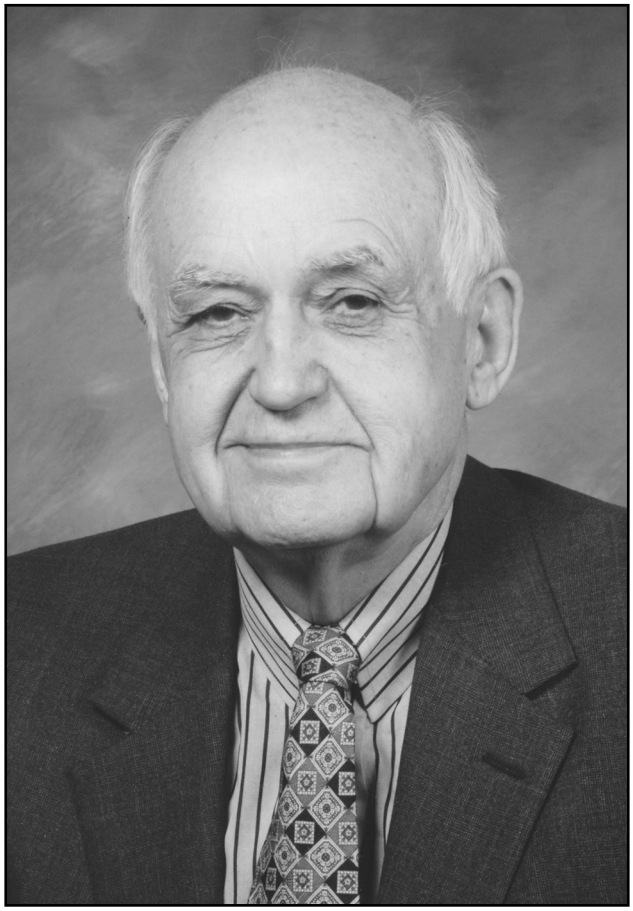
MAURICE R. HILLEMAN



MERCK RESEARCH LABORATORIES

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THE WORLD lost a true public health hero when Maurice R. Hilleman, Ph.D., died of cancer on 11 April 2005, at the age of eighty-five. Maurice literally changed the world with his extraordinary contributions in numerous disciplines: virology, epidemiology, immunology, cancer research, and, especially, vaccine research and development.

Maurice was perhaps the single most influential public health figure of the twentieth century, if one considers the millions of lives saved and the countless people who were spared suffering because of his work. Over the course of his career, Maurice and his colleagues developed more than forty vaccines. Of the fourteen vaccines currently recommended in the United States, Maurice developed eight.

Straight-shooting and sometimes irascible, Maurice combined a phenomenal intellect with the ability to get things done. He locked his eye on a target and went after it, with boundless energy, purpose, and enthusiasm. He had an engaging, dry sense of humor, often tinged with a sense of irreverence.

To fully appreciate Maurice, it is instructive to understand how his upbringing affected the way he approached life and tackled problems. Maurice was born into a family of western pioneers in Miles City, Montana, on the banks of the Tongue and Yellowstone rivers. His great-uncle had served as an Indian scout in the United States cavalry in the days following Custer's last stand. After his mother died in childbirth, leaving his father with several boys to raise, Maurice was adopted by an aunt and uncle. Although both families lived side by side on the same farm and shared a strong work ethic, they held quite different philosophies on life. His biological father was devoutly religious, and his brothers were destined to become Lutheran preachers. His uncle, on the other hand, was a freethinker and encouraged Maurice to challenge authority and think "outside the box."

Amazingly, Maurice almost did not make it to college, thinking the family could not afford it. After high school, he got a job at the local J. C. Penney store, starting in as a "basement boy." Halfway through the summer, one of his brothers said to his father, "Hey, aren't you going to send that kid to college?" So Maurice registered at Montana State College, where he received a four-year scholarship. At Montana State he majored in biology, which combined botany and bacteriology. Maurice said that he hated the botany part of the curriculum and defied the dean, refusing to take the required botany courses. He ultimately forged his own path, switching majors to chemistry while taking all the microbiology courses. He graduated at the top of his class, motivated largely, he later said, by a strong desire to get out of Montana. He went on to graduate school at the University of Chicago, where he

was groomed for a career in academics. Maurice, however, was determined to go into industry, an idea that was unheard of at Chicago. His fixation was to get a job and make a living, not to go around, as Maurice put it, "being a fuzzy-headed professor."

Maurice took a job at Squibb. He plunged right into the thick of things and developed his famous management style, overseeing the research and development process from start to finish, conducting basic research studies, initiating product development, and pushing through the final product. While at Squibb, he developed a vaccine for Japanese encephalitis as well as vaccines for rabies, smallpox, typhus, and influenza.

In 1948 Maurice accepted a position at the Walter Reed Army Medical Research Institute, which was then the global epicenter for infectious disease research. Inspired by the memory of the terrible influenza pandemic of 1918–19, public health officials and scientists were concerned, as they are today, about preventing the next global encounter with influenza. It was at Walter Reed that Maurice became a leading authority on influenza and helped solve many mysteries of influenza viruses. During the 1947 flu season, the seasonal influenza vaccine was not protective, and Maurice set out to figure out why. He studied influenza virus strains from different years and showed that there was a continuous drift from year to year in the makeup of viral surface proteins. In 1947, however, there had been an abrupt shift of the virus, and the circulating virus was substantially different from the previous year, such that the existing vaccine offered little protection. Fortunately, the world was spared a major pandemic that year, because of the low virulence of the virus. It was Maurice's meticulous attention to detail that revealed the phenomenon of "shift" and "drift" of the influenza virus and how it dictates the epidemiology of the disease, concepts that are very much in play today as we brace for the next pandemic.

From that point on, Maurice was keenly aware that another major shift in the influenza virus could trigger a pandemic. In early April 1957, he read a news story in the *New York Times* about thousands of mothers in Hong Kong lining up at health clinics, holding infants with glassy-eyed stares. He instantly knew that the next flu pandemic had hit. He sent for specimens, analyzed them, and predicted that the influenza strain circulating in Hong Kong would cause a pandemic. In true Hilleman style, he put out a press release on 22 April 1957 telling the world that there would be a pandemic when school started in the fall. He sent virus samples to manufacturers. In an effort to ensure a large supply of fertilized chicken eggs to manufacture vaccine, he asked chicken breeders not to kill the roosters in their flocks. Through his

initiative, forty million doses of vaccine were produced in the United States, likely saving tens of thousands of lives.

Soon after, Maurice left Walter Reed and ventured north to Merck, where he would spend the next forty-five years. It was here that his vaccine work really took off. He turned the organization around, instilling a new respect for vaccine research. He and his colleagues guided numerous vaccines through the laborious process from promising concept to licensed product. Among his successes are vaccines against measles, mumps, rubella, pneumonia, meningitis, and chickenpox, and the first vaccine against a cancer-causing virus, hepatitis B.

One of his more significant achievements was the development of the mumps vaccine in 1963, when his six-year-old daughter, Jeryl Lynn, came down with a case of the disease. He swabbed the back of her throat and took the samples back to the laboratory in the middle of the night. From those samples, he isolated the mumps virus, which is still known as the "Jeryl Lynn" strain, and developed the vaccine from those cultures. His younger daughter, Kirsten, was a volunteer in early clinical trials of the vaccine. The mumps vaccine was licensed in 1967 and now constitutes part of the standard MMR inoculation. Today, only a few hundred cases of mumps are reported in the United States each year.

Another major achievement came with the development of a vaccine against rubella, or German measles. Between 1963 and 1965, one of the country's worst rubella outbreaks occurred, causing at least twenty thousand fetal and infant deaths, and another twenty thousand cases of permanent brain damage in children born to mothers infected during pregnancy. Maurice and his team developed techniques for culturing and attenuating the virus in duck eggs, opening the door to a rubella vaccine, which was licensed and distributed in 1969. Today, rubella is extremely rare, with fewer than twenty-five cases reported each year since 2001 in the United States.

One of his most important innovations was the first vaccine effective against hepatitis B. Because the virus could not be cultivated in cell culture, he could not follow the path established with the polio, measles, mumps, and rubella vaccines. Using a surface antigen, Maurice and his colleagues developed a successful vaccine that they initially tested on volunteers (including Maurice) inside the Merck Research Laboratories. Approved in 1981, this vaccine led to the development at Merck of the first recombinant vaccine for human use, a vaccine effective against hepatitis B and in widespread use around the world.

In addition to his vaccine work, Maurice made many pioneering discoveries in basic virology and immunology. For example, he discovered or co-discovered several viruses including hepatitis A, SV40, and several adenoviruses and rhinoviruses. He also purified and characterized

interferon and discovered that double-stranded RNA could induce its production, leading to protection against viral challenge.

Toward the end of his career, Maurice took on the enormous challenge of developing a vaccine against HIV/AIDS. Through his work in this field I came to know Maurice as colleague, close adviser, and dear friend. He clearly and incisively helped to define the obstacles to developing an AIDS vaccine and the steps that academia, industry, and the government should take to meet this challenge.

Despite Maurice's enormous accomplishments, his name has never been a household word. Few people, even in the scientific community, were aware of the scope of his achievements. I once asked my postdoctoral fellows whether they knew who had developed the measles, mumps, rubella, hepatitis B, and chickenpox vaccines; they had no idea. When I told them it was Maurice Hilleman, they said, "Oh, you mean that grumpy guy who comes to all of the AIDS meetings?" Maurice was not someone disposed to taking personal credit for his achievements. He was always quick to give credit to his team members. It was never about him. Rather, the reward was in the products developed, the lives saved. Only after his death, when the press finally realized the magnitude of his lifetime accomplishments, did Maurice get the broad recognition that he so justly deserved.

Maurice Hilleman may be gone, but he has left his mark on so many areas of science and public health and made such a lasting impression on so many people that his legacy will continue for decades and generations to come. It has been an honor and privilege to know such a great man.

Elected 1997

ANTHONY S. FAUCI
Director, National Institute of Allergy and Infectious Diseases
National Institutes of Health

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