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VACCINES ON THE FRONTLINE AGAINST INFECTIOUS DISEASES

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The World Health Organisation estimates that vaccines prevent 2-3 million deaths every year.¹ This paper explains what vaccines are, how they work, how they are tested and what they offer for the future.

BACKGROUND

Vaccines harness the capacity of our immune system to provide protection against diseases caused by pathogens, such as bacteria and viruses, by the process we call 'immunisation'.

Our awareness of immunisation traces back thousands of years. The ancient Greeks observed that people who recovered from the bubonic plague did not suffer the plague again. It was also common knowledge that survivors of smallpox became resistant to the disease, and survivors were often called on to nurse the sick.² In the Middle Ages, people in India and China would expose uninfected people to small amounts of material from the smallpox lesions of sufferers, in the hope that they would be protected.³

The modern era of vaccination began in the 18th century through the pioneering work of British doctor Edward Jenner.² Jenner observed that milkmaids who suffered mild skin infections from cowpox were resistant to smallpox. He embarked on what we now recognise as the first scientific attempt to control an infectious disease through the deliberate use of vaccination.

In Australia, vaccines have had a profound impact in the decades following their introduction. Deaths from diphtheria, pertussis (whooping cough), tetanus, polio and measles have either fallen to zero or close to zero.⁴

Following the start of community vaccination against measles in 1970, for example, the number of measles-related deaths fell from 146 in the decade 1966-1975 to zero in 1996-2005.

Routine vaccination (Box 1)⁵ has also led to a decline in the number of infections.

"It was a terrific thrill to be involved in a program which in 10 years removed from the Earth a disease which, at the time we started, was credited with 20 million cases and two million deaths every year."

- Professor Frank Fenner in 2002, on accepting the Prime Minister's Prize for Science in Australia for his role in eradicating smallpox.

Box 1: Childhood vaccination in Australia

Routine childhood immunisations given through the *Immunise Australia Program* currently provide protection against 13 diseases (below), most of which can cause serious illness and sometimes death.

- diphtheria
- haemophilus influenzae type b (Hib)
- hepatitis B
- measles
- meningococcal C
- mumps
- whooping cough (pertussis)
- pneumococcal disease
- polio (poliomyelitis)
- rotaviral gastroenteritis
- rubella (German measles)
- tetanus
- chickenpox (varicella)

Adapted from The Australian Immunisation Handbook 2013(10th ed), <http://www.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home>

HUMANITY'S SHIELD

Across the globe, vaccination is recognised as a critical tool in the fight against disease.

Several highly infectious and debilitating diseases are now rare because they are prevented by vaccines. Smallpox has been eradicated throughout the world, a triumph in which Australian immunologist Professor Frank Fenner played a central role.

Global deaths caused by measles fell from 535 300 in 2000 to 139 300 in 2010.⁶

Polio is on the brink of being eradicated, with the number of cases world-wide falling by more than 99 per cent since 1988.⁷ In 1988, more than 125 countries recorded polio cases. Today only three – Afghanistan, Pakistan and Nigeria – have yet to eradicate the disease.

Constant vigilance

While governments and health professionals have worked hard to spread the benefits of vaccination, the re-emergence of vaccine-preventable diseases in the United States, the United Kingdom, France and Japan demonstrates the need for constant vigilance.⁸

In 2013, a measles outbreak in the United Kingdom mainly affected children whose parents had opted against the measles-mumps-rubella (MMR) vaccine.⁸ A claimed but now discredited 'link' between the MMR vaccine and autism played a significant role in spreading fear.⁹ Such fears can be amplified in communities which have not seen or experienced the diseases that vaccinations prevent.

HOW DO VACCINES WORK?

Our immune system is a complex network of cells and organs that have evolved to defend the body against 'foreign invaders'.¹⁰ Much of the defence is mounted by specialist cells that are mobilised following an infection.

Chief among these are the **B cells** and **T cells**.

B cells are like factories that make precision weapons. The weapons are proteins called antibodies. Antibodies attached to an invader make it useless, or flag it for elimination by other cells of the immune system.

T cells join the offence against infection. Killer T cells directly destroy invaders; whilst helper T cells assist the B cells to do their job.

When the immune system first encounters a pathogen it 'remembers' it by keeping a small pool of long-lasting 'memory' B cells against that pathogen.¹⁰ These cells reside mainly in the spleen and circulate in small numbers in blood.¹¹

They represent a rapid response force that deal with subsequent infections. It is this memory that is the foundation of our resistance to future infections with the same pathogen.

Building the body's defences

Vaccinations are designed to trigger a protective immune response against a specific pathogen, without causing illness. Some vaccines can also protect against the longer-term complications of infections, which include liver cancer and cervical cancer.

Modern vaccines usually have two main ingredients: **antigens**, and **adjuvants**.¹⁰

Antigens are killed or weakened pathogens or pathogen components. Some vaccines contain virus or bacteria killed by heat or chemical treatment. Others contain live virus or bacteria that have been weakened by growing them under particular conditions in the laboratory. For example, the measles vaccine contains weakened forms of the virus that do not cause disease.

An **adjuvant** amplifies an immune response above what is caused by the antigen alone. The aluminium salt alum, for example, creates a depot of antigens at the site of injection, boosting the recruitment of immune cells to the site. Alum also helps deliver antigens to the draining lymph nodes where an

immune response to the antigen begins. The safety record of aluminium adjuvants is reflected in the fact that they have now been in use for 70 years.¹²

Herd immunity

In countries with high vaccination rates, such as Australia¹³, the spread of disease is limited.

This indirectly protects unvaccinated or vulnerable individuals (such as newborn babies and cancer patients undergoing chemotherapy) through what is known as ‘herd immunity’.

The threshold required to secure this benefit depends on both the disease and the vaccine. For example, herd immunity for measles requires 83-94 per cent vaccine coverage in the community (Table 1).¹⁴

Table 1: Herd immunity thresholds for vaccine preventable diseases

Disease	Herd Immunity
Diphtheria	85%
Measles	83-94%
Mumps	75-86%
Pertussis	92-94%
Polio	80-86%
Rubella	83-85%
Smallpox	80-85%

Adapted from The Centers for Disease Control and Prevention, History and epidemiology of global smallpox eradication, <http://www.bt.cdc.gov/agent/smallpox/training/overview/pdf/eradicationhistory.pdf>

VACCINE PRODUCTION

The process of making vaccines is complex and depends on the type of vaccine. As an overview of the steps involved, consider vaccines for influenza. The process involves three key steps: growing the weakened forms of the virus; isolating and purifying the virus or its components; and making them into vaccines.¹⁴

The first step is to grow the virus. Chicken eggs are commonly used to grow the influenza virus.

The next step is to isolate and purify the weakened virus (for the nasal spray vaccine) or antigens derived from it (for the injected vaccine).

If required, the final formulation step includes the addition of adjuvants.

Vaccines can contain trace quantities of material used during the production process. These can include nutrients (for example, egg proteins) and chemicals used to kill the virus.

Regulatory authorities require vaccine makers to test for such material and ensure that they do not exceed safety limits.¹⁵

VACCINES ARE SAFE AND EFFECTIVE

The risks of severe effects from diseases are far greater than the risks of side effects from vaccinations in use in Australia.^{3,15}

Serious complications, such as severe allergic reactions, are extremely rare. The vast majority of side effects which are observed are mild and short-lived, such as swelling and redness at the site of injection (Figure 1).¹⁶ Fevers following vaccination are much less common.

Figure 1: Calculating vaccine risks

COMMON: MORE THAN 1 IN 100 DOSES

Redness, swelling or soreness at the site of an injection are common for many vaccines, as are mild fevers. Nausea, vomiting and diarrhoea have been reported for a few.

LESS COMMON: 1 IN 100 TO 1 IN 100,000

High fevers can occur in this range, as can fever-induced convulsions from vaccines such as that for measles, mumps and rubella (1 in 3000 doses).

RARE: 1 IN 100,000 TO 1 IN 1 MILLION

Severe allergic reactions to vaccines are generally uncommon, in the order of 1 in 1 million.

INCONCLUSIVE: NOT ENOUGH DATA

Guillain-Barré syndrome, a paralytic disorder, has been associated with some seasonal influenza vaccines, but a causal link has not been established.

Adapted from Calculating risks, US Centers for Disease Control and Prevention. <http://www.nature.com/news/2011/110525/full/473436a/box/1.html>

The safety and effectiveness of any vaccine used in Australia is established with a series of rigorous testing processes (Figure 2)³, with the bar set very high.

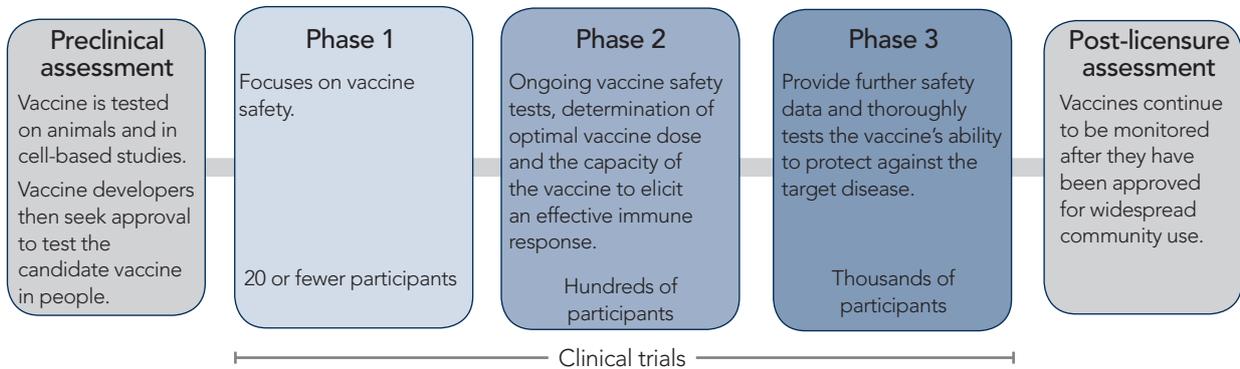
THE NEW FRONTIER

There are no effective vaccines against tuberculosis (TB), malaria and human immunodeficiency virus (HIV), currently the world’s three deadliest infectious diseases (Table 2).¹⁷

These three diseases ‘hide’ within affected individuals and do not elicit natural immunity, so vaccine developers need to use innovative strategies and technologies.¹⁸

Figure 2: Stages of vaccine testing

Following regulatory approval, a candidate vaccine enters three phases of clinical trials, each involving an increasing number of human volunteers.



Source: *The Science of Immunisation, The Australian Academy of Science, 2012.*

Table 2: The world's most infectious diseases

Disease	Number of carriers	Deaths
Tuberculosis	2 billion	1.3 million
Malaria	207 million	627, 000
HIV	35.3 million	1.6 million

Data reported in 2011 (Tuberculosis) and 2012 (Malaria and HIV)

Source: (Bourzac K, *Nature* vol 507, 2014, s4-7).

These include targeting every stage of the complex life cycle of the malaria parasite, using novel genetic analysis to reveal the different immune responses elicited by TB, and gaining further insights into the weaknesses of HIV through basic science.

While the Ebola virus and its horrific symptoms have been known since the 1970s, efforts to develop an Ebola vaccine have been accelerated by the scale of the current epidemic in West Africa. An Ebola vaccine, developed through a public-private partnership, is showing positive preliminary results in early clinical trials.¹⁸

New strains of the influenza virus are expected to cause three severe influenza pandemics every century.¹⁹ The last pandemic in 2009 turned out to be mild, but exposed our limited capacity to produce influenza vaccines, with a global production capacity of 850 million doses.¹⁹

Major changes are required in both influenza vaccine production and pandemic preparedness to produce and quickly supply the billions of doses that could be required during a severe influenza pandemic.

New technologies are also under development to improve vaccine delivery.³ Priorities include vaccines that need to be given only once, needle-free vaccination and plant-based edible vaccines.

"New vaccines nearly always give public health its biggest leap forward. Of course, everyone would love to see a vaccine developed for the high-mortality killers, like HIV and malaria, and a better vaccine for tuberculosis."

- Dr Margaret Chan, Director-General of the World Health Organisation, 2011.

CONCLUSION

Scientific and technological advances in vaccine development hold the promise of a future free from most infectious diseases. Recent disease epidemics in developed nations demonstrate that a fall in vaccine coverage in the community will inevitably lead to the reemergence of diseases of the past. The challenge for all nations is to foster both the science and the scientific awareness of vaccination to keep our communities safe.

References are available at chiefscientist.gov.au

About this series

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