

# New vaccines for global health

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Vaccination and provision of clean water have probably had more impact on global health than any other intervention. Since Edward Jenner's work in 1796, vaccination has saved millions of lives.

The approach developed by Jenner of using a harmless ("attenuated") organism to protect against a related but dangerous one underlies the success of the tuberculosis (BCG), measles and poliomyelitis vaccines used today.

The discovery of bacteria and their role in the causation of many major infectious diseases, such as tuberculosis, diphtheria, tetanus and typhoid, led to the development of several new vaccines. These vaccines were based on chemical inactivation of the toxins produced by these bacteria or on the use of whole bacteria that had been killed or attenuated in some way.

The development of vaccines against major viral diseases such as poliomyelitis and measles had to await the discovery of how to grow viruses in cell cultures before it was possible to provide sufficient quantities of virus to make vaccines to protect all the world's children.

Initially, vaccines were available only to children living in wealthy, industrialised countries and even in the 1960s, half of all children living in many developing countries died before reaching the age of five years, frequently from a vaccine-preventable disease. In the 1970s, the World Health Organisation set out to make established vaccines available to all children. This has been remarkably successful and currently about 75% of children receive the basic vaccines that they need. Recent successes include vaccination with hepatitis B which also leads to the prevention of hepatocellular cancer, a complication of hepatitis B infection, and the introduction of vaccines for human papilloma virus (HPV) holds great promise for the prevention of cancer of the uterine cervix.

Vaccination of livestock has also made a major contribution to global health. There is increasing recognition that the health of human and animal populations are intertwined (One Health). Recently a major success has been achieved with the eradication of rinderpest, an important infection of cattle which is closely related to measles.

Despite these successes, in most developing countries, infectious diseases are still responsible for the majority of childhood deaths. Pneumonia and diarrhoeal diseases are the most important causes of these deaths followed by malaria, tuberculosis and HIV. Use of vaccination to prevent diarrhoea and pneumonia has been complicated by the fact that many different bacteria and viruses can cause them. However, effective vaccines have been developed against *Streptococcus pneumoniae* (the pneumococcus), the most significant cause of severe pneumonia in young children, and against rotavirus, the most significant cause of diarrhoea.

In the cases of HIV and malaria, both organisms are able to vary the structure of key antigens which are the target of protective immune responses induced by vaccines, so that a vaccine that protects against one strain may not protect against others. The HIV virus is particularly adept at rapidly generating diversity. Development of vaccines against malaria is complicated because of the complex life cycle of the parasite which involves stages in the mosquito, the human liver and blood.

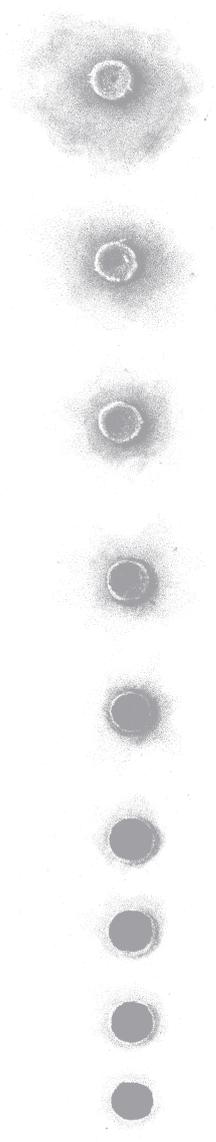
More recently, the frontiers of vaccinology have widened with attempts to develop therapeutic vaccines against cancer, chronic infections and other non-infectious diseases. For example, candidate vaccines to treat Alzheimer's disease, hypertension and even nicotine addiction are being explored

Every  
45 seconds

a child in Africa dies  
from malaria  
(World Health Organisation)

Main image - The vaccine vesicle from *A Treatise on the Cow-Pox...*, John Ring, 1803. From the Royal Society archive.

Archive image - Jenner's handwritten draft of the first vaccination. The original manuscript of Jenner's Inquiry is in the library of the Royal College of Surgeons.



Recent scientific developments could accelerate the development of new vaccines. The genomes of many important human and animal pathogens, including several strains of the most important ones, have now been sequenced. Modern genetic methods have made it possible to transfer genetic material from one organism to another. Thus, genetic material from a dangerous pathogen against which a vaccine is required can be transferred into a harmless carrier bacterium or virus which can then be used as a vaccine that induces the required immune response.

Many vaccines in current use need to be refrigerated. This poses problems for immunisation programmes in developing countries. One major advance would be the development of vaccines that could be stored at a high ambient temperature. Recent research has shown that it is possible to produce heat stable vaccines by mixing them with stabilising compounds and preserving them on glass fibre membranes.

Currently most vaccines are given by injection with a needle and syringe. This is a cumbersome process and carries a risk of spreading blood borne infections, such as hepatitis and HIV, if syringes are reused. Alternative approaches include oral administration, currently used for poliomyelitis vaccine, and nasal sprays used for some influenza vaccines. Some vaccines need to be injected so research is taking place on the use of tiny painless micro-needles, administered via a skin patch.

Technological advances should result in the development of several new vaccines within the next few years. However, these vaccines are likely to be more expensive. The global community must ensure that these new vaccines are available to the population of the developing world, who will benefit from them most, through supportive funding.

## From the archive

10. Caswell:  
The man, as usually to observe the  
of the infection, I selected a healthy  
not eight years old for the purpose  
and taken for the Cow-pox. The matter  
then from a suppurated sore on the  
of a young child, who was infected by  
antoin's Cow-pox, inoculated on the 14th of  
1796, into the arm of the Boy, by means  
of a fine needle, and about three  
lines of an inch long: on the 7th day  
found it surrounded with a white  
& disagreeable little itching, look-  
ing like a small red spot, and  
the whole of this day he was pruned  
with a feather, & had within a fortnight  
upon the day following, he was  
to walk. The appearance, and progress  
of the disease, as a state of inflammation,  
very much the same as that of the  
when managed by a cautious practitioner,  
the inflammation, I perceived was that  
of a suppurated rather a dark hue, and  
a suppurated cover, spreading round  
the sore, took on rather more of an  
oblong look, than an ordinary  
when a suppurated matter has  
the usual form of the cow-pox.

It is well known that Edward Jenner FRS was one of the first people to approach vaccination scientifically, in the late 18th century. However, less well known is that he was initially advised against publishing it – by none less than Sir Joseph Banks, the formidable President of the Royal Society. While this might seem like a terrible lapse of judgement on Banks' part, in fact he offered rather shrewd counsel to Jenner that his evidence was slim and he should perform more experiments before challenging accepted medical wisdom.

It was an era in which physicians might just as easily be accused of spreading disease by using such methods. Banks suggested that Jenner follow the example of the Royal Society's secretary James Jurin who had, a generation before, gathered and published data on smallpox inoculation for a decade, gradually accumulating evidence for the treatment's efficacy. Following this advice, Jenner's new treatment was first trialled in 1796 and by

1798 he was finally ready to publish the first in a series of papers: *Inquiry into the causes of and effects of the variolae vaccinae a disease... known by the name of cow-pox.*

Jenner's simple idea was to use one disease, cowpox, to protect against another, the more deadly smallpox. He had discussed the notion with the great London doctor John Hunter FRS during the 1770s and studied immunity linked to cowpox while practicing as a rural surgeon. By the time of Jenner's first vaccination, he was therefore reasonably sure of the likely successful outcome.

Even with Jenner's evidence, the widespread adoption of vaccination took quite some time, lasting into the mid-19th century. More than a century later, the critical importance of vaccination in global health was brought home by the complete eradication of smallpox – a medical triumph confirmed in 1980. Which disease will be next?