

## Stanley Alan Plotkin (1932- )

Stanley Alan Plotkin developed vaccines in the United States during the mid to late twentieth century. Plotkin began his research career at the Wistar Institute in Philadelphia, Pennsylvania, where he studied the rubella virus. In pregnant women, the rubella virus caused congenital rubella syndrome in the fetus, which led to various malformations and birth defects. Using WI-38 cells, a line of cells that originated from tissues of aborted fetuses, Plotkin successfully created RA27/3, a weakened strain of the rubella virus, which he then used to develop a rubella vaccine. Plotkin's rubella vaccine has prevented birth defects due to congenital rubella in developing fetuses and newborns.

Plotkin was born 12 May 1932 in New York City, New York, to parents Lee and Joseph Plotkin, who had immigrated to the United States from England. Plotkin's father worked as a commercial telegrapher while his mother cared for Plotkin and his younger sister, Brenda. As an adolescent, Plotkin attended the Bronx High School of Science in New York City, New York. When Plotkin was fifteen, he read two books, *Arrowsmith*, a novel by Sinclair Lewis, and *Microbe Hunters*, a non-fiction science drama by Paul de Kruif. Both books told stories of scientists striving to discover the causes of diseases and to create vaccines against them. Plotkin later credited those books as his inspiration for studying science and medicine. After graduating from the Bronx High School of Science in 1948, Plotkin enrolled at New York University in New York City.

Plotkin graduated with his bachelor's degree from New York University in 1952 and applied to the State University of New York Medical School at the Downstate Medical Center in Brooklyn, New York. While at the Downstate Medical Center, Plotkin worked in the lab of Robert Austrian, who studied infectious diseases like pneumonia and meningitis caused by the bacteria, streptococcus pneumoniae. One classmate recalled that Plotkin had an insatiable curiosity and emphasized finding practical solutions to human health problems through rigorous experimentation, traits that Plotkin later attributed to his time spent working with Austrian. After Plotkin received his medical degree from the State University of New York Medical School in 1956, he moved to Cleveland, Ohio, where he spent a year as a pediatric intern at Cleveland Metropolitan General Hospital.

In 1957, Plotkin planned to volunteer for the US Air Force rather than be drafted for military service in the Vietnam War. According to Plotkin, he wanted to join the Air Force to learn to fly planes. But because of his medical training, Plotkin instead served for three years in the Epidemic Intelligence Service of the Centers for Disease Control in Atlanta, Georgia.

As an officer of the Epidemic Intelligence Service, Plotkin studied anthrax at the Wistar Institute. Plotkin later revealed that he requested that specific appointment because he hoped to work with the new director of the Wistar Institute, Hilary Koprowski, who had developed a preliminary oral polio vaccine. Polio was a common childhood disease that caused flu-like symptoms and sometimes affected the central nervous system, paralyzing some children. In addition to studying anthrax, Plotkin also studied the poliovirus in Koprowski's lab. He researched alternative, experimental polio vaccines and tested the new polio vaccines in the Belgian Congo, later called the Democratic Republic of the Congo.

During his initial research at the Wistar Institute, Plotkin taught at the School of Medicine at the University of Pennsylvania in Philadelphia, Pennsylvania, in 1959. To obtain credentials as a pediatrician, Plotkin worked as a resident physician at the Children's Hospital of Philadelphia in Philadelphia, Pennsylvania, in 1961. In 1962, he left Philadelphia and transferred his pediatric residency to the Hospital for Sick Children in London, England. Plotkin later stated that he enjoyed his residency there because he believed the hospital attracted some of the most difficult medical cases and some of the best pediatric consultants in England. After obtaining his pediatric credentials, Plotkin

returned to Philadelphia in 1963 where he resumed teaching in pediatrics as an assistant professor at the University of Pennsylvania. He also resumed research at the Wistar Institute with institute director Koprowski.

Upon returning to the Wistar Institute in 1963, Plotkin began studying the rubella virus. The rubella virus caused a common but often mild disease that caused rashes and flu-like symptoms in those infected. However, pregnant women infected with the rubella virus could pass the virus to their fetuses, who got congenital rubella syndrome. Congenital rubella syndrome can lead to miscarriage or birth defects in the heart, brain, eyes, and ears of the fetus. In 1963, an epidemic of rubella and congenital rubella syndrome broke out in Europe. In 1964 and 1965, the epidemic spread to the United States, causing birth defects in thousands of infants. After that epidemic, many researchers, including Plotkin, accelerated the development of a vaccine for rubella. According to Plotkin, he realized the importance of preventing rubella in pregnant women to prevent congenital rubella in their fetuses and the subsequent birth defects in infants.

Throughout the 1960s, Plotkin strove to develop a vaccine for rubella at the Wistar Institute. Plotkin built upon work conducted by virologists Thomas Huckle Weller and Franklin Allen Neva as well as Paul Douglas Parkman, all of whom isolated strains of the rubella virus in 1962 in the US. In the early 1960s cell biologists Leonard Hayflick and Paul Moorhead at the Wistar Institute developed the WI-38 strain, a human cell strain created using aborted fetal tissue. WI-38 cells, named after the Wistar Institute where they were developed, were among the first non-cancerous human cells that could be maintained for long periods of time without substantial degradation, making them well-suited for laboratory research. Using WI-38 cells, Plotkin cultured a new strain of the rubella virus called RA 27/3, a weakened strain of the rubella virus, which he and his research team then used to create a rubella vaccine in 1969.

However, Plotkin was not the only one to create a rubella vaccine. In 1968 at a National Institutes of Health conference, several rubella vaccine developers debated which of four possible vaccines was the best candidate for further production. Of the proposed vaccines, only Plotkin's had used diploid human cells while other laboratories had used cells from ducks, dogs, and rabbits. Diploid human cells, like the WI-38 cells Plotkin used, have the same number of chromosome pairs as typical human body cells. Plotkin argued that diploid human cells were a better medium for growing weakened virus strains for vaccines because they better represented the human cells to be vaccinated.

Plotkin's primary opposition at the conference was Albert Sabin, who had successfully created an oral polio vaccine, similar to Koprowski's, that was widely used in the Soviet Union. Sabin objected that vaccines developed with human cells, like WI-38, contaminated vaccines with cancer causing viruses, a common theory at the time. Plotkin countered that there was not sufficient evidence to indicate such danger. He further asserted that Sabin's objections came from religious, not factual, reasons due the origins of the WI-38 cells in aborted fetal tissues. Plotkin's arguments convinced his colleagues of the benefits of his RA 27/3 rubella vaccine, eventually convincing Sabin himself. In 1969, Plotkin published his experimental results about his rubella vaccine, which became available for public use shortly thereafter.

After advocating for his rubella vaccine, Plotkin continued to balance his study of viruses and vaccines with his medical career. In the late 1960s, Plotkin collaborated with Koprowski and Tadeusz Wiktor at the Wistar Institute to create a vaccine for rabies, which became licensed for public use beginning in 1980. Plotkin also continued teaching pediatrics at the School of Medicine at the University of Pennsylvania where he remained a professor until 1991. In 1972, Plotkin became the director of the infectious disease department as well as a senior physician in pediatrics at the Children's Hospital of Philadelphia, where he remained for decades to follow. In addition to his vaccine research, Plotkin became a professor of virology at the Wistar Institute in 1974. In 1980, Plotkin married Susan, the coordinator of the pediatric AIDS Program at the Children's Hospital of Philadelphia. The couple had two children, Michael and Alec.

Throughout the 1980s, Plotkin continued to develop vaccines for infectious diseases. In the early 1980s, Plotkin created several experimental vaccines for chickenpox, caused by the varicella virus, though those vaccines never made it to public production. In 1988, Plotkin published the first edition of *Vaccines*, a textbook detailing the history, theory, and creation of vaccines. The US National

Foundation for Infectious Diseases in Bethesda, Maryland, considered Vaccines, in its sixth edition as of 2013, to be the authoritative textbook in the field of vaccinology. Plotkin continued to seek out new vaccines, and in 1988, he published a paper for a preliminary vaccine for rotavirus, which causes severe diarrhea in infants and young children.

In 1991, a private vaccine company, Pasteur Mérieux Connaught Vaccines, offered Plotkin a position as the company's medical and science director. Plotkin accepted and relocated to Paris, France, with his family later that year. In 1997, he returned to the US as a consultant for the multinational vaccine producer, Aventis Pasteur, later called Sanofi Pasteur, headquartered in Lyon, France. In 2006, Plotkin, collaborated with vaccine researchers Fred Clark and Paul Offit in the US to create a rotavirus vaccine, which they called RotaTeq, based on research Plotkin had started nearly twenty years earlier. Also that year, at the age of 74, Plotkin learned to pilot an airplane, fulfilling his earlier ambition.

Plotkin received many awards for his work as a physician and medical researcher. For his contributions to preventative medicine, in 1987, the American College of Physicians awarded Plotkin the Bruce Medal, and in 1993, the Pan American Group for Rapid Viral Diagnosis presented him with the Clinical Virology Award. In 1998, Plotkin also received the French Legion Medal of Honor. To honor his scientific work in vaccines and combatting infectious diseases, Plotkin received the Sabin Foundation Medal in 2002, the Maxwell Finland Award in 2009, and the Hamdan Award Medical Research Excellence in 2014.

Although retired, in the second decade of the twenty-first century, Plotkin consulted on issues of vaccines and remained involved with infectious disease and vaccine research, particularly for cytomegalovirus, which can cause infants to be born with abnormalities. He was a professor emeritus at the University of Pennsylvania and at the Wistar Institute.

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