The Measles, Mumps, and Rubella (MMR) Vaccine [1]

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In 1971 Maurice Hillemanat at the Merck Institute of Therapeutic Research, a pharmaceutical company in West Point, Pennsylvania, created the measles, mumps, and rubella (MMR) vaccine. The vaccine combined three separate vaccines for measles, mumps, and rubella, common and sometimes fatal diseases. Measles causes a red skin rash and severe fevers that can be fatal. Mumps causes fever and swelling of the salivary glands in the mouth and jaw, while rubella causes milder fevers and skin rashes. Pregnant women that contract rubella sometimes pass the virus to their fetuses, causing congenital rubella syndrome, which results in malformations of the eyes, ears, heart, and brain in the fetuses. The MMR vaccine has protected millions of people from contracting the potentially deadly diseases of measles, mumps, and rubella, as well as prevented the development congenital rubella syndrome in the fetuses.

Hilleman developed the MMR vaccine while working in the vaccine research laboratories at Merck. There, Hilleman created forty different vaccines over his career. During his time at Merck, Hilleman created the vaccines for both measles and mumps, which he later incorporated into the MMR vaccine. He developed his first measles vaccine in 1963 and a subsequent improved version of that vaccine in 1968. In 1967, Hilleman developed his mumps vaccine using samples of mumps virus which he isolated from his five-year-old daughter, Jeryl Lynn Hilleman, who had contracted the mumps. Though Hilleman created a rubella vaccine himself in 1969, he used the rubella vaccine developed that year by Stanley Plotkin at the Wistar Institute, in the MMR vaccine instead.

Plotkin used human fetal cells to develop his rubella vaccine, whereas Hilleman had used animal cells in his rubella vaccine. Using human cells rather than animal cells enabled Plotkin to develop a rubella vaccine that was better adapted to protect against the disease in humans [2] and produced fewer negative side effects after vaccination.

When a virus infects an individual, that individual's immune system begins to make antibodies specific to that virus to combat the infection. Antibodies are proteins that recognize and bind to the specific chemical signatures of the virus, marking the virus as a target for removal by the other parts of the immune system. Even after the immune system eliminates the infection, the antibodies remain to protect against future similar infections. The immune system continues to produces those antibodies, providing immunity from, or protection against, future infections from the same type of virus.

The MMR vaccine contains within it small amounts of attenuated (weakened) or inactive viruses, which are not infectious. Even if the virus is inactive or attenuated, the immune system still responds as if the virus were active. Because the virus is inactive or attenuated, the virus does not cause a full-strength infection with accompanying symptoms. However, the immune system still produces the same antibodies that it would if it were a full-strength infection. When an individual vaccinated with the MMR vaccine encounters the full-strength version of the virus, the antibodies specific to measles, mumps, and rubella provide immunity against those viruses, meaning they prevent infection. By exposing individuals to a mild version of viral infections, the MMR vaccine gives the immune system an opportunity to build defenses against weaker measles, mumps, and rubella infections before it encounters the full-strength viruses.

When the MMR vaccine was developed in 1971, it did not protect against measles, mumps, and rubella in a new way. Instead, it was a combination vaccine, a vaccine that contained the ingredients of multiple other vaccines, specifically vaccines against measles, mumps, and rubella. With combination vaccines, physicians could immunize against multiple diseases with a single injection rather than multiple vaccinations over time. Combination vaccines enabled quicker and more thorough vaccination coverage in the public. As a combination vaccine, the MMR vaccine contains attenuated viral material from measles, mumps, and rubella viruses. Each dose of the MMR vaccine became typically administered via injection, often in the upper part of recipient's arm, resulting in few, if any, side effects from the MMR vaccine. The most common side effects are minor and include mild fevers or rashes. In rarer cases, about one in every 3,000 people receiving the vaccine, the MMR vaccine could cause temporary joint pain or stiffness in teens or adults, as well as high fevers that may lead to seizures.

Though a single dose of the MMR vaccine protects against contracting measles, mumps, and rubella, it is most effective after two doses of the vaccine spread out over time. The second dose of the MMR vaccine is more than a booster to immunity gained from the first dose. Instead, the second dose helps to produce immunity in individuals that did not receive it from the first dose. A single dose of the MMR vaccine imparts immunity against measles in about 93 percent of recipients, mumps in about 78 percent of recipients, and rubella in about 90 percent to 95 percent of recipients. The second dose increases immunity against measles to about 97 percent, against mumps to about 88 percent of recipients, and against rubella to over 99 percent. However, even after two doses, there may still be a small portion of recipients that do not obtain immunity against rubella.

By the end of the twentieth century, the US Centers for Disease Control and Prevention (CDC), headquartered in Atlanta, Georgia, recommended that children receive their first dose of the MMR vaccine between twelve and fifteen months of age.

They encouraged parents to wait until after a child's first year to begin vaccination because until about that time children retain passive protection against measles, mumps, and rubella from antibodies passed to them from their mothers. Those antibodies destroy any measles, mumps, or rubella viruses, including those present in the MMR vaccine, rendering the vaccine ineffective in producing immunity. After the first year, the mother's antibodies are no longer present in the child, but the child's immune system cannot produce those antibodies itself, leaving the child unprotected against infection from measles, mumps, and rubella and ready for immunization with the MMR vaccine. The CDC suggested that children receive their second dose between ages four and six, although children could receive their second does MMR vaccine as early as twenty-eight days after receiving their first does without negative effects on health or disease immunity.

Though medical personnel widely used the MMR vaccine to better promote individual and public health, concerns later arose over the safety of administering the vaccine. In 1998, the medical journal *The Lancet* published an article in which Andrew Wakefield and his colleagues in the UK claimed that there was a causal link between the MMR vaccine and autism spectrum disorders. That publication sparked much public speculation and debate about the safety of vaccines like the MMR vaccine, particularly those that contained thimerosal. Thimerosal is a mercury-based preservative included in many vaccines to prevent microbes from contaminating the vaccines.

People were concerned that thimerosal, a mercury-based preservative included in many vaccines to prevent microbes from contaminating them, caused increased rates of autism spectrum disorders in the US. In response to growing public concerns, the United States Congress held hearings to debate the effects of thimerosal in vaccines and any possible links to autism spectrum disorders. The Congressional reports from those hearings called for federal health agencies to determine the impact mercury-based compounds on individuals' health.

However, multiple studies conducted and reviewed by the Institute of Medicine, now called the National Academy of Medicine in Washington, D.C., and the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, demonstrated that there is no link between vaccines or thimerosal and autism spectrum disorders. From 2003 to 2015, there were at least nine studies conducted or funded by the CDC investigating the relationship between thimerosal in vaccines. None of those studies found any evidence to support the claim that thimerosal caused autism spectrum disorders. Studies conducted by the Institute of Medicine in 2004 and 2011 further disconfirmed that vaccines containing thimerosal caused autism spectrum disorders. In 2013, a CDC study concluded that there was no evidence that vaccines, in particular the MMR vaccine, caused and autism spectrum disorders. Thorough and repeated research has demonstrated that the MMR vaccine is not only safe for use, but also highly effective in preventing against potentially deadly diseases. In 2010, *The Lancet* retracted Wakefield's 1998 paper due to incorrect statements contained within.

The MMR vaccine has prevented deaths and defects caused by childhood diseases. Of the diseases that the MMR vaccine protected against, measles was the deadliest. In the early part of the twentieth century, records reported an average of 6,000 deaths per year in the US due to measles. In the ten years before the advent of measles vaccines in 1963, an estimated 3.5 million people in the US contracted the disease each year. After the introduction of the MMR vaccine in 1971, the number of cases in the US dropped to between 22,000 and 75,000 cases per year. By the mid-1980s, the number of US measles cases had decreased to fewer than 4,000 cases per year. Since its licensing in 1971, the MMR vaccine has prevented millions of cases of rubella in children as well as pregnant women, further preventing malformation in the fetuses of rubella-infected mothers due to congenital rubella syndrome. Later, a CDC study of vaccinated children born between 1994 and 2013 estimated that the MMR vaccine prevented nearly 150 million cases and over 57,000 deaths from measles, mumps, and rubella. Furthermore, the CDC estimated between 1999 and 2004, when the World Health Organization, headquartered in Geneva, Switzerland, increased global efforts to vaccinate people against measles, they likely prevented about 1.4 million deaths.

Worldwide, medical personnel administered more than 500 million doses of the MMR vaccine between 1999 and 2006. In that time, the use of the MMR vaccine has improved the health of children and women by preventing measles, mumps, and rubella and preventing congenital rubella syndrome in the fetuses of pregnant women.

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Subject

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Topic
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Publisher
Arizona State University. School of Life Sciences. Center for Biology and Society. Embryo Project Encyclopedia.

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Format
Articles [28]

Last Modified
Wednesday, July 4, 2018 - 04:40

DC Date Accessioned
Thursday, March 30, 2017 - 21:28

DC Date Available
Thursday, March 30, 2017 - 21:28

DC Date Created
2017-03-30

DC Date Created Standard
Thursday, March 30, 2017 - 07:00

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