ARMING THE IMMUNE SYSTEM

In 1796, English physician Edward Jenner introduced the first vaccine, for smallpox, when he infected a young boy with cowpox. In the years since, vaccines — a name derived from the Latin word for cow — have been developed for many diseases, saving millions of lives. But the fight to conquer infectious disease continues.

By Neil Savage; infographic by Alisdair Macdonald

IMMUNE STIMULATION

Vaccines can be administered orally, nasally or by injection: into the muscle mass, into the layer between skin and muscle or into the outer layer of skin. They stimulate an immune response that gives the body the ability to mount a swifter defence to the same pathogen if it is encountered again.

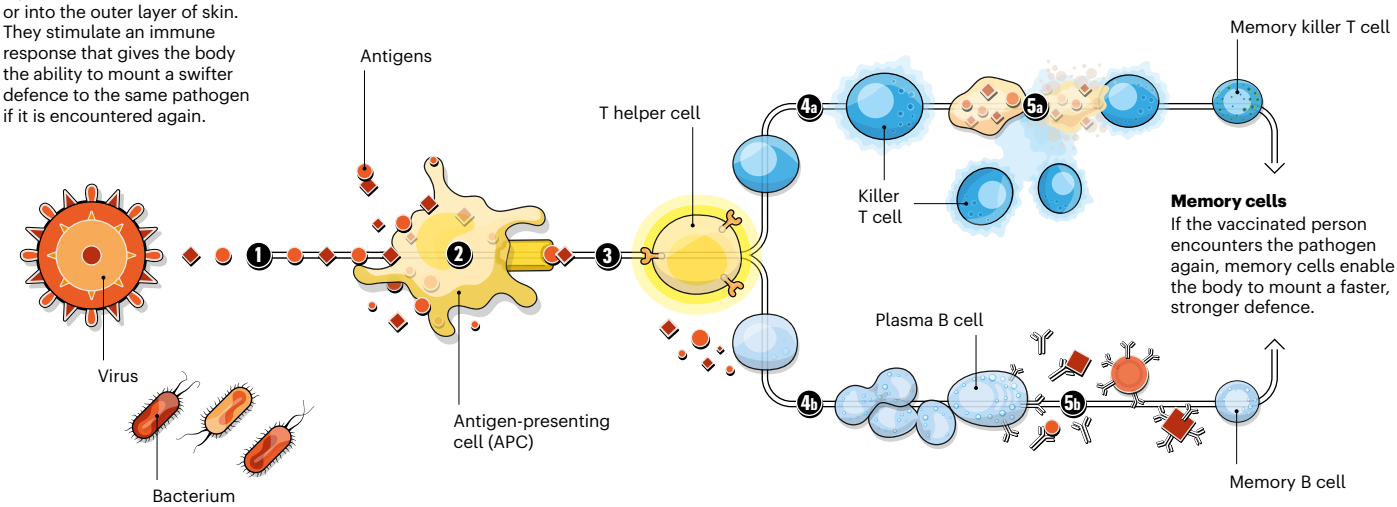
1. Antigens, often in the form of molecules on the surface of viruses or bacteria, are introduced into the bloodstream.

2. Antigen-presenting cells (APCs) capture and ingest the antigen, then display pieces of it on their surfaces.

3. APCs move to where immune cells cluster. They activate T helper cells, which trigger activity in killer T cells (4a) and the maturation of B cells (4b).

4a. Naive killer T cells become active killer T cells specific to the antigen.

5a. If the vaccine contains a live attenuated virus that infects cells, killer T cells will then target and destroy those cells.



Memory cells
If the vaccinated person encounters the pathogen again, memory cells enable the body to mount a faster, stronger defence.

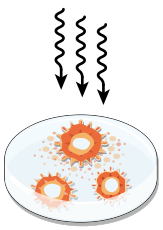
4b. Naive B cells, activated either by T helper cells or directly by antigens, become plasma B cells specific to the antigen.

5b. Plasma B cells produce antibodies that bind to antigens, preventing them from entering cells and marking them for destruction by killer T cells.

VACCINE VARIETIES

There are several types of vaccine in use, each with their own strengths and weaknesses. Many are administered along with adjuvants — substances such as aluminium salts, lipids and RNA that strengthen the immune response.

Inactivated vaccine

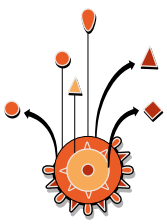


The pathogen is treated with heat or chemicals to kill it before it is introduced into the body.

- ▲ Easy to store and transport.
- ▲ Low risk of causing an infection.
- ▼ Elicits weaker immune response.
- ▼ May require several doses and boosters.

Examples: polio, hepatitis A, rabies

Subunit vaccine

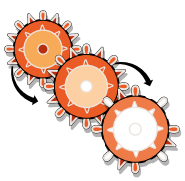


One or more parts of the pathogen, such as a protein, are isolated and used to evoke an immune response.

- ▲ Low risk of adverse reaction.
- ▲ Can be used in people with weakened immune systems.
- ▼ Can be difficult to manufacture.
- ▼ May require boosters.

Examples: hepatitis B, influenza, pertussis

Live, attenuated vaccine

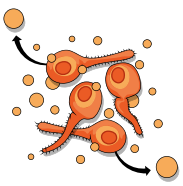


A virus is weakened, often by repeatedly passing it through a tissue culture in which it replicates poorly.

- ▲ Activates killer T cells.
- ▲ One or two doses can provide lifelong immunity.
- ▼ Must be refrigerated.
- ▼ Less safe for people with weakened immune systems.

Examples: measles, mumps, rubella, varicella, rotavirus

Toxoid vaccine



A toxin produced by the pathogen, instead of the pathogen itself, is deactivated and used to produce the immune response.

- ▲ Unable to cause disease or to spread.
- ▲ Stable, so easy to distribute.
- ▼ May require boosters to maintain immunity.

Examples: diphtheria, tetanus

IN DEVELOPMENT

DNA vaccine

DNA from pathogens, sometimes attached to another virus or bacterium, is used to generate an immune response.

In human trials for herpesvirus, influenza and Zika virus.

Recombinant vector vaccine

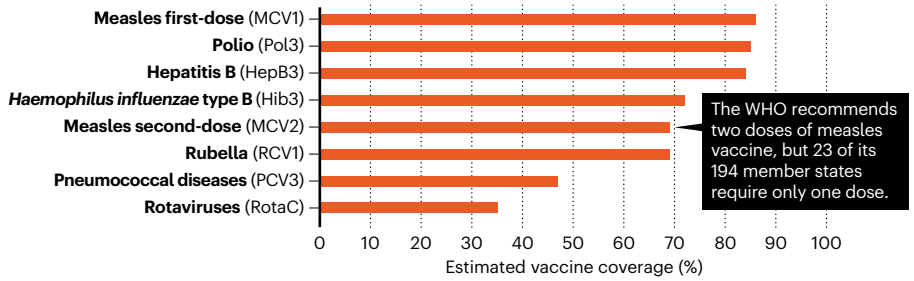
Live but harmless viruses are genetically engineered to express an antigen to a dangerous virus, which the immune system can target.

Being explored for Zika virus, HIV and Ebola.

BUILDING COVERAGE

Vaccines initially developed in the 1950s and 1960s, such as those for polio and measles, are commonly administered globally. Those introduced more recently, such as that for rotavirus, are less widely used.

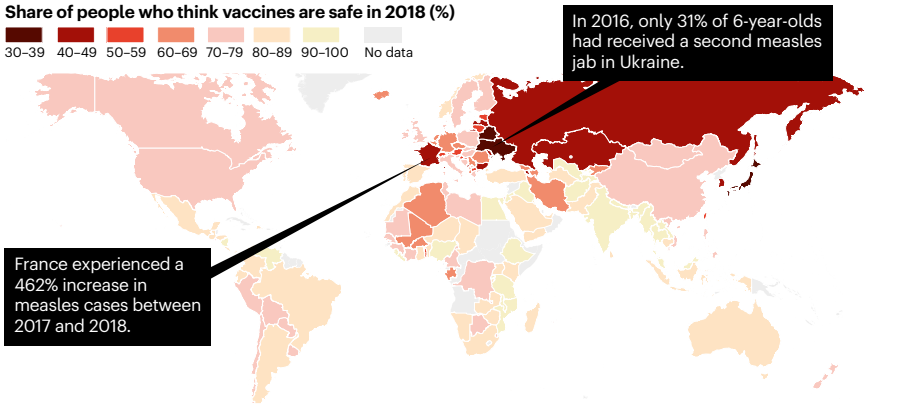
Global vaccine coverage in 2018



THE LUXURY OF HESITANCY

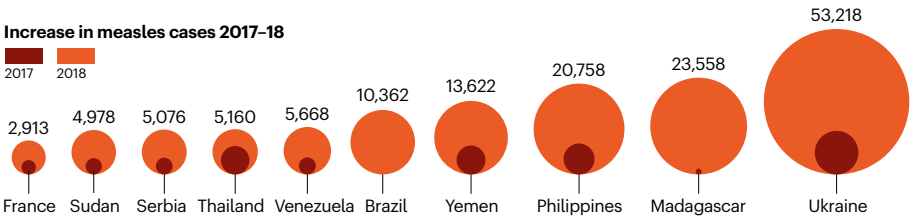
Although 79% of people globally think that vaccines are safe, trust varies widely between nations. Europe has some of the lowest levels of perceived safety — a finding that might partly explain the surge in measles cases seen in Ukraine in 2018. But other factors besides hesitancy to vaccinate also affect the spread of infections.

Share of people who think vaccines are safe in 2018 (%)



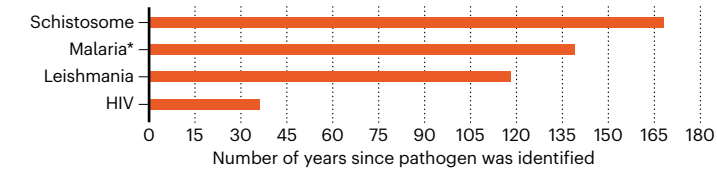
Nature publications remain neutral with regard to contested jurisdictional claims in published maps.

Increase in measles cases 2017–18



LONG ROAD TO NEW VACCINES

Development programmes are under way for a number of deadly diseases that currently lack a vaccine. In many cases, the pathogen responsible was identified decades ago, but effective vaccination strategies have proved elusive.

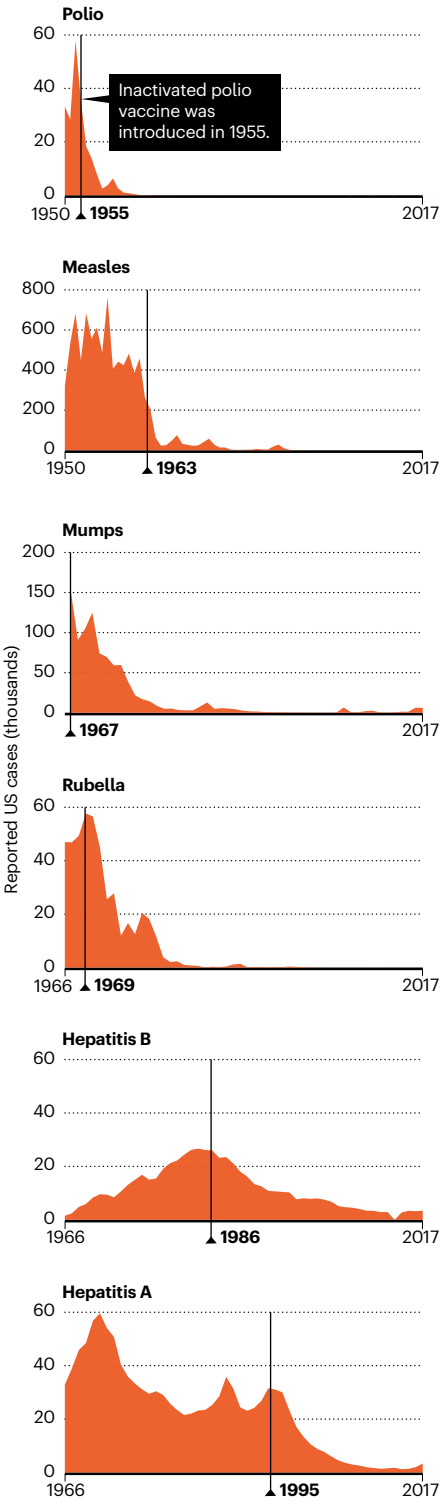


~1.5 MILLION deaths from these four diseases in 2016.

*A pilot study of a malaria vaccine began in three countries in 2019.

SAVING LIVES

Case numbers of certain infectious diseases in the United States dropped precipitously after effective vaccines for each were widely adopted.



SOURCES: Immune stimulation: WHO/CDC/www.historyofvaccines.org; Vaccine varieties: US Dept. Health & Human Services/www.historyofvaccines.org; Building coverage: WHO; The luxury of hesitancy: Gallup Wellcome Global Monitor 2018 (Wellcome, 2019); Long road to new vaccines: S. Vanderslott & M. Roser https://ourworldindata.org/vaccination (2019)/WHO; Saving lives: S. W. Roush *et al. J. Am. Med. Assoc.* **298**, 2155–2163 (2007)/CDC.