A Forgotten Pioneer of Vaccines

By RICHARD CONNIFF

We live in an epidemiological bubble and are for the most part blissfully unaware of it. Diseases that were routine hazards of childhood for many Americans living today now seem like ancient history. And while every mother could once identify measles in a heartbeat, now even the best hospitals have to call in their eldest staff members to ask: “Is this what we think it is?”

To a remarkable extent, we owe our well-being, and in many cases our lives, to the work of one man and to events that happened 50 years ago this spring.

At 1 a.m. on March 21, 1963, an intense, irascible but modest Merck scientist named Maurice R. Hilleman was asleep at his home in the Philadelphia suburb of Lafayette Hill when his 5-year-old daughter, Jeryl Lynn, woke him with a sore throat. Dr. Hilleman felt the side of her face and then the telltale swelling beneath the jaw indicating mumps. He tucked her back into bed, about the only treatment anyone could offer at the time.

For most children, mumps was a nuisance disease, nothing worse than a painful swelling of the salivary glands. But Dr. Hilleman knew that it could sometimes leave a child deaf or otherwise permanently impaired.

He quickly dressed and drove 20 minutes to pick up proper sampling equipment from his laboratory. Returning home, he woke Jeryl Lynn long enough to swab the back of her throat and immerse the specimen in a nutrient broth. Then he drove back to store it in the laboratory freezer.

The name Maurice Hilleman may not ring a bell. But today 95 percent of American children receive the M.M.R. — the vaccine for measles, mumps and rubella that Dr. Hilleman invented, starting with the mumps strain he collected that night from his daughter.

It was by no means his only contribution. At Dr. Hilleman’s death in 2005, other researchers credited him with having saved more lives than any other scientist in the 20th century. Over his career, he devised or substantially improved more than 25 vaccines, including 9 of the 14 now routinely recommended for children.
“One person did that!” said Dr. Anthony S. Fauci, a longtime friend of Dr. Hilleman’s and now director of the National Institute of Allergy and Infectious Diseases. “Truly amazing.”

As a young man in Montana, Maurice Hilleman had intended only to become a manager at the J. C. Penney store. He turned out not to have the perfect retail personality. (Asked later in life what he was proudest of in his career, he replied, “Being able to survive while being a bastard.”)

After getting a Ph.D. in microbiology at the University of Chicago, he went on to spend most of his career at Merck, but the corporate personality also eluded him. He had a sailor’s vocabulary, and his brand of peer review often included shipboard expletives (though he used them “in a constructive way,” Dr. Fauci said with a smile).

But everyone recognized Dr. Hilleman’s genius at discovering and perfecting vaccines, which he pursued, Dr. Fauci said, with a rare combination of “exquisite scientific knowledge” and an “amazingly practical get-it-done personality.”

Vaccines are tools for coaxing the immune system to resist a disease without producing the actual symptoms, and making them was as much an art as a science. “It’s not like there was a formula for this,” said Dr. Paul A. Offit, a Philadelphia pediatrician, vaccine developer and the author of “Vaccinated,” a 2007 biography of Dr. Hilleman.

The general practice was to isolate a disease organism, figure out how to keep it alive in the laboratory, then weaken or “attenuate” it by passing it over and over through a series of cells, typically from chicken embryos, until it could no longer reproduce in humans but could still elicit an immune response. Other steps followed, particularly for Dr. Hilleman, who was obsessed with safety and with stripping away unwanted side effects.

That spring of 1963, the Food and Drug Administration also granted the first license for a vaccine against measles. Much of the early work on the virus had been done in the laboratory of John F. Enders at Boston Children’s Hospital, but the vaccine still commonly produced rashes and fevers when Dr. Hilleman began to work on it.

Under pressure from public health officials to stop a disease then killing more than 500 American children every year, Dr. Hilleman and Dr. Joseph Stokes, a pediatrician, devised a way to minimize the side effects by giving a gamma globulin shot in one arm and the measles vaccine in the other. It was the beginning of the end of the disease in this country.
Dr. Hilleman then went on to refine the vaccine over the next four years, eventually producing the much safer Moraten strain that is still in use today. As always, he kept himself in the background: The name stands for “more attenuated enders.”

One other crucial event in the development of M.M.R. happened that spring of 1963: An epidemic of rubella began in Europe and quickly swept around the globe. In this country, the virus’s devastating effect on first-trimester pregnancies caused about 11,000 newborns to die, according to the Centers for Disease Control and Prevention. An additional 20,000 suffered birth defects, including deafness, heart disease and cataracts.

Dr. Hilleman was already testing his own vaccine as the epidemic ended in 1965. But he agreed to work instead with a vaccine being developed by federal regulators. It was, he later recalled, “toxic, toxic, toxic.” By 1969, he had cleaned it up enough to obtain F.D.A. approval and prevent another rubella epidemic. Finally, in 1971, he put his vaccines for measles, mumps and rubella together to make M.M.R., replacing a series of six shots with just two.

Or rather not finally. In 1978, having found a better rubella vaccine than his own, Dr. Hilleman asked its developer if he could use it in the M.M.R. The developer, Dr. Stanley Plotkin, then of the Wistar Institute in Philadelphia, was momentarily speechless. It was an expensive choice for Merck, and might have been a painful one for anyone other than Dr. Hilleman.

“It’s not that he didn’t have an ego. He certainly did,” Dr. Plotkin recalled in a recent interview. “But he valued excellence above that. Once he decided that this strain was better, he did what he had to do,” even if it meant sacrificing his own work.

Given Dr. Hilleman’s obsession with safety and effectiveness, it came as a bitter surprise toward the end of his life when his vaccine was at the center of what Dr. Offit called “a perfect storm of fear.” In 1998, The Lancet, a respected British medical journal, published an article alleging that M.M.R. had caused an epidemic of autism.

The lead author, Dr. Andrew Wakefield, became a media celebrity, and some parents began to balk at having their children immunized; the vaccine’s very success had made them forget just how devastating measles, mumps and rubella could be. Dr. Hilleman, who might reasonably have been expected to win a Nobel Prize, got hate mail and death threats instead.
Multiple independent studies would eventually demonstrate that there is no link between M.M.R. and autism, and Dr. Wakefield’s work has been widely discredited. In 2010, the British medical authorities stripped him of the right to practice medicine, and The Lancet retracted the 1998 article.

It came too late, not just for Dr. Hilleman, who by then had died of cancer, but also for many parents who mistakenly believed that avoiding the vaccine was the right way to protect their children. In 2011 alone, a measles outbreak in Europe sickened 26,000 people and killed 9. Because the disease is contagious enough to pick up from a traveler walking by in the airport, cases still also occur in this country among the unvaccinated.

But Dr. Hilleman would probably still find reason to be encouraged. The Measles and Rubella Initiative, a global campaign organized in 2001, has given the M.M.R. vaccine to a billion children in this century, preventing 9.6 million deaths from measles alone, for less than $2 a dose. According to Dr. Stephen L. Cochi, a global immunization adviser at the C.D.C., the initiative is “on the verge of setting a target date” to eradicate the disease.

In this country, the strain that Dr. Hilleman collected from his daughter that night in 1963 has reduced the incidence of mumps to fewer than 1,000 cases a year, from 186,000. Characteristically, he named it not for himself but for his daughter. Jeryl Lynn Hilleman, now a financial consultant to biotech start-ups in Silicon Valley, turns the credit back on her father.

He was driven, she said in an interview, “by a need to be of use — of use to people, of use to humanity.”

“All I did,” she added, “was get sick at the right time, with the right virus, with the right father.”