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In Unvaccinated Children, Measles Cripples Immune Protection

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Measles infection can cripple the body's ability to remember viruses and bacteria for the long term, according to two investigations into the immune systems of unvaccinated children. This "immune amnesia" can leave individuals more vulnerable to future viral or microbial infections, even those they have encountered before, for months.

Based on these findings, published Oct. 31 in [*Science*](https://science.sciencemag.org/cgi/doi/10.1126/science.aay6485) and [Science Immunology](http://immunology.sciencemag.org/lookup/doi/10.1126/sciimmunol.aay6125), the researchers emphasize once more the need for widespread vaccination against measles, which affects seven million people annually worldwide, causing more than 100,000 deaths. Their studies highlight the importance of the vaccine not just in curbing infection, but also in preventing more severe consequences of the infection, like the debilitation of "herd immunity" to other kinds of pathogens.

"Many people today who have never seen measles think that measles just causes a skin rash and fever, but underneath, measles is decimating large fractions of crucial protective immunological memory, placing children at risk for all other infectious diseases," said Michael Mina, assistant professor of epidemiology at the School of Public Health at Harvard University and first author of the paper published in Science.

Nearly every child experienced measles infection before the introduction of the first measles vaccine in 1963. Wherever the vaccine was implemented, a 20% to 50% reduction in childhood deaths followed. Between 2000 and 2017, the measles vaccine helped lead to an 80% reduction in measles cases, saving an estimated 21.1 million lives.

As is the case with many infectious diseases, limited access to vaccines continues to drive persistence of measles in under-resourced populations around the world. In recent years, antivaccination campaigns and the rise of nonvaccinating religious communities have contributed to a resurgence of measles infection even in areas of the world where the vaccine is readily available. Since 2018, reduced vaccination alone has led to a nearly 300% increase in measles cases.

The two Science studies grew from a clinical study of a 2013 measles epidemic that spread across populations of orthodox Protestants in the Netherlands. Dutch orthodox Protestants are a religious minority consisting of about 250,000 individuals representing denominations that separated from the Dutch Reformed Church, the formerly dominant Protestant group until the 1930s. The community leaves the decision to vaccinate to its individual members, and certain denominations can have either high, medium or low vaccination rates.

The measles epidemic in this community afforded an opportunity for scientists to collect samples from unvaccinated individuals infected with the virus. Rik de Swart, associate professor of bioscience at Erasmus University Medical Center in the Netherlands, collected blood samples from 77 four- to 17-year-old unvaccinated children in the community before and after measles infection, with the consent of their parents. According to de Swart, the participation level in the study was relatively high, and most parents were very involved.

"In general, the orthodox Protestant community [in the Netherlands] does not mistrust science, nor do they have confidence issues with the efficacy or safety of vaccines," said de Swart. He pointed to a [study](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3434025/) by Dutch scientists in 2012 that showed religious reasons, punishment by God according to their faith, and fear of making the wrong decision were the predominant factors preventing parents from vaccinating their children.

De Swart sent the samples he collected to Mina and his research team, as well as a second team of researchers that includes Velislava Petrova, a postdoctoral researcher at the Wellcome Sanger Institute and first author of the Science Immunology paper. Working with de Swart, the two teams explored the hypothesis that measles can suppress the immune system for months or years after the disappearance of visible symptoms like the characteristic measles rash. This hypothesis had already been supported by previous studies, including evidence that associates measles with up to 50% of childhood deaths from infectious diseases. However, the biological basis for this effect has remained unknown.

Mina and his colleagues used a tool called VirScan, developed by two of the Science study's authors, Stephen Elledge, professor of genetics and medicine at Harvard Medical School, and Tomasz Kula of Brigham and Women's Hospital in Boston, to analyze the responses of virus-neutralizing antibodies in the children before and after measles infection. Tracking tens of thousands of antibodies to thousands of viral and microbial proteins in the blood, the researchers found that measles wiped out 11% to 73% of the antibody repertoire across individuals two months after infection, severely compromising immune memory even after recovery.

"We had envisioned that there would be loss of antibodies," said Mina. "However, we did not think that in some children the loss would exceed 50% of their overall pre-existing immune memory." Antibody depletion was not observed in infants vaccinated against measles, mumps and rubella, they found.

Using the same blood samples, Petrova and colleagues sequenced antibodies produced by B cells — one of the primary immune cells able to recognize a virus and deploy attacks against it — from the unvaccinated children before and after measles infection. Their data indicated immune suppression by measles in two ways: incomplete repopulation of the B cell pool and reduction of B cell clones, which led to compromised B cell immune memory of measles.

Both teams hope to continue exploring this research question for a longer time period in unvaccinated populations. "The biggest limitation is that we only were able to evaluate the immune memory response over two to three months following measles," said Mina. In macaque studies conducted by his team, more than 50% of the antibodies were still missing five months after measles recovery with no hint of returning, Mina noted, suggesting that "immune amnesia" may last longer than two to three months."

"This work lends much needed biological evidence that measles has longer lasting and more devastating effects on immunity that we previously recognized," said Mina. "I think the idea that, if a child gets measles they may be at increased risk to all other infectious diseases, should be a strong motivator for measles vaccines."