Obituary

Maurice R. Hilleman (1919–2005)

During the twentieth century, life expectancy in industrialized countries almost doubled. Improvements in nutrition and sanitation certainly played a major role, but the central factor responsible was the development of childhood vaccines. A particular name can be attached to this achievement — that of Maurice R. Hilleman.

Hilleman ranks with the most brilliant and productive creators of vaccines of all time, with a stature comparable to that of Edward Jenner and Louis Pasteur. But his career was hardly foreseeable. Born in remote Miles City, Montana, as the last of eight children (his mother and twin sister dying during the birth), Hilleman grew up on his uncle's farm, "where things got done" — as Hilleman himself often said. He was later renowned for bringing the same attitude to work in the laboratory. He would never go home before an experiment was finished, and whenever possible was continually driven to translate results in basic or applied research to practical ends.

Growing up on a lonely ranch, Hilleman soon became interested in biology. He talked to the farm animals, trying to hypnotize and train them, but eventually discovered Charles Darwin's *Origin of Species*. Caught reading this book in church did nothing to enhance his popularity in a community of staunch Lutheran Protestants.

Indeed, Hilleman's career almost never got started. When he graduated in 1937, his family had no plans for him to go to college and instead he took a job as a stock boy at a local store. However, one of his older brothers, returning home for the summer, persuaded Hilleman that his talents were being wasted and he enrolled at Montana State University on a scholarship. There, in order to be finished by mid-term, he would often run a semester's worth of organic-chemistry experiments simultaneously. He won a fellowship to the University of Chicago and finished in 1944 with a prizewinning PhD dissertation on the bacterium *Chlamydia*. At that time, it was not possible to accurately subtype bacterial or viral families, but Hilleman developed the appropriate techniques by immunizing animals with different isolates and studying antigenic cross-recognition by the resulting antibodies.

Hilleman's scientific successes continued when he joined the pharmaceutical company E. R. Squibb in 1944. Because of the danger of Japanese encephalitis in the Pacific offensive during

Creator of vaccines that continue to prevent death and disease on a global scale

the Second World War, his first challenge was to develop a vaccine against this viral disease. He completed the task within a few months, then cooperated with Nobel laureate Wendell Stanley from The Rockefeller University to develop the first highly immunogenic influenza vaccine with low toxicity.

In 1948, Hilleman left industry to concentrate on basic research at the Walter Reed Army Institute of Research in Washington. Among many other achievements, he discovered antigenic drift in influenza viruses, the phenomenon by which point mutations allow the virus to evade the full force of the continuously evolving herd immunity. He also discovered antigenic shift, that rare genetic reassortment that can occur during influenza double-infections and that leads to influenza strains against which herd immunity does not yet exist.

In 1957, this knowledge allowed Hilleman to warn the US authorities and the World Health Organization (WHO) that an influenza pandemic was about to emerge, a threat that had been overlooked by the WHO. He had noticed a report in *The New York Times* of a severe outbreak of respiratory disease in Hong Kong. Hilleman obtained samples, isolated a new influenza

strain and convinced manufacturers to produce 40 million doses of a vaccine. When, as predicted by Hilleman, the new virus reached the United States in September 1957, those at greatest risk were already being immunized.

Hilleman's productivity really shifted into high gear after 1957, when he joined Merck Research Laboratories in West Point, Pennsylvania. He was given full responsibility to plan and direct vaccine research and development. During the next 30 years, Hilleman and his co-workers produced more than 40 viral and bacterial vaccines. They developed the concept of combined live virus vaccines, which culminated in the global marketing of the measles–mumps–rubella (MMR) vaccine that is estimated to save the lives of almost two million children each year. Other remarkable vaccines against hepatitis A and hepatitis B followed. His hepatitis B vaccine was also the first anticancer vaccine, as it prevents hepatocellular carcinoma, a consequence of infection.

The following episode exemplifies Hilleman's dedication to science. One night in 1963, he was awakened by his little daughter Jeryl Lynn who was sick with a sore throat. He rightly diagnosed mumps, took a throat swab and isolated the virus. This virus strain was then used to develop a vaccine, and Hilleman, assisted by his wife Lorraine, a trained nurse, immunized their second daughter Kirsten in one of the first successful clinical trials.

Hilleman's accomplishments in basic and applied research have been of seminal importance to medical biology and human health. They have increasingly received recognition for their insight and ingenuity — it is no exaggeration to state that they have changed the world. Together with antibiotics such as penicillin, the products of Hilleman's hard work and skill have prevented and continue to prevent the suffering of billions, and the deaths of millions. In acknowledgement of his work, he received many honours and prizes, among them the Albert Lasker Public Service Award and the US National Medal of Science.

Hilleman was an indefatigable worker, still publishing and giving seminars until a few weeks before his death on 11 April. He was our godfather in the scientific community: usually quiet, yet precisely intervening and creative in discussions, approachable for youngsters and always helpful, he was our benchmark. His many friends will remember him, as should the whole of mankind.

Reinhard Kurth

Reinhard Kurth is at the Robert-Koch-Institut, Nordufer 20, 13353 Berlin, Germany.
e-mail: schwarzk@rki.de