## What is 'immune amnesia?' This long-term side effect of measles is newly relevant.

Measles, one of the most contagious viruses in existence, can have devastating impacts, including deadly complications that arise years after the initial infection. Here's what we know.

As the United States sees an increase in measles cases-including 23 confirmed cases between December 1, 2023 and January 23, 2024, and seven more in Florida-the Centers for Disease Control and Prevention cautions that these outbreaks reflect a growing global threat.

Measles, known for its characteristic red rash, is caused by the morbillivirus virus, and is spread through the air. For every 10 unvaccinated people who are exposed to the virus, nine of them will get sick, making it one of the most contagious viruses in existence. Although most measles cases are mild, an infection can cause several potentially serious complications, including conditions that emerge months to years after the initial infection.

Before the introduction of the measles vaccine in 1963, the U.S. had an estimated three-four million cases every year, which resulted in roughly 48,000 hospitalizations, 400-500 deaths, and 1,000 cases of encephalitis. After the introduction of the vaccine, these numbers dropped by more than 99 percent.
"In a sense, we are victims of our own success, because when it's out of sight and out of mind, it's not considered a problem," says Luis Ostrosky, an infectious disease physician and epidemiologist at UTHealth Houston.

One of the major issues is that given how contagious measles is, preventing outbreaks requires that a very high percentage of people need to be vaccinated. As Camille Sabella, an infectious disease physician at the Cleveland Clinic, explains, unless a community has a very high rate of vaccination, "you are going to have outbreaks," he says. "It really has a way of finding the people who are susceptible."

Susceptible people include children who are too young to have received their first dose of the vaccine, immunocompromised people, who are ineligible for the vaccine, as well as children who have only received one dose; two doses are needed for maximum effectiveness.

## The risks of getting measles

Measles is characterized by a fever, cough, runny nose, red, watery eyes, and a bright red rash. People who are infected are contagious for up to four days before the onset of the rash, and for about four days after.

Although most people who get measles will make a full recovery, the disease "has significant morbidity associated with it, and significant mortality as well," Sabella says.

According to the CDC, one out of five unvaccinated people who get measles will need to be hospitalized. One out of every 20 children who get measles will develop pneumonia, which is the leading cause of death from measles in children. The other major risk is encephalitis-brain swellingwhich affects an estimated one out of 1,000 children within a week of being infected with measles.

A small number of people infected with the measles virus, may later develop a condition called subacute sclerosing panencephalitis (SSPE), which occurs when the virus infects the brain, where it remains dormant until it progresses to SSPE years later. SSPE is characterized by cognitive decline, behavior changes, issues with motor functioning-such as uncontrollable movements and seizuresand blindness.

In the later stages of the disease, patients may lose their ability to walk, or go into a coma. There is no cure for SSPE. "It is 100 percent fatal," says Rik de Swart, a virologist at Erasmus University Rotterdam, in the Netherlands. "It is really a terrible disease." For every 100,000 cases of measles, there will be between four and 11 cases of SSPE, with these case numbers rising to 18 for children who get measles before the age of one.

## Measles causes immune amnesia

In the decades following the introduction of the measles vaccine, the risk of dying in childhood dropped between 30 to 86 percent (depending on the country), far more than could be attributed to a decline in measles-related deaths.

Scientists discovered that the vaccine saved lives because in addition to measles protection, children were no longer dying from other common childhood infections, such as_diarrhea or respiratory illnesses.
"It has been known for decades that those who recover from measles become immunosuppressed," says Mansour Haeryfar, a professor of immunology at Western University in London, Ontario, and are much more vulnerable to dying from other unrelated infections.

Researchers figured out that although considered a respiratory virus-because it is spread through the air-the measles virus infects and kills the memory cells of the immune system, explains de Swart, who co-authored the paper which was published in Nature Communications in 2018.

These memory cells are responsible for recognizing and destroying pathogens it has encountered in the past. Once the virus destroys them, they are replaced with cells that predominantly recognize the measles virus. This enables the body to fight off another measles infection, but impairs its ability to recognize other common pathogens, such as the common cold or the influenza virus.

However, as de Swart notes, the good news is that this effect is not permanent. "It's not like you lose everything," de Swart says. "If you are given time, and you are not, at the wrong moment, exposed to the wrong pathogen, your system will restore to its normal self."

This immune amnesia is most pronounced in the months following a measles infection but can persist for years.

## The impact of measles on a concurrent pandemic

Given how measles can suppress the immune response, experts fear that an increase in cases will make future pandemics more severe.

In a 2021 study, researchers modeled the impact of lower measles vaccination rates on pandemics and found that relatively small drops in vaccination rates can make it harder to contain another pandemic due to immune amnesia.
"You can believe you have herd immunity, but because of a small effect of a lack of measles vaccination, you don't," says Miguel Muñoz, a professor at the University of Granada, and one of the authors of the 2021 paper. "The results can be dramatic."

## How effective is the measles vaccine?

The measles vaccine, which is administered in two doses-the first between the ages of 12 and 15 months and the second between years four and six-offers long-lasting protection against infection.

One dose of the vaccine is about 93 percent effective at preventing infection; two doses provide 97 percent protection, which lasts a lifetime.
"It is one of the most effective vaccines that we have available to us," Ostrosky says. "We only very rarely need to revaccinate someone." For those people who aren't sure about their vaccination status, their immunity against measles can be confirmed through laboratory testing, or in lieu of testing, they can receive another dose of the vaccine.

