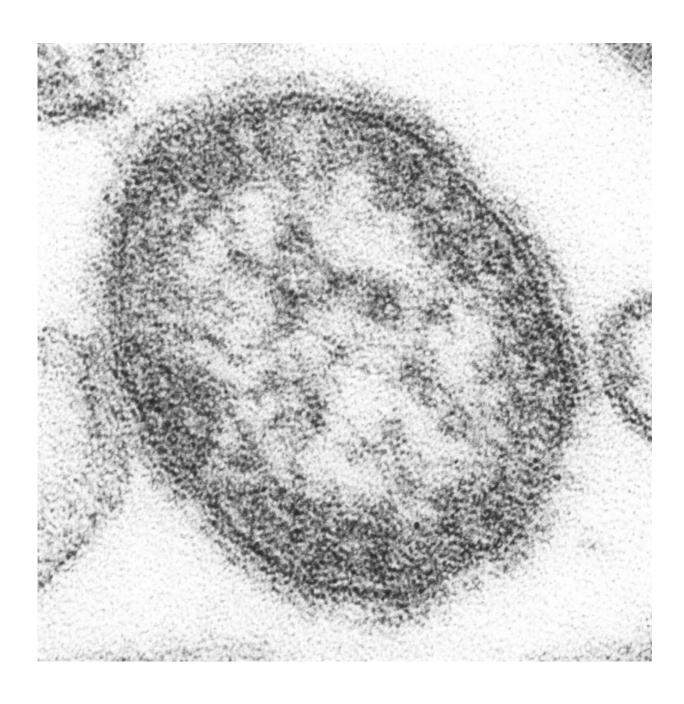


## Measles infection wipes our immune system's memory leaving us vulnerable to other diseases

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An electron micrograph of the measles virus. Credit: CDC/ Courtesy of Cynthia S. Goldsmith

Scientists have shown how measles causes long-term damage to the immune system, leaving people vulnerable to other infections. Researchers from the Wellcome Sanger Institute, University of Amsterdam and their collaborators revealed that the measles virus deletes part of the immune system's memory, removing previously existing immunity to other infections, in both humans and ferrets. Importantly, the team showed for the first time that measles resets the human immune system back to an immature baby-like state with only limited ability to respond to new infections.

Reported in *Science Immunology*, the study explains why children often catch other <u>infectious diseases</u> after <u>measles</u>, and highlights the importance of vaccination against measles. The research has great implications for <u>public health</u>, as falling vaccination rates are resulting in rising cases of measles, which could also cause an increase in cases of other dangerous infections such as flu, diphtheria or tuberculosis, even in people who were previously immune.

The measles virus causes coughing, rashes and fever, and can lead to potentially fatal complications including pneumonia and encephalitis—inflammation of the brain. Measles leads to more than 100,000 deaths per year worldwide in unvaccinated communities.

**Related:** Study details the mechanism and scope of measles-induced immune amnesia in the wake of infection



A highly effective measles vaccine was introduced into the UK in the late 1960s and in 2017 measles had been completely eliminated from the UK. However, measles is highly contagious and measles cases are rising again as the UK vaccination rate has dropped below the required level of 95 per cent of the population. This has lead to the UK losing its World Health Organisation (WHO) measles elimination status recently.

It is known that measles weakens the <u>immune system</u>, even after the initial <u>infection</u> has cleared, but it has not been known how. During a measles infection, people have fewer <u>white blood cells</u>, which protect the body against disease, and this is seen in the clinic as a low white blood cell count. However, after a few weeks, the patient's white blood cell count goes back up to previous levels and they have recovered from the measles, yet they are still much more susceptible to other infectious diseases.

To find out what measles does to the immune system, researchers looked at a group of non-vaccinated people in the Netherlands. Blood samples were first taken from healthy volunteers from this community, who were followed-up for repeat sampling after a measles outbreak in 2013.

The researchers sequenced antibody genes from 26 children, before and 40-50 days after their measles infection. The team discovered that specific immune memory cells that had been built up against other diseases, and were present before the measles virus infection, had disappeared from the children's blood. This would leave them vulnerable against infectious diseases they had previously been immune to.

Dr. Velislava Petrova, lead author from the Wellcome Sanger Institute and Cambridge University, said: "This study is a direct demonstration in humans of 'immunological amnesia', where the immune system forgets how to respond to infections encountered before. We show that measles directly causes the loss of protection to other infectious diseases."



Researchers then tested this 'immunological amnesia' directly in ferrets, showing that infection with a measles-like virus reduced the level of flu antibodies in ferrets that had been previously vaccinated against flu. These ferrets also had worse flu symptoms when infected with flu virus after the measles-like infection.

Professor Paul Kellam, an author on the paper from Imperial College London, and previously from the Wellcome Sanger Institute, said: "We showed that measles-like viruses can delete pre-existing flu immune memory from ferrets. Even after the ferrets had been successfully vaccinated against flu, the measles-like virus reduced levels of flu antibodies resulting in the animals becoming susceptible to flu infection again and experiencing more severe flu-like symptoms. This shows that measles could reverse the effects of vaccination against other infectious diseases."

The researchers also discovered that the <u>measles virus</u> resets the immune system to an immature state that can only make a limited repertoire of antibodies against disease. This means that measles makes it difficult for the immune system to respond to any new infections, increasing the risk of secondary diseases.

Professor Colin Russell, senior author from the University of Amsterdam, Netherlands, said: "For the first time we see that measles resets the immune system and it becomes more baby-like, limiting how well it can respond to new infections. In some children the effect is so strong it is similar to being given powerful immunosuppressive drugs. Our study has huge implications for vaccination and public health as we show that not only does measles vaccination protect people from measles, but also protects from other infectious diseases."

The study reveals that it is extremely important that everyone who can be vaccinated, is vaccinated, to prevent the resurgence of measles and other



diseases that we have developed immunity to in childhood or for which we vaccinate.

After measles, some children still show signs of immune suppression for up to five years although they appear healthy when their white blood cell counts are measured. This study shows how genetic techniques can reveal new mechanisms of disease that are undetectable using routine clinical tests, and that further research is needed to understand the full effects of measles.

Dr. Charlie Weller, Head of Vaccines at Wellcome, said: "Measles is highly contagious and its potentially devastating consequences are well known. This study finds that measles also has the potential to weaken our body's existing immune response to other diseases, leaving us vulnerable to infections. These findings further strengthen the vital role the MMR vaccine plays in public health and protecting us from deadly disease. It is yet another reminder of how important vaccines are as a vital resource in eliminating infectious disease."

More information: Science Immunology (2019). science.sciencemag.org/lookup/ ... 1126/science.aay6125

## Provided by Wellcome Trust Sanger Institute

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