1.5 FUNDAMENTALS OF IMMUNISATION

1.5.1 Overview

Vaccines are complex biological products designed to induce a protective immune response effectively and safely. Vaccines contain one or more antigens (or immunogens) that stimulate an active immune response. These are generally protein- or polysaccharide (sugar)-based substances. The number and derivation of the antigen(s) contained in each vaccine vary. Most vaccines work by inducing B-lymphocytes to produce antibodies that bind to and inhibit pathogenic organisms or their toxins. Generation of T-cell-mediated (cellular) immunity is also important for some vaccines.

Vaccines, like all medicines, are regulated in Australia by the Therapeutic Goods Administration (TGA). Before they are made available for use they are rigorously tested in human clinical trials to confirm that they are safe and that they stimulate protective immune responses. Vaccines are also evaluated to ensure compliance with strict manufacturing and production standards. This testing is required by law and is usually conducted both during the vaccine’s development and after its registration. In addition, once they are in use, the safety of vaccines is monitored by the TGA and other organisations using different methods, including passive and active surveillance for adverse events following immunisation (see 1.5.5 Vaccine safety and adverse events following immunisation).

1.5.2 Passive immunisation

Passive immunity is the direct transfer or administration of antibodies to a non-immune person to provide immediate protection. One example of passive immunisation is the transfer of maternal antibodies to the fetus, which provides some short-lived protection of the newborn infant against certain infections.\(^\text{1,2}\) Another example is the administration of a product containing antibodies (or immunoglobulins, IgG) pooled from blood donors, in order to provide temporary protection to a non-immune person who has recently been exposed to infection.\(^\text{3}\) The protection afforded is immediate, but lasts for only a few weeks as the half-life of IgG is approximately 3 to 4 weeks. Regular immunoglobulin infusions are also indicated for some immunocompromised persons who are deficient in antibody. A separate use of immunoglobulins is in the treatment of a number of specific immune-mediated conditions in order to modulate the disease course. For further information regarding the use of intravenous immunoglobulin for this purpose, refer to Criteria for the clinical use of intravenous immunoglobulin in Australia (www.nba.gov.au/ivig/index.html).

For more information on passive immunisation see Part 5 Passive immunisation.

1.5.3 Active immunisation

Active immunisation involves the use of vaccines to stimulate the immune system to produce a protective immune response. Vaccines usually induce an immune response that mimics the host’s response to natural infection, but without the harmful consequences of the infection itself. In addition to antibody responses, many vaccines also stimulate cell-mediated immunity. Immunity following active immunisation generally lasts for months to many years, depending on the nature of the vaccine as well as host factors.\(^\text{1,2}\) Protective immunity is induced by antigen(s) contained within the vaccine. This may be a toxoid (a bacterial toxin that has been rendered non-toxigenic, e.g. for tetanus or diphtheria); killed or inactivated bacteria or viruses, such as hepatitis A vaccines; live attenuated bacteria or viruses, such as measles, mumps and rubella vaccines; or subunit components of a pathogen that only contain the antigen(s) of interest, such as the hepatitis B vaccine.\(^\text{1,3}\)

In addition to containing the immunising antigen(s), vaccines may also contain the following:

- Adjuvants, which enhance the immune response to an antigen; an example is aluminium hydroxide.
- Preservatives, which reduce the risk of contamination; some examples are 2-phenoxyethanol, which is also used in many cosmetics and pharmaceuticals, and thiomersal, which is used in the Q fever vaccine but is not present in any of the vaccines on the National Immunisation Program for young children.
- Stabilisers, which improve the shelf-life and help to protect the vaccine from adverse conditions; examples are sucrose, mannitol, lactose and gelatin. Stabilisers are also used in most confectionery and many pharmaceuticals.
- Emulsifiers or surfactants, which alter the surface tension of the liquid vaccine; examples are polysorbate-80 and sorbitol. Emulsifiers are added to most ice creams and many pharmaceuticals.
- Residuals, which are minute or trace amounts of substances that remain after the manufacture of the vaccine; examples of residuals detectable in some vaccines are formaldehyde, antibiotics such as neomycin or polymyxin, and egg proteins.

Further details of a particular vaccine’s constituents can be found in either the product information (PI) or the consumer medicines information (CMI) for individual vaccines. This information is presented in the shaded box for each vaccine under the disease-specific chapters in Part 4 of this Handbook (current June 2012); however, it is important to note that...
In addition, information on the components contained in vaccines that are available under the Australian National Immunisation Program is provided in Appendix 3 of this Handbook, and further details on vaccine composition can be found in Appendix 4: Commonly asked questions about vaccination.

The recommended number of doses and age of administration vary for each vaccine. These recommendations are based on the type of vaccine, disease epidemiology (the age-specific risk for infection and for complications), and the anticipated immune response of the recipient (including whether transplacental transfer of maternal antibodies will inhibit the immune response in an infant). Several doses of a vaccine may be required to induce protective immunity, particularly in younger children.

Homeopathic preparations do not induce immunity and are never an alternative to vaccination (see Appendix 4: Commonly asked questions about vaccination).

Detailed information on the background, available vaccines and recommendations for vaccines used in active immunisation are provided in the disease-specific chapters in Part 4 of this Handbook.

1.5.4 Vaccine efficacy, vaccine effectiveness and vaccine failure

The terms vaccine efficacy and vaccine effectiveness are often used interchangeably. However, in general terms, vaccine efficacy refers to estimates of protection obtained under the idealised conditions of a randomised controlled trial (RCT). It is usually expressed as the percentage reduction in a person’s risk of disease if vaccinated compared to the risk if not vaccinated. Vaccine effectiveness refers to estimates of protection obtained under ‘real world’ rather than trial conditions, for example, in immunisation programs after vaccine registration. Sometimes vaccine effectiveness is also taken to include the broader impact of a vaccination program on overall disease incidence in the population, including any additional herd protection conferred to unvaccinated individuals.

The extent and duration of protection provided by vaccination varies and is influenced by many factors. For example, some vaccines, such as the pneumococcal and meningococcal polysaccharide vaccines, provide protection for a few years only. This is because polysaccharide antigens induce antibodies without the involvement of T-lymphocytes (T-cell independent response). T-cell lymphocyte involvement is needed for long-term immune memory; without it, protection is relatively short-lived and immunity wanes, sometimes requiring revaccination. In addition, polysaccharide vaccines are less immunogenic in children aged <2 years. The process of conjugating (or linking) capsular polysaccharides to a protein carrier creates conjugate vaccines that can induce antibody production with the help of T-lymphocytes (T-cell dependent response). This results in higher-quality and longer-term immunity, including in children <2 years of age. Conjugated vaccines are available for Haemophilus influenzae type b, Neisseria meningitidis (serogroups A, C, W135 and Y) and pneumococcal disease.

Vaccination failure can be due to either vaccine failure or failure to vaccinate (i.e. that an indicated vaccine was not administered appropriately for any reason). Sometimes a vaccinated person may develop infections despite being vaccinated (vaccine failure). Often such infections result in a milder or more attenuated form of disease, for example, chickenpox developing despite varicella vaccination or whooping cough developing after 2 or more doses of pertussis vaccine. Vaccine failure can be categorised in two ways. ‘Primary’ vaccine failure occurs when a fully vaccinated person does not form an adequate immune response to that vaccine. This might occur because a vaccine is defective due to a manufacturing fault or, more typically, because of inadequate storage (e.g. breakage of the cold chain) or expiry of the shelf-life. Primary vaccine failure may also occur because the recipient’s immune response is ineffective, which may be relatively specific for that vaccine or part of a broader immunodeficiency. ‘Secondary’ vaccine failures occur when a fully vaccinated person becomes susceptible to that disease over time, usually because immunity following vaccination wanes over time. As discussed above, the duration of the protective effect of vaccination varies depending on the nature of the vaccine and the type of immune response elicited, the number of doses received, and host factors. Some vaccinated persons may get further immune stimulation from natural infection or colonisation, which aids in maintaining ongoing protection.

1.5.5 Vaccine safety and adverse events following immunisation

What is an adverse event following immunisation?

The term ‘adverse event following immunisation’ (AEFI) refers to any untoward medical occurrence that follows immunisation, whether expected or unexpected, and whether triggered by the vaccine or only coincidentally occurring after receipt of a vaccine. The adverse event may be any unfavourable or unintended sign, abnormal laboratory finding, symptom or disease.
Adverse events following immunisation (AEFI) should be reported promptly, either according to relevant state or territory protocols or directly to the TGA (for detailed information on reporting and management of AEFI, see 2.3 Post-vaccination).

The safety of vaccines is very important as vaccines are given to prevent disease and target all or many members of the population, most of whom are healthy. All vaccines available in Australia must pass stringent safety testing before being approved for use by the TGA. This testing is required by law and is usually done over many years during the vaccine’s development. In addition, the TGA monitors the safety of vaccines once they are registered.

From the time a vaccine comes into use, there is an ongoing review of both vaccine safety and efficacy through a variety of mechanisms, such as further clinical trials and surveillance of disease and vaccine adverse events. One important component of ensuring that vaccines are safe is to monitor the occurrence of AEFI. In Australia, there are regional and national surveillance systems that collect reports of any adverse events following immunisation. All AEFI reported are added to the national Adverse Drug Reactions System (ADRS) database, which is operated by the TGA. (See also 2.3 Post-vaccination.) Each year, reports presenting data and analysis of AEFI in Australia are published in the journal Communicable Diseases Intelligence, accessible via the Australian Government Department of Health website (www.health.gov.au/internet/main/publishing.nsf/content/cda-pubs-cdi-cdiintro.htm).

In some cases, other specific studies will be conducted to ensure that vaccine safety is closely monitored once a vaccine is in use. For example, the risk of intussusception (IS) following rotavirus vaccines has been closely monitored in Australia and elsewhere because of the association of a previously licensed vaccine with an unacceptably high risk of IS.

Adverse reactions to vaccines (also known as ‘vaccine side effects’) do sometimes occur. It is usually not possible to predict which individuals may have a mild or, rarely, a serious reaction to a vaccine. However, by following guidelines regarding when vaccines should and should not be used, the risk of adverse events can be minimised. As vaccines are usually given to healthy people, any adverse event that follows soon after immunisation may be perceived as due to the vaccine. The fact that an adverse event occurs after an immunisation does not prove the vaccine caused the event. A causal association is rarely certain, but is most likely when the AEFI is both typical (even if very rare) and when there is no other plausible explanation, for example, an injection site reaction occurring a day after vaccination or typical anaphylaxis occurring within minutes of vaccination. Many AEFIs are less specific and/or have plausible alternative explanations, including coincidence. Such associations can only be assessed by large-scale epidemiological studies or specific tests, for example, in the case of allergy, by allergy testing or challenge. Even when an AEFI is typical, it may be nonetheless unrelated to vaccination (see 2.3 Post-vaccination).

Vaccine adverse events fall into two general categories: local or systemic. Local reactions are defined as reactions occurring at the site of vaccine administration (usually pain, redness or swelling at the injection site) and are generally the least severe and most frequently occurring AEFI. Systemic reactions most commonly include fever, headache and lethargy.8,9 Allergic reactions can also occur, although anaphylaxis, the most severe form of an allergic response, is rarely caused by vaccination. It is not possible to completely predict which individuals may have a reaction to a vaccine.

Each chapter in the Handbook indicates under which circumstances vaccine administration is contraindicated or where precautions are required. A contraindication to vaccination usually occurs when a person has a pre-existing condition that significantly increases the chance that a serious adverse event will occur following receipt of a specific vaccine. A contraindication may also occur when there is insufficient safety data regarding a vaccine’s use and there is a theoretical risk of harm. In general, vaccines should not be given where a contraindication exists, except under advice from your local state or territory health department (Appendix 1 Contact details for Australian, state and territory government health authorities and communicable disease control).

A precaution is a condition that may increase the chance of an adverse event following immunisation or one that may compromise the ability of the vaccine to produce immunity. When a precaution exists, there may still be circumstances when the benefits of giving the vaccine outweigh the potential risks; however, special care and the provision of appropriate advice to the vaccine recipient may be required (see 3.3.1 Vaccination of persons who have had an adverse event following immunisation).

In 2010, a national review of the management of adverse events that occurred following influenza vaccine administration was performed.10 The review made a number of recommendations to further improve the monitoring of vaccine safety in Australia. Any changes to the system(s) for monitoring or reporting of AEFI in Australia will be reflected in future updates to the Handbook and will also be available from the Immunise Australia website (www.immunise.health.gov.au).

References

A full reference list is available on the electronic Handbook or website www.immunise.health.gov.au.


