

History

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American doctor, Thomas Peebles, was the first to isolate the measles virus, in 1954. In 1958, Sam Katz, MD, working with Thomas Peebles and other researchers tested the first vaccine. However, it caused measles symptoms (rash) in some cases.

John Enders and colleagues created the first licensed vaccine in 1963 (in the United States).



The modern-day measles, mumps and rubella (MMR) vaccine was created by Merck Vaccines in 1968.

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Sabin's OPV became very popular and remained the main method of polio vaccination because it was so easy to administer and it worked very quickly.

The IPV, however, retained one major advantage over the OPV: The killed viruses in IPV cannot revert to virulent forms as can the viruses in OPV. And in another respect, the two vaccines are basically the same: The IPV is as good as OPV in preventing polioviruses from spreading through the bloodstream.

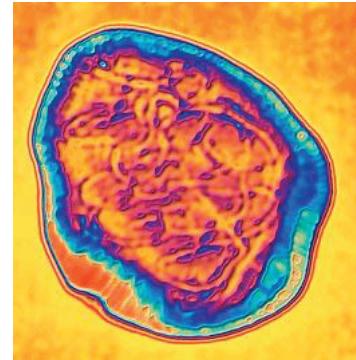
In 1997, an improved version of Jonas Salk's inactivated poliovirus vaccine began to be given to U. S. children instead of the OPV. An average of 8-10 cases of vaccine-derived polio per year were caused by the OPV (about one case per 2.4 million doses distributed)

By 2000, transition to an all-IPV schedule would be complete.

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Although the Persian physician Rhazes was the first to attempt distinguishing smallpox from the measles (in the year 900), Sydenham was the first to do so successfully and in detail (in 1676).

In 1757, Scottish physician Francis Home, MD, transmitted measles from infected patients to healthy individuals via blood, demonstrating that the disease was caused by an infectious agent



In 1916, French researchers Charles Nicolle, MD, and Ernest Conseil, MD, showed that measles patients have specific protective antibodies in their blood. The researchers then demonstrated that serum from measles patients could be used to protect against the disease.

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Measles

Measles is an extremely contagious disease caused by a virus from the paramyxovirus family and spread by air. Its symptoms include fever and coughing as well as its infamous rash. Typically, fever occurs before the measles rash; however, with the appearance of the rash, the existing fever may rise to temperatures of 104°F or higher.

These symptoms usually begin one to two weeks after infection with the measles virus; most people recover within two to three weeks. Complications are common (30% of the cases). It includes pneumonia or encephalitis. It can lead to death event in developed countries



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1951: Jonas Salk and his team developed a method of cultivating poliovirus in monkey kidney tissue.

1952: Salk and team began its first tests on humans of their killed-virus polio vaccine.

1954: The Vaccine Advisory Committee approved a field test of Salk's inactivated polio vaccine (IPV). In all, over 1.3 million children participated in the trial.



1959: Albert Sabin forged a bond with Soviet health officials, who were interested in a cheaper alternative to Salk's vaccine. A massive vaccination campaign began, in which Sabin's oral polio vaccine (OPV) was fed to 10 million Soviet children.

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In Vienna, Karl Landsteiner, MD (1868–1943), and Erwin Popper, MD (1879–1955), announced that the infectious agent in polio was a virus.

Popper and Landsteiner deduced the viral nature of polio by carefully filtering preparations of spinal cord fluid from a person who had died of polio. The filters were known to trap bacteria. When Popper and Landsteiner injected the filtered preparations into monkeys, the monkeys developed polio. The researchers then concluded that an infectious particle smaller than bacteria caused the disease.



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British researcher Andrew Wakefield, along with twelve co-authors, published a paper in *The Lancet* claiming evidence of measles virus in the digestive systems of autistic children. Wakefield suggested a relationship between the MMR (measles, mumps and rubella) vaccine and autism. Vaccination rates in England dropped in response, from more than 90% to 80% or lower – well below the level required for herd immunity to measles.

In 2010, *Britain's General Medical Council* ruled that Wakefield had engaged in misconduct during the course of conducting and publishing the study. Subsequently, *The Lancet* formally retracted the paper; in May 2010, Wakefield was banned from practicing medicine in Britain.

Despite this and the lack of any evidence to support a link between vaccines and autism, some groups remain convinced of the allegations first raised by Wakefield in 1998.

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Poliomyelitis

Poliomyelitis (polio) is a highly infectious neurological disease, which, in severe cases, can cause paralysis. It is transmitted between people through contact via nasal and oral secretions, or contact with contaminated feces. The virus enters through the mouth and multiplies throughout the digestive tract.

There are three types of polio, each with different symptoms:

1/ *Abortive polio* is the mildest form. Symptoms include viral-like symptoms such as fever, fatigue, headache, sore throat, nausea and diarrhea.

2/ *Non-paralytic polio* involves the same symptoms as abortive polio, but with additional neurological symptoms such as sensitivity to light and neck stiffness.

3/ *Paralytic polio* is the most severe form, beginning with virus-like symptoms, progressing to loss of reflexes, muscle pain and spasms, followed by paralysis. Fewer than 1–2 % of people with the disease are paralysed.

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Pasteur attenuated the bacteria for use in the vaccine.

He happened upon the method of attenuation by accident: in his lab, he was studying fowl cholera by injecting chickens with the live bacteria and recording the fatal progression of the illness. He had instructed an assistant to inject the chickens with a fresh culture of the bacteria before a holiday. The assistant, however, forgot. When the assistant returned a month later, he carried out Pasteur's wishes. The chickens, while showing mild signs of the disease, survived. When they were healthy again, Pasteur injected them with fresh bacteria. The chickens did not become ill. Pasteur eventually reasoned the factor that made the bacteria less deadly was exposure to oxygen.



Louis Pasteur produced the first laboratory-developed vaccine: the vaccine for chicken cholera (*Pasteurella multocida*).

Quotation from www.historyofvaccines.org

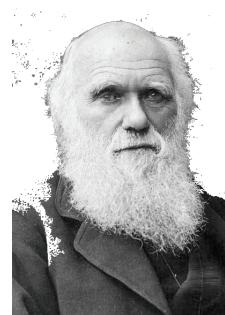
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www.chemheritage.org

The attenuation of pathogens did challenge the theory of evolution presented by Darwin: Do the attenuated pathogen belong to the same species as the virulent one? How could this new feature be selected? In the point of view of Pasteur, the theory of Lamarck could explain better attenuation (triggered by environmental changes) than the theory of Darwin.



Jean-Baptiste de Lamarck
1744-1829

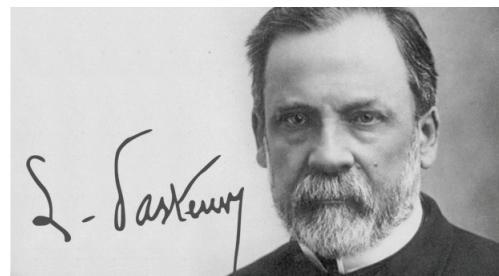


Charles Darwin
(1809-1822)

In the early 1870s Pasteur had already acquired considerable renown and respect in France, and in 1873 he was elected as an associate member of the "Académie de Médecine". Nonetheless, the medical establishment was reluctant to accept his germ theory of disease, primarily because it originated from a chemist. However, during the next decade, Pasteur developed the overall principle of vaccination and contributed to the foundation of *immunology*.

Encyclopædia Britannica

Pasteur used the term vaccine for disease others than smallpox. The French word "vaccine" was used for the first time in 1880 by Pasteur presenting his results on Avian cholera



Louis Pasteur (1822-1895)

Synonyms : Fowl cholera or *avian pasteurellosis* or avian hemorrhagic septicemia or chicken cholera. Avian cholera has been recognized as a distinct disease associated with domestic fowl for more than 200 years.

Epizootics occurred through the 1800s in domestic birds across several European countries, including France, Bohemia, Austria, Russia, Italy, and Hungary

Outbreaks are commonly associated with dense concentrations of susceptible birds and can involve hundreds to thousands of birds of many species.

Even in large epizootics with extensive mortality, it is uncommon to observe sick birds. They often have been observed in apparent good health the day prior to death.

<https://www.pasteur.fr/fr/institut-pasteur/l-histoire/louis-pasteur/l-oeuvre-louis-pasteur/troisieme-epoque-1877-1887>



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Everywhere, vaccination is encouraged (in Europe and in the United States) over variolation

"It is inconsistent for a government to encourage vaccination and not forbid inoculation" (Dr Jean de Carro, 1802)

1805: First compulsory vaccination attempted in France

Marianne Elisa of Lucca (Napoleon's sister) became the first ruler to try making vaccination compulsory. She was unable, however, to determine a practical method of enforcement.

1853: Vaccination Act in England

The *Vaccination Act* of 1853 ordered mandatory vaccination for infants up to 3 months old, and the Act of 1867 extended this age requirement to 14 years, adding penalties for vaccine refusal. The laws were met with immediate resistance from citizens who demanded the right to control their bodies and those of their children. The *Anti-Vaccination League* and the *Anti-Compulsory Vaccination League* formed in response to the mandatory laws, and numerous anti-vaccination journals sprang up.

Quotation from www.historyofvaccines.org

Edouard Jenner, a young English doctor learned from a milkmaid that she believed herself protected from smallpox because she had caught cowpox from a cow



Edward Jenner (1749-1823)

Quotation from www.historyofvaccines.org

First test

Edward Jenner tested the hypothesis that infection with cowpox could protect a person from smallpox infection. Jenner inoculated eight-year-old James Phipps with matter from a cowpox sore on the hand of milkmaid Sarah Nelmes. Phipps suffered a local reaction and felt poorly for several days but made a full recovery. Few months later, Jenner inoculated Phipps with matter taken from a fresh human smallpox sore, as if he were variolating the boy, in an attempt to challenge the protection from cowpox. Phipps remained healthy. Jenner next demonstrated that cowpox matter transferred in a human chain, from one person to the next, provided protection from smallpox.

Jenner's Inquiry published

After the Royal Society rejected his report of his achievement, Jenner self-published a pamphlet called *An Inquiry into the Causes and Effects of the Variolæ Vaccinæ, a Disease discovered in some of the Western Counties of England, particularly Gloucestershire, and known by the name of the Cow Pox*. It outlined Jenner's success in protecting James Phipps from smallpox infection with material from a cowpox pustule, in addition to 22 related cases. Initially, the *Inquiry* received little attention. This changed when Henry Cline, an associate of Jenner living in London, used dried vaccine material provided by Jenner to demonstrate once again that vaccination with cowpox material prevented future smallpox infection. From this point on, word about the *Inquiry* quickly spread.

Quotation from www.historyofvaccines.org

Cow pox or *Variolæ vaccinæ*

Cowpox is an uncommon illness in cattle, usually mild, that can be spread from a cow to humans via sores on the cow. During an infection, dairy workers may have pustules on their hands. Sufferers can spread the infection to other parts of the body



Cowpox infections on cow
The Historical Medical Library
of The College of Physicians of Philadelphia

We know now that the cowpox virus belongs to the Orthopox family of viruses. Orthopox viruses also include monkeypox virus and variola viruses, which cause smallpox.

Quotation from www.historyofvaccines.org

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Immunization by inoculation of a virus

Variolation is a smallpox immunization technique once practiced in many locations worldwide. Variolation involved the *transfer of matter from a smallpox sore* into a cut in the skin of an uninfected person. The variolated person would generally experience a *local reaction* or mild form of the disease and thereafter be *immune to smallpox*. Variolation, however, carried the risk of severe infection and death.



Lady Mary Wortley Montagu
(1689–1762)

Quotation from www.historyofvaccines.org

On her return to London in 1721, Lady Montague had the surgeon, Charles Maitland, inoculate her daughter before the physicians of the Royal Court. This caught the attention of the Princess of Wales, who later had Maitland treat her own children. Because it was not just any mothers who had their children treated to prevent smallpox, but two aristocratic women, including the wife of the heir to the throne, this significantly publicized the new practice and its possibilities.

Maitland went on to perform experiments on orphans and on prisoners (who received full pardons for their risk) with the blessings of the English crown. Prisoners and orphans alike survived and proved immune to smallpox.

Despite the risks of infection from variolation, the number of cases of smallpox plummeted. The mortality rate in uninoculated children was 1:14, but 1:91 in children who had been inoculated. Thus variolation spread throughout Europe, spurred by the inoculation of many of Europe's ruling dynasties. In the United States, although happening independently and without a clear-cut aristocracy, the role requirement for a famous and respected public figure was similar (see box, "Cottoning to inoculations")

Quotation from MMD 2001; written by C. S. W. Koehler

1718: Variolation in Turkey

Lady Mary Montagu (1689–1762) had her son variolated in Constantinople by Dr. Charles Maitland. Lady Montagu, whose husband was ambassador to Turkey, had been disfigured by smallpox around 1715. She had heard about variolation upon her arrival in Turkey, and was anxious that her six-year-old son, Edward, have the procedure. She later wrote to a friend:

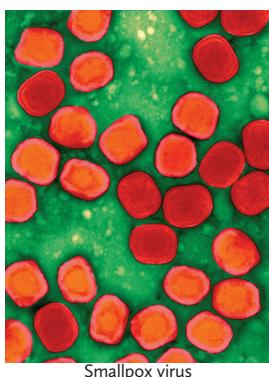
"I am going to tell you a thing that I am sure will make you wish yourself here. The small-pox, so fatal, and so general amongst us, is here entirely harmless by the invention of ingrafting, which is the term they give it. There is a set of old women who make it their business to perform the operation every autumn... The old woman comes with a nut-shell full of the mater of the best sort of smallpox, and asks what veins you please to have opened... She immediately rips open that you offer her with a large needle... and puts into the vein as much venom as can lie upon the head of her needle... Every year thousands undergo this operation... There is no example of any one that has died in it; and you may believe I am well satisfied of the safety of the experiment... I am patriot enough to take pains to bring this useful invention into fashion in England; and I should not fail to write to some of our doctors very particularly about it, if I knew any one of them that I thought had virtue enough to destroy such a considerable branch of their revenue for the good of mankind."

Lady Mary Wortley Montagu, *Modern History Sourcebook*

Symptoms of a typical smallpox infection began with a fever and lethargy about two weeks after exposure to the virus. Headache, sore throat, and vomiting were common as well. In a few days, a raised rash appeared on the face and body, and sores formed inside the mouth, throat, and nose. Fluid-filled pustules would develop and expand, in some cases joining together and covering large areas of skin. In about the third week of illness, scabs formed and separated from the skin.

About 30% of smallpox cases of the *Variola major* type ended in death, typically in the second week of infection. Most survivors had some degree of permanent scarring, which could be extensive. Other deformities could result, such as loss of lip, nose, and ear tissue. Blindness could occur as a result of corneal scarring. *Variola minor* was less severe and caused fewer of those infected to die.

The history of smallpox holds a unique place in human health and medicine. One of the deadliest diseases known to humans, smallpox is also the only disease to have been eradicated by vaccination.



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Quotation from www.historyofvaccines.org