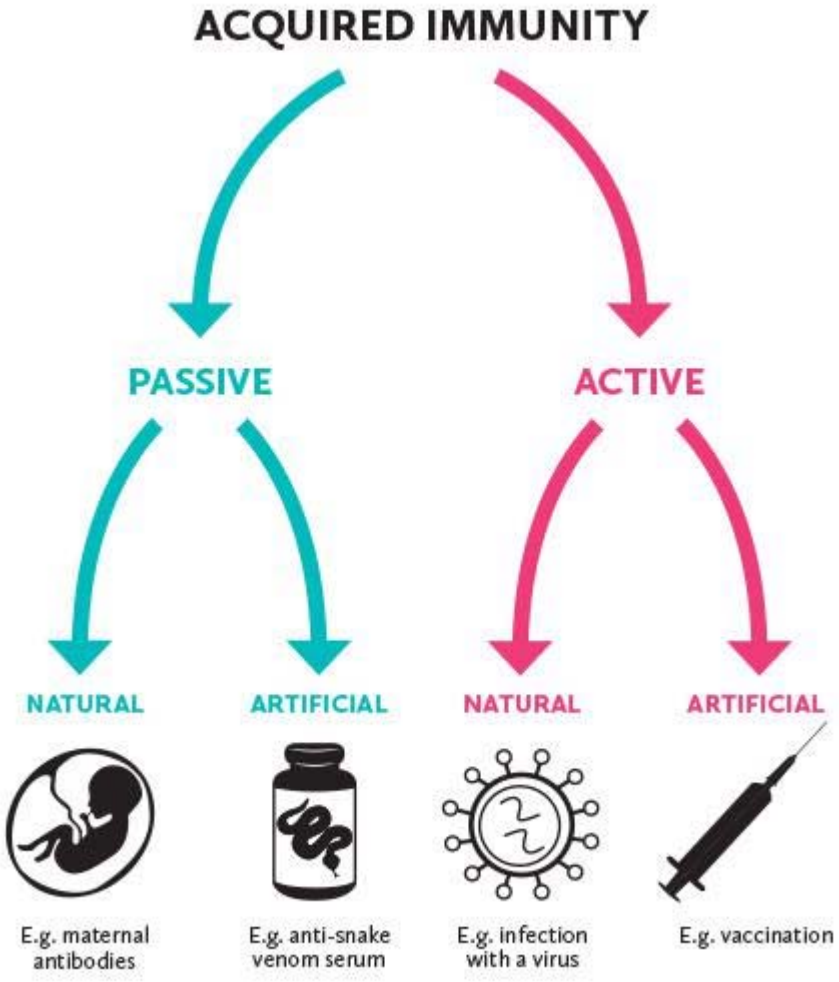
Immunity and vaccination

There are several different types of immunity

During the first few months of our lives, we were all protected from infections by antibodies passed on to us by our mothers – in the uterus (via the placenta), and in breast milk. This type of immunity is known as passive immunity.



The antibodies last only a few months, though, so infants must quickly start developing their own long-lasting active immunity to protect them against different diseases. The thymus gland, where T cells mature, is most active just after birth and before puberty.

Before they are six months old, babies in the UK are immunised against diphtheria, tetanus, whooping cough, polio, rotavirus, meningitis C and other infections. The components of each vaccine encourage the immune system to develop its own defences against the disease. This is known as 'artificial' active immunity, whereas the kind of immunity that develops when the immune system comes into contact with the infectious agents of disease – often making you ill – is known as 'natural' active immunity.

Being immune to a disease means that you shouldn't get ill with the same infection again. If a virus evolves, though, you can still catch the new strain.

Take a look at our animation to see how immunological memory is developed. Each time the body is exposed to a particular pathogen, the antibody response becomes quicker, and more sustained, providing better immunological protection.

Vaccines come in different forms

Vaccinations work by giving the immune system a controlled first exposure to a disease. Exposed to the antigens in the vaccine, your immune cells start making antibodies and also produce long-lived memory T cells and memory B cells. If your immune system encounters the same antigen again, the memory cells ensure that many specific antibodies are made quickly and in greater quantity, so you are much less likely to get ill from that disease.

What is in a vaccine? Some use only pieces of the DNA – certain antigens or DNA encoding antigenic memory B cells – that trigger an immune response but don't cause disease on their own. Other vaccines contain dead (inactivated) pathogens. Some vaccines, such as the measles, mumps and rubella (MMR) vaccine, are made with live attenuated (weakened) versions of the pathogen. Live vaccines are usually the best at provoking an immune response but they have to be kept refrigerated. They also pose the very small risk that the live pathogen will mutate to an infectious form. For example, it's estimated that the live virus in the oral polio vaccine can cause paralysis in about 1 in 2.5 million doses of the vaccine. Ideally, vaccines against a particular pathogen will be delivered into the body the same way as the pathogen itself, such as a vaccine against influenza that is inhaled.

So why don't we have vaccines for all diseases? For some, scientists haven't been able to provoke a strong enough immune response using the usual vaccine designs. For others, there may be several promising vaccines, but rigorous safety and efficacy testing means that it may take years before a vaccine becomes available. Or it may be that more funding is needed.

Vaccination can completely wipe out some diseases, as in the case of smallpox, which was declared eradicated in 1980. In other cases, to keep a disease from spreading, a high proportion of the population must be vaccinated. This is called 'herd immunity'. The measles outbreak in Wales in 2013 was due to falling vaccination levels, which meant that infected people were more likely to come into contact with others who were unprotected.

Vaccines: how and when are they given?

How are vaccines given?

Vaccines generate immunity across the body as a whole, but they can also provoke specific immune responses in specific bodily areas. For this reason, the varying delivery methods of vaccines are important.

Vaccines are most effective if they can stimulate the creation of antibodies where pathogens are likely to invade and harm the body, for instance in mucous membranes. So, to ensure that their action is suitably targeted, the delivery routes of vaccines often mimic the invasion routes of pathogens.

For example, the oral polio vaccine is ingested in order to stimulate the creation of antibodies in the lining of the intestines, as this is where the poliovirus ends up and multiplies after entering the body in contaminated food and water. The oral cholera vaccine generates one localised set of antibodies that stop *Vibrio cholerae* bacteria from attaching themselves to the intestinal wall, and another set that prevents the bacteria's toxins from binding to the intestine's mucous membrane.

Intranasal (up-the-nose) delivery of vaccines achieves the same effect, but in the mucous membrane of the nasal cavity. This delivery method is used to combat diseases that need to overcome the nasal mucous barrier in order to infect the body, such as influenza.

However, specific delivery routes are also sometimes necessary to minimise the chances of vaccines having adverse effects on the body. Vaccines containing aluminium-based adjuvants often cause inflammation (granulomas) unless they are injected into muscle tissue. The BCG (Bacille Calmette–Guérin) vaccine for tuberculosis is injected into the topmost layer of the skin – a process known as intradermal injection – to avoid it causing damage to blood vessels and nerves.

Some vaccines – such as those for yellow fever and MMR (measles, mumps and rubella) – work best when released slowly into the body. For this reason they are injected into the layer of fat between the skin and muscle. The limited blood flow in this area prevents the vaccine from being distributed around the body too quickly. This method is known as subcutaneous injection.

Why do we have different vaccines at different ages?

Vaccines are given to people when they are at risk of contracting a disease. Many vaccines are given at a young age because children's bodies may not be strong enough to fight off naturally occurring diseases, which puts them at risk. Measles, for example, killed 122,000 people globally in 2012, and is one of the leading causes of death among young children – this is why children are given a measles vaccination at an early age.

Some vaccines are given to children because they work less effectively in adults. For example, when immunising those at risk of contracting tuberculosis, the NHS recommends giving the BCG before the age of 16, and never past 35 – at this age it simply isn't effective in stimulating an immune response.

However, some diseases become a risk only later in life and so childhood vaccination is not needed. Human papillomavirus (HPV), which can cause cervical cancer, is transferred through sexual contact, so the HPV vaccine is commonly given to girls only once they have reached puberty. (See our cervical cancer case study for more.)

Likewise, before the age of 65 most adults aren't at risk of becoming seriously ill from influenza. However, as the body ages, its ability to fight flu decreases. Because of this, anyone over the age of 65 in the UK is entitled to a free annual flu vaccination, to protect against strains of the disease from recent years.

Differences and changes in risk explain why vaccine programmes vary from region to region and over time. For example, in the UK the BCG is only offered to children who live in an area where contracting tuberculosis is a real risk, such as inner-city London; children in low-risk areas do not receive the vaccine. For diseases that have been eradicated, such as smallpox, vaccination programmes no longer exist.

Why and how are vaccines kept cold?

The antigens in a vaccine are biological matter, and so will denature if exposed to high temperatures. This can reduce or even entirely destroy a vaccine's potency. Biological molecules also degrade naturally over time, and reducing their temperature slows the rate of degradation. However, vaccines containing aluminium-based adjuvants cannot be frozen, as sub-zero temperatures upset the adjuvants' structures, rendering them ineffective.

This is why the World Health Organization (WHO) recommends keeping most vaccines between 2°C and 8°C – though there are some exceptions. The oral polio vaccine, for instance, is notoriously unstable, and so WHO recommends storing it between –25°C and –15°C ahead of it being distributed for administration.

Keeping vaccines cold right up until they are administered (known as 'maintaining the cold chain') is a big challenge in lower-income countries. Many such countries have hot climates and limited, intermittent electricity supplies, making constant refrigeration difficult. Thankfully, there are a number of solutions.

One method is to use passive coolers – large vacuum flasks filled with ice that can keep vaccines cool for up to a month. Other options include battery-powered and solar-powered fridges.

However, the ultimate solution, which is currently being explored, is to create new thermo-stable vaccines that can be stored and transported at a variety of different temperatures without any loss of potency.

Vaccines: what's inside?

A vaccine contains the antigens, or 'non-self' markers, of a pathogen, to provoke an immune response and stimulate the production of antibodies. This process, in essence, mimics real-life infection and allows the body to 'learn' how to identify the same pathogen in the future.

These antigens may be delivered by putting a whole, weakened pathogen into the body (eg whole bacteria or viruses), or by taking the antigens from a pathogen and delivering these alone.

Live attenuated vaccines

Different vaccines deliver antigens in different ways. Some vaccines – such as the BCG (Bacille Calmette–Guérin), which protects against tuberculosis – contain a live version of the whole pathogen. However, in such cases the pathogen's strength (virulence) is weakened (attenuated) before it is given, to reduce the chance of infection.

Inactivated vaccines

Some vaccines contain an inactive version of a pathogen, one that has been killed – for instance by using heat or a chemical called formaldehyde. The immune system can still recognise and respond to the pathogen, but as the pathogen cannot reproduce, it poses no risk of infection. Cholera, hepatitis A and rabies vaccines all contain inactivated pathogens.

Toxoid vaccines

The symptoms of some diseases are caused by harmful products of bacteria, known as toxins. Vaccines for these diseases, which include tetanus, use inactivated versions of toxins (called toxoids) to stimulate an immune response.

Subunit vaccines

Other vaccines contain only the antigens of a pathogen that best stimulate a response – these are known as subunit vaccines. By including only the essential antigens, and not the whole pathogen itself, these vaccines are much less likely to cause an adverse reaction, and pose no risk of infection. However, subunit vaccines tend to induce a weaker immune response than live attenuated vaccines.

Conjugate vaccines

Finally, some pathogens can be hard for the immune system to identify, and so require a special type of vaccine.

Bacteria coated with sugar molecules known as polysaccharides are able to mask the antigenic material on their surface, making it difficult for the immune system to recognise them and mount a response (especially in children). To fight against this, conjugate vaccines are created: the bacteria's sugar coatings are isolated as subunits and then chemically joined to larger, more readily identifiable carrier proteins. These new constructions, being recognisable, stimulate an immune response that creates antibodies that can also recognise and fight against the coated bacteria in the future.

Other ingredients

As well as these active ingredients, vaccines also contain:

- fluid, such as sterile water, saline or a protein-containing fluid, to suspend the contents
- stabilisers, such as albumin, gelatine or sugars, to help the active ingredients remain unchanged when exposed to adverse conditions, such as extreme temperatures or changes in light, humidity or acidity
- preservatives, such as phenols or antibiotics, to prevent the growth of dangerous bacteria and fungi in the vaccine.

Some vaccines also contain adjuvants: substances such as aluminium compounds that strengthen the immune response to the vaccine's antigens. These are commonly used in subunit vaccines.

Vaccines may also contain trace elements of substances used during their manufacture: for example, some vaccines are grown using fertilised hens' eggs and so may contain traces of egg protein, and inactivated vaccines may contain extremely small traces of formaldehyde.

How well do vaccines work?

How effective are vaccines, and why do they require boosters?

Vaccines are very effective at providing individuals with immunity to certain diseases, though they don't provide immunity in 100 per cent of cases. Every person's immune system is different: some people won't create antibodies in response to a vaccine's antigens and therefore won't become immune.

Rates of effectiveness vary from vaccine to vaccine: a three-dose course of the inactivated polio vaccine is 99 per cent effective, whereas the effectiveness of typhoid vaccines is only around 70 per cent.

A further complication is that the effects of some vaccinations wear off over time. Two doses of the MMR (measles, mumps and rubella) vaccine will usually provide 20 years' protection against measles, but the effects of a typhoid vaccine will typically wear off after three years. Scientists are currently trying to work out why this happens. This is why we have boosters – to 'remind' our immune system how to identify certain pathogens and top up our immunity.

At the population level vaccines are highly effective. They have eradicated some diseases, such as smallpox, and vastly reduced the threat of others. In the UK in the 1940s and 1950s annual deaths from measles numbered in the hundreds.

Success is achieved through herd immunity. No vaccine is 100 per cent effective, and not everyone in a population will be vaccinated; however, if most of a population are vaccinated and become immune to a disease, its ability to spread will be vastly reduced. This protects people without immunity from infection too.

What risks are associated with vaccines?

Vaccines are very safe in the Western world – national regulatory authorities govern their testing and manufacture, which ensures that they are safe for human use.

Even so, not everyone may be able to be vaccinated. People allergic to trace elements such as egg protein or pork gelatine have to avoid vaccines that are grown using these substances. Some people may be allergic to the antibiotics used in some vaccines. This is why antibiotics that are known to often cause allergic reactions, such as penicillin, are generally not used in them.

It is recommended that pregnant women avoid taking live vaccines, to prevent live pathogens affecting their unborn child. Likewise, adults recovering from certain illnesses are advised to delay taking certain vaccines until they have recovered. For example, the NHS says you shouldn't have a flu jab while you are recovering from a fever.

There are many rumours about negative side-effects of vaccines, which are not just untrue but potentially very damaging. A false claim linking the MMR vaccination to autism in the UK in the 1990s caused levels of vaccination to fall significantly in some parts of the country. This led to a reduction in herd immunity, which has resulted in outbreaks of measles and mumps in recent years. Both these diseases can cause encephalitis, a rare but potentially deadly inflammation of the brain.

The greatest risks surrounding vaccination are in low-income countries. These risks concern not the vaccines themselves, but their regulation and administration. Unreliable regulatory authorities in some countries may not be able to stop fake vaccines being produced; failure to keep the vaccines cold right up until they are administered (the so-called 'cold chain') may result in spoiled, ineffective vaccines being administered; and insufficient education among those administering vaccines may result in needles being reused, risking the spread of blood-borne diseases such as HIV/AIDS.

Vaccination does not just benefit the vaccinated

Childhood vaccination against infectious diseases has saved countless lives. The main beneficiary, of course, is the child who gets vaccinated. But those not given a vaccine also gain, thanks to herd immunity.

If most people in a population are vaccinated, a pathogen cannot spread – it cannot come into contact with enough susceptible hosts to sustain an infection. The degree of vaccine coverage needed to create herd immunity varies between infections but is rarely more than 90 per cent.

If people choose not to vaccinate their children, there is often little risk that their child will become ill. But they are freeloading off the majority – they gain the benefits without facing any risks.

And if lots of parents go down this route, the risk of an outbreak rises dramatically. This is a particular problem for children who for medical reasons cannot be vaccinated, and so have to rely on herd immunity. Fears about a possible link between the MMR (measles, mumps and rubella) vaccine and autism (considered extremely unlikely by the overwhelming majority of experts) lowered the vaccine's coverage to danger levels, threatening herd immunity. As a refusal to vaccinate places others at risk, some have argued that vaccination should be compulsory. In the USA it is effectively compulsory – children cannot attend school unless they have had the MMR vaccine.

Others argue that individuals should have the right to decide for themselves whether to vaccinate their children, having made their own decision about the risks involved.