

THE IN A HURRY SERIES

Vaccines

in a Hurry

How they work and why they matter

Max Brocklesby

BOOKSINAHURRY.COM

Contents

The Whole Thing in One Page 4

Why You Should Care 5

The Core Ideas 7

How It Actually Works 21

What People Get Wrong 32

Use It 36

Terms 41

Go Deeper 45

Notes and Sources 46

Bibliography 53

The Whole Thing in One Page

A vaccine is often pictured as a shield: injection in, protection on. That picture is too solid. Pathogens enter, multiply and damage tissue on their own timetable. The adaptive response begins with a different problem. It must recognise what has arrived, find the rare cells able to respond, multiply them and produce enough useful antibodies and killer cells. During a first encounter, that can take days. A vaccine changes the starting line.

It presents a selected antigen, or instructions for making one, in a form designed to cause far less harm than the disease. Innate immune signals mark the material as worth attention. Antigen-presenting cells carry fragments to lymph nodes. Matching B cells and T cells are selected, multiplied and improved. Some become short-lived factories for antibodies or active effector cells. Others remain as memory. When the pathogen later appears, the response can begin with more suitable cells, better antibodies and less delay.

That is the common mechanism. The engineering varies. Live attenuated vaccines reproduce enough to resemble infection. Inactivated vaccines cannot replicate. Toxoids train against a bacterial toxin. Subunit and conjugate vaccines isolate useful targets. Viral vectors deliver genetic instructions inside another virus. Messenger RNA gives cells a temporary recipe for an antigen. No platform is best in the abstract. The right choice depends on the pathogen, the population, the immune response required, the acceptable risks, the manufacturing process and the conditions in which doses must travel.

Protection is not one outcome. A vaccine may prevent infection, reduce symptoms, sharply cut severe disease, shorten infectiousness or do several of these at once. It may work differently in infants, older adults and immunocompromised people. Its effect can wane, pathogens can change, and extra doses can restore or redirect protection. A claim such as 90 per cent effective means little until you ask: against what endpoint, in whom, compared with what, and for how long?

Safety also has two clocks. Trials can detect common effects and measure whether disease is prevented. Rare harms may become visible only after millions of doses, so surveillance continues. A report of illness after vaccination is evidence of sequence, not proof of cause. Investigators compare observed events with background rates, examine timing and biology, look across data systems and change recommendations when the balance differs by product or group. Confidence should rest on that process, not on pretending risk is zero.

Then comes the part hidden by the syringe. A useful vaccine must be manufactured consistently, released in sound batches, kept within suitable conditions, delivered on time, recorded, afforded and accepted. Individual protection can then become population protection if vaccination reduces transmission and susceptible people are not clustered together. Smallpox was eradicated because a vaccine was joined to surveillance and targeted delivery. Tetanus cannot be eradicated through community immunity because it does not pass from person to person. The biology sets the possibilities. The programme decides how much of them becomes real.

Vaccines matter because they let prevention arrive before the danger. Their greatest successes can push disease so far from daily life that the reason for vaccination fades, while the appointment, the sore arm and the disputed claim remain visible. Success can hide much of its own evidence. Failure returns in bodies.

That is the book.

Why You Should Care

In 1977, a hospital cook in Somalia developed smallpox. Ali Maow Maalin recovered, contacts were traced, and no later naturally occurring case was found. Three years afterwards, the World Health Assembly declared the disease eradicated. A virus that had killed, blinded and scarred people for millennia no longer circulated anywhere in humans. Medicine has cured many patients. Vaccination helped remove a human disease from the world.

That result was exceptional, but the scale beneath it is larger. A 2024 modelling study of fifty years of the World Health Organization's Expanded Programme on Immunization estimated that vaccination against fourteen pathogens had averted about 154 million deaths since 1974, most among children younger than five. The figure is a modelled counterfactual, not a count of named people. That is precisely why vaccine impact is hard to see. Prevention leaves no recovered patient, dramatic operation or bottle on the bedside table. It leaves a person who did not become ill and an outbreak that did not happen.

The effects also arrive in forms that the old image of childhood infection misses. Hepatitis B vaccination can prevent later liver cancer. Human papillomavirus vaccination prevents persistent infections that can become cervical and other cancers years afterwards. England's programme has already produced large reductions in cervical precancer and cervical cancer among cohorts offered vaccination, with the strongest effects in those offered it at ages twelve and thirteen. A dose given before exposure can alter a cancer statistic decades later.

The present frontier is not a single new technology. It is the widening range of problems to which the same logic can be applied. Messenger RNA made the speed of the COVID-19 response visible, but the platform rested on decades of work in RNA chemistry, delivery and immune signalling. Malaria made the opposite difficulty visible. A parasite with a complex life cycle, immense global burden and a talent for immune evasion resisted easy solutions. Two vaccines are now recommended by the WHO for children in endemic areas, as part of combined malaria control. A 46-month evaluation in Ghana, Kenya and Malawi, published in 2026, found that routine introduction of RTS,S was associated with a 13 per cent reduction in all-cause mortality excluding injuries among vaccine-eligible children. That was a delivered programme result in three settings, not a product-efficacy percentage. It shows why the vial and the programme cannot be separated.

You should care for a more personal reason too. Vaccine claims are unusually easy to state and unusually hard to interpret. A relative risk

reduction can be presented without the absolute risk. An adverse event report can be treated as a verdict. A trial result can be carried into another age group, variant or year. A vaccine that protects well against hospitalisation can be called useless because infections still occur. A recommendation can be discussed as though it were timeless, when schedules depend on local disease, age, pregnancy, health, previous doses and changing evidence.

This book will give you a way through those arguments without asking you to worship institutions or distrust them by reflex. You will learn what the immune system is being asked to remember, what each platform delivers, what the trial measured, what surveillance can establish, where population effects come from and where they do not. You will also see the limits: incomplete protection, real adverse effects, failed candidates, unequal access and the political cost of mistakes concealed or explained badly.

Vaccination is a technology whose proper unit is both a cell and a society. It changes molecular recognition inside one person, then may change the routes available to an infection across millions. Follow that chain and the subject becomes clearer, more interesting and harder to reduce to a slogan.

The Core Ideas

A Head Start, Not a Wall

For many vaccine-preventable diseases, the contest begins before the adaptive response is ready. One virus becomes many viruses; one bacterium becomes a population; a toxin reaches vulnerable tissue. Adaptive immunity also depends on multiplication, but it starts from a much smaller base. Among billions of lymphocytes, only a fraction recognise a useful target. Those cells must be found, activated and copied before they can matter.

This turns many infections into a race. The pathogen has the advantage of arriving first. The adaptive response has the advantage of being able to become more precise as it develops. During a first encounter, precision is

slow. Antigen must reach the right places. Matching B cells and T cells must receive enough signals to act. Antibody-producing cells must emerge. T cells able to coordinate or kill infected cells must expand. By then, a fast pathogen may have spread through tissue or triggered inflammation that continues even after its numbers begin to fall.

Vaccination moves the immune system forwards without requiring the full disease. It increases the number of relevant cells, improves the fit and function of some antibodies, and can leave antibodies already circulating. On later exposure, the body does not begin from ignorance. It may neutralise part of the incoming pathogen quickly, contain spread, clear infected cells sooner or keep the pathogen below the level at which severe damage becomes likely.

That explains why a vaccine need not prevent every infection to prevent many deaths. The nose or throat may be infected before circulating immunity can stop entry. Memory cells may still accelerate the response enough to protect the lungs, nervous system or other vulnerable tissue. Protection against infection, symptoms and severe disease can therefore differ. Calling the vaccine a wall encourages the wrong verdict: one detected infection becomes proof that the wall failed. The better question is how the encounter changed.

Rabies shows the timing model from the opposite direction. Vaccination can be useful after exposure because the virus usually travels slowly from the wound towards the nervous system. Wound care, rabies immunoglobulin where indicated, and a vaccine series can give immunity time to develop before the virus reaches its decisive site. This is post-exposure prophylaxis, not a reversal of established rabies once symptoms appear. The vaccine works because the race still has time left in it.

The model has limits. Some pathogens change their exposed targets. Some hide inside cells, persist, suppress immunity or establish themselves before a recall response can act. Some diseases are driven by toxins, so the useful target is the toxin rather than the bacterium. Some vaccines generate strong blood responses but weaker immunity at the mucosal surface where entry

occurs. Age, pregnancy, medicines and immune disorders can alter the response. The head start is designed, measured and conditional.

Keep the timing. A vaccine does not make exposure impossible. It changes what is waiting when exposure occurs, and therefore changes what the pathogen is able to do before the response catches it.

The Target and the Alarm

The immune system cannot remember “a disease” as a general idea. It encounters molecules. Vaccine design therefore begins with selection: which part of the pathogen, toxin or infected cell should be shown, in what shape, at what dose, and with what signals around it?

The selected material is the antigen. It may be an entire weakened organism, a killed organism, a purified protein, a sugar from a bacterial capsule, an inactivated toxin, or a protein made temporarily from delivered genetic instructions. Within that antigen are smaller features, called epitopes, that antibodies or T-cell receptors can recognise. The useful target must be accessible at the right moment and similar enough to the version encountered during infection. An abundant protein hidden inside a virus may be easy to manufacture yet poor for antibodies that must block entry. A surface protein may be promising until mutation alters it. A toxin may be a better target than the bacterium producing it.

Recognition alone is not enough. Immune systems evolved to distinguish danger and context, not to respond maximally to every harmless protein. A purified antigen can disappear with little consequence unless innate sensors and antigen-presenting cells treat the encounter as worth organising around. Live vaccines provide many of those signals through limited replication. Other vaccines use an adjuvant, a substance or formulation that strengthens or shapes the response. Aluminium salts have been used for decades. Newer adjuvants combine defined components to recruit and activate cells in more directed ways.

The useful distinction is target and alarm. The antigen says, “recognise this”. The surrounding context helps say, “pay attention, carry this to the lymph

node, and build a response of the needed kind". An adjuvant is not a general chemical irritant added to make the body suffer. Its value lies in improving antigen uptake, local signalling, cell recruitment or the quality and persistence of the response. A sore arm and fever can accompany innate activation, but discomfort is neither the aim nor a reliable measure of protection.

Route is part of the instruction. An injection into muscle usually builds strong systemic responses through nearby lymph nodes. Oral or nasal delivery can engage immune tissue closer to a pathogen's point of entry, but the material must survive mucus, enzymes and other barriers. The same antigen placed in a different site can produce a different balance of circulating antibodies, mucosal antibodies and resident cells. Where the vaccine goes is therefore part of what it tells the immune system to prepare.

Too much alarm can be harmful, and the loudest response is not always the best one. Protection against an extracellular toxin may depend heavily on neutralising antibodies. Protection against a pathogen living inside cells may require a stronger T-cell component. A response aimed at the wrong site or a non-protective epitope can look impressive in a laboratory assay while doing little against disease. In rare circumstances, a poorly shaped response can worsen later disease, which is why candidates are tested for the kind of immunity they induce, not only its size.

Age changes the design problem. Young infants have developing immune systems and may carry maternal antibodies that help protect them but can sometimes reduce responses to certain antigens. Older adults may respond less strongly or less durably. Polysaccharide capsules are difficult targets for young children when given alone. Conjugate vaccines solve that problem by chemically linking the sugar to a carrier protein, recruiting T-cell help and creating a stronger, more durable response. The bottle contains chemistry; the achievement is organisational.

This is why vaccine design cannot be reduced to copying a fragment of a pathogen. The target, its shape, its delivery and the immune context form one instruction. A vaccine succeeds when that instruction prepares the

response that the future encounter will demand.

Memory Is a Living Population

Immune memory sounds like a stored file. It is closer to a managed population. After vaccination, some cells die within days, some antibodies fall over months, some plasma cells continue secreting antibodies from bone marrow, and some memory B cells and T cells persist while changing in number and quality. Protection is the result of those moving parts, not a binary mark stamped into the body.

The process begins when rare matching cells are selected. Activated B cells can become plasma cells that release antibodies. With help from T cells, some enter germinal centres inside lymph nodes and the spleen. There they multiply, mutate the genes that shape their antibodies, and compete for antigen and survival signals. Cells making antibodies that bind more effectively are favoured. This is affinity maturation: evolution compressed into a small temporary structure inside the body. Some of the winners become long-lived plasma cells; others become memory B cells able to respond quickly and continue adapting after re-exposure.

T cells leave different forms of memory. Helper T cells support B cells and coordinate other immune functions. Cytotoxic T cells can recognise and kill infected cells displaying the relevant antigen fragments. Memory populations may circulate, remain in lymphoid organs or take up residence in tissues. A blood test can therefore measure something important while missing other important things. Antibody concentration is often useful, and for some vaccines a defined level predicts protection well. It is not a universal scoreboard for immunity.

This makes waning less mysterious. Circulating antibodies can decline while memory cells remain. Protection against infection may fall first because stopping entry requires antibodies to be present at the moment of exposure. Protection against severe disease may last longer if memory can expand before damage reaches its worst stage. In other cases, the pathogen acts too quickly for recall alone, or the remaining memory is too sparse, so

maintaining antibody above a threshold matters. Different pathogens produce different clocks.

A booster is another encounter under controlled conditions. It can raise antibody levels, recruit memory cells, create new germinal-centre activity and broaden or improve the responding population. That does not mean the previous dose was useless. Some schedules are designed from the start as a series because priming and maturation need repeated exposure. Some boosters compensate for waning. Others update the target when the pathogen changes. The same word covers several jobs.

Spacing matters because immune development takes time. Repeating a dose immediately is not always equivalent to allowing cells to expand, contract and mature before recalling them. Yet longer is not automatically better. The schedule must balance immune response against the period during which the person remains vulnerable. An infant at immediate risk cannot wait for an elegant interval designed for a healthy adult. Programme schedules are compromises between biology, exposure, attendance and feasibility.

Memory also varies between people. Genetics, age, previous infections, microbiota, nutrition, medicines, pregnancy and immune conditions can alter the response. A population average can hide a group with weaker protection. That is one reason some recommendations include extra doses, higher antigen content or different products for particular ages or risks.

The practical lesson is to stop asking whether immunity exists and ask what is present, where, against which target, at what level, and how quickly it can be recalled. Memory is durable in some respects and fragile in others because it is alive.

Different Platforms Solve Different Delivery Problems

A vaccine platform is the method used to present antigen and context. The platforms are often arranged as generations, with the newest treated as the most advanced. That is poor engineering. A bridge, a ferry and a tunnel solve different crossing problems. Vaccine platforms solve different delivery problems, and old methods can remain better suited to a particular pathogen or programme.

Live attenuated vaccines use an organism weakened so that it can reproduce to a limited extent without causing ordinary disease in most recipients. Because the antigen is made over time and appears in several forms, these vaccines can produce broad, durable responses and sometimes strong mucosal immunity. The same biological activity creates constraints. A live vaccine may be unsuitable for some severely immunocompromised people or during pregnancy, and attenuation must remain stable. Storage can be demanding. A rare vaccine-derived problem can become important when millions receive it.

Inactivated vaccines contain organisms rendered unable to replicate. They cannot revert to a replicating form, but killing can alter antigen shape and removes the signals supplied by replication. Multiple doses or adjuvants may be needed. Toxoid vaccines take a different route. Diphtheria and tetanus are dangerous chiefly because of toxins. Chemically inactivating the toxin while preserving its recognisable structure teaches antibodies to neutralise the weapon rather than attack every bacterial component.

Subunit vaccines narrow the target further to selected proteins or other components. This can improve control and safety but may reduce the range of signals and epitopes, increasing dependence on adjuvants and careful formulation. Recombinant technology allows an antigen to be made in yeast, insect or mammalian cells rather than harvested from large quantities of the pathogen. The hepatitis B surface antigen vaccine became a landmark of this approach.

Polysaccharide vaccines use sugars from bacterial capsules. Those sugars can trigger antibody without strong T-cell help, which limits memory and performs poorly in young children. Conjugation links the sugar to a protein carrier. A B cell binding the sugar takes up the whole conjugate, presents carrier-protein fragments to helper T cells, and gains the signals needed for class switching, maturation and memory. Hib conjugate vaccines turned a weak infant antigen into the basis of effective childhood prevention.

Viral-vector vaccines place genetic instructions for an antigen inside a different virus that has been altered for delivery. Cells make the antigen, giving the immune system some features of an intracellular infection without exposure to the target pathogen. Pre-existing or newly formed immunity to the vector can reduce later delivery. Replicating and non-replicating vectors have different properties and risks.

Messenger RNA vaccines package temporary instructions, commonly in lipid nanoparticles, so cells produce an antigen for a limited period. In authorised products, ribosomes read the delivered mRNA in the cytoplasm. Its intended function does not require entry into the nucleus, and the platform supplies no machinery for integration into chromosomes. The platform separates antigen design from much of the pathogen-specific manufacturing process, which can speed redesign once a sequence is known. It also demands control of RNA stability, delivery, innate sensing and storage conditions. Modified nucleosides and improved lipid delivery were products of long research, not emergency improvisation.

Platform choice affects the immune response, speed, scale, stability, dose, route, cost and suitability for different groups. It does not settle them. A beautifully engineered antigen can fail because it targets the wrong stage. A potent live vaccine can be a poor fit for a population with common immune suppression. A stable low-cost formulation may save more lives than a stronger product that cannot reach clinics intact. Modernity is not the outcome. Protection under real conditions is.

Protection Has More Than One Endpoint

A vaccine result usually arrives as a percentage, and the percentage is often the least informative part. Before reading it, four questions are needed: protection against what, in which people, over what period, compared with whom?

In a randomised trial, efficacy commonly compares the risk of a defined outcome in vaccinated and control groups. If disease occurs in 10 people per thousand in one group and 2 per thousand in the other, the relative reduction is 80 per cent. The absolute reduction is 8 cases per thousand under those trial conditions. Both are correct. They answer different questions. Relative change describes proportional performance; absolute change depends heavily on how common the outcome was during the study.

The endpoint may be laboratory-confirmed infection, symptomatic disease, severe disease, hospital admission, death, persistent infection, a precancerous lesion or another specified result. These outcomes sit at different points in the chain from exposure to harm. A vaccine can have modest effect on infection yet strong effect on hospitalisation because immune recall limits progression. It can reduce a cancer precursor without anyone being able to observe the prevented cancer until years later. It can stop a toxin from causing disease without preventing the bacterium from being present.

Efficacy is measured under the conditions of a study. Effectiveness describes performance in ordinary use, where recipients differ, appointments are missed, storage may fail, clinicians follow varied practice, and exposure changes by season and place. A lower effectiveness estimate does not automatically mean the product failed in ordinary use. It may reflect a different endpoint, age mix, variant, dosing interval, follow-up period or background risk. Comparing percentages across studies without aligning those features is numerical theatre.

Protection can also extend beyond the recipient. If vaccination reduces the

chance of becoming infected, the duration of infection or infectiousness, it can reduce opportunities for onward spread. People who remain susceptible may then receive indirect protection. This is community immunity, and it is a network effect rather than a halo around each unvaccinated person. It depends on transmission, contact patterns, vaccine action, coverage, clustering and time. A national average can look high while a school, neighbourhood or close-knit community contains enough susceptible people for an outbreak.

There is no universal immunity threshold. The rough threshold rises as transmission becomes easier, but the simple calculation assumes homogeneous mixing, durable protection and a vaccine that blocks transmission in a fixed way. Real populations violate each assumption. Measles exposes small gaps because it is highly transmissible. Tetanus provides the clean counterexample: the bacterium's spores enter wounds from the environment and cases do not sustain person-to-person spread. Your tetanus vaccination protects you, but your vaccinated neighbour does not remove spores from the soil.

Population outcomes can include control, elimination and eradication. Control reduces disease to an accepted level but requires continuing effort. Elimination interrupts transmission in a defined area while importation remains possible. Eradication means worldwide interruption, allowing routine control measures eventually to stop. Smallpox met unusual conditions: humans were the main reservoir, cases were recognisable, surveillance and contact vaccination were workable, and the vaccine could break transmission. Most pathogens do not offer that combination.

A sound vaccine claim therefore names its endpoint and scale. Individual disease prevention, reduced severe outcomes, fewer transmissions and eradication are connected, but they are not interchangeable. The percentage becomes useful only after the result has been defined.

Safety Is a Comparison and a Surveillance System

No medical intervention is risk-free, and neither is non-intervention. Vaccine safety is therefore a comparison between specified risks in specified people, backed by a system designed to find what was missed.

Development begins before a large trial. Researchers characterise the antigen and formulation, study immune responses and toxicity, and establish how the product can be manufactured. Early human studies examine dose, common reactions and immune response in small groups. Later studies widen the population and test a clinical endpoint in hundreds or thousands, often many thousands. Regulators assess the evidence together with manufacturing controls and the disease burden in the intended population. A tolerable balance for older adults facing high risk may differ from the balance for healthy adolescents facing a rarer outcome.

Trials have a mathematical limit. A study of thirty thousand people can detect common reactions and a strong disease effect. It may miss a harmful event occurring once in one hundred thousand doses, especially if the event also occurs without vaccination. That is why authorisation begins a new phase of evidence rather than ending the inquiry. Health records, active surveillance networks, registries, linked databases and spontaneous reporting systems can detect patterns after use at scale.

Spontaneous reports are commonly misunderstood. A person can report an illness that followed vaccination whether or not anyone thinks the vaccine caused it. This openness is useful because an unexpected pattern cannot be found if reports are filtered through certainty. It also means the database contains coincidences. In any week, some recently vaccinated people will have seizures, miscarriages, heart attacks or new diagnoses because those events occur in the population. Timing generates a hypothesis. It does not settle it.

Investigators then ask whether the event occurs more often than its background rate, clusters in a plausible time window, changes with dose or product, appears in more than one system, has a credible mechanism, and

declines when exposure changes. Different study designs have different biases. A safety signal may be confirmed, narrowed to a subgroup, attributed to another cause or left uncertain. Recommendations can change by age, sex, interval or product when benefit and risk differ. That is the system working, though poor communication can make revision look like proof that everything before it was fraudulent.

Real vaccine injuries exist. Denying them is both false and strategically foolish. The 1955 Cutter incident followed release of some inactivated polio vaccine containing live poliovirus. Children were paralysed, transmission reached contacts, vaccination paused, and manufacturing oversight was strengthened. A later example shows the surveillance sequence. Post-authorisation surveillance in the United States confirmed a rare excess of myocarditis and pericarditis after mRNA COVID-19 vaccination, concentrated in adolescent and young adult males and most often within a week after a second dose. Estimated risk differed by product, age, dose and interval, so advice was adjusted for particular groups rather than applied uniformly. The signal did not mean every report of chest pain was vaccine-caused, but its rarity did not make the excess unreal. The ethical response is to measure, disclose, compensate where appropriate and alter practice, while comparing the harm with the disease the product prevents.

Manufacturing is part of safety because a vaccine is a biological product made in batches. The process must control identity, purity, potency, sterility and consistency. A candidate can be sound in concept and fail through contamination, incomplete inactivation, unstable formulation or poor storage. Regulators inspect facilities, review production, require batch testing and continue monitoring changes. The recipe alone is not the product; the controlled process is.

The right attitude is neither “vaccines are safe” as an unqualified slogan nor “a report proves danger”. Ask which product, dose, group, outcome and time window are under discussion. Ask what the comparator is. Then ask what evidence system could detect a rare problem and whether the result has survived that test.

The Vial Is Only the Beginning

A vaccine can produce excellent trial results and prevent little disease. The gap is filled by an operating system: financing, factories, raw materials, quality control, forecasting, procurement, transport, refrigeration, clinics, trained staff, records, reminders, surveillance, public consent and enough time in the day to deliver the dose.

The chain can fail at any link. A country may approve a product but be unable to buy enough. Supply may exist globally but arrive in the wrong vial size or after the high-risk season. A refrigerator can accidentally freeze a product that freezing damages, even while its display suggests that everything is cold. A child can receive a first dose but miss the later dose needed for stronger or longer protection. A clinic can have stock while families cannot lose wages, travel safely or obtain an appointment. Coverage is the visible end of many hidden systems.

In 2025, the WHO estimated that 13.5 million infants received no initial dose of a diphtheria-tetanus-pertussis-containing vaccine, the standard operational marker for “zero-dose” status. These children are not distributed randomly. They are often concentrated where conflict, poverty, displacement, weak services or exclusion affect other health care too. Reaching them is not a matter of correcting one belief. It may require mobile teams, secure access, reliable records, local workers, smaller packages, different opening hours or a health system that has given families a reason to return.

Schedules translate immune biology into workable appointments. They place doses before likely exposure, allow enough time for priming and maturation, account for maternal antibody and age, and fit visits that health services can deliver. The best theoretical interval can be a poorer public-health choice if few people complete it. Combining vaccines reduces visits but increases manufacturing and regulatory complexity. A new recommendation changes procurement, training, software, consent materials and waste, not only a line in a clinical guide.

Trust belongs inside this operating system. People judge vaccines through institutions, personal experience, social identity, past mistreatment, convenience and the conduct of those asking. Some questions are factual and answerable. Others concern who carries risk, who profits, whether uncertainty was admitted and whether the service will respond if harm occurs. Calling every hesitation ignorance avoids the harder work of making institutions competent and worthy of confidence.

Programmes also alter the disease environment. High uptake can cut transmission, protect people who respond poorly and make outbreaks rare. Success then changes the evidence available to everyday perception. The appointment and possible reaction remain visible; the ward that did not fill disappears. A generation with no memory of polio paralysis or congenital rubella may perceive less immediate benefit because earlier vaccination lowered the risk around it. This can create a feedback loop: success reduces disease, reduced disease can weaken demand, and lower uptake can restore opportunity to the pathogen.

Smallpox eradication shows what happens when the system and the biology align. Mass vaccination mattered, but the final campaign depended heavily on surveillance, rapid investigation, case isolation and vaccination around detected cases. The vaccine created the possibility; field operations closed the last chains of transmission. Malaria shows a different settlement. Vaccines now add protection for children, but they are used with nets, diagnosis, treatment and other control measures because neither the parasite nor the ecology offers a single-tool victory.

Return to the starting line. Inside one person, vaccination prepares a faster response. Across a population, programmes decide who receives that advantage and whether susceptible people remain connected in ways that sustain spread. The vial contains biological potential. Public health is the work of making that potential arrive.

How It Actually Works

Before the vaccine

Long before anyone knew what a virus was, people noticed that surviving smallpox usually protected against having it again. In several parts of Asia, Africa and the Ottoman world, practitioners turned that observation into variolation. Material from a smallpox lesion was introduced into a healthy person through the skin or nose, producing a deliberate infection that was often milder than naturally acquired disease.

Often was doing dangerous work. Variolated people could develop severe smallpox, die, or transmit infection to others. The method still reduced risk compared with facing smallpox unprepared in a society where exposure was common. It was prevention by controlled danger, based on experience rather than a theory of immunity.

Variolation did not travel in one direction from a single inventor. European accounts described techniques in China and the Ottoman Empire, while African knowledge entered the North American debate. During Boston's 1721 epidemic, Cotton Mather cited the practice described by Onesimus, an enslaved African man, and physician Zabdiel Boylston carried it out despite hostility. The comparison was uncontrolled by modern standards, yet recorded deaths were lower among inoculated people than among recorded natural cases. The episode matters because the origin story is a network of practices, risks and observations rather than a lone European insight.

Lady Mary Wortley Montagu encountered Ottoman inoculation while living in Constantinople. Smallpox had killed her brother and scarred her. She had her son variolated there in 1718, then promoted the practice after returning to Britain and arranged inoculation for her daughter during the epidemic of 1721. The procedure became a public argument involving physicians, clergy, aristocrats, prisoners, orphans and royal children. The moral problem was already recognisable: accept a smaller chosen risk now to reduce a larger uncertain risk later.

Cowpox changes the bargain

Edward Jenner did not invent the idea of acquired protection, and he was not the first person to suspect that cowpox could protect against smallpox. His achievement was to investigate, test and publicise a safer substitute for variolation.

In May 1796, Jenner took material from a cowpox lesion on the hand of Sarah Nelmes and introduced it into the arm of James Phipps, an eight-year-old boy. After Phipps recovered, Jenner exposed him to smallpox material by variolation and reported that he did not develop the disease. The experiment would fail modern consent and research standards. It also supplied a powerful proof of concept: protection could be induced with a related infection that did not carry the ordinary risk of smallpox.

Jenner published his evidence in a 1798 inquiry whose title used *Variolae Vaccinae*, cowpox. The Latin root tied the method to the cow; the word vaccination appeared in print soon afterwards. The method spread, was modified by many hands, and gradually displaced variolation. It was not perfect. Cowpox material varied, arm-to-arm transfer could carry other infections, protection waned, and revaccination became necessary. Yet the bargain had changed. Deliberate smallpox was no longer the only route to planned protection.

Protection still depended on material supply. Before stable laboratory production, vaccination often moved arm to arm: fluid from a fresh vaccine lesion was transferred to the next recipient. The chain could fail if the material lost activity, and it could carry contaminants. Later use of calves, better preservation, potency standards and organised vaccination services turned Jenner's observation into a more reproducible product. The history did not move from superstition to science in one jump. It moved from variable biological practice towards controlled manufacture.

The mechanism remained unknown. Viruses were not visible, antibodies had not been described, and germ theory had not been established. Vaccination began as a useful observed pattern before it became an

explained technology. That sequence matters. Medicine often learns that an intervention works before it can say exactly why, then uses mechanism to make the intervention safer, more consistent and easier to extend.

From observation to attenuation

Nineteenth-century bacteriology turned vaccination from a particular smallpox practice into a general strategy. Louis Pasteur and others showed that microorganisms could be cultivated and altered. A pathogen weakened by heat, oxygen, passage through another host or laboratory growth might retain enough identity to induce protection while causing less disease.

Pasteur used the word vaccination for this wider class of methods, honouring Jenner even when no cow was involved. Work on chicken cholera and anthrax helped establish attenuation as a deliberate laboratory process. In 1885, after animal experiments, Pasteur's group treated Joseph Meister, a boy bitten repeatedly by a dog believed to be rabid, with preparations of infected rabbit spinal cord dried for different lengths of time. Meister survived. The case brought fame, funds and controversy. It also showed that a vaccine could be given after exposure when the pathogen's route left time for immunity to develop.

Bacteriology opened another route. Some bacteria damage the body mainly through secreted toxins. Researchers learned to inactivate diphtheria and tetanus toxins with heat and chemicals while preserving shapes recognised by antibodies. These toxoids could train neutralisation without exposing a person to active toxin. Gaston Ramon developed practical toxoid methods in the 1920s and also observed that certain added substances increased the immune response, helping establish the logic of adjuvants.

The new science brought new dangers. Cultures could be contaminated. Attenuation could be incomplete. Potency varied. A biological product could not be guaranteed by its formula alone because the manufacturing process shaped what emerged. Vaccination was becoming more powerful and more industrial, so standardisation had to grow with it.

Polio and the price of scale

Polio made the promise of vaccination visible on television and the risks of production visible in courtrooms. Most poliovirus infections caused no paralysis, but the small fraction that reached the nervous system could destroy motor neurons and leave children unable to breathe without mechanical support. In epidemic summers, pools closed, parents feared crowds, and hospital wards filled with iron lungs.

By 1949, researchers had learned to grow poliovirus in tissue culture without relying on nervous tissue. Jonas Salk used formaldehyde to inactivate virus from three poliovirus types. A vast field trial in 1954 compared disease among vaccinated children and controls. On 12 April 1955, the vaccine was announced as effective and licensed in the United States.

Within weeks, cases of paralysis were linked to vaccine made by Cutter Laboratories. Some virus in certain lots had not been fully inactivated. Vaccinated children developed polio, and infection spread to contacts. The programme paused while investigators traced what had happened. The incident exposed weaknesses in production assumptions, testing and regulatory requirements. It did not show that inactivated vaccination was impossible. It showed that a process able to leave live virus behind required tighter control than the rules had demanded.

The response clarified a principle that now sounds obvious: a test must match the failure it is meant to exclude. Following a written recipe or measuring average potency was insufficient if small pockets of surviving virus could escape detection. Manufacturers changed filtration, inactivation, sampling and release controls; regulators required stronger evidence from each lot. Safety was not recovered by promising more care. The process was redesigned so that the dangerous failure became harder to produce and easier to find.

Albert Sabin pursued a different product: live attenuated poliovirus taken by mouth. Oral vaccine was easy to deliver, replicated in the gut and could produce strong intestinal immunity, helping interrupt transmission. It became

central to the global eradication effort. Its strength carried a rare cost. Attenuated virus can mutate during replication and, in poorly immunised populations, vaccine-derived strains can circulate and cause paralysis. As wild poliovirus has been pushed back, programmes have had to manage risks created by the tool used to defeat it, changing formulations and expanding inactivated vaccine use.

The contrast is the field in miniature. Salk's vaccine is unable to replicate and protects strongly against paralytic disease, but is less powerful at stopping intestinal infection. Sabin's can suppress transmission more effectively in many settings, but replication creates a small biological hazard. There is no platform victory detached from purpose. The right product depends on whether the immediate aim is protecting an individual from paralysis, extinguishing community transmission, or managing the final stages of eradication.

Making targets instead of growing diseases

Cell culture, protein chemistry and molecular biology allowed vaccine makers to separate the useful target from more of the pathogen. The rubella vaccine developed by Stanley Plotkin and colleagues relied on human cell culture and careful attenuation. Maurice Hilleman led or contributed to vaccines against measles, mumps, hepatitis A, hepatitis B and other infections. His career shows vaccine research as sustained industrial work rather than a sequence of isolated heroic moments.

Conjugate vaccines solved a specific childhood problem. The polysaccharide capsule of *Haemophilus influenzae* type b can evade early defences, yet capsule sugar alone produces a weak, short-lived response in infants. Linking the sugar to a carrier protein recruits T-cell help. Invasive Hib disease fell steeply after conjugate vaccines entered routine use, and the same design principle was extended to pneumococcal and meningococcal vaccines.

Recombinant DNA allowed manufacturers to make an antigen without cultivating the complete pathogen. Yeast cells engineered to produce

hepatitis B surface antigen supplied material that assembles into particles resembling the virus's outer form but contains no viral genome. Human papillomavirus vaccines use recombinant capsid proteins that self-assemble into virus-like particles. These particles display the target densely enough to induce strong neutralising antibodies while being unable to infect or reproduce.

The destination can be decades away. HPV vaccination aims to prevent persistent infection before exposure, thereby preventing cellular changes that can progress to cancer. In England, cohorts offered vaccination at ages twelve and thirteen later showed the largest reductions in cervical precancer and cervical cancer. The intervention occurs in adolescence; part of the benefit appears in cancer registries years later. Vaccine evidence can therefore require patience as well as scale.

A programme becomes global

In 1974, the WHO created the Expanded Programme on Immunization to widen routine access to vaccines against tuberculosis, diphtheria, tetanus, pertussis, polio and measles. The scientific products already existed. The harder problem was making protection routine across countries with different budgets, roads, electricity supplies, workforces and disease patterns.

Smallpox supplied the decisive demonstration. The intensified global eradication programme began in 1967. Vaccination coverage mattered, but the final campaign did not depend on injecting every person on Earth. Teams searched for cases, investigated rumours, isolated patients, traced contacts and vaccinated around outbreaks. The visible rash made surveillance possible. Humans formed the essential reservoir. The vaccine could be delivered in difficult conditions and could break transmission. The last naturally occurring case was recorded in Somalia in 1977. In 1980, the World Health Assembly certified eradication.

Two modest technologies helped field operations work. The bifurcated needle held a small dose between two prongs and could be used rapidly

after limited training. Freeze-dried vaccine tolerated difficult transport better than earlier liquid material. Neither changed the immune principle. They made it deliverable where vaccine, roads and staff were scarce and waste could end a campaign. Eradication joined case finding to a product and tool suited to the places in which the last chains survived.

That victory did not produce a general recipe. Measles can be eliminated locally but returns quickly through immunity gaps and importation. Tetanus spores remain in the environment. Influenza changes and has animal reservoirs. Malaria parasites move through humans and mosquitoes and pass through several biological stages. Eradication requires a favourable pathogen, a suitable intervention, sensitive surveillance, political cooperation and relentless delivery. Remove one and the finish line moves away.

The wider programme still changed survival. A 2024 modelling analysis attributed roughly 154 million lives saved over the expanded programme's first fifty years to vaccination against fourteen pathogens. Models reconstruct what would have happened without vaccination, so the result carries assumptions and uncertainty. Its scale reflects a plain operational fact: a dose that already exists can save nobody until routine services reach the next child.

Platforms under pressure

The COVID-19 pandemic compressed decades of vaccine development into public view. Once the viral sequence was available, several groups could insert the selected antigen into platforms already being developed. Viral vectors, protein subunits, inactivated virus and messenger RNA all reached large trials.

Messenger RNA drew the greatest attention because no mRNA vaccine had previously been authorised for widespread human use. The apparent leap rested on long work. Researchers had learned to make RNA more stable, reduce unhelpful innate sensing through nucleoside modification, and package it in lipid nanoparticles that could enter cells. Katalin Karikó and

Drew Weissman's 2005 work on modified nucleosides became one important part of that chain. The pandemic supplied urgent funding, rapid recruitment, high disease incidence and willingness to manufacture doses before trial results were known.

Speed did not come from doing every task one after another. Trial phases and factory preparation overlapped; regulators reviewed data as they accumulated; companies accepted the financial risk of manufacturing a product that might fail. Large randomised trials still had to show defined outcomes and common adverse effects. Rare risks emerged only after rollout, confirming why monitoring at scale remained necessary.

The acceleration did not remove uncertainty. Trials involving tens of thousands could estimate efficacy against selected endpoints and detect common reactions, but they could not reveal every rare harm, future variant or duration of protection. Linked records and active surveillance later identified rare product-specific risks and allowed recommendations to differ by age, sex, dose and available alternatives. The episode showed both halves of rapid development: prior platform knowledge can shorten the route to large trials, while evidence after rollout remains part of the route rather than proof that no testing occurred.

Malaria shows a slower form of pressure. The parasite changes form between mosquito, liver and blood, presents different antigens at different stages and has coevolved with human immunity. After decades of development, RTS,S became the first malaria vaccine recommended by the WHO in 2021; R21 followed in 2023. Both target the parasite before its blood stage and are recommended alongside other malaria control measures for children in endemic areas. By July 2026, the WHO reported that twenty-five African countries had introduced malaria vaccination. The products add protection; nets, diagnosis, medicines and surveillance remain necessary.

From candidate to dose

Modern development begins by defining the intended use. A vaccine for infants, pregnant women, older adults or travellers faces different immune responses, disease risks and acceptable trade-offs. Researchers choose an antigen and platform, develop assays, study animals where informative, and build a manufacturing process capable of producing consistent material.

Early human studies examine dose, tolerability and immune response. Later studies expand safety data, compare schedules and test whether the vaccine prevents a clinical endpoint. Randomisation helps separate vaccine effect from differences between people. Blinding can reduce biased diagnosis and reporting. The trial protocol defines cases in advance because changing the endpoint after seeing results can manufacture success.

Sometimes a clinical endpoint would require a trial too large or slow to be practical. A well-established immune correlate can then support comparison of schedules, age groups or updated versions, provided that the measurement has been tied convincingly to protection. That is an efficient bridge, not a universal shortcut. A neutralising-antibody level established for one antigen, assay and population may not transfer unchanged to another. The bridge is only as sound as the relationship underneath it.

Manufacturing develops alongside clinical evidence. Facilities must control starting materials, contamination, inactivation or attenuation, formulation, filling and storage. National authorisation routes differ. Some authorities perform a complete review; others use work-sharing or rely partly on assessments by recognised regulators. WHO prequalification and emergency-listing procedures can support procurement and national decisions, but they do not replace national authority. Across those routes, manufacturing assessment covers the process and facilities and may include lot testing for identity, purity, potency and sterility. A change of factory, cell line or process can require evidence that the resulting product remains comparable.

Scale-up can alter a biological product. A larger vessel, purification step, stabiliser or filling line may change particle size, protein shape, residual material or loss during storage. Developers do not prove that one research batch works and then copy the label. They must show that commercial lots remain comparable to the material studied and that the process stays within validated limits. Biological manufacture is controlled variation, not perfect repetition.

After authorisation, programmes decide who should receive the vaccine and when. Trials, disease surveillance, cost, supply, equity and feasibility all matter. Effectiveness studies test performance in ordinary use. Safety systems search for rare events. Genomic and epidemiological surveillance may reveal a changing target. Recommendations are revised as disease burden, population immunity and evidence change.

The result seen by the recipient is a few seconds with a needle, a spray or drops. Behind it sits a chain of choices about molecules, endpoints, factories, transport and public priorities. That chain is the vaccine.

How we know

Vaccine knowledge comes from methods that answer different questions. Laboratory studies show binding, neutralisation, cell responses and mechanisms, but an immune measurement is not automatically a clinical benefit. Randomised trials estimate efficacy against endpoints defined in advance and detect common adverse effects, yet their participants and follow-up may not represent every population or year. Observational studies estimate effectiveness after rollout but must address differences in exposure, health, care-seeking and vaccine uptake. Linked health records and active surveillance can compare rates of rare outcomes; spontaneous reports generate signals but lack an unvaccinated comparison and cannot alone establish causation. Disease surveillance shows population change, while transmission models estimate the counterfactual that prevention removed. Programme evaluations remain setting-specific because disease burden, coverage, co-interventions and services differ. Historical accounts are strongest where laboratory records, official reports and independent evidence converge; famous discovery stories often compress collective work. The claims in this book are therefore matched to the method: trials for defined efficacy, surveillance for rare signals, programme evaluations for delivered impact, and models for events that did not occur.

What People Get Wrong

“The vaccine gives you the disease”

Most vaccines cannot cause the infection they prevent. Inactivated organisms do not replicate. Toxoids contain inactivated toxin. Protein, conjugate and virus-like particle vaccines supply selected components. Messenger RNA supplies temporary instructions for selected antigens, not the machinery of the pathogen. A sore arm, fever or fatigue reflects inflammation and immune signalling, not proof that the target disease has begun. Symptoms alone cannot identify their cause. A fever after vaccination may be an expected short reaction, an unrelated infection acquired before the appointment, or a rare adverse effect. The product, timing, symptom pattern and diagnostic evidence matter because similar words can describe biologically different events.

The correction needs a boundary. Live attenuated vaccines contain organisms able to reproduce to a limited extent. They can cause mild symptoms resembling part of the infection and, in rare circumstances, disease in a susceptible recipient. Oral polio vaccine can rarely cause paralysis or seed vaccine-derived circulation where population immunity is low. This is why live products have specific contraindications and why programmes change products as risks change.

The useful question is not whether a vaccine contains “the virus”. Ask whether the material can replicate, which parts are present, and what harm is biologically possible in the recipient under discussion.

“Vaccinated means infection-proof”

Sterilising immunity, in which infection is stopped before it becomes established, is one possible result. It is not the definition of vaccination. A pathogen may enter the nose, throat or gut before blood antibodies and recalled cells can control it. The encounter can still be shorter, less intense and far less likely to reach vulnerable tissue.

This is why one vaccine can have different effects against infection,

symptoms, hospital admission and death. Detecting infections after vaccination does not by itself show that protection against severe outcomes has disappeared. The opposite error is also possible: strong protection against individual disease does not prove that transmission is sufficiently reduced to protect others.

The denominator matters. When millions of vaccinated people encounter a circulating pathogen, some breakthrough infections are expected even with strong protection. Counting vaccinated cases without the number vaccinated, their exposure and their baseline risk can make a working vaccine look ineffective.

The wall metaphor created the confusion. Vaccines alter probabilities and timing. They do not issue guarantees. A fair test names the outcome, period, population and circulating strain, then compares like with like.

“Natural infection is the better teacher”

Infection can produce broad and durable immunity. It can also produce pneumonia, paralysis, congenital damage, cancer, long-term symptoms or death. Calling it a better teacher omits the tuition fee.

The immune response is not graded by how ill someone became. A vaccine can focus attention on a protective target while avoiding much of the pathogen's damage and immune evasion. HPV virus-like particles can induce strong neutralising antibodies without infection. Tetanus disease may not generate dependable immunity because the amount of toxin capable of causing illness can be too small to produce a protective response, so recovered patients still need vaccination. Broader exposure is not automatically more protective. Infection may present many antigens while directing much of the response towards targets that do not prevent harm. Some pathogens also suppress, distract or exhaust immune functions. Quality, location and timing matter more than the number of components encountered.

There are cases where prior infection changes the number or timing of doses recommended, and hybrid exposure can broaden responses. That is

a clinical and epidemiological question, not a reason to seek disease. The proper comparison is planned exposure to selected antigen against the risks and uncertainty of the infection itself.

“Boosters mean the first doses failed”

Many vaccine series are designed as several doses from the beginning. The first exposure primes rare cells. Later exposure expands them, raises antibody concentrations and gives B cells another round of selection and maturation. Calling dose two evidence that dose one failed is like calling the second lesson proof that the first taught nothing. Primary series are not maintenance in disguise. For some antigens, the first dose establishes recognition while later doses create the antibody level and durability on which ordinary protection depends. Judging the series after its first step is judging an unfinished intervention.

Other boosters do compensate for waning, update the target or protect a group whose first response was weaker. These are different jobs. Antibodies may fall while memory remains, yet some pathogens act too quickly for memory alone. Influenza strains change. Ageing alters immune response. A schedule adapts protection to those facts.

The critical question is why another dose is advised. A planned primary series, a periodic restoration and an updated antigen should not be collapsed into the same story. Nor does the need for maintenance make the earlier protection worthless.

“mRNA vaccines alter your DNA”

Messenger RNA is a working copy of genetic instructions. In an mRNA vaccine, cells take up the RNA, and ribosomes read it in the cytoplasm to make the encoded antigen for a limited period. The RNA is then broken down through ordinary cellular processes.

Human chromosomal DNA is held in the nucleus. In authorised mRNA vaccines, the delivered RNA performs its intended function in the cytoplasm, while the platform supplies no machinery to integrate it into the genome.

The fact that RNA and DNA both carry sequence information does not make them interchangeable; location and molecular machinery determine what each can do. Cells already handle enormous quantities of their own messenger RNA. Sequence information alone is not a route into chromosomes. Integration would require additional machinery that the authorised vaccine platform does not supply.

Claims about integration sometimes borrow mechanisms from retroviruses, which use specialised enzymes and life cycles absent from authorised mRNA vaccines. A concern should be tested against the product's components and cell biology, not the word genetic. The platform does instruct cells temporarily. That is how it works. Temporary instruction is not genome alteration.

“Vaccines cause autism”

The modern claim began with a 1998 report describing twelve children and proposing a link involving the measles, mumps and rubella vaccine. A case series with no suitable control group could not estimate whether vaccination changed autism risk. The paper was later retracted after serious problems in conduct and reporting, yet its narrative travelled much further than the correction. Retraction matters, but replication matters more. A false claim can survive by being recast as evidence that institutions punished its author. Independent studies across countries, designs and vaccine schedules answer the scientific question rather than the grievance: children receiving MMR do not show the predicted excess of autism.

The relevant question has since been tested in far larger populations. A nationwide Danish cohort study followed 657,461 children and found no increased autism risk associated with MMR vaccination, including among groups thought more susceptible. That result agrees with the wider body of epidemiological evidence. Research has also failed to support claims that thiomersal or aluminium-containing childhood vaccines cause autism.

Timing helped the myth. Autistic differences often become noticeable during the same early years in which routine vaccines are given. Sequence feels

causal, especially when parents are searching for an explanation. Large comparative studies exist to separate that powerful impression from risk.

“A reported event is a proved side effect”

Safety systems invite reports of illnesses that occur after vaccination, including events with no established causal link. That openness is a feature. A signal cannot be noticed if reporters must prove it first.

The resulting database is not a list of verified injuries. Millions of people experience miscarriages, seizures, strokes, infections and new diagnoses each year. Some will occur shortly after a dose by chance. Investigators compare observed and expected rates, examine timing, product and dose patterns, use linked records and controlled designs, and ask whether a biological mechanism fits. They can compare the same person's risk in different time windows, match groups with similar characteristics, or test whether one product shows a pattern that another does not. No method is perfect. Agreement across methods is what turns a signal into a causal conclusion.

The reverse mistake is treating every unconfirmed report as irrelevant. Rare harms have been found through post-use monitoring, and recommendations have changed. Report first, investigate next, conclude last. Confusing those stages either manufactures certainty from coincidence or suppresses the evidence needed to detect a real problem.

Use It

Name the endpoint

Whenever you hear that a vaccine “works” or “doesn’t work”, ask what event was counted. Infection, symptoms, a positive test, hospital admission, severe disease, death, persistent infection and onward transmission are different endpoints. A product can perform strongly against one and less strongly against another without contradiction.

Then add time. Protection measured for three months after a dose cannot

be carried unchanged into a second year. Add population. Results in healthy adults do not settle performance in infants, older people or those with immune suppression. Add the version of the pathogen where relevant. A precise claim will often become less dramatic and more useful once these conditions are restored.

This lens prevents two common manipulations. One side cannot dismiss protection against severe disease by pointing only to infections. The other cannot promise community protection from evidence that measured only symptoms in recipients. First name the endpoint. Then decide whether it answers the question being argued about.

Put the denominator back

A safety story without a denominator can frighten; a benefit story without one can advertise. “Fifty reports” means little without knowing how many doses were given, over what period, to which people, and how often the same event would otherwise occur. “Ninety per cent effective” needs the underlying risks and endpoint.

Compare risks on the same scale. A rate per million doses should not be set beside a percentage per infection. A short post-vaccination window should not be compared with a lifetime disease risk. Relative and absolute effects should travel together when decisions depend on baseline risk. If severe disease is rare in one group and common in another, the same relative vaccine effect can produce a different absolute benefit.

The denominator also exposes selection. A passive reporting system counts reports, not proven cases, and may receive more attention after publicity. A clinic study can miss people who never reach clinics. Numbers become evidence only when you know who had a chance to enter them.

Separate the product from the programme

A vaccine has properties. A vaccination programme has results. Confusing them hides where failure occurred.

Suppose a product prevents disease under the tested schedule, but many

people receive one dose of a two-dose series, doses arrive after the seasonal peak, or storage damages potency. Low population impact does not prove the antigen was useless. The product worked under conditions the programme did not reproduce. The opposite also occurs. A programme can show impressive decline because disease was already falling, higher-risk people changed behaviour, or another intervention arrived at the same time. Observed improvement does not automatically measure vaccine effect.

Look for the bridge between trial and use: eligibility, uptake, completion, timing, handling, surveillance and exposure. Then ask whether the study design separates those factors. This is especially important when countries produce different results with the same named vaccine. The difference may lie in age, schedule, pathogen, health system or data, not in national virtue.

Trace the factory-to-arm chain

The syringe is the final centimetre of a long physical system. Follow it backwards. Was the batch released at the intended potency? Did the formulation tolerate heat, light or freezing? Was the correct product ordered in enough quantity? Were multi-dose vials used before expiry? Could the clinic record which lot went into which person?

Then follow the person forwards. Was the dose given at the right age and interval? Was a later dose completed? Did the recipient belong to a group for whom the response or risk differs? Did surveillance find the expected decline in disease? Could a rare safety pattern be linked back to product, lot and timing?

This lens turns vague arguments about access into operational questions. A dose can fail without any scientific scandal: the refrigerator froze it, the road flooded, the appointment required a day's lost pay, the record system split one person into two identities. Those are not side issues to vaccine impact. They are the route by which impact exists.

Ask who protects whom

“Community immunity” can sound like a fixed public good generated once coverage crosses a magic line. Replace the line with a contact network.

Who meets whom, how often, and where are susceptible people clustered? Does vaccination reduce acquisition, infectiousness or duration enough to interrupt those contacts? How quickly does protection wane? Can the pathogen arrive from elsewhere? A high national average can conceal a local chain of susceptible households, schools or workplaces. A lower average can still protect particular groups if coverage is concentrated around them, though that protection may be brittle.

Some people benefit greatly from others being vaccinated because they cannot receive a product or respond poorly. Others receive little indirect benefit. Tetanus does not spread between people, so only personal vaccination addresses the environmental risk. A claim about social duty is strongest when the transmission mechanism supports it and weakest when community effect is assumed from individual efficacy.

Read recommendations as local engineering

A recommendation is a decision made for a population at a time, not an eternal verdict on a molecule. It combines disease burden, age-specific risk, product performance, adverse effects, existing immunity, supply, cost, feasibility and competing health priorities. Change any of those and the schedule may change.

This explains why countries can recommend different products or intervals without one of them rejecting science. Their outbreaks, health systems, budgets and licensed products may differ. It also explains why guidance changes. New safety data can narrow a product to groups with a more favourable balance. Falling disease can change the value of another dose. A new variant or formulation can alter the target. Better evidence can correct an earlier judgement.

Read the date, country, eligible group, dose history and reason. Do not

carry advice for a pregnant woman, a traveller, an infant or an older adult into another person by analogy. For a personal decision, current clinical guidance and individual medical advice outrank a general book.

The limits

Vaccines cannot solve every infectious disease. Some pathogens change their exposed antigens rapidly, establish latent reservoirs, suppress immune responses or present different targets at different life stages. HIV has resisted decades of vaccine development despite immense effort. Current BCG vaccination protects young children against some severe forms of tuberculosis but does not provide the reliable adult pulmonary protection needed to end transmission. Malaria vaccines add useful protection without replacing nets, diagnosis and treatment.

Protection is uneven. Infants, older adults and immunocompromised people may respond differently. Access is unequal. Rare serious adverse effects occur. Manufacturing errors and misleading communication have caused real harm. Trust cannot be injected and should not be demanded without accountability.

Vaccination also creates evolutionary pressure, though the outcome is not a slogan. Pathogens can change under immune selection, but mutation occurs during replication, and preventing infections can reduce the opportunities on which selection acts. Whether escape evolves depends on biology, transmission and the kind of immunity induced. The honest position is conditional.

The one thing to keep

Keep the starting line.

Before vaccination, the pathogen and the adaptive response begin their race at different times. After vaccination, selected antibodies and cells may already be present, and memory can expand sooner. That altered start can mean no infection, a milder illness, survival instead of death, or less opportunity to pass the pathogen onwards. Which result occurs depends on

the target, platform, person and time.

Then widen the view. A factory must reproduce the antigen. A regulator must judge evidence. A cold chain must preserve the dose. A clinic must reach the person before exposure. A record must bring them back when another dose is due. A safety system must notice the rare pattern. A community must decide whether the institution asking for trust has earned it.

Vaccines are often discussed as substances, with arguments trapped inside the vial. They are better understood as advance preparation joined to delivery. The immune system is given time it would not otherwise have; the programme decides who receives that time. Once you see both starting lines, biological and social, claims about success and failure become much harder to fake.

Terms

Antigen. A molecule or structure recognised by the immune system. In vaccines it is the selected target, or the product made from delivered instructions, around which protection is built.

Epitope. The particular part of an antigen contacted by an antibody or T-cell receptor. One antigen contains several epitopes, not all equally exposed, conserved or protective.

Adjuvant. A vaccine component that strengthens or shapes immune activation. It can improve antigen uptake, innate signalling, cell recruitment, antibody quality, persistence or responses in less responsive groups.

Innate immunity. Rapid defence using barriers, sensors and cells that recognise broad signs of infection or damage. Vaccines use innate signals to initiate and shape slower adaptive responses.

Adaptive immunity. Antigen-specific defence produced by B cells and T cells. It expands after recognition, can improve during a response and leaves memory that changes later encounters.

Antigen-presenting cell. A cell that takes up antigen, processes it and

displays fragments to T cells. Dendritic cells are especially important for connecting local vaccination to lymph-node responses.

Lymphocyte. A white blood cell involved in adaptive immunity. B cells can make antibodies and memory; helper and cytotoxic T cells coordinate responses or kill infected cells.

Antibody. A protein made by B-cell descendants that binds a specific target. Antibodies can block attachment, neutralise toxins, recruit other immune functions or mark material for removal.

Neutralising antibody. An antibody that directly prevents a pathogen or toxin performing a required action, such as entering a cell. Binding alone does not guarantee neutralisation or clinical protection.

Memory cell. A long-lived B cell or T cell left after exposure. It responds faster than a naive cell, though recall speed and location may still limit protection against infection.

Germinal centre. A temporary structure in lymph nodes or the spleen where activated B cells mutate, compete and receive T-cell help. It is a workshop for improved antibodies and memory.

Affinity maturation. The process by which selected B-cell clones produce antibodies that bind antigen more effectively. Repeated exposure can continue this selection and improve the response's quality.

Correlate of protection. An immune measurement associated with protection against a defined outcome. A useful correlate can support decisions, but association, mechanism and transfer across populations require separate evidence.

Serology. The study or measurement of antibodies in blood. It can detect seroconversion or estimate an antibody titre, but a positive result is not automatically proof of clinical protection.

Immunogenicity. The ability of a product to generate measured immune responses. High immunogenicity can support development, but the

measured response must still be linked to protection that matters. It is not clinical efficacy.

Reactogenicity. Expected short-term reactions caused by the immediate response to vaccination, such as soreness or fever. Reactogenicity describes reactions; it is not a score for effectiveness.

Primary series. The initial dose or set of doses intended to establish protection. Several doses may be designed into the series because priming, maturation and response strength develop over time.

Booster. A later dose given to expand primed cells, raise antibody, improve quality, restore waning protection or update the antigen. The term covers several distinct purposes.

Live attenuated vaccine. A vaccine using an organism weakened enough to avoid ordinary disease in most recipients while retaining limited replication. It can induce broad immunity but carries specific contraindications.

Inactivated vaccine. A vaccine containing a pathogen rendered unable to replicate. Once inactivation is complete it cannot reproduce, though the product may need adjuvant and repeated doses to produce durable protection.

Toxoid. A bacterial toxin altered so it cannot cause its usual harm while retaining recognisable structure. Tetanus and diphtheria vaccines train antibodies against toxins through this method.

Subunit vaccine. A vaccine containing selected components rather than the whole pathogen. Greater control over the target can reduce unnecessary material while increasing dependence on formulation and adjuvant.

Conjugate vaccine. A vaccine that links a bacterial polysaccharide to a carrier protein. The link recruits T-cell help, improving infant responses, antibody quality and immune memory.

Viral-vector vaccine. A vaccine using a modified virus to deliver genetic instructions for another pathogen's antigen. Vector immunity, replication ability, tissue targeting and storage affect its performance.

mRNA vaccine. A vaccine delivering temporary messenger RNA instructions, usually inside lipid particles, so cells make an antigen. In authorised products the RNA acts in the cytoplasm, supplies no machinery for chromosomal integration and is broken down after use.

Efficacy. The proportional reduction in a defined outcome among vaccinated people compared with a control group under study conditions. The endpoint, population, schedule and follow-up must be stated.

Effectiveness. Vaccine performance in ordinary use. It reflects product properties together with recipient differences, adherence, storage, circulating strains, health services, exposure and evaluation design.

Adverse event following immunisation. Any unfavourable medical occurrence after vaccination, whether caused by the vaccine or not. The term preserves timing while causality is investigated through comparison and biological evidence.

Community immunity. Indirect protection produced when immunity reduces transmission through a contact network. It depends on pathogen biology, vaccine effects, coverage, clustering, waning and importation, so no universal threshold exists.

Cold chain. The temperature-controlled route from manufacture through storage and transport to administration. Some vaccines are damaged by heat, light or freezing, so correct conditions are product-specific. Failure may leave a dose looking normal while reducing potency.

Go Deeper

Paul A. Offit, *Vaccinated: One Man's Quest to Defeat the World's Deadliest Diseases* (Smithsonian Books, 2007). The most inviting next step is a biography of Maurice Hilleman, whose work connected laboratory science, industry and the routine childhood schedule. Offit writes with admiration and a clear pro-vaccination position, so this is not a detached social history. It is excellent on the practical, collective labour behind vaccines commonly attached to more famous names, and on how one research programme produced several different products. Read it after this book to see how laboratory choices became manufacturing processes, trials and a routine schedule.

Edward Jenner, *An Inquiry into the Causes and Effects of the Variolae Vaccinae* (1798). Read the primary evidence and notice how little theory Jenner possessed. The booklet is short, includes case histories and reveals vaccination being assembled from observation, experiment, analogy and persuasion before viruses or antibodies were known. Its experiments on children violate modern standards, and its causal reasoning is uneven. That discomfort is part of its value: a founding medical text can be both transformative and ethically unacceptable by current rules. Follow the sequence of cases rather than only the famous first experiment; Jenner's argument is less clean and more revealing than the legend.

Meredith Wadman, *The Vaccine Race: Science, Politics, and the Human Costs of Defeating Disease* (Viking, 2017). Wadman follows the development of human cell lines and rubella vaccines through scientific rivalry, abortion politics, regulation and contested research ethics. It is the best choice for seeing why a vaccine is never only an antigen. Cell culture, institutional power, consent, intellectual credit and manufacturing all enter the product. The narrative is detailed and sometimes grim, but it makes the hidden infrastructure of twentieth-century vaccination unusually tangible. It also shows that ethical and technical progress do not advance at the same speed.

Walter A. Orenstein, Paul A. Offit, Kathryn M. Edwards and Stanley A. Plotkin, *Plotkin's Vaccines*, 8th edition (Elsevier, 2023). This is the field's large reference work, not a book to read straight through. Begin with the chapters on vaccine immunology, correlates of protection, manufacturing, adjuvants and general immunisation practice, then use the disease chapters as needed. It is technical, expensive and tied partly to licensed products and recommendations that change. Its strength is the opposite of this book's: depth, qualification and detail when compression is no longer enough. Use the index and chapter bibliographies; recommendations age, while the mechanistic and evidential distinctions remain valuable.

Notes and Sources

Current scientific, regulatory and programme claims were checked on 3 September 2026. Where a source page was published in 2026 but reports 2025 data, both dates are stated. Vaccine schedules and recommendations vary by country, age, risk and time; this book explains the decision structure rather than reproducing one current schedule.

The Whole Thing in One Page and Why You Should Care

The book's central model, vaccination as a change to the immune system's starting position before exposure, is a synthesis of standard vaccine immunology rather than a claim that every infection follows one clock. Pollard and Bijker's guide to vaccinology and the general chapters in *Plotkin's Vaccines* support the account of antigen presentation, B-cell and T-cell activation, germinal centres, antibodies, memory and platform choice. The model is bounded in the text where mucosal entry, toxins, immune evasion, age and immune suppression alter the result.

Smallpox dates follow the WHO eradication record: intensified global work began in 1967, the last known natural case occurred in Somalia in 1977, and eradication was declared in 1980. Ali Maow Maalin was the last person known to acquire naturally occurring smallpox; his illness was variola minor,

not variola major. The programme's dependence on surveillance, case investigation and vaccination around detected transmission is documented in Fenner and colleagues' official history.

The estimate of 154 million deaths averted between 1974 and 2024 comes from Shattock and colleagues' modelling of fourteen pathogens across fifty years of the Expanded Programme on Immunization. It is retained as a modelled counterfactual with uncertainty, not presented as a direct count. The study also estimated that most deaths averted were among children younger than five.

The England HPV example comes from Falcaro and colleagues' 2024 population-based observational study, which extended the programme analysis through June 2020. It compared cervical cancer and grade 3 cervical intraepithelial neoplasia rates across birth cohorts with different eligibility for the national programme. The largest reductions were in women offered vaccination at ages twelve to thirteen. The study concerns England and the bivalent vaccine era; it is not treated as a universal effect size for every HPV product or programme.

The malaria programme result comes from Mwapasa and colleagues' 2026 evaluation of the 2019 to 2023 Malaria Vaccine Implementation Programme in Ghana, Kenya and Malawi. Administrative clusters were assigned to earlier or later RTS,S introduction, then evaluated through routine delivery. Introduction was associated with a 13 per cent reduction in all-cause mortality excluding injuries among vaccine-eligible children. This is a programme result in three settings with their observed coverage and accompanying malaria control, not the clinical efficacy percentage of RTS,S or R21. The WHO's July 2026 coverage release reported that twenty-five African countries had introduced malaria vaccination at national or subnational level.

Mechanism and Core Ideas

The distinction between antigen target and innate context follows modern vaccine immunology. An adjuvant can improve antigen uptake, innate signalling, cell recruitment and response quality; its purpose is not to create discomfort. Statements about route are intentionally conditional because intramuscular, oral, intranasal and intradermal delivery can produce different systemic, mucosal and tissue responses depending on product and pathogen.

The account of germinal centres, affinity maturation, plasma cells and memory populations follows Pollard and Bijker and the immunology chapters in *Plotkin's Vaccines*. Plotkin's review of correlates of protection supports the warning that an immune measurement becomes useful only when linked to a defined clinical outcome. Some vaccines have strong accepted correlates; others depend on several immune functions or lack a single transferable threshold.

The platform survey describes categories rather than ranking them. Pardi and colleagues support the mRNA platform account; Karikó and colleagues' 2005 study establishes the importance of nucleoside modification in reducing unwanted RNA sensing. Current UK Spikevax product information and WHO product assessment state that delivered mRNA acts in the cytoplasm, does not enter the nucleus or interact with the genome, does not replicate and is expressed transiently. These sources support the authorised product mechanism, not a claim about every experimental RNA construct.

The conjugate-vaccine mechanism is standard: coupling a polysaccharide to a carrier protein allows a polysaccharide-specific B cell to recruit T-cell help, improving class switching, maturation and memory in young children. The hepatitis B and HPV examples use recombinant antigens without a complete infectious genome. Live attenuated products retain limited biological activity and therefore have product-specific contraindications and rare risks that do not apply to non-replicating platforms.

The definitions of efficacy, effectiveness and indirect effects follow Halloran, Struchiner and Longini. A percentage must be tied to an endpoint, comparator, population, schedule and follow-up period. Fine, Eames and Heymann support the treatment of community immunity as a setting-dependent transmission effect rather than a universal threshold. Tetanus is the counterexample because environmental spores cause cases without sustained person-to-person transmission.

The rabies passage follows current WHO guidance: post-exposure prophylaxis includes immediate wound care, a vaccine course and rabies immunoglobulin where indicated. It works before clinical rabies becomes established by preventing the virus from reaching the central nervous system. The book does not imply that vaccination reverses symptomatic rabies.

The development and manufacturing account is supported by FDA guidance on phased human studies, concurrent assessment of manufacturing, facility review, lot-to-lot consistency and post-approval lot release. WHO assessment documents support the distinction among national authorisation, work-sharing, emergency listing and prequalification. The exact route and legal effect vary across jurisdictions. The text therefore describes common evidential and manufacturing functions rather than presenting the United States process as universal.

Historical and operating evidence

The origins of variolation are distributed and incompletely documented. Boylston's review and National Library of Medicine material support established use in parts of Asia, Africa and the Ottoman world before European adoption. The Boston account rests on contemporary records concerning Onesimus, Cotton Mather and Zabdiel Boylston. Mortality comparisons were not randomised, depended on incomplete case records and cannot be read as a modern efficacy trial.

Lady Mary Wortley Montagu's promotion of Ottoman inoculation in Britain and the 1721 inoculation of her daughter are well documented. Jenner's

1796 experiment and 1798 publication are described from his own *Inquiry* and Baxby's bicentenary analysis. James Phipps was a child in Jenner's household orbit and could not provide consent by modern standards. Jenner did not invent acquired immunity or the first cowpox practice; his historical importance lies in experimental demonstration, publication and mobilisation of a safer substitute for variolation. Jenner used the Latin-rooted *Variolae Vaccinae* for cowpox; his friend Richard Dunning used the word vaccination in print in 1800.

The discussion of arm-to-arm vaccination, calf lymph, preservation and potency standards draws on Fenner and colleagues and vaccine histories. These changes matter because biological material varied between transfers and could carry contamination. The narrative avoids a single clean transition from folk practice to laboratory science.

Pasteur's attenuation work and the Joseph Meister treatment are supported by Geison's archival history and standard vaccine histories. The dog was believed rabid, and Pasteur's group used progressively less attenuated spinal-cord preparations after the bite. The case's scientific and ethical interpretation remains contested, so the text presents survival, publicity and controversy without claiming that one dramatic case alone proved the regimen.

The Cutter incident follows Nathanson and Langmuir's epidemiological reconstruction. Some 1955 lots contained incompletely inactivated poliovirus, causing vaccine-associated cases and transmission to contacts. The incident led to tighter production, testing and regulatory controls. The comparison of inactivated and oral polio vaccines is deliberately functional: inactivated vaccine strongly protects against paralytic disease, while oral vaccine has offered important intestinal and transmission advantages but can rarely cause vaccine-associated paralysis or seed circulating vaccine-derived poliovirus where population immunity is low.

The rubella, hepatitis B, Hib conjugate and HPV passages rely on Wadman, Offit, *Plotkin's Vaccines* and the updated England HPV outcome study. Named individuals appear where their work reveals a mechanism or

institution; they are not treated as solitary inventors of programmes produced by large teams.

The WHO established the Expanded Programme on Immunization in 1974 around six initial diseases: tuberculosis, diphtheria, tetanus, pertussis, polio and measles. The smallpox operating details, including surveillance-containment, the bifurcated needle and freeze-dried vaccine, follow Fenner and colleagues.

The COVID-19 acceleration account distinguishes elapsed calendar time from evidential tasks. Karikó and Weissman's nucleoside work and Pardi and colleagues' platform review predate the pandemic. During the emergency, trial stages, rolling review, manufacturing preparation and financial risk overlapped. Large randomised trials still measured prespecified clinical endpoints and common adverse effects; post-authorisation surveillance remained necessary for rare events and changing conditions.

Evidence behind the corrections

The live-vaccine qualification prevents the claim that no vaccine can ever produce infection-like illness. Oral polio vaccine supplies the clearest programme-level exception. The WHO and Global Polio Eradication Initiative describe circulating vaccine-derived strains as rare consequences of prolonged circulation in under-immunised populations, not evidence that inactivated or subunit products behave the same way.

Tetanus disease does not reliably induce protective immunity because a disease-causing amount of toxin can be below the amount needed to generate dependable antitoxin. WHO and CDC guidance therefore recommend immunisation after recovery when indicated. This example is retained to show that severity or breadth of natural exposure does not guarantee better memory.

The mRNA correction is limited to authorised vaccine products and the machinery they contain. It does not claim that RNA can never affect DNA through any biological route. Retroviruses possess specialised

reverse-transcription and integration machinery; authorised mRNA vaccines do not supply that system.

The autism section distinguishes the history of the 1998 case series from the epidemiological question. Hviid and colleagues followed 657,461 Danish children and found no increased autism risk associated with MMR vaccination, including in prespecified higher-risk groups. WHO's December 2025 vaccine-safety committee review summarises the wider evidence against causal links involving MMR, other childhood vaccines, thiomersal and aluminium-containing vaccine ingredients.

FDA guidance on the Vaccine Adverse Event Reporting System states that a report means symptoms occurred after vaccination, not that vaccination caused them. Shimabukuro and colleagues explain how passive reports support signal detection while remaining vulnerable to under-reporting, stimulated reporting, incomplete information and the absence of a suitable denominator. Current CDC guidance supplies the deliberately setting-specific myocarditis example: in United States surveillance, cases were rare and occurred most often in adolescent and young adult males within seven days after a second mRNA dose. Product, age, dose and interval affected the assessment. This example demonstrates signal confirmation and recommendation refinement; it is not used as a universal rate or a current schedule. Confirmed safety conclusions require comparison with background rates and stronger designs.

Use It and Terms

The practical lenses are interpretive tools derived from the evidence structure: define the endpoint, restore denominators, separate product properties from programme performance, trace the physical delivery chain, map transmission and read recommendations in their local setting. They are not a personal clinical schedule. Current national guidance and individual medical advice take precedence for pregnancy, immune suppression, travel, previous reactions, missed doses and age-specific decisions.

The discussion of evolutionary pressure is intentionally conditional.

Vaccination can favour antigenic variants under some circumstances, while preventing infection can also reduce pathogen replication and the supply of mutations. Escape depends on the pathogen, target, breadth and location of immunity, transmission conditions and fitness costs. The book rejects both claims that vaccines cannot influence evolution and that escape is an inevitable consequence of use.

Current data and recommendations

The global coverage figures are WHO estimates for 2025 published on 15 July 2026. They include 13.5 million zero-dose children, meaning children who received no initial diphtheria-tetanus-pertussis-containing dose under the operational definition, 85 per cent coverage for a third diphtheria-tetanus-pertussis dose, 84 per cent first-dose measles coverage and 33 per cent first-dose HPV coverage among girls. Only the zero-dose figure is used in the narrative because it directly supports the programme argument. Coverage estimates can be revised as national reporting improves.

Malaria rollout status was checked against the WHO immunisation coverage release dated 15 July 2026. It reported that twenty-five African countries had introduced malaria vaccines at national or subnational level. Because rollout is changing quickly, this status should be rechecked immediately before publication.

Bibliography

Primary and original evidence

Falcaro, Milena, Kate Soldan, Busani Ndlela and Peter Sasieni. “Effect of the HPV Vaccination Programme on Incidence of Cervical Cancer and Grade 3 Cervical Intraepithelial Neoplasia by Socioeconomic Deprivation in England: Population Based Observational Study.” *BMJ* 385 (2024): e077341. DOI: 10.1136/bmj-2023-077341.

Halloran, M. Elizabeth, Claudio J. Struchiner and Ira M. Longini Jr. “Study

Designs for Evaluating Different Efficacy and Effectiveness Aspects of Vaccines.” *American Journal of Epidemiology* 146, no. 10 (1997): 789-803. DOI: 10.1093/oxfordjournals.aje.a009196.

Hviid, Anders, Jørgen Vinsløv Hansen, Morten Frisch and Mads Melbye. “Measles, Mumps, Rubella Vaccination and Autism: A Nationwide Cohort Study.” *Annals of Internal Medicine* 170, no. 8 (2019): 513-520. DOI: 10.7326/M18-2101.

Jenner, Edward. *An Inquiry into the Causes and Effects of the Variolae Vaccinae*. London: Sampson Low, 1798.

Karikó, Katalin, Michael Buckstein, Houping Ni and Drew Weissman. “Suppression of RNA Recognition by Toll-Like Receptors: The Impact of Nucleoside Modification and the Evolutionary Origin of RNA.” *Immunity* 23, no. 2 (2005): 165-175. DOI: 10.1016/j.immuni.2005.06.008.

Mwapasa, Victor, Kwaku Poku Asante, Paul Milligan, et al. “Impact of Introducing RTS,S/AS01E Malaria Vaccine on Mortality in Young Children in Ghana, Kenya, and Malawi: An Observational Evaluation of a Cluster-Randomised Implementation Programme.” *The Lancet* 407, no. 10541 (2026): 1796-1808. DOI: 10.1016/S0140-6736(26)00248-5.

Nathanson, Neal and Alexander D. Langmuir. “The Cutter Incident: Poliomyelitis Following Formaldehyde-Inactivated Poliovirus Vaccination in the United States during the Spring of 1955. I. Background.” *American Journal of Hygiene* 78 (1963): 16-28. DOI: 10.1093/oxfordjournals.aje.a120327.

Nathanson, Neal and Alexander D. Langmuir. “The Cutter Incident: Poliomyelitis Following Formaldehyde-Inactivated Poliovirus Vaccination in the United States during the Spring of 1955. II. Relationship of Poliomyelitis to Cutter Vaccine.” *American Journal of Hygiene* 78 (1963): 29-60. DOI: 10.1093/oxfordjournals.aje.a120328.

Plotkin, Stanley A. “Correlates of Protection Induced by Vaccination.” *Clinical and Vaccine Immunology* 17, no. 7 (2010): 1055-1065. DOI:

10.1128/CVI.00131-10.

Shattock, Andrew J., Helen C. Johnson, So Yoon Sim, et al. "Contribution of Vaccination to Improved Survival and Health: Modelling 50 Years of the Expanded Programme on Immunization." *The Lancet* 403, no. 10441 (2024): 2307-2316. DOI: 10.1016/S0140-6736(24)00850-X.

Shimabukuro, Tom T., Michael Nguyen, David Martin and Frank DeStefano. "Safety Monitoring in the Vaccine Adverse Event Reporting System." *Vaccine* 33, no. 36 (2015): 4398-4405. DOI: 10.1016/j.vaccine.2015.07.035.

Reviews and syntheses

Fine, Paul, Ken Eames and David L. Heymann. "'Herd Immunity': A Rough Guide." *Clinical Infectious Diseases* 52, no. 7 (2011): 911-916. DOI: 10.1093/cid/cir007.

Orenstein, Walter A., Paul A. Offit, Kathryn M. Edwards and Stanley A. Plotkin, eds. *Plotkin's Vaccines*. 8th ed. Philadelphia: Elsevier, 2023.

Pardi, Norbert, Michael J. Hogan, Frederick W. Porter and Drew Weissman. "mRNA Vaccines: A New Era in Vaccinology." *Nature Reviews Drug Discovery* 17, no. 4 (2018): 261-279. DOI: 10.1038/nrd.2017.243.

Pollard, Andrew J., and Else M. Bijker. "A Guide to Vaccinology: From Basic Principles to New Developments." *Nature Reviews Immunology* 21 (2021): 83-100. DOI: 10.1038/s41577-020-00479-7.

History and interpretation

Baxby, Derrick. "Edward Jenner's Inquiry after 200 Years." *BMJ* 318, no. 7180 (1999): 390. DOI: 10.1136/bmj.318.7180.390.

Boylston, Arthur. "The Origins of Inoculation." *Journal of the Royal Society of Medicine* 105, no. 7 (2012): 309-313. DOI: 10.1258/jrsm.2012.12k044.

Fenner, Frank, Donald A. Henderson, Isao Arita, Zdeněk Ježek and Ivan D. Ladnyi. *Smallpox and Its Eradication*. Geneva: World Health Organization, 1988.

Geison, Gerald L. *The Private Science of Louis Pasteur*. Princeton: Princeton University Press, 1995.

Offit, Paul A. *Vaccinated: One Man's Quest to Defeat the World's Deadliest Diseases*. Washington, DC: Smithsonian Books, 2007.

Wadman, Meredith. *The Vaccine Race: Science, Politics, and the Human Costs of Defeating Disease*. New York: Viking, 2017.

Institutional and current sources

Centers for Disease Control and Prevention. "Safety Considerations for COVID-19 Vaccines." Updated 4 November 2025; checked 3 September 2026.

Centers for Disease Control and Prevention. "Tetanus." In *Epidemiology and Prevention of Vaccine-Preventable Diseases*, 14th ed. Washington, DC: Public Health Foundation, 2021; online chapter checked 3 September 2026.

electronic Medicines Compendium. "Spikevax LP.8.1 0.1 mg/mL Dispersion for Injection: Summary of Product Characteristics." Current UK product information checked 3 September 2026.

Food and Drug Administration. "Vaccine Adverse Event Reporting System Questions and Answers." Silver Spring, MD: FDA, checked 3 September 2026.

Food and Drug Administration. "Vaccine Development 101." Silver Spring, MD: FDA, checked 3 September 2026.

World Health Organization. "BCG Vaccines: WHO Position Paper, February 2018." *Weekly Epidemiological Record* 93, no. 8 (2018): 73-96; checked 3 September 2026.

World Health Organization. "WHO Expert Group's New Analysis Reaffirms There Is No Link between Vaccines and Autism." Statement, 11 December 2025; checked 3 September 2026.

World Health Organization. "Immunization Coverage." Fact sheet, 15 July

2026; checked 3 September 2026.

World Health Organization. "Malaria Vaccines: RTS,S and R21." Questions and answers, 2026; checked 3 September 2026.

World Health Organization. *Recommendation for an Emergency Use Listing of COVID-19 Vaccine Moderna*. Version dated 17 May 2021; checked 3 September 2026.

World Health Organization. "Rabies." Fact sheet, 5 June 2024; checked 3 September 2026.

World Health Organization. "Smallpox." Eradication record, checked 3 September 2026.