital, McKusick agreed on the condition that the clinic could become a Division of Medical Genetics dedicated to the treatment of hereditary diseases, which he viewed as the ultimate in chronic diseases. From the beginning, McKusick attracted a remarkably talented and diverse group of trainees and junior colleagues from the United States, Great Britain, and beyond to the renamed Moore Clinic. The recruits were chosen for their expertise in biochemistry, cytology, statistics, and other disciplines needed to build a medical genetics center. This history is fascinatingly evoked by several of his disciples, each of whom went on to make major contributions to the field, and the Moore Clinic itself would become a prototype for scores of departments of medical genetics across the country.

The weekly meetings of the Moore Clinic were supplemented by a monthly journal club at McKusick's house. At these sessions each of the fellows was called upon to report on new genetic results from the literature, which were to be summarized on index cards. At the evening's close, McKusick collected the index cards and subsequently used them to prepare an annual review of the genetic literature. Ultimately, these index cards were to form the building blocks for what was, in some respects, McKusick's most enduring contribution, a compilation of concise clinical descriptions of all known Mendelian diseases that would be published in successive iterations of the storied Mendelian Inheritance in Man. All told, there would be 12 print editions of this book, which spanned the years 1966 to 1995, and continues to thrive online.

A second enduring expression of McKusick's passion for collecting and disseminating genetic knowledge was the Bar Harbor Course, which he launched in 1960 in conjunction with the Jackson Laboratory. Thousands of people at all levels made the pilgrimage to Mount Desert Island to hear the new gospel of medical genetics, as they still do. The course never ceased to captivate McKusick who had listened to it on a live video stream on the day he died.

McKusick's interest in genetics and disease was an all-consuming passion, which left little time for the ordinary diversions of life. As his son Ken relates with wry humor, his father could not have told you who Barry Bonds was, the name of any of the Beatles or of a single actor or character in The Honeymooners, Star Trek, M*A*S*H, Cheers, or Seinfeld. In one telling incident, McKusick's rheumatologist wife Anne relates how McKusick called one morning to inquire “with his endearing obliviousness” about bringing home 26 geneticists for dinner.
When, in 1973 after nearly 20 years spent studying rare genetic disorders, McKusick was appointed Chief Physician and Chairman of the Department of Medicine at the Johns Hopkins Medical School, his initially skeptical residents were amazed to find how quickly he regained mastery over mainstream medicine. But the clinical and academic threads of his life had always been deeply intertwined. The synergy of his interests was first evident in his groundbreaking work on Marfan syndrome and other inherited connective tissue disorders in the 1950s. By studying autopsy reports, McKusick had discovered that cardiovascular disease was present in a far higher percentage of Marfan victims than had been previously thought, and in the 1970s he established that fully 90% of Marfan deaths were due to cardiovascular causes. This led him to propose the use of β-blockers to reduce stress on the aorta, and by the 1990s randomized studies clearly showed that the use of β-blockers significantly reduced the frequency of dissection and the need for surgical intervention in the treated group.

His second remarkable success as physician-scientist was in his treatment of the Amish, and his more than 40-year-long association with them is described in several of these essays. By chance, in 1962, McKusick learned of the high frequency of dwarfism among the Amish. The fact that the most common form of the disorder—achondroplasia—was an autosomal dominant that greatly reduced fitness led McKusick to hypothesize that the Amish might be suffering from an as yet unrecognized autosomal recessive form. Ultimately, McKusick's inspired conjecture would prove correct, and he would uncover two new recessive forms of dwarfism as well as a dozen other previously uncharacterized rare recessive diseases among the Amish. In so doing, McKusick was the first to demonstrate the immense rewards to be reaped from the study of isolated, closed, highly inbred populations.

Characteristically, McKusick got to know his Amish patients well, and arranged for them to have free genetic counseling as well as free consultations with Johns Hopkins orthopedists, neurologists, and neurosurgeons. In a sign of their deep gratitude to him, he was awarded a lifetime membership in the Little People of America for his contribution to their care.

From the beginning of his genetics work, McKusick understood the central importance of building a map of the human genes, and he spent most of his adult life characterizing and cataloging single gene defects and mapping them to chromosomes. In the late 1960s he was the first to assign a human autosomal gene to a specific chromosome. In 1973, he secured funding for the first Human Gene Mapping workshop and together with Frank Ruddle championed the use of human-rodent somatic cell hybrids to do the mapping, which made it possible to assign genes to specific chromosomes. With the new advances in molecular biology and, particularly, in the ability to sequence DNA, McKusick recognized that the field of medical genetics was about to explode, and he became a powerful advocate for the Human Genome Project. As a result of the new sequence data it became possible to find the actual mutations that were responsible for the gene defects that he had so painstakingly characterized and located, and the ultimate goal of diagnosing and treating genetic disorders has been achieved for many conditions.

The many facets of McKusick's remarkable career are drawn together in this commemorative volume, which is in part a testament to the powerful imprint he made on his many protégés. Because McKusick was so much at the center of the development of medical genetics, the book provides an in-depth introduction to the subject. At the same time, readers get a glimpse of the
price that such a life extracts from family and close friends who, in this case, at least had the
comfort of knowing that they were sacrificing for a truly grand project. In her eulogy of her
friend and mentor, Clair Francomano explained the qualities that McKusick taught and lived by:
“Work very hard, always stay positive, and share what we know, widely and deeply, with
whoever will stop to listen and learn” (p. 213).

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