

Vaccines

September 2015

Summary

- Vaccines have made a huge contribution to health; reducing illness, death, and long-term disability from a host of diseases which commonly afflicted populations before widespread immunisation.
- For all vaccines currently available the risk from the disease greatly outweighs any adverse effect the vaccine might have. Severe complications due to vaccines are extremely rare although it is still important to communicate the facts about vaccines to the public.
- More research is needed to develop effective vaccines against many infectious diseases where no effective vaccine currently exists. Importantly, vaccines are also showing promise in the prevention or treatment of non-communicable diseases, such as cancer and potentially Alzheimer's disease.

What are vaccines?

Vaccines work by teaching the body's immune system to recognise a harmful infection. Most vaccines contain a harmless element of the infectious agent – either a killed part of the germ or one that is alive but unable to cause the disease (attenuated) – that stimulates the immune system to recognise the pathogen by producing antibodies against it. The production of these antibodies against inert components of the disease builds immunity without triggering the disease itself, and means the immune system is able to subsequently recognise the pathogen and mount an appropriate immune response as a reaction to encountering the infection naturally. This means the person won't become ill following exposure to the germ and is therefore immune. In many cases a single dose of the vaccine is sufficient to confer lifelong immunity. For others, such as with 3-in-1 Td/IPV vaccine for tetanus, diphtheria and polio, the acquired immunity degrades over time and a booster dose may be required to "top up" the level of antibodies. Vaccines are primarily preventative (given before potential exposure to a disease) but some can be effective when delivered a very short time after infection, such as with rabies.¹

Importance of vaccination

Vaccines are one of the most effective ways of preventing infectious disease and have had a major impact in reducing illness, death, and long-term disability from conditions that were common before widespread vaccination campaigns. In fact, vaccines were responsible for completely eradicating smallpox, an infectious disease responsible for an estimated 300-500 million deaths during the 20th century, with the last known case occurring in Somalia in 1977. As such, smallpox vaccines are generally considered to be amongst the most successful interventions in the history of medicine.

As another example, during the 1950's there were as many as 7,760 annual notifications of paralytic poliomyelitis in the UK.² Following the introduction of an effective polio vaccine, cases fell rapidly, with the last natural polio infection acquired in the UK occurring in 1984.³ Today, thanks to a collaborative international immunisation programme, the global incidence of polio has been reduced by 99% and the disease remains endemic in only a very small number of developing countries.⁴

Vaccination provides protection to the individual against specific diseases. Sometimes these individuals are immunised because they belong to a high risk group, such as with seasonal flu jabs and the elderly. However, as well as providing benefits to the individual,

mass immunisation – such as those vaccines which are offered free of charge on the NHS to all infants – also confer wider protection to the community through herd immunity. Herd immunity is brought about when enough people have been vaccinated against an infection that the disease is unable to circulate within the population. This means even those who have not been vaccinated are much less likely to come into contact and subsequently develop the disease.

Herd immunity is a critical component in controlling the prevalence of dangerous contagious diseases and protecting the wider population from illness. Individuals who are unable to be vaccinated, such as very young infants, individuals with poorly functioning immune systems (such as those undergoing treatment for cancer), and people with severe immune diseases, are protected from infections because there are enough vaccinated individuals to ensure diseases cannot spread.

However, herd immunity can be lost if the number of people vaccinated in a population falls below a critical proportion. Public anxiety over the safety of vaccines, in particular MMR (see box 1), is thought to have contributed to a decrease in vaccination coverage against some infections. Following the MMR controversy the number of children receiving the MMR vaccine dipped in the early 2000's and as a result there have been several outbreaks of measles in the UK. In the late 1990's the number of confirmed measles cases in the UK remained consistently below 100 but had risen to 2,016 cases in 2012.⁵ Unfortunately, there have been several needless deaths during these outbreaks.

Safety of vaccination

As with all medical interventions, vaccination is not entirely risk free. Any vaccine can have side effects, though these are largely constrained to minor reactions, for instance pain or tenderness at the site of an injection. In extremely rare cases more serious reactions can occur, such as a severe allergic reaction (anaphylaxis). However these adverse events are exceptionally rare and great care is taken to identify individuals for whom the vaccine might not be safe. Vaccines are used because the risk of disease greatly outweighs any adverse effect the vaccine might have. As an illustration, measles virus will cause encephalomyelitis (dangerous and sometimes fatal swelling of the brain and spinal cord) in approximately 1 in every 1000 infected persons. The risk of encephalitis from the MMR vaccine is less than 1 per 1 million doses, or about 1,000 times less than the risk from measles infection.⁶

As with all pharmaceuticals, vaccines are subject to stringent testing before they are approved for use and undergo constant surveillance post-licensure to ensure any problems are acted upon immediately.

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The MMR controversy

MMR is a triple vaccine that protects against three separate illnesses in a single injection – measles, mumps and rubella. In the late 1990's the vaccine was the subject of major controversy after a paper by Andrew Wakefield et al reported a link between the vaccines and autism. In the wake of the publicity caused by the research the uptake of MMR fell, reaching its nadir in 2003/04 when MMR coverage at 24 months (the age at which children should be completely immunised) fell to 79.9%.⁷ The World Health Organisation has set a minimum MMR coverage target of 95%. The latest figures in England remain below this target at 92.7%.⁷

Since the publication of that research several independent bodies, including NHS and Cochrane Library reviews, have concluded that there is no evidence of a link between the MMR vaccine and autism.

The original paper has now been discredited and was officially retracted by *The Lancet*, the journal in which it was published. The research was later declared fraudulent by the *British Medical Journal*. In addition the lead author, Dr Andrew Wakefield, was found to have multiple undeclared conflicts of interest and has since been struck off the Medical Register.

The need for more research

The development of vaccines and their contribution to the health of global populations is one of the 20th century's greatest achievements. Yet there is more that can be done.

Many millions continue to be affected by infectious diseases that have no effective vaccine, including HIV, RSV (the most common cause of bronchitis in children aged under 2 in the UK and worldwide), and tropical diseases such as dengue and malaria. Moreover, developing effective vaccines against unpredictable emergent or re-emergent infections, where it is often difficult for vaccine developers to foresee any significant return on investment, means many diseases affecting predominantly developing economies continue to have no effective vaccine. The recent outbreak of Ebola demonstrates the consequences of being unprepared against such infections while the example of pandemic flu (such as H1N1 or "swine flu") indicates the recurrent and unpredictable nature of infectious disease threats.

Yet while the success of vaccines has been rooted in the prevention of infectious disease, pioneering research suggests a new focus on the impact vaccination can have on chronic diseases. Cancer is one such condition where considerable effort is underway to harness the body's immune system to protect against or fight the disease. The HPV vaccine is the only currently available vaccine

that was specifically designed and developed to protect against cancer, but recent successes in the field of cancer immunotherapy offer promising new hope for cancer patients. In addition to cancer, Alzheimer's is another disease at the centre of major efforts to develop therapeutic vaccines using immunotherapy to target the proteins that contribute to declining brain function.

The UK's contribution to the development of vaccines has a long and proud history, beginning with Jenner's discovery and proof of vaccination in the 18th century and leading to the present day where UK immunologists and institutions remain at the centre of global efforts to understand and prevent diseases amenable to vaccination. Our immunisation programme is universally admired internationally and UK scientists in both public and private settings remain at the forefront of vaccines discovery, development, and manufacture.

Nevertheless, there is a need to continue to develop this programme as new vaccines, or improved forms of existing vaccines, come onto the market. For example, 2013 saw the introduction of a new children's flu vaccine, administered nasally, to prevent infection of influenza in infant populations, where it can be very dangerous. The same year saw the launch of a shingles vaccine for the over-70s to protect elderly patients against shingles, which can be extremely painful and uncomfortable for older people, while in September 2015 England will become the first country in the world to introduce a publicly funded meningitis B vaccine for all babies. A coherent government strategy is required to continue to support the research, development and roll-out of new vaccines and bring these benefits to the wider public. Currently, the Joint Committee on Vaccination and Immunisation advises the Government on the implementation of vaccination strategies. However, their recommendations must be backed up by the necessary funding and Government support to continue to bring new health benefits to the general population.

In the last 200 years vaccines have eliminated smallpox, largely eradicated polio, and severely diminished death and disability for a range of once common infections. As researchers continue to explore new possibilities for vaccines research and look to extend their application beyond infectious disease, there is reason for considerable confidence that the next 200 years will herald similar landmark achievements.

¹WHO (2015). Rabies. Guide for post-exposure prophylaxis

²Oxford Vaccine Group (2013). Polio.

³Public Health England (2013). The Green Book: Immunisation against infectious disease. Chapter 26: Poliomyelitis.

⁴WHO (2014). Poliomyelitis.

⁵Oxford Vaccines Group (2014). Measles.

⁶WHO (2014). Observed rate of vaccine reactions: Measles, Mumps and Rubella vaccines.