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Immunisation Handbook

2017

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Disclaimer

This publication, which has been prepared for, and is published by, the Ministry of Health, is for the assistance of those involved in providing immunisation services in New Zealand.

While the information and advice included in this publication are believed to be correct, no liability is accepted for any incorrect statement or advice. No person proposing to administer a vaccine to any other person should rely on the advice given in this publication without first exercising his or her professional judgement as to the appropriateness of administering that vaccine to another person.

Feedback

Comments on this book and suggestions for future editions are invited, to enhance the usefulness of future editions. These should be sent to the Manager Immunisation, Ministry of Health, at the address below.

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Foreword

With the publication of the *Immunisation Handbook 2017* (the *Handbook*), it is once again appropriate to extend the Ministry of Health's thanks to everyone involved in supporting, promoting or delivering immunisations to the people of New Zealand. This *Handbook* has been designed as a comprehensive source of information on immunisation, to support you in the work you do.

Since the July 2014 edition of the *Handbook*, there have been two subsequent editions ie, the 2014 (2nd ed) and 2014 (3rd ed) released online. Both of these editions were updated with a few amendments and PHARMAC's revised eligibility criteria for some of the vaccines for individuals at increased risk of the relevant vaccine-preventable diseases.

On 1 January 2017, PHARMAC approved funding for human papillomavirus vaccine for boys and girls up to the age of 27 years, and these changes were included in the 2014 (3rd ed) online *Handbook* versions. From July 2017 varicella vaccine will be introduced to the National Immunisation Schedule and is expected to significantly reduce the burden of varicella disease, particularly in young infants.

Immunisation coverage has continued to improve and as at 31 December 2016, 93.3 percent of 8-month-olds and 93.1 percent of 2-year-olds were fully immunised for the quarter. Significant progress has been made for immunisation at age 5 years in recent years, with coverage increasing from 82 percent in June 2015 to 89 percent in December 2016. Gains have consistently been made for Māori infants and children, with an increase in coverage at age 8 months from 78 percent in 2012 to 91 percent in December 2016. In the Human Papillomavirus (HPV) Immunisation Programme, equity has continued to be achieved for young Māori and Pacific women, and 12 district health boards achieved or exceeded the 2016 HPV immunisation coverage target of 65 percent of 12-year-old girls having received all three HPV doses.

At a population level, the effects of increasing immunisation coverage are clearly discernible, with fewer cases of vaccine-preventable diseases as coverage increases. In New Zealand, we have seen significant decline

in hepatitis B, *Haemophilus influenzae* type b, genital warts and, in infants, pneumococcal and rotavirus diseases since the introduction of vaccines.

The health community deserves praise for this improvement, but at the same time must continue with its efforts to increase coverage toward the point where herd immunity against the most infectious diseases can be achieved.

I congratulate you on these past achievements and encourage your ongoing commitment to improving immunisation coverage and reducing vaccine-preventable diseases in New Zealand. Pharmacists can now assist with achieving this goal. Due to a reclassification of the influenza, meningococcal, Tdap and zoster vaccines, pharmacists who have undergone Ministry-approved vaccinator training can now administer these vaccines to adults. In 2017 pharmacists have also been able to provide funded influenza vaccinations to those aged 65 years and older and to pregnant women. This provides more opportunities for people to be vaccinated against these infectious diseases.

Immunisation is an important opportunity for health professionals to interact with people from all walks of life: mothers with newborns, school-age children, and adults either working or retired. Your attitude and the conversations you have with people affect their attitudes toward immunisation and their engagement with the health care system in general. We hope this *Handbook* will help your interactions with your patients and their families/whānau.

In closing, I would like to thank the members of the Handbook Advisory Group who updated the *Handbook* – and also all the peer reviewers. I trust this edition, like its predecessors, will prove a valuable resource for health professionals.

Chai Chuah
Director-General of Health and Chief Executive

The Immunisation Handbook Advisory Group

The Immunisation Handbook Advisory Group provided expert technical and medical advice for the *Immunisation Handbook 2017*. The Ministry of Health wishes to thank them for their time and commitment during the *Handbook* update and rewrite. The Handbook Advisory Group members are as follows.

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Main source books

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Department of Health and Ageing. 2017. *The Australian Immunisation Handbook* (10th edition, updated 2017). Canberra, ACT: Department of Health and Ageing.

Ministry of Health. 2012. *Communicable Disease Control Manual 2012*. Wellington: Ministry of Health.

Plotkin SA, Orenstein WA, Offit PA (eds). 2013. *Vaccines* (6th edition). Philadelphia, PA: Elsevier Saunders.

New Zealand epidemiology data

Information on New Zealand epidemiology is sourced from data collated by the Institute of Environmental Science and Research (ESR), on behalf of the Ministry of Health, or from Analytical Services, Ministry of Health.

For the most up-to-date epidemiological data, see the ESR Public Health Surveillance (www.surv.esr.cri.nz) and Ministry of Health (www.health.govt.nz/nz-health-statistics) websites.

Commonly used abbreviations

23PPV	23-valent pneumococcal polysaccharide vaccine
ADT	adult diphtheria and tetanus vaccine
AEFI	adverse event following immunisation
AFP	acute flaccid paralysis
AIDS	acquired immunodeficiency syndrome
AOM	acute otitis media
BCG	bacillus Calmette–Guérin vaccine
CARM	Centre for Adverse Reactions Monitoring
CPR	cardiopulmonary resuscitation
CRS	congenital rubella syndrome
DHB	district health board
DMARD	disease-modifying anti-rheumatic drug
DNA	deoxyribonucleic acid
DT	diphtheria and tetanus vaccine
DTaP	diphtheria, tetanus and acellular pertussis vaccine
DTaP-IPV	diphtheria, tetanus, acellular pertussis and inactivated polio vaccine
DTaP-IPV-HepB/Hib	diphtheria, tetanus, acellular pertussis, inactivated polio, hepatitis B and *Haemophilus influenzae* type b vaccine
DTwP	diphtheria, tetanus and whole-cell pertussis vaccine
DTwPH	diphtheria, tetanus, whole-cell pertussis and *Haemophilus influenzae* type b vaccine
ESR	Institute of Environmental Science and Research
GBS	Guillain–Barré syndrome
GP	general practitioner
GSK	GlaxoSmithKline (New Zealand) Limited
HAV	hepatitis A virus
HBcAg	hepatitis B core antigen
HBeAg	hepatitis B e antigen

HBIG	hepatitis B immunoglobulin
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HepB	hepatitis B vaccine
Hib	*Haemophilus influenzae* type b
HIV	human immunodeficiency virus
HPV	human papillomavirus
HSCT	haematopoietic stem cell transplant
HZ	herpes zoster
HZV	herpes zoster vaccine
ICD	International Classification of Diseases
IG	immunoglobulin
IgG	immunoglobulin G
IM	intramuscular
IMAC	Immunisation Advisory Centre
IPD	invasive pneumococcal disease
IPV	inactivated polio vaccine
ITP	idiopathic thrombocytopenic purpura (also known as immune thrombocytopenia)
IV	intravenous
IVIG	intravenous immunoglobulin
LAIV	live attenuated influenza vaccine
MCV4-D	quadrivalent meningococcal conjugate vaccine (conjugated to diphtheria toxoid)
Medsafe	New Zealand Medicines and Medical Devices Safety Authority
MenCCV	meningococcal C conjugate vaccine
MeNZB	meningococcal B vaccine
MMR	measles, mumps and rubella vaccine
MMRV	measles, mumps, rubella and varicella vaccine
MSD	Merck Sharp & Dohme (New Zealand) Limited
NHI	National Health Index

NIR	National Immunisation Register
NTHi	non-typeable *Haemophilus influenzae*
NZBS	New Zealand Blood Service
OPV	oral polio vaccine
PCR	polymerase chain reaction
PCV7	7-valent pneumococcal conjugate vaccine
PCV10	10-valent pneumococcal conjugate vaccine
PCV13	13-valent pneumococcal conjugate vaccine
PFU	plaque-forming unit
PHARMAC	Pharmaceutical Management Agency
PMS	practice management system (also known as patient management system)
PRP	polyribosylribitol phosphate
PSNZ	Pharmaceutical Society of New Zealand
PTAC	Pharmacology and Therapeutics Advisory Committee
QIV	quadrivalent inactivated vaccine
RIG	rabies immunoglobulin
RNA	ribonucleic acid
RV1	rotavirus vaccine (monovalent)
RV5	rotavirus vaccine (pentavalent)
SBVS	School-Based Vaccination System
SC	subcutaneous
SCID	severe combined immune deficiency
STI	sexually transmitted infection
SUDI	sudden unexpected death in infancy
TB	tuberculosis
Td	adult tetanus and diphtheria vaccine
Tdap	adult tetanus, diphtheria and acellular pertussis vaccine
TIG	tetanus immunoglobulin
TIV	trivalent inactivated vaccine
UK	United Kingdom
US	United States of America

VAPP	vaccine-associated paralytic poliomyelitis
VLP	virus-like particle
VTC	vaccinator training course
VV	varicella vaccine
VZV	varicella zoster virus
WHO	World Health Organization
ZIG	zoster immunoglobulin

Introduction

The purpose of the *Immunisation Handbook 2017* (the *Handbook*) is to provide clinical guidelines for health professionals on the safest and most effective use of vaccines in their practice. These guidelines are based on the best scientific evidence available at the time of publication, from published and unpublished literature.

> The information contained within the *Handbook* was correct at the time of publication. This edition of the *Handbook* will remain current unless amended electronically via the Ministry of Health website (www.health.govt.nz/our-work/preventative-health-wellness/immunisation) or until the next edition or update is published.

Changes to the *Handbook* in 2017

All chapters have been updated and revised since the 2014 edition. The following changes have been made.

- There is a new section at the end of each disease chapter called 'Variations from the vaccine data sheets'.
- The content from chapter 2 'Processes for safe immunisation' has been reformatted into pre-vaccination, vaccine administration and post-vaccination sections.
- The 'Passive immunisation' section of chapter 1 has been moved to its own appendix (Appendix 6).
- The 'Cold chain: vaccine storage, transport and destruction' appendix has been removed and its content is now included in the Ministry of Health document *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017* (available at www.health.govt.nz/coldchain).

- The 'Notifiable disease case definitions and laboratory tests' appendix (Appendix 8) has been removed. Health care providers should use the Ministry of Health's *Communicable Disease Control Manual 2012* (available at www.health.govt.nz/publication/communicable-disease-control-manual-2012) for case definition and laboratory test information.
- There is a new appendix, 'High-incidence TB countries' (Appendix 8), with a list of countries with tuberculosis (TB) rates of ≥40 per 100,000 population.

The National Immunisation Schedule

The National Immunisation Schedule (the Schedule) is the series of publicly funded vaccines available in New Zealand (see Table 1). Some vaccines are also offered as targeted programmes in response to a recognised need (see Table 2). See also section 2.1.7 for a summary of the primary immunisation requirements for adults (funded) and other funded and unfunded recommendations for this age group.

On 1 July 2012 the management and purchasing of vaccines transferred from the Ministry of Health to PHARMAC. All publicly funded vaccines are now listed on PHARMAC's Pharmaceutical Schedule (see www.pharmac.govt.nz), and the district health boards (DHBs) are responsible for funding these once PHARMAC has listed them.

PHARMAC considers medicine and vaccine funding applications from pharmaceutical suppliers, health professionals, consumer groups and patients. Usually, manufacturers/suppliers decide whether to make an application for funding. Normally this will follow registration and approval of the medicine or vaccine by Medsafe. PHARMAC will generally only consider an application for a medicine or vaccine to be funded once it has been registered and approved by Medsafe.

Following a vaccine funding application, PHARMAC will assess the vaccine, seek clinical input (for vaccines this may be from the immunisation subcommittee of the Pharmacology and Therapeutics Advisory Committee [PTAC] or from PTAC itself), and conduct an economic analysis. The recommendations from the immunisation subcommittee are then considered by PTAC, who will provide advice to PHARMAC. PHARMAC then decides what priority the application has for funding, and consults with the Ministry of Health on capacity and

implementation issues that may be associated with introducing a new vaccine. Depending on the outcome of that process, PHARMAC may then negotiate with the supplier. If an agreement is reached, PHARMAC will consult with the health sector on a funding proposal.

The Ministry of Health remains responsible for and manages the National Immunisation Programme. The National Immunisation Programme:

- aims to prevent disease through vaccination and to achieve coverage that prevents outbreaks and epidemics
- is accountable for achieving the Immunisation Health Target
- monitors disease burden and those at risk
- provides guidance to the sector on immunisation, cold chain and resources
- ensures immunisation providers deliver services that meet the needs of their population
- implements the National Immunisation Schedule
- delivers trusted and effective vaccine programmes
- provides immunisation resources, including the *Immunisation Handbook*
- improves information and data systems
- manages the National Immunisation Register (NIR).

The Ministry of Health works with PHARMAC to ensure there is a strong link between vaccine decisions, management and the National Immunisation Programme.

Although funding decisions will be communicated to the sector, vaccinators are advised to regularly check the Pharmaceutical Schedule and any online updates (www.pharmac.govt.nz) for changes to funding decisions, and the online edition of the *Immunisation Handbook* (www.health.govt.nz/our-work/preventative-health-wellness/immunisation) for the latest immunisation information.

Changes to the National Immunisation Schedule in 2018

Table 1 shows the 2018 National Immunisation Schedule, and Table 2 shows the vaccines funded for special groups at higher risk of some diseases.

Changes to vaccine funding in 2018 are as follows.

1. From 2018, the quadrivalent inactivated influenza vaccine (Influvac Tetra; see chapter 10 'Influenza') will be the Schedule vaccine for pregnant women and for adults aged 65 years and older.

2. From 1 April 2018, one dose of herpes zoster vaccine (HZV, Zostavax; see chapter 22 'Zoster') will be introduced for:
    - individuals at age 65 years, or
    - catch-up of individuals aged 66–80 years, inclusive (the catch-up programme ceases on 31 March 2020).

Table 1: National Immunisation Schedule, commencing 1 April 2018

Antigen(s)	DTaP-IPV-HepB/Hib	PCV10	RV1	MMR	Hib	VV	DTaP-IPV	Tdap	HPV9	Td	Influenza	HZV
Brand	Infanrix-hexa	Synflorix	Rotarix	Priorix	Hiberix	Varilrix	Infanrix-IPV	Boostrix	Gardasil9	ADT Booster	Influvac Tetra	Zostavax
Manufacturer	GSK	GSK	GSK	GSK	GSK	GSK	GSK	GSK	Seqirus/ MSD	Seqirus	Mylan	MSD
Pregnancy								●[a]			●	
6 weeks	●	●	●									
3 months	●	●	●									
5 months	●	●										
15 months		●		●	●	●[b]						
4 years				●			●					
11 or 12 years[c]								●	● 2 doses[c]			
45 years										●		
65 years										●	● annually	●[d]

a Tdap is for women during every pregnancy, from 28 to 38 weeks' gestation.

b VV is funded for children born on or after 1 April 2016.

c HPV is funded for individuals aged 26 years and under: 2 doses for those aged 14 years and under; 3 doses for those aged 15–26 years; 3 doses for those aged 9–26 years with certain medical conditions, plus an additional dose post-chemotherapy.

d There is a catch-up programme from 1 April 2018 until 31 March 2020, with 1 dose of HZV funded for individuals aged 66–80 years, inclusive.

2018 changes to targeted programmes for special groups

Vaccines funded for special groups are described in Table 2 below. Changes to existing programmes in 2018 are as follows.

1. Hepatitis B vaccine (HepB, HBvaxPRO; see chapter 8 'Hepatitis B') is funded for individuals with eligible conditions. However, in 2018 there is a shortage of the HBvaxPRO 5 μg and HBvaxPRO 10 μg vaccines. If the HBvaxPRO 5 μg or HBvaxPRO 10 μg vaccines are not available, the Engerix-B 20 μg vaccine may be used instead. (Supplies of the HBvaxPRO 40 μg vaccine are unaffected.)

2. Influenza vaccine is funded for individuals aged 6 months to under 65 years with eligible conditions (see chapter 10 'Influenza'). From 2018, the following quadrivalent inactivated influenza vaccines will be used:
    - Fluarix Tetra for children aged 6 months to under 3 years (ie, aged 6–35 months)
    - Influvac Tetra for adults and children aged 3 years and older.

Table 2: Funded vaccines for special groups – in addition to the routine schedule

Note: Vaccinators are advised to regularly check the Pharmaceutical Schedule and any online updates (www.pharmac.govt.nz) for changes to funding decisions for special groups. See also chapter 4 'Immunisation of special groups'.

Vaccine	Individuals eligible for funded vaccine
Haemophilus influenzae type b (Hib) (chapter 6)	For (re-)vaccination of patients who are: • post-haematopoietic stem cell transplant (HSCT) or chemotherapy • pre- or post-splenectomy or with functional asplenia • pre- or post-solid organ transplant • pre- or post-cochlear implants • undergoing renal dialysis and other severely immunosuppressive regimens For use in testing for primary immune deficiency[a]
Hepatitis A (chapter 7)	Transplant patients Children with chronic liver disease Close contacts of hepatitis A cases
Hepatitis B (HepB) (chapter 8)	Household or sexual contacts of patients with acute or chronic hepatitis B virus (HBV) infection Babies of mothers with chronic HBV infection need both hepatitis B vaccine (HepB) and hepatitis B immunoglobulin (HBIG) at birth Children aged under 18 years who have not achieved positive serology and who require additional vaccination HIV-positive patients Hepatitis C-positive patients Following non-consensual sexual intercourse Patients following immunosuppression[b] Solid organ transplant patients Post-HSCT patients Following needle-stick injury Dialysis patients Liver or kidney transplant patients
Human papillomavirus (HPV) (chapter 9)	People aged 9 to 26 years inclusive: • with confirmed HIV infection • transplant (including stem cell) patients • post-chemotherapy

Continued overleaf

Vaccine	Individuals eligible for funded vaccine
Annual influenza vaccine (chapter 10)	Patients aged 6 months to <65 years who: • have any of the following cardiovascular diseases: – ischaemic heart disease – congestive heart failure – rheumatic heart disease – congenital heart disease – cerebrovascular disease • have either of the following chronic respiratory diseases: – asthma, if on a regular preventative therapy – other chronic respiratory disease with impaired lung function • have diabetes • have chronic renal disease • have any cancer, excluding basal and squamous skin cancers if not invasive • have any of the following other conditions: – autoimmune disease – immune suppression or immune deficiency – HIV – transplant recipients – neuromuscular and central nervous system diseases/disorders – haemoglobinopathies – are children on long-term aspirin – have a cochlear implant – errors of metabolism at risk of major metabolic decompensation – pre- and post-splenectomy – Down syndrome • are pregnant • are children aged 4 years and under who have been hospitalised for respiratory illness or have a history of significant respiratory illness • are children aged under 18 years living in the Seddon/Ward and rural Eastern Marlborough region (within the Nelson Marlborough District Health Board) and Kaikoura and Hurunui areas (within the Canterbury District Health Board) • are children aged under 18 years who have been displaced from their homes in Edgecumbe and the surrounding region • are patients who are compulsorily detained long-term in a forensic unit within a DHB hospital[c]

Continued overleaf

Vaccine	Individuals eligible for funded vaccine
Measles, mumps and rubella (MMR) (chapters 11, 13 and 18)	(Re-)vaccination of patients following immunosuppression[b]
Meningococcal C conjugate vaccine (MenCCV) and quadrivalent meningococcal conjugate vaccine (MCV4-D) (chapter 12)	Pre- and post-splenectomy or with functional or anatomical asplenia HIV Complement deficiency (acquired or inherited) Pre- or post-solid organ transplant Close contacts of meningococcal cases HSCT (bone marrow transplant) patients Following immunosuppression[b]
Pertussis-containing vaccines (chapter 14)	Pregnant women between 28 and 38 weeks' gestation (Re-)vaccination of patients who are: • post-HSCT or chemotherapy • pre- or post-splenectomy • pre- or post-solid organ transplant • undergoing renal dialysis or other severely immunosuppressive regimens

Continued overleaf

Vaccine	Individuals eligible for funded vaccine
13-valent pneumococcal conjugate vaccine (PCV13) and 23-valent pneumococcal polysaccharide vaccine (23PPV) (chapter 15)	PCV13 and 23PPV for (re-)vaccination of high-risk children aged under 5 years: • on immunosuppressive therapy or radiation therapy (vaccinate when there is expected to be a sufficient immune response) • with primary immune deficiencies • with HIV infection • with renal failure or nephrotic syndrome • who are immune-suppressed following organ transplantation (including HSCT) • with cochlear implants or intracranial shunts • with cerebrospinal fluid leak • who are receiving corticosteroid therapy for more than 2 weeks, and who are on an equivalent daily dosage of prednisone of 2 mg/kg per day or greater, or children who weigh more than 10 kg on a total daily dosage of 20 mg or greater • with chronic pulmonary disease (including asthma treated with high-dose corticosteroid therapy) • preterm infants, born before 28 weeks' gestation • with cardiac disease, with cyanosis or failure with diabetes • with Down syndrome • who are pre- or post-splenectomy, or with functional asplenia 1 dose of PCV13 for catch-up of high-risk children (over the age of 17 months and under 18 years who have received 4 doses of PCV10), and 2 doses of 23PPV for catch-up of high-risk children aged under 18 years. PCV13 and 23PPV for (re-)vaccination of patients aged 5 years and older: • with HIV • pre- or post-HSCT[d] or chemotherapy[d] • pre- or post-splenectomy or with functional asplenia • pre- or post-solid organ transplant • undergoing renal dialysis • with complement deficiency (acquired or inherited) • with cochlear implants • with primary immune deficiency • PCV13 and 23PPV for use in testing for primary immune deficiency.[a]

Continued overleaf

Vaccine	Individuals eligible for funded vaccine
Inactivated polio vaccine (IPV) (chapter 16)	(Re-)vaccination of patients following immunosuppression[b]
Tetanus and diphtheria (Td) (chapter 19)	(Re-)vaccination of patients following immunosuppression[b] Boosting of patients with tetanus-prone wounds For use in testing for primary immune deficiency[a]
Bacillus Calmette–Guérin (BCG) (chapter 20 and Appendix 8)	For infants at increased risk of tuberculosis (TB): • living in a house or family with a person with current or past history of TB; or • having one or more household members or carers who within the last 5 years lived in a country with a rate of TB ≥40 per 100,000 for 6 months or longer; or • during their first 5 years will be living 3 months or longer in a country with a rate of TB ≥40 per 100,000
Varicella vaccine (VV) (chapter 21)	Non-immune patients: • with chronic liver disease who may in future be candidates for transplantation • with deteriorating renal function before transplantation • prior to solid organ transplant • prior to any elective immunosuppression[b] • for post-exposure prophylaxis of immune-competent hospital in-patients Patients at least 2 years after bone marrow transplantation, on advice of their specialist Patients at least 6 months after completion of chemotherapy, on advice of their specialist HIV-positive patients with mild or moderate immunosuppression who are non-immune to varicella, on advice of their HIV specialist Patients with inborn errors of metabolism at risk of major metabolic decompensation, with no clinical history of varicella Household contacts of paediatric patients who are immunocompromised, or undergoing a procedure leading to immunocompromise, where the household contact has no clinical history of varicella Household contacts of adult patients who have no clinical history of varicella and who are severely immunocompromised or undergoing a procedure leading to immunocompromise, where the household contact has no clinical history of varicella

a Upon the recommendation of an internal medicine physician or paediatrician.

b The period of immunosuppression due to steroid or other immunosuppressive therapy must be longer than 28 days.

c This is a Pharmaceutical Schedule Section H – Hospital Medicines List funding restriction.

d PCV13 is funded pre- or post-HSCT or chemotherapy. 23PPV is only funded post-HSCT or chemotherapy.

Eligibility for publicly funded vaccines

Only vaccines given according to the Schedule are available free of charge, unless there is a specific funded programme in response to a recognised need (see Table 2). The immunisation benefit is paid by DHBs to providers for the administration of:

- all childhood Schedule vaccines
- influenza vaccine to eligible children and adults (ie, at higher risk of disease)
- HZV to individuals at age 65 years and for catch-up (until 31 March 2020) of individuals aged 66-80 years, inclusive
- hepatitis A, HepB, Hib, human papillomavirus (HPV), inactivated polio vaccine (IPV), MMR, meningococcal conjugate, pertussis, pneumococcal conjugate and/or polysaccharide, and varicella vaccines only, for eligible children and adults (ie, at higher risk of disease).

Currently there is no funding provided for the administration of tetanus and diphtheria (Td) boosters given at ages 45 and 65 years, although the vaccine is free.

The *Health and Disability Services Eligibility Direction 2011* (the Eligibility Direction) issued by the Minister of Health sets out the eligibility criteria for publicly funded health and disability services in New Zealand. Only people who meet the eligibility criteria defined in the Eligibility Direction can receive publicly funded (ie, free or subsidised) health and disability services.

Regardless of their immigration and citizenship status, all children aged under 18 years are eligible to receive Schedule vaccines, and providers can claim the immunisation benefit for administering the vaccines. All children are also eligible for Well Child Tamariki Ora services.

Non-residents who were aged under 18 years when they commenced HPV vaccination are currently funded to complete the course, even if they are aged 18 years or older when they complete it.

Further information on eligibility can be found on the Ministry of Health website (www.health.govt.nz/eligibility).

Notifiable diseases

All diseases preventable by vaccines on the Schedule (or as part of a targeted programme) are notifiable, except for HPV, seasonal influenza, rotavirus, varicella and herpes zoster.

Note: Rotavirus infections presenting as gastroenteritis are notifiable as acute gastroenteritis.

> It is a legal requirement (Health Act 1956) that health professionals notify their local medical officer of health of any notifiable disease they suspect or diagnose so that appropriate action (eg, public health prevention and control activities) can be undertaken.

Notification processes, and the diseases to which they relate, have been updated in the Health Act and supporting Health (Infectious and Notifiable Diseases) Regulations 2016. See the Ministry of Health document *Guidance on Infectious Disease Management under the Health Act 1956* (available at www.health.govt.nz/publication/guidance-infectious-disease-management-under-health-act-1956) for an explanation, as well as the processes and forms for notifiable diseases.

The case definitions used by the medical officer of health to classify the notified case for surveillance purposes (and to assist in identifying appropriate prevention and control activities) and the laboratory tests required to confirm the diagnosis can be found in the *Communicable Disease Control Manual 2012*. For the most up-to-date information, refer to the online version (available at www.health.govt.nz/publication/communicable-disease-control-manual-2012).

1 General immunisation principles

It is not necessary to have an in-depth knowledge of the immune system to understand the first principles of vaccinology. The immune system is an extremely complex inter-connected system, but certain aspects involved in the process of inducing specific immunity through vaccination inform vaccination practice.

As protective immunity develops over time, the timing of vaccine doses, along with a basic understanding of the different types of vaccines, becomes important.

1.1 Immunity and immunisation

Immunity is the biological state of being able to resist disease: the primary objective of vaccination is to induce an immunological memory against specific diseases, so that if exposure to a disease-causing pathogen occurs, the immune response will neutralise the infection before disease can occur.

1.1.1 Immune recognition

One of the primary ways in which the immune system achieves elimination of pathogens and other unwanted foreign material is through a 'self' tag. Each cell in the body is equipped with a type of molecule that identifies the individual from any other, much like a barcode. Pathogens not only lack a 'self' tag, they also contain a range of material termed 'virulence factors' that the immune system recognises as danger signals.

Antigens (antibody generators) are the drivers of an immune response. Antigens are usually part of a foreign protein or glycoprotein; molecular shapes that the immune system recognises as foreign and trigger an adaptive immune response. While some vaccines contain the entire weakened or attenuated organism (such as measles, mumps and rubella vaccines), increasingly vaccines now contain purified antigens (as in acellular pertussis, HPV or pneumococcal vaccines).

The first process that occurs when a foreign antigen, such as a vaccine antigen, is introduced to the body is the recognition that the antigen is non-self. The antigen is taken up at the local site (such as the injection site) by professional phagocytic cells called antigen-presenting cells; for example, macrophages and dendritic cells. Once inside the antigen-presenting cells, degradation of the foreign protein (or microbe) occurs and tiny fragments are carried to the cell surface and displayed along with a 'self' tag molecule. These antigen-presenting cells then make their way through the lymph to the local lymph node where the adaptive immune response is initiated.

1.1.2 Induction of the adaptive immune response

> The response that occurs the first time an antigen is 'seen' by the immune system is called the primary immune response.

The adaptive immune response occurs in lymphoid tissue, primarily the lymph nodes, of which there are 500–600 distributed throughout the body, including the spleen.

The adaptive immune response to most vaccines occurs at the draining lymph node proximal to the site of injection. The spleen and lymph nodes are densely populated with important effector lymphocytes of the immune response: the T-cells and B-cells. The lymph that flows through the nodes brings with it the vaccine antigen that has been captured at the injection site by the specialised antigen-presenting cells. Once in the lymph node the vaccine antigen, in combination with the cell that has carried it there, comes into contact with the specific T-cells and B-cells.

Among the trillions of specific T and B lymphocytes (~10^{16} possibilities) there (usually) exists a match for the antigen. The process that occurs once these cells recognise each other is the primary immune response and it matures over a period of four to six weeks.

An early outcome of the interaction between these antigen-presenting cells and T and B lymphocytes is the production of antibody-producing B-cells. Antibody can be measured in the blood as soon as 4–7 days, but is usually more effectively measured weeks to months later. Initially, this is low in quantity and of low affinity for the antigen (binds weakly to the antigen), and primarily consists of the antibody subtype immunoglobulin M (IgM), often referred to as 'early antibody'. It peaks at around 7–10 days then declines relatively quickly (see Figure 1.1).

For most vaccine-preventable diseases this process is too slow following infection, and disease occurs before an effective immune response can be mounted. Injecting a subunit part of the disease in the form of vaccine readies the immune response so an effective immune response can be mounted more rapidly when the wild disease is encountered.

1.1.3 Development of immune memory and the secondary response

The response that occurs the second time an antigen is 'seen' by the immune system is called the secondary immune response.

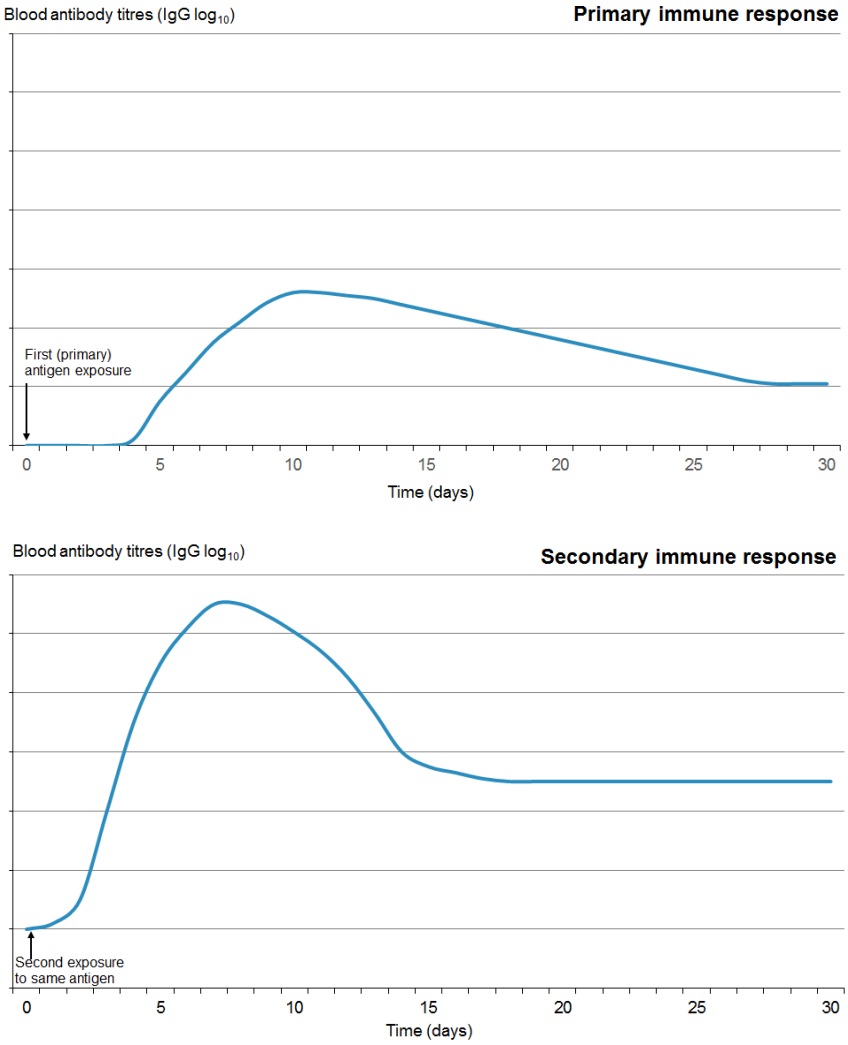
Following the primary immune response, a reaction occurs within the lymph node. Over a period of around two months, cells that are less specific for the specific antigen are deleted, and those that are highly specific are retained and divide. During this time immunological memory cells also develop.

The next time the same antigen is introduced, either as a pathogen component or as a further dose of vaccine subunit, the immunological memory cells will recognise it and begin to proliferate. Highly specific antibody (primarily of the IgG subtype, but also IgA) is rapidly produced in large amounts. The lag phase is much shorter than the primary immune response (see Figure 1.1), just 1–4 days; the antibody peaks very quickly and lasts much longer.

The immune system has been readied by the vaccine; if the actual disease pathogen enters the body, then it is recognised by the immune system and is prevented from causing disease.

Figure 1.1: Comparison of primary and secondary immune responses to protein-containing vaccines

Secondary responses are faster (peaking at day 7) than the primary immune response and the antibody titres are higher, more prolonged and of higher neutralising capacity.

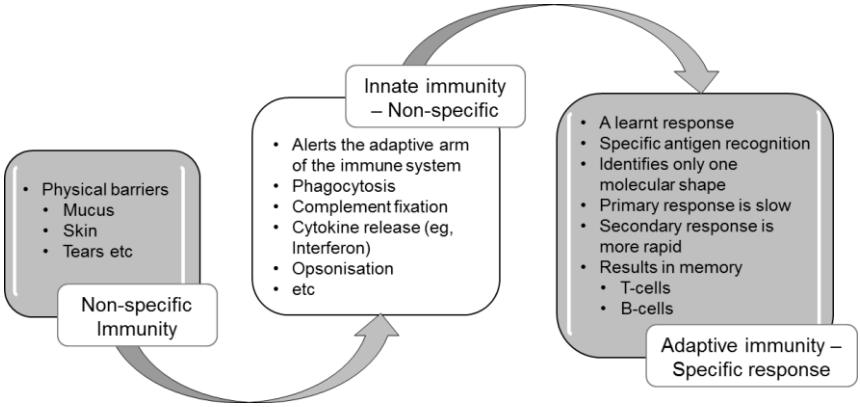


Innate immunity

Most infectious microbes (also known as micro-organisms) are prevented from entering the body by barriers such as skin, mucosa, cilia and a range of anti-microbial enzymes. Any microbes that breach these surface barriers are then attacked by other components of the innate immune system, such as polymorphonuclear leucocytes (neutrophils), macrophages and complement.

This non-specific immune response termed 'innate' is robotic and does not involve learnt or adaptive mechanisms. The cells and proteins of the innate immune system are able to recognise common microbial fragments and can kill microbes without the need for prior exposure. The cells of the innate immune system also interact with the cells of the adaptive immune system (eg, lymphocytes) to induce a cascade of events that results in the development of adaptive immunity and immune memory, as summarised in Figure 1.2.

Figure 1.2: Summary of non-specific innate and adaptive (specific) immunity



1.1.4 Acquisition of adaptive immunity

Specific antibody can be acquired either naturally via infection or 'artificially' using vaccines by teaching the immune system to respond to specific parts of the potential pathogenic antigens. This is termed adaptive or learnt immunity.

Naturally acquired immunity

Naturally acquired immunity occurs either actively by experiencing the infection or passively through the transfer of maternal antibodies from mother to fetus or infant (transplacentally or in breastmilk).

Artificially acquired immunity

'Artificially' acquired immunity occurs either actively through vaccination or passively through administration of immunoglobulin (IG) (see Appendix 6).

While actively acquired immunity lasts from years to life, passively acquired immunity lasts from weeks to months as the transferred antibodies decay and are not renewed.

1.1.5 Maternally derived immunity

The passive transfer of antibody from mother to fetus provides an opportunity to provide protection to the neonate against several diseases before they are old enough to be vaccinated themselves. Maternal vaccination boosts the immunity of the mother, inducing high levels of maternal antibody. This antibody is actively transported across the placenta to concentrate at protective levels by birth (in term infants).

Important diseases that maternal vaccination is effective at preventing include neonatal tetanus, influenza and pertussis in the infant for the first weeks or months of life (see section 4.1 and the relevant disease chapters).

1.1.6 Summary

- Successful immune responses occur following the recognition of, and appropriate response to, a foreign antigen.
- Specialised but non-specific cells, called antigen-presenting cells, take up, transport and present the vaccine antigen to antigen-specific T-cells and B-cells within the lymph nodes and spleen.
- The first wave of antibodies produced are short lived and of low affinity.

- Immune memory takes at least four months to fully develop, but the antibody and memory cells that arise are of high affinity.
- Immune memory can be boosted. This is called a secondary immune response.
- Adaptive immunity is learnt and acquired actively through disease or vaccination.
- Passive immunity is acquired through maternal transfer and administration of IG.
- Maternal vaccination offers passive protection to infants for the first weeks or months of life.

1.2 From personal protection to community (herd) immunity

By protecting individuals, vaccination can also protect the wider community. This herd immunity occurs when the vaccine coverage is high, meaning an infectious case is unlikely to encounter susceptible contacts, so transmission stops.

When a vaccine is able to prevent carriage and transmission of a human-only pathogen such as polio virus, measles virus or *Streptococcus pneumoniae*, the whole population benefits, and these agents can be reduced and even eliminated. This phenomenon, called herd or community immunity, can prevent infections spreading and therefore protect vulnerable members of the population, such as the very young, very old, or those with underlying conditions that increase their risk from infectious diseases (immunocompromised). These individuals may not themselves be able to receive some vaccines (eg, live vaccines) or may not mount an effective immune response to other vaccines.

The population benefits depend on the disease itself and the nature of the vaccine. A recent example of herd immunity in New Zealand is the significant reduction in rotavirus hospital discharge rates in children aged under 5 years following the July 2014 introduction of rotavirus vaccine for infants (see section 17.3.2).

1.2.1 Reproduction number (R_0) and herd immunity threshold (H)

A measure of the infectiousness of a disease is the basic reproduction number (R_0). This is the number of secondary cases generated by a typical infectious individual when the rest of the population is susceptible. In other words, R_0 describes the spreading potential of an infection in a population.[1] Measles is one of the most infectious diseases, with an R_0 of 12–18 (Table 1.1). In other words, one person with measles is likely to infect up to 18 other susceptible people. Pertussis is similarly infectious.

If a significant proportion of the population are immune, then the chain of disease transmission is likely to be disrupted. The herd immunity threshold (H) is the proportion of immune individuals in a population that must be exceeded to prevent disease transmission. For example, to prevent measles or pertussis transmission, 92–94 percent of the population must be immune (Table 1.1).

R_0 must remain above 1 in order for an infection to continue to exist. Once R_0 drops below 1 (such as in the presence of an effective vaccination programme), the disease can be eliminated. The greater the proportion of the population that is immune to the infection, the lower the R_0 will be. For example, data[2] indicates that a quadrivalent HPV vaccine programme with 70 percent coverage in young women may lead to the near disappearance of genital warts from the heterosexual population because the R_0 for HPV types 6 and 11 (causing genital warts) falls to below 1 (see 'Herd immunity' in section 9.4.2).

Table 1.1: Approximate basic reproduction numbers (in developed countries) and implied crude herd immunity thresholds[a] for common vaccine-preventable diseases[b]

Infection	Basic reproduction number (R_0)	Crude herd immunity threshold, H (%)
Diphtheria	6–7	83–85
Influenza[c]	1.4–4	30–75
Measles[d]	12–18	92–94
Mumps	4–7	75–86
Pertussis	5–17	92–94
Polio[e]	2–20	50–95
Rubella	6–7	83–85
Varicella	8–10	Not defined

Notes

a The herd immunity threshold (H) is calculated as $1-1/R_0$.

b The values given in this table are approximate: they do not properly reflect the range and diversity among populations, nor do they reflect the full immunological complexity underlying the epidemiology and persistence of these infections.

c The R_0 of influenza viruses varies among subtypes.

d Herd immunity thresholds as low as 55% have been published.

e This is complicated by uncertainties over immunity to infection and variation related to hygiene standards.

Adapted from: Fine PEM, Mulholland K. 2013. Community immunity. In: Plotkin SA, Orenstein WA, Offit PA (eds). *Vaccines* (6th edition). Philadelphia, PA: Elsevier Saunders. Table 71.2.

1.2.2 Summary

- Vaccines provide not only individual protection, but for many of the diseases we vaccinate against there is also a population effect called herd/community immunity.
- Some diseases are extremely infectious and require a very high proportion of the community to be immune to prevent transmission (particularly measles and pertussis).

1.3 The importance of immunisation coverage

High immunisation coverage not only means more individuals are protected but is vital to achieve herd immunity. High coverage reduces the spread of disease to those who have not been vaccinated for medical reasons (eg, children with leukaemia while receiving treatment) or because of age (eg, infants who are too young to respond to some vaccines). High coverage also reduces the spread of disease to those who may not mount an effective immune response to vaccines because of an underlying condition (eg, those on immunosuppressive regimes).

The World Health Organization (WHO) and the New Zealand government target for immunisation coverage is for at least 95 percent of children to be fully vaccinated by age 2 years. The New Zealand target includes a marker for on-time immunisation of 95 percent by age 8 months, as well as at age 2 years. This target is based on the need for:

- on-time immunisation coverage, particularly three doses of pertussis-containing vaccine for infants in the primary series and the first dose of measles vaccine at age 15 months
- achieving high herd immunity, particularly to prevent measles transmission.

For the three months ending 31 December 2017, 92.2 percent of New Zealand children were fully immunised by age 8 months and 92.3 percent were fully immunised by age 2 years. Up-to-date national and DHB immunisation coverage data is available on the Ministry of Health website (www.health.govt.nz/national-and-dhb-immunisation-data).

1.4 Classification of vaccines

There are three broad categories of vaccine type: live attenuated (weakened), killed/inactivated, and subunit. Examples of the different types of vaccines are summarised in Table 1.2.

Table 1.2: Classification of vaccines, with examples

Live attenuated	Inactivated or whole killed	Subunit
Measles Mumps Rubella Varicella Rotavirus Tuberculosis (BCG) Zoster	Poliomyelitis (IPV) Hepatitis A Some influenza vaccines	Toxoid: • diphtheria • tetanus Polysaccharide: • pneumococcal (23-valent) Conjugate: • pneumococcal (10- and 13-valent) • *Haemophilus influenzae* type b • meningococcal (monovalent and quadrivalent) Recombinant: • hepatitis B • human papillomavirus Other subunit: • pertussis, acellular • influenza

Note: Travel vaccines have been omitted from the above table.

1.4.1 Live attenuated vaccines

Live vaccines contain pathogens, usually viruses, which have been weakened (attenuated) so that they are able to replicate enough to induce an immune response but not cause disease. Immunity from live vaccines is usually very long-lived. The live vaccines on the National Immunisation Schedule are MMR, varicella, rotavirus and herpes zoster vaccines.

1.4.2 Killed and inactivated vaccines

Killed vaccines contain whole bacteria that have been killed. The whole-cell pertussis vaccine is an example of a killed vaccine. There are no killed vaccines on the Schedule.

Inactivated vaccines contain viruses that have been inactivated in some way, such as splitting, so they are unable to replicate or cause disease. Examples of inactivated vaccines are influenza and polio vaccines.

1.4.3 Subunit vaccines

Subunit vaccines contain microbial fragments or particles that can induce an immune response which protects against disease. These are produced using a range of methods including recombinant engineering, detoxification processes and splitting and purification.

Toxoid vaccines

In some bacterial infections (eg, diphtheria, tetanus), the clinical manifestations of disease are caused not by the bacteria themselves but by the toxins they secrete. Toxoid vaccines are produced by harvesting a toxin and altering it chemically (usually with formaldehyde) to convert the toxin to a toxoid. The toxoid is then purified. Toxoid vaccines induce antibodies that neutralise the harmful exotoxins released from these bacteria.

Recombinant vaccines

Recombinant vaccines, such as those used against HBV and HPV, are made using a gene from the (disease-causing) pathogen. The gene is inserted into a cell system capable of producing large amounts of the protein of interest. The protein produced is capable of generating a protective immune response. For example, the gene for the hepatitis B surface antigen (HBsAg) is inserted into yeast cells, which replicate and produce large amounts of HBsAg. This is purified and used to make vaccine. The advantage of this approach is that it results in a very pure vaccine that is efficient to produce.

Polysaccharide and conjugate vaccines

Polysaccharides are strings of sugars. Some bacteria, such as *Streptococcus pneumoniae* and *Neisseria meningitidis*, have large amounts of polysaccharide on their surface, which encapsulate the bacteria. The polysaccharide capsules protect the bacteria from the host's immune system and can make the bacteria more virulent. Historically, it has been difficult to stimulate an effective immune response to these polysaccharide capsules using vaccines, particularly in children aged under 2 years.

First-generation capsular polysaccharide vaccines contained antigens isolated from the different polysaccharide capsules (eg, 23PPV, see chapter 15). Polysaccharide vaccines are poorly immunogenic, and they only induce a primary immune response. They produce low affinity antibodies (which do not bind well to the antigen) and, because they do not elicit T-cell responses, immune memory is not strong. Multiple priming doses (even a single dose) can cause hyporesponsiveness in both children and adults to further doses. There is also concern that repeated doses could result in 'clonal deletion' where the specific B-cell pool becomes depleted due to successive primary responses.

The new generation conjugate vaccines (eg, PCV13 and MCV4-D) contain carrier proteins that are chemically attached to the polysaccharide antigens. Attaching relatively non-immunogenic polysaccharides to the highly immunogenic carrier proteins means that by activating a T-cell response, conjugate vaccines induce both high-affinity antibodies against the polysaccharide antigens, and immune memory.

Examples of carrier proteins and vaccines that use them are:

- tetanus toxoid, used in the meningococcal C conjugate vaccine (MenCCV; NeisVac-C)
- a non-toxic recombinant variant of diphtheria toxin (CRM197), used in the 13-valent pneumococcal conjugate vaccine (PCV13; Prevenar 13)
- diphtheria toxoid (D), used in the quadrivalent meningococcal conjugate vaccine (MCV4-D; Menactra)
- outer membrane protein, used in some Hib vaccines.

The new generation conjugate vaccines are limited by the number of polysaccharides that can be covalently linked to the carrier molecule, so there is still a role for polysaccharide vaccines to broaden the number of serotypes recognised. For example, PCV13 has 13 serotypes, compared to 23PPV with 23 serotypes. Conjugate vaccine technology is expected to improve so that polysaccharide vaccines can eventually be phased out.

Principles and implications for using polysaccharide and conjugate vaccines

- Because of their improved immune response, where possible use protein conjugate polysaccharide vaccines in preference to plain polysaccharide vaccines.
- To ensure broad protection against disease, use a conjugate vaccine to prime the immune system before using the polysaccharide vaccine to increase the number of serotypes recognised. For example, high-risk children are primed with PCV13 then boosted with 23PPV (see section 15.5).
- To avoid or minimise hyporesponsiveness, individuals should have a maximum of three lifetime doses of polysaccharide vaccine.
- Children aged under 2 years should not receive polysaccharide vaccines as they are likely to be ineffective.

1.4.4 Summary

- Vaccines introduce antigens to the immune system in the form of live, killed/inactivated or subunit vaccines.
- Polysaccharide vaccines do not induce immune memory and have been associated with hyporesponsiveness to later doses. Polysaccharide-conjugated vaccines overcome these problems.

1.5 Vaccine ingredients

In addition to the antigen, a vaccine may contain a range of other substances; for example, an immune enhancer (adjuvant) and/or a preservative. Traces of residual components from the manufacturing process may also be present in the vaccine. For further information on vaccine content, see chapter 3 and the vaccine sections within the disease chapters of this *Handbook*.

1.5.1 Adjuvants

Adjuvants are substances that enhance the immune response to an antigen through a range of mechanisms, including improving the delivery of the antigen to the innate immune system and to the lymphoid organs. Use of adjuvants also means that less antigen (which can be difficult to produce) is needed (antigen sparing).

Adjuvants licensed for human use include aluminium salts (eg, aluminium hydroxide and aluminium phosphate), oil-in-water emulsions (MF59, Novartis; AS03, GSK) and a bacterial endotoxin (AS04, GSK). Most non-live vaccines require an adjuvant, and most vaccines still use aluminium adjuvants. The amount of aluminium contained in a vaccine is very small compared with that present in our daily intake from food and water, including breastmilk.

1.5.2 Preservatives

Preservatives prevent the contamination of vaccines, particularly in multi-dose vials. 2-phenoxyethanol is an example of a preservative used in some vaccines. It is also used in many cosmetics and baby care products. Many vaccines do not contain a preservative. Mercury-based preservatives (thiomersal) are not used in vaccines on the New Zealand National Immunisation Schedule.

1.5.3 Stabilisers

Stabilisers protect the vaccine from adverse conditions (such as exposure to heat), inhibit chemical reactions and prevent components from separating. Examples include sucrose, lactose, albumin, gelatin, glycine and monosodium glutamate (MSG).

1.5.4 Surfactants/emulsifiers

These are wetting agents that alter the surface tension of a liquid, like a detergent does. Surfactants assist particles to remain suspended in liquid, preventing settling and clumping. A commonly used surfactant is polysorbate 80, made from sorbitol (sugar alcohol) and oleic acid (an omega fatty acid). It is also commonly used in foods such as ice-cream.

1.5.5 Residuals

Residuals are traces of substances that remain in the vaccine as an inevitable consequence of the manufacturing process. Regulatory bodies vary as to which trace substances must be specified. Residuals may include virus-inactivating agents (such as formaldehyde), antibiotics and other substances used in the manufacturing process, such as egg protein and gelatin.

1.6 Safety monitoring of vaccines in New Zealand

1.6.1 The approval of vaccines for use in New Zealand

Vaccines, like all medicines, have benefits and risks of harm. Before a medicine or vaccine is approved for use, it must be tested in clinical trials to determine its efficacy and safety profile. Information about efficacy and potential risks of harm is identified from the clinical trial data and assessed before the medicine or vaccine is approved for use.

Known information about each medicine and vaccine is published for health professionals in a manufacturer's data sheet, available on the Medsafe website (www.medsafe.govt.nz). Consumer medicine information is usually also published.

Once the vaccine is used freely (ie, outside of the clinical trials), further information becomes available on its safety profile. Some adverse reactions are rare and may not be seen until a very large number of people have received the medicine or vaccine. This is one of the reasons why it is important to monitor all medicines and vaccines after they have been approved (registered). Note that some vaccines that are approved for use by Medsafe may not have been made available for distribution by the manufacturer or supplier.

Most countries (including New Zealand) have a safety monitoring system, which includes a voluntary spontaneous reporting scheme, to help identify any possible safety concerns. These reporting systems feed into the WHO Collaborating Centre for International Drug Monitoring, called the Uppsala Monitoring Centre, located in Sweden. This means

that international data, often covering millions of doses, is available for Medsafe, which is the medicines regulator responsible for monitoring information to ensure that approved vaccines remain acceptably safe for use in New Zealand. Vaccine safety is never reviewed in isolation from the expected benefits of the vaccine; it is always looked at in terms of the risk–benefit balance.

In addition, the WHO plays an important role in vaccine safety through its Strategic Advisory Group of Experts on Immunization and the Global Advisory Committee on Vaccine Safety.

1.6.2 The New Zealand spontaneous reporting scheme

Two terms are used to describe spontaneous reports. *Adverse events* are undesirable events experienced by a person, which may or may not be causally associated with the vaccine. *Adverse reactions* are undesirable effects resulting from medicines or vaccines (ie, they are causally associated).

Spontaneous reports are case reports of adverse events that people have experienced while or after taking a medicine or having a vaccine. Medsafe contracts the collection, review and analysis of this information to the New Zealand Pharmacovigilance Centre at the University of Otago in Dunedin.

Health care professionals and consumers are encouraged to report adverse events following immunisation (AEFIs) to the Centre for Adverse Reactions Monitoring (CARM), which is part of the New Zealand Pharmacovigilance Centre. Pharmaceutical companies also submit adverse event reports.

Further information about suspected adverse reactions (and events following immunisation) reported in New Zealand can be found in the *Suspected Medicine Adverse Reaction Search* (SMARS) on the Medsafe website (www.medsafe.govt.nz/projects/B1/ADRDisclaimer.asp). See below for details about how to report to CARM and what information should be reported.

1.6.3 AEFI reporting process – notifying CARM

When obtaining consent for immunisation, vaccinators should also seek consent to report any adverse events that may occur, because AEFI reporting is considered part of immunisation programme quality control monitoring and public safety.

How to report to CARM

Adverse events may be reported to CARM by:

- the electronic adverse reaction reporting tool available in practice management software programmes
- online reporting at https://nzphvc.otago.ac.nz/report/
- using the iPhone/iPad iOS application (available at https://nzphvc.otago.ac.nz/app)
- downloading and printing a reporting form (https://nzphvc.otago.ac.nz/reporting), then mailing the completed form to the address below
- completing a Freepost Yellow Card (available from CARM), and also found in the *MIMS New Ethicals* and inside the back cover of some editions of *Prescriber Update*
- by telephone, email or fax (see below). Outside office hours, a telephone-answering machine will take messages.

Send reporting forms to:

Freepost 112002
The Medical Assessor
Centre for Adverse Reactions Monitoring (CARM)
University of Otago Medical School
PO Box 913
Dunedin 9710

Telephone: (03) 479 7247
Fax: (03) 479 7150
Email: carmnz@otago.ac.nz
Website: www.otago.ac.nz/carm

In terms of guidance, the sort of information the reporting form generally requires is a patient identifier (gender, age, initial), a medicine, a reaction and the reporter's contact details.

What should be reported?

Health professionals/vaccinators should report:

- all serious suspected AEFI and other reactions of clinical concern to established vaccines, such as those described in Table 1.3 below. The AEFIs should be reported regardless of whether or not they consider the event to have been caused by the vaccination, and they should still be reported even if the effect is well recognised
- all suspected adverse reactions (including minor reactions) to newly introduced vaccines, or those being used for new indications or being delivered by a different route.

Individuals or parents/guardians should be encouraged to notify vaccinators of any AEFI that they consider may have been caused by the vaccination. Alternatively, individuals or parents/guardians may wish to notify CARM themselves, or they can contact their general practice or the Immunisation Advisory Centre (IMAC) (0800 IMMUNE / 0800 466 863) to help with notification.

If in doubt, report it.

Table 1.3: Examples of AEFIs to be reported

Timeframe	Event
All vaccines	
Within 24 hours of vaccination	Anaphylactic reaction (acute hypersensitivity reaction) Anaphylaxis Persistent inconsolable screaming (more than 3 hours) Hypotonic-hyporesponsive episode Fever >40°C
Within 5 days of vaccination	Severe local reaction Sepsis Injection site abscess
Within 12 days of vaccination	Seizures, including febrile seizures Encephalopathy
Within 3 months of vaccination	Acute flaccid paralysis* (AFP), including Guillain–Barré syndrome (GBS) Brachial neuritis (usually occurs 2–28 days after tetanus-containing vaccine) Thrombocytopenia (usually occurs 15–35 days after MMR)
Between 1 and 12 months after BCG vaccination	Lymphadenitis Disseminated BCG infection Osteitis/osteomyelitis
No time limit	Intussusception after rotavirus vaccine Any death, hospitalisation, or other severe or unusual events of clinical concern that are thought by health professionals or the public to possibly be related to vaccination
Newly introduced vaccines, or those with new indications or being delivered by a different route	
No time limit	All suspected adverse reactions

* AFP in children is also monitored by the New Zealand Paediatric Surveillance Unit as part of polio eradication surveillance (see chapter 16).

Seriousness of AEFIs

Reports of suspected adverse reactions or AEFIs can be categorised as serious or non-serious. This categorisation system is a tool used to try and prioritise safety concerns. It is not a reflection of the importance of the events to the consumer or their health care professional. Because a report is defined as serious based on what is reported, it is possible to have both serious and non-serious cases reporting the same type of event; for example, headache.

International convention defines the seriousness of reports based on the outcome or nature of the reported event as documented in the report, *irrespective of whether there is any association to the medicine or vaccine*.

Serious events are based on the following international criteria:

- hospitalisation (or prolonged hospitalisation) of the patient
- life-threatening event
- persisting disability of the patient
- intervention required to prevent permanent impairment
- congenital anomaly
- death of the patient.

CARM assessment of causality

The WHO recommends that individual reports of adverse reactions to vaccines are assessed for causality. This assessment is a tool used to help detect new safety concerns; it is not a determination of whether a vaccine caused an adverse reaction.

The person reporting the event will receive a letter of response from CARM commenting on the adverse effect, the causal relationship, the number of other similar events, and advice about future use of the vaccine in the individual. Also, where applicable, CARM will provide a validated AEFI code to the NIR.

The information provided by CARM:

- needs to be communicated to the individual and parent/guardian (if applicable)
- must be entered in the medical notes
- will help to identify those individuals who should receive follow-up vaccination in a controlled environment, such as a hospital.

1.6.4 What does Medsafe do with this information?

Medsafe and CARM analyse spontaneous reports in conjunction with other information to determine whether there are any new potential safety signals. Medsafe seeks the advice of independent experts through the Medicines Adverse Reactions Committee, or may form working groups of experts to provide advice. Medsafe works closely with other regulatory authorities from around the world.

Medsafe undertakes a risk–benefit assessment of safety signals to decide if action is required. Further information on risk–benefit assessment is provided on the Medsafe website (www.medsafe.govt.nz/Consumers/Safety-of-Medicines/Medsafe-Evaluation-Process.asp).

Most safety signals are not supported by any additional information, and no action is taken, although Medsafe may continue to monitor the issue closely. A small number of possible safety signals are confirmed as real. In these cases, Medsafe has a number of regulatory actions it can take, including withdrawing the product.

In New Zealand, it is less likely that any new rare side-effects to vaccines will be detected because of the small number of people immunised compared to other countries. Therefore, Medsafe uses international data available from the WHO, other regulators and pharmaceutical companies to help assess any reports of rare events following immunisation and to determine if they may be new events linked to immunisation.

1.6.5 Advantages and limitations of spontaneous reports

Spontaneous reports have been shown to be a very simple way of identifying potential or possible safety signals with medicines, and over 90 countries have a spontaneous reporting system. They can be used to monitor the safety of medicines in real-life use over the lifetime of the medicine, and for all types of people.

The limitations of using spontaneous reports include under-reporting, a lack of reliable information on the extent of use of the medicine, and wide variations in the clinical details provided about the event and the history of the patient. Spontaneous reports are heavily subject to

reporting bias, such as media or other attention on an issue. They are also not very effective at detecting adverse reactions that occur a long time after starting the medicine.

For these reasons, such reports are only used to identify safety signals. These signals require further formal epidemiological study before they can be validated or discounted. Information obtained from spontaneous reports needs to be interpreted with caution.

Understanding vaccine safety and spontaneous reporting

Spontaneous report patterns can be variable, and they depend on many factors. Summaries of reported events following immunisation *are not* lists of known or proven adverse reactions to vaccines. They cannot be used to determine the frequency of adverse reactions to vaccines in the whole population, and they cannot be used to directly compare the relative safety of vaccines. They must not be interpreted and used as such.

Health care professionals and consumers are encouraged to report any suspicions that an event they have experienced may have been caused by vaccination. Therefore, reports sent to CARM may be:

- real adverse reactions to the vaccine
- anxiety or nervousness about needles or the process of vaccination
- coincidental events that would have occurred anyway.

With any vaccine, the adverse events that are generally reported include:

- injection-site reactions
- well-recognised events, such as headaches, dizziness, muscle aches, mild fever and tiredness
- mild allergic reactions, such as mild rashes and itching
- rare but serious allergic reactions, called anaphylaxis, which can occur in response to any medicine or vaccine and some foods – health care professionals giving vaccines are trained to recognise the symptoms of serious allergic reactions and promptly treat them
- events due to anxiety, such as fear or anticipation of the needle injection (eg, fainting)

- coincidental medical conditions
- new adverse events (ie, those not already listed in the prescribing information [data sheet]).

There will always be a number of coincidental events reported because vaccines are given to large sections of the population. In some cases, vaccines are specifically targeted at people with underlying medical conditions (eg, the influenza vaccine). The challenge is to be able to distinguish these coincidental 'background' events from those that may have been caused by the vaccine. There are a range of research methods for assessing the risk of an event after a vaccine compared with the risk with no vaccine exposure.

The time between immunisation and an event can be important in determining whether the event was coincidental. Most reactions to vaccines occur within a very short time of immunisation, usually within days.

Another important approach taken when assessing vaccine safety is comparing the number of reports for a specific event with the expected background rate for that event. When doing this, it is important to ensure that definite diagnoses of the events reported were made and to adjust the background rate for any differences in population groups and seasonal variations.[3]

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1. Fine PEM, Mulholland K. 2013. Community immunity. In: Plotkin SA, Orenstein WA, Offit PA (eds). *Vaccines* (6th edition). Philadelphia, PA: Elsevier Saunders.
2. Read TRH, Hocking JS, Chen MY, et al. 2011. The near disappearance of genital warts in young women 4 years after commencing a national human papillomavirus (HPV) vaccination programme. *Sexually Transmitted Infections* 87(7): 544–7.
3. Sexton K, McNicholas A, Galloway Y, et al. 2009. Henoch-Schönlein purpura and meningococcal B vaccination. *Archives of Disease in Childhood* 94(3): 224–6.

2 Processes for safe immunisation

Who can administer a vaccine?

Vaccines are prescription medicines, so they can only be administered by:

- a nurse practitioner
- a medical practitioner
- a registered midwife
- a designated prescriber (which includes a registered nurse fulfilling the designated prescriber criteria)
- a person authorised to administer the medicine in accordance with a prescription or a standing order.

In the case of an approved immunisation programme, vaccines can be administered without a prescription or standing order by:

- a person who is authorised by either the Director-General of Health or a medical officer of health under Regulation 44A of the Medicines Regulations 1984 (see Appendix 4).

Several vaccines have been considered by the Medicines Classification Committee and reclassified from prescription medicines to restricted medicines when administered by a registered pharmacist (who meets the conditions of the classification; see Appendix 4, 'Pharmacist vaccinators'). It is the reclassification of a vaccine to a restricted medicine that gives a pharmacist vaccinator the authority to administer the vaccine without a prescription.

- See section 2.1 'Pre-vaccination' for cold chain management, informed consent, pre-vaccination screening, contraindications, spacing of doses, catch-up, and adult vaccination.
- See section 2.2 'Vaccine administration' for preparation, route, vaccination techniques by age, and multiple injections.

- See section 2.3 'Post-vaccination' for post-vaccination advice, pain and fever recommendations, anaphylaxis and emergency management, and documentation and insurance.

2.1 Pre-vaccination

The 'Immunisation standards for vaccinators' and the 'Guidelines for organisations storing vaccines and/or offering immunisation services' apply to the delivery of all Schedule vaccines and those not on the Schedule. See Appendix 3.

The vaccinator is responsible for ensuring all the vaccines they are handling and administering have been stored at the recommended temperature range of +2°C to +8°C at all times (see 'Cold chain management' below and the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*[1]). Information on vaccine presentation, preparation and disposal can be found in Appendix 7.

Vaccinators are expected to know and observe standard occupational health and safety guidelines in order to minimise the risk of spreading infection and needle-stick injury (see Appendix 7).

All vaccinations on the New Zealand National Immunisation Schedule are given parenterally (by injection) except for the rotavirus vaccine which is given non-parenterally (orally). For non-parenteral vaccine administration, follow the manufacturer's instructions.

2.1.1 Cold chain management

All vaccines must be stored and/or transported within the recommended temperature range of +2°C to +8°C at all times. Refer to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*[1] for detailed vaccine storage, transportation and destruction information.

The 'cold chain' is defined as 'the system of transporting and storing vaccines within the recommended temperature range of +2°C to +8°C from the place of manufacture to the point of vaccine administration (the individual)'. The integrity of the cold chain is dependent not only on the equipment used for storage, transportation and monitoring but also on the people involved and the processes/practices they undertake.

Table 2.1: Key points for cold chain management

All vaccinators are responsible for ensuring the vaccines they administer have been stored correctly.
All immunisation providers storing vaccines must use a pharmaceutical refrigerator.
The pharmaceutical refrigerator minimum and maximum temperatures must be monitored and recorded at the same time on a daily basis.
All immunisation providers must monitor the refrigerator with an electronic temperature recording device (eg, a data logger) that records and downloads data on a weekly basis. This should be compared with the daily minimum/maximum recordings.
All immunisation providers who store vaccines and/or offer immunisation services must achieve Cold Chain Accreditation.
Each immunisation provider must have a written cold chain management policy in place and ensure their policy is reviewed and updated annually. Each vaccinator is responsible to ensure they are able to access this policy, as it will contain important practice information on vaccine storage.
If the vaccine refrigerator temperature goes outside the recommended +2°C to +8°C range • Label the vaccines 'not for use'. If the refrigerator is currently running within the +2°C to +8°C range, leave the labelled vaccines in your refrigerator. If the refrigerator is not within the +2°C to +8°C range, pack your labelled vaccines into a chilly bin, with a temperature monitoring device and consider transporting to your back-up provider (details for this are in your cold chain policy). • Download the data logger and check for inconsistencies or temperature fluctuations; note any temperature fluctuations outside the +2°C to +8°C range, and the time period. • Contact your local immunisation coordinator for advice and further actions. • Document the steps and actions you have taken.

2.1.2 Informed consent

What is informed consent?

Informed consent is a fundamental concept in the provision of health care services, including immunisation. It is based on ethical obligations that are supported by legal provisions (eg, the Health and Disability Commissioner Act 1994, Code of Health and Disability Services Consumers' Rights 1996, Health Information Privacy Code 1994, Privacy Act 1993 and Privacy Amendment Act 2013).

Providing meaningful information to enable an informed choice, and seeking informed consent, is a duty that all health and disability providers must meet to uphold the rights of health and disability consumers. Informed consent includes the right to be honestly and openly informed about one's personal health matters. The right to agree to treatment carries with it the right to refuse and withdraw from treatment.

Informed consent is also an external expression of a health care provider's pivotal ethical duty to uphold and enhance their patient's autonomy by respecting the patient's personhood in every aspect of their relationship with that individual.

The informed consent process

Informed consent is a process whereby the individual and/or their representative (if the individual does not have the capacity to consent) are appropriately informed in an environment and manner that are meaningful. Then, having been well informed, they are willing and able to agree to what is being suggested without coercion.

Regardless of age, an individual and/or their parent/guardian must be able to understand:

- that they have a choice
- why they are being offered the treatment/procedure
- what is involved in what they are being offered
- the probable benefits, risks, side-effects, failure rates and alternatives, and the risks and benefits of not receiving the treatment or procedure.

With regard to vaccination, the individual or parent/guardian needs to understand the benefits and risks of vaccination, including those to the child and community, in order to make an informed choice and give informed consent.

The essential elements of the informed consent process are effective communication, full information and freely given competent consent. The specific rights in the Code of Health and Disability Services Consumers' Rights that represent these three elements are:

- Right 5: Right to effective communication
- Right 6: Right to be fully informed
- Right 7: Right to make an informed choice and give informed consent.[2]

For example, section 7(1) of the Code states that 'services may be provided to a consumer only if that consumer makes an informed choice and gives informed consent, except where any enactment, or the common law, or any other provision of the Code provides otherwise.' Information on the Code of Health and Disability Services Consumers' Rights can be found on the Health and Disability Commissioner's website (www.hdc.org.nz).

Health professionals have legal obligations to obtain informed consent prior to a procedure and prior to data collection (eg, data collected for the NIR). Unless there are specific legal exceptions to the need for consent, the health professional who acts without consent potentially faces the prospect of a civil claim for exemplary damages, criminal prosecution for assault (sections 190 and 196 of the Crimes Act 1961), complaints to the Health and Disability Commissioner, and professional disciplining.

Ensuring that an individual has made an informed choice regarding treatment options has been included in the Health Practitioners Competence Assurance Act 2003. This Act ensures that health practitioners are, and remain, competent and safe to practise. For example, the Nursing Council of New Zealand competencies for the Registered Nurse Scope of Practice, Competency 2.4, 'ensures the client has adequate explanation of the effects, consequences and alternatives of proposed treatment options' (see the Nursing Council of New Zealand website, www.nursingcouncil.org.nz).

Privacy, and control over personal information

The right to authorise, or to exert some control over, the collection and disclosure of personal information about oneself is a right closely allied to that of consent to treatment and is also relevant to personal integrity and autonomy. The Health Information Privacy Code 1994 gives people the right to access, and seek correction of, health information about them (Rules 6 and 7). It also requires health agencies collecting

identifiable information to be open about how and for what purpose that information will be stored, and who will be able to see it (Rule 3).

Parents and guardians have a similar right of access to information about their children under section 22F of the Health Act 1956. This right is limited in that access requests can be refused if providing the information would be contrary to the interests or wishes of the child.

Further information about privacy and health information can be found on the Privacy Commissioner's website (www.privacy.org.nz), or by calling the privacy enquiries line: 0800 803 909.

Immunisation consent in primary care

Parents should be prepared during the antenatal period for the choice they will have to make about their child's vaccination. During the third trimester of pregnancy, the lead maternity carer must provide Ministry of Health information on immunisation and the NIR. This is a requirement under clause DA21(c) of the Primary Maternity Services Notice 2007, pursuant to section 88 of the New Zealand Public Health and Disability Act 2000.

Vaccine hesitancy

> Vaccine hesitancy refers to delay in acceptance or refusal of vaccines despite availability of vaccination services. Vaccine hesitancy is complex and context specific varying across time, place and vaccines. It includes factors such as complacency, convenience and confidence.
>
> WHO: Addressing Vaccine Hesitancy (www.who.int/immunization/programmes_systems/vaccine_hesitancy/en/)

Effective communication and active listening are key components of the informed consent process, especially when health care providers are working with vaccine-hesitant individuals/parents/guardians.

- Be willing to initiate the conversation, avoid leaving it to others.
- Tailor content to the needs of the individual.
- Ensure respect and acknowledgement of concerns.
- Use plain language, open-ended questions and active listening.
- Avoid medical jargon, or ensure it is explained.

- Offer resources.
- Finish with an effective immunisation recommendation.

Information for parents, guardians and health care providers

Health care providers must offer information without individuals or parents/guardians having to ask for it. The depth of information offered or required may differ, but it should at least ensure that the individual or parent/guardian understands what the vaccine is for and the possible side-effects, as well as information about the vaccination programme, the NIR and the risks of not being vaccinated (see chapter 3).

Every effort should be made to ensure that the need for information is met, including extra discussion time, use of an interpreter and alternative-language pamphlets. (Ministry of Health immunisation pamphlets are produced in several languages, and are available from the local authorised provider or can be ordered, viewed and/or downloaded from the HealthEd website: www.healthed.govt.nz)

Issues to discuss with individuals or parents/guardians about immunisation include:

- the vaccine-preventable diseases
- the vaccines used on the Schedule (ie, the funded vaccines that are available)
- how vaccines work, known risks and adverse events, and what the vaccine is made of, in case of known allergies
- the collection of immunisation information on the NIR from birth, or as part of a targeted immunisation programme (eg, the information that will be collected, who will have access to it and how it will be used; see section 2.3.5 for more information on the NIR)
- the choice to vaccinate.

Informed consent is required for each immunisation episode or dose. Presentation for an immunisation event should not be interpreted as implying consent. Individuals and parents/guardians have the right to change their mind at any time. Where consent is obtained formally but not in writing, the provider should document what was discussed, and that consent was obtained and by whom.

Ministry of Health information

Ministry of Health immunisation information for parents and guardians is available on the Ministry of Health's website (www.health.govt.nz/immunisation). Parents and guardians may also order, view or download Ministry of Health immunisation information from the HealthEd website (www.healthed.govt.nz) or from the local authorised resource provider, including:

- Immunise Your Child on Time (leaflet, available in English [HE1327] and other languages)
- Childhood Immunisation (health education booklet [HE1323]).

Further immunisation consent information for health care providers is also available in Appendix 3 of this *Handbook* 'Immunisation standards for vaccinators and Guidelines for organisations offering immunisation services'. Responses to commonly asked questions and suggestions for addressing myths and concerns are available in chapter 3 of this *Handbook* 'Vaccination questions and addressing concerns'.

Other information sources

- Australian Government Department of Health and Ageing. 2013. *Myths and Realities: Responding to arguments against vaccination: A guide for providers* (5th edition). See the Australian Government immunisation website: www.immunise.health.gov.au
- Offit PA, Moser C. 2011. *Vaccines and Your Child – Separating fact from fiction*. New York, NY: Columbia University Press.
- The vaccine manufacturers' data sheets, available on the Medsafe website (www.medsafe.govt.nz). Both consumer and health care provider versions are available.
- Other immunisation-related websites (see Appendix 9).

Alternatively, contact:

- the Immunisation Advisory Centre (IMAC) on freephone 0800 IMMUNE or (0800 466 863), or see the IMAC website (www.immune.org.nz)
- the immunisation coordinator (a list and contact details are available at www.immune.org.nz).

Immunisation consent in other settings (eg, schools)

In mass immunisation campaigns, such as those undertaken at schools, the consent requirements are different from those that apply to the vaccination of individuals in primary care. The parent/guardian may not be with the child on the day of immunisation, so immunisation should proceed only after the parent/guardian has had the opportunity to read the immunisation information and discuss any areas of concern. Consent forms are provided for immunisations given in schools by public health nurses. For children aged under 16 years who are being immunised at school, written consent must be obtained from the parent/guardian. Individuals who are aged 16 years or older may self-consent.

Consent and children

Under the Code of Rights, every consumer, including a child, has the right to the information they need to make an informed choice or to give informed consent. The law relating to the ability of children to consent to medical treatment is complex. There is no one particular age at which all children can consent to all health and disability services. The presumption that parental consent is necessary in order to give health care to those aged under 16 years is inconsistent with common law developments and the Code of Rights.

The Code of Rights makes a presumption of competence (to give consent) in relation to children, although New Zealand is unusual in this respect (ie, the obligations regarding consent of minors are greater in New Zealand than in many other jurisdictions).

A child aged under 16 years has the right to give consent for minor treatment, including immunisation, providing he or she understands fully the benefits and risks involved. In 2002 the Health and Disability Commissioner provided an opinion of a child's consent to a vaccine, whereby the Commissioner was satisfied that a 14-year-old was competent to give informed consent for an immunisation event due to an injury where a tetanus toxoid vaccine would be commonly given. More details of this opinion can be found on the Health and Disability Commissioner's website (www.hdc.org.nz – Case: 01HDC02915).

Further information on informed consent can be found on the Health and Disability Commissioner's website (www.hdc.org.nz).

2.1.3 Pre-vaccination screening

Prior to immunisation with *any* vaccine, the vaccinator should ascertain if the vaccinee (child or adult) has a condition or circumstance which may influence whether a vaccine is given, deferred or contraindicated. Refer to Table 2.2 below, which provides a checklist of conditions or circumstances to screen for, along with the appropriate action to take and a rationale.

The vaccinator will also need to determine which vaccines the vaccinee is due to have, assess the vaccinee's overall current vaccination status and address parental concerns. The vaccinator also needs to advise the individual/parent/guardian they will need to remain for 20 minutes post-vaccination.

Table 2.2: Pre-vaccination screening and actions to take

Condition* or Circumstance	Action	Rationale
Is unwell today: • fever >38°C • acute systemic illness	Defer all vaccines until afebrile. Note: Children with minor illnesses (without acute symptoms/signs) should be vaccinated.	To avoid an adverse event in an already unwell child, or to avoid attributing symptoms to vaccination.
Is a preterm infant and had apnoeas following immunisation in hospital (6-week and/or 3-month event)	Re-admission for the next infant immunisation and respiratory monitoring for 48 to 72 hours may be warranted,[3] but do not avoid or delay immunisation.	There is a potential risk of apnoea in infants born before 28 weeks' gestation.
Previously had a severe reaction to any vaccine	Careful consideration will be needed depending on the nature of the reaction. If in doubt about the safety of future doses, seek specialist advice.	Anaphylaxis to a previous vaccine dose or any component of the vaccine is an absolute contraindication to further vaccination with that vaccine.

Continued overleaf

Condition* or Circumstance	Action	Rationale
Anaphylaxis to vaccine components (eg, gelatin, egg protein, neomycin)	Refer to the relevant vaccine data sheet (www.medsafe.govt.nz) for the components. If an individual has had anaphylaxis to any component contained in a vaccine, seek specialist advice. Egg allergy, including anaphylactic egg allergy, is not a contraindication to MMR or influenza vaccination (see sections 10.6.3 and 11.6.3).	Vaccinators need to be aware of the possibility that allergic reactions, including anaphylaxis, may occur after any vaccination without any apparent risk factors (see section 2.3.3). Delayed hypersensitivity to a prior vaccine dose or a component of a vaccine is not a contraindication to further doses, but it is important to distinguish these from anaphylaxis.
Appropriate spacing between doses of the same vaccine (when was the last vaccination, and what was it?)	See section 2.1.5 and check the relevant disease chapters and catch-up schedules. (See below for live parenteral vaccines.)	The general rule is for a minimum of 4 weeks between doses of a primary series and 4 months between the priming dose(s) and the booster.
Had a live parenteral vaccine within the last 4 weeks – if in doubt, check the individual's immunisation status on the NIR (if applicable)	Delay live attenuated parenteral vaccines to 4 weeks.	The antibody response to the first dose may interfere with the response to the second. They may be given on the same day without interference. Note that this does not apply to rotavirus vaccine, which is a non-parenteral vaccine.
Had an injection of immunoglobulin or a blood transfusion within the last 11 months and is now due for a live vaccine	Check which product the person received and the interval since administration, and refer to Table A6.1. Delay vaccination if necessary.	Live virus vaccines should be given at least 3 weeks before, or deferred for up to 11 months after, doses of human normal immunoglobulin or other blood products. The interval will be determined by the blood product and dose received.

Continued overleaf

Condition* or Circumstance	Action	Rationale
Has a disease that lowers immunity, is receiving treatment that lowers immunity or is an infant of a mother who received immunosuppressive therapy during pregnancy	See chapter 4 'Immunisation of special groups'. In some cases, specialist advice may need to be sought before vaccination. Note: Persons living with someone with lowered immunity should be vaccinated, including with live viral vaccines (see section 4.3.1).	The safety and effectiveness of the vaccine may be suboptimal in persons who are immunocompromised. Live attenuated vaccines may be contraindicated.
Is planning a pregnancy	See section 4.1.1 'For women planning pregnancy'. Ensure women and household members have received all vaccines recommended for their age group. Women should know if they are immune to rubella (section 18.5.3) and varicella (section 21.5.4). Advise women not to become pregnant within 4 weeks of receiving live viral vaccines.	Vaccinating before pregnancy may prevent maternal illness, which could affect the infant, and may confer passive immunity to the newborn.
Is pregnant	See sections 4.1.2 'During pregnancy' and 4.1.3 'Breastfeeding and post-partum'. Influenza and Tdap vaccines are recommended.	Vaccinating (with inactivated vaccines) during pregnancy may prevent maternal illness, which could affect the infant, and may confer passive immunity to the newborn.
	Live vaccines should be avoided until after the delivery.	Deferring administration of live vaccines until after delivery is a precautionary safety measure. Studies of women who inadvertently received a live vaccine during pregnancy and their infants have not identified any adverse effects.

Continued overleaf

Condition* or Circumstance	Action	Rationale
Undiagnosed or evolving neurological condition (for pertussis-containing vaccines only)	Seek specialist advice.	There is the potential for confusion about the role of vaccination in the context of a clinically unstable illness. The risks and benefits of withholding vaccination until the clinical situation has stabilised should be considered on an individual basis.
Thrombocytopenia or bleeding disorders	Administer intramuscular vaccines with caution: • use a 23-gauge or smaller needle and apply firm pressure to the injection site (without rubbing) for at least 10 minutes.	A haematoma may occur following intramuscular administration. The subcutaneous route is still recommended by some authorities – seek specialist advice when appropriate.
Individuals who are currently being treated with immune checkpoint inhibitors, as well as those who have discontinued treatment within the past 6 months.	Seek specialist advice.	There is a theoretical risk that vaccines may trigger an autoimmune response in these individuals. See the 'Oncology patients treated with immune checkpoint inhibitors' discussion in section 4.3.3.

* See chapter 4 'Immunisation of special groups' for more information about pregnancy and lactation and for information about infants with special immunisation considerations, immune-deficient and immunosuppressed individuals, immigrants and refugees, travel, and occupational and other risk factors.

Adapted from: Department of Health and Ageing. 2016. *The Australian Immunisation Handbook* (10th edition; updated August 2016). Canberra, ACT: Department of Health and Ageing. Table 2.1.2.

2.1.4 Contraindications

No individual should be denied vaccination without serious consideration of the consequences, both for the individual and for the community. Where there is any doubt, seek advice from the individual's general practitioner (GP), a public health medicine specialist, medical officer of health, consultant paediatrician or IMAC.

> Anaphylaxis to a previous vaccine dose or any component of the vaccine is an absolute contraindication to further vaccination with that vaccine. (Note that egg-related anaphylaxis and influenza or MMR vaccines are exceptions.) **For more detail on anaphylaxis, see section 2.3.3.**

Live viral vaccines should not be given to pregnant women, nor, in general, to immunosuppressed individuals (see chapter 4).

Seek specialist advice for individuals being treated with immune checkpoint inhibitors, as well as those who have discontinued treatment within the past 6 months. See 'Oncology patients treated with immune checkpoint inhibitors' in section 4.3.3.

See the relevant disease chapter section for more specific vaccine contraindications.

Conditions that are not contraindications to immunisation

The conditions in Table 2.3 are not contraindications to the immunisation of children and adults (see also section 3.1).

Table 2.3: Conditions that are *not* contraindications to immunisation

Individuals with these conditions should be vaccinated with all the recommended vaccines.

Mildly unwell, with a temperature ≤38°C
Asthma, hay fever, eczema, 'snuffles', allergy to house dust
Treatment with antibiotics or locally acting steroids
A breastfeeding mother or a breastfed child
Neonatal jaundice
Low weight in an otherwise healthy child
The child being over the usual age for immunisation – use age-appropriate vaccines, as per the catch-up schedules in Appendix 2 (the exception is rotavirus vaccine, see section 17.5.2)
A previous hypotonic-hyporesponsive episode (see section 2.3.3)
Clinical history of pertussis, measles, mumps or rubella infection – clinical history without laboratory confirmation cannot be taken as proof of immunity (even when an individual is proven to be immune to one or two of either measles, mumps or rubella, there is still the need for immunisation against the other/s, see the relevant chapters)
Prematurity, but an otherwise well infant – it is particularly important to immunise these children, who are likely to suffer severe illness if infected; immunisation is recommended at the usual chronological age (see 'Preterm and low birthweight infants' in section 4.2.1)
Stable neurological conditions, such as cerebral palsy or Down syndrome
Contact with an infectious disease
Egg allergy, including anaphylaxis, is not a contraindication to MMR vaccine (see section 11.6.3) or influenza vaccine (see section 10.6.3)
Family history of vaccine reactions
Family history of seizures
Family history of sudden unexpected death in infancy (SUDI)
Child's mother or household member is pregnant or immunocompromised

2.1.5 Spacing of doses

In general, follow the recommendations in the manufacturers' data sheets.

Principles for spacing of doses of the same vaccine

The immune response to a series of vaccines depends on the time interval between doses. The general rule is for a minimum of four weeks between doses of a primary series; however, the immune response may be better with longer intervals. A repeat dose of the same vaccine given less than four weeks after the previous dose may result in a reduced immune response. Specific recommendations for a rapid schedule by the manufacturer may apply for some vaccines.

Generally, a minimum interval of four to six months between priming dose(s) and the booster dose allows affinity maturation of memory B cells, and thus higher secondary responses (see section 1.1).

It is not necessary to repeat a prior dose if the time elapsed between doses is more than the recommended interval.

Spacing of different vaccines

Two or more parenterally administered live vaccines may be given at the same visit; for example, MMR and VV. However, when given at different visits, a minimum interval of four weeks is recommended. This interval is to avoid the response to the second vaccine being diminished due to interference from the response to the first vaccine. **Note that no interval is required between administration of bacillus Calmette–Guérin (BCG) and rotavirus vaccines.**

Unless there is a specific recommendation against it, an inactivated or subunit vaccine can be administered either simultaneously or at any time before or after a different inactivated, subunit or live vaccine.

Concurrent administration of vaccines

Best practice is to follow the Schedule. Changing the timing of visits or increasing the number of visits to avoid multiple injections delays protection against potentially serious diseases and may also lead to incomplete immunisation.

> Where a number of different injectable vaccines are given on the same day, they must be administered in separate syringes, at different sites.

2.1.6 Catch-up programmes for unimmunised or partially immunised children

The objective of a catch-up programme is to complete a course of vaccinations that provides adequate protection. Catch-up programmes should be based on documented evidence of previous vaccination (eg, the child's *Well Child Tamariki Ora My Health Book*, NIR or overseas immunisation records).

When children have missed vaccine doses, it is important to bring them up to date as quickly as possible. Where more than one vaccine is overdue, it is preferable to give as many as possible at the first visit. For children aged 15 months and older, MMR is the priority.

> See Appendix 2 for determining catch-up requirements and planning a catch-up programme.

If the vaccinator is uncertain about how to plan a catch-up programme, they should contact the local immunisation coordinator, IMAC, medical officer of health or public health service.

Once catch-up is achieved, the child should continue as per the Schedule.

Vaccination of children with inadequate vaccination records

Children *without a documented history of vaccination* are recommended to have a full course of vaccinations appropriate for their age. In cases of doubt, it is safe to repeat vaccine doses: it is preferable for the individual to receive an unnecessary dose than to miss out a required dose(s) and not be fully protected.

2.1.7 Adult vaccination (aged 18 years and older)

Whenever adults are seen in general practice or by immunisation providers, there is an opportunity to ensure they have been adequately protected against the following diseases and have received at least a primary immunisation course as described in Table 2.4. If the requisite number of doses has not been received, catch-up vaccination is recommended and funded (see Appendix 2).

Women of childbearing age should know whether or not they are immune to rubella (see chapter 18) and varicella (see chapter 21).

Table 2.4: Primary immunisation requirements for adults (funded)

Disease	Number of vaccine doses
Tetanus	3 doses
Diphtheria	3 doses
Poliomyelitis	3 doses
Measles, mumps, rubella	2 doses
HPV (aged 26 years and under)	3 doses*

* Individuals who were under age 27 years when they commenced HPV vaccination are currently funded to complete the 3-dose course, even if they are older than 27 years when they complete it.

See Table 2.5 for adult vaccination recommendations, including vaccinations recommended for at-risk groups (funded vaccines are in the shaded boxes). See also chapter 4 'Immunisation of special groups' for information about immunisation during pregnancy and lactation (section 4.1), of immunocompromised individuals (section 4.3), of immigrants and refugees (section 4.4), for travel (section 4.5), and for those with occupational and other risk factors (section 4.6).

Table 2.5: Adult (≥18 years) vaccination recommendations, excluding travel requirements

Vaccine	Recommended and funded	Recommended but not funded
Hib (chapters 4 and 6)	(Re-)vaccination of patients post-haematopoietic stem cell transplant (HSCT) or chemotherapy; pre- or post-splenectomy or with functional asplenia; pre- or post-solid organ transplant, pre- or post-cochlear implants, renal dialysis and other severely immunosuppressive regimens	
Hepatitis A (chapter 7)	Transplant patients Close contacts of hepatitis A cases[a]	Patients with chronic hepatitis B or C infection; men who have sex with men; adults at occupational risk
Hepatitis B (chapter 8)	Household or sexual contacts of patients with acute or chronic HBV infection HIV-positive patients Hepatitis C-positive patients Following non-consensual sexual intercourse Following immunosuppression[b] Solid organ transplant patients Post-HSCT patients Following needle-stick injury Dialysis patients Liver or kidney transplant patients	Non-immune adults at risk including occupational or other risk factors
HPV (chapter 9)	Individuals aged 18–26 years[c,d] Individuals aged 18–26 years:[c,d] • with confirmed HIV infection • transplant (including stem cell) patients • an additional dose post-chemotherapy	Adults ≥27 years:[c,d,e] • who have had little previous exposure to HPV and are now likely to be exposed • who are men who have sex with men • with HIV
Annual influenza vaccine (chapter 10)	Pregnant women Individuals aged 65 years and older Individuals aged under 65 years with eligible conditions	All other adults

Continued overleaf

Vaccine	Recommended and funded	Recommended but not funded
MMR (chapters 11, 13 and 18)	Any individual susceptible to any one of these three diseases (Re-)vaccination following immunosuppression[b]	
MenCCV and MCV4-D (chapters 4 and 12)	For patients who are pre- or post-splenectomy or with functional asplenia; with HIV; with complement deficiency (acquired, including monoclonal antibody therapy against C5, or inherited); who are pre- or post-solid organ transplant Close contacts of meningococcal cases[a] HSCT (bone marrow transplant) patients Patients following immunosuppression[b]	Young adults in communal accommodation Laboratory personnel routinely exposed to *N. meningitidis*
Pertussis-containing vaccine (chapters 4 and 14)	Tdap for pregnant women from 28 to 38 weeks' gestation of every pregnancy Tdap for (re-)vaccination of patients who are post-HSCT or chemotherapy; pre- or post-splenectomy; pre- or post-solid organ transplant, renal dialysis and other severely immunosuppressive regimens	Tdap instead of Td if likely to be in contact with infants aged under 12 months
PCV13 and 23PPV (chapters 4 and 15)	(Re-)vaccination of patients with HIV; pre- or post-HSCT[f] or chemotherapy;[f] pre- or post-splenectomy or with functional asplenia; pre- or post-solid organ transplant; renal dialysis; complement deficiency (acquired or inherited); cochlear implants; primary immune deficiency	PCV13 followed by 23PPV for those with certain conditions PCV13 followed by 23PPV for those aged 65 years or older
IPV (chapter 16)	Any unvaccinated or partially vaccinated individual (Re-)vaccination following immunosuppression[b]	
Td (chapters 5 and 19)	Td for susceptible individuals (including following immunosuppression); boosters[g] at 45 and 65 years; boosting of patients with tetanus-prone wounds	Tdap instead of Td if likely to be in contact with infants aged under 12 months

Continued overleaf

Vaccine	Recommended and funded	Recommended but not funded
Varicella (chapter 21)	Non-immune patients: • with chronic liver disease who may need a transplant in the future • with deteriorating renal function before transplantation • prior to solid organ transplant • prior to any elective immunosuppression[b] • for post-exposure prophylaxis of immune-competent hospital in-patients Patients at least 2 years after bone marrow transplant[h] Patients at least 6 months after completion of chemotherapy[h] HIV-positive patients who are non-immune to varicella, with mild or moderate immunosuppression[h] Patients with inborn errors of metabolism at risk of major metabolic decompensation, with no clinical history of varicella Household contacts of paediatric patients who are immunocompromised or undergoing a procedure leading to immunocompromise, where the household contact has no clinical history of varicella Household contacts of adult patients who have no clinical history of varicella and who are severely immunocompromised or undergoing a procedure leading to immunocompromise, where the household contact has no clinical history of varicella	Susceptible adults

Continued overleaf

Vaccine	Recommended and funded	Recommended but not funded
HZV (chapter 22)	From 1 April 2018, 1 dose of HZV is funded for: • individuals at age 65 years, or • catch-up of individuals aged 66–80 years, inclusive (the catch-up programme ceases on 31 March 2020).	HZV may be considered, but is not funded, for individuals aged 50–64 years who are: • at increased risk of shingles and who may benefit from being vaccinated earlier than the routine schedule • household contacts of an immunosuppressed individual.

a Only 1 dose of vaccine is funded for close contacts.

b Note that the period of immunosuppression due to steroid or other immunosuppressive therapy must be longer than 28 days.

c Individuals who started with HPV4 may complete their remaining doses with HPV9.

d Individuals who were <27 years when they commenced HPV vaccination are currently funded to complete the 3-dose course, even if they are ≥27 years when they complete it.

e HPV9 vaccine is registered for use in females aged 9–45 years and in males aged 9–26 years. However, there are no theoretical concerns that the efficacy or safety of HPV vaccine in males up to the age of 45 years will differ significantly from females of the same age or younger males.

f PCV13 is funded pre- or post-HSCT or chemotherapy. 23PPV is only funded post-HSCT or chemotherapy.

g The administration charge for the Td booster is not funded, although the vaccine is free.

h On the advice of their specialist.

2.2 Vaccine administration

2.2.1 Minimising pain and distress at the time of vaccination

The WHO's Strategic Advisory Group of Experts on Immunization (SAGE) key recommendations for minimising pain and distress at the time of vaccination are:[4]

- do not aspirate (draw back) when giving vaccines
- administer vaccines from the least to the most painful for all ages
- breastfeed before and during vaccine injection

- position (hold the infant/young child, individuals aged 3 years and older should sit up, parental presence)
- for infants, give oral rotavirus vaccine before injections (the vaccine contains sucrose that can reduce pain)
- use neutral words at the time of vaccination; avoid language that increases anxiety
- provide appropriate distractions
- consider using topical anaesthetics (only if the cost is acceptable to the family).

See also section 2.3.2 and the IMAC factsheet *Mitigating Vaccination Pain and Distress* (available at www.immune.org.nz/resources/written-resources).

2.2.2 Preparing for vaccine administration

Key points for administering injectable vaccines

Vaccines should not be mixed in the same syringe, unless the prescribing information sheet specifically states it is permitted or essential (eg, DTaP-IPV-HepB/Hib).

Careful use of a longer needle will cause less damage than a short needle.

To avoid tracking, make sure all the vaccine has been injected before smoothly withdrawing the needle.

Correct vaccine administration is important, and vaccinators have a responsibility to see that vaccines are given:

- in the optimal site
- using the appropriate needle size for vaccine effectiveness and patient safety.

The use of alternative sites will be based on professional judgement, including knowledge of the potential risks at each site and recommendations in the manufacturer's data sheet.

The guidelines below will help to make the experience less distressing for the individual, parent/guardian and/or whānau, and vaccinator.

Table 2.6: Guidelines for vaccine administration

Preparation	Immunisation event
Vaccinate in a private and appropriate setting.	Draw up injections out of sight, if possible. Medical paraphernalia is commonplace to vaccinators, but it may heighten the anxiety of some individuals.
Prepare the area/room layout to suit the vaccinator and vaccination event.	Ensure the individual or parent/guardian has had the opportunity to discuss any concerns and has given informed consent.
Be familiar with the vaccines (eg, their correct preparation, administration and the potential for adverse events).	Be prepared to include other family members and whānau in the discussion, and explain to older children accompanying infants why the injections are being given and what will happen.
Be aware of the individual's immunisation history (eg, submit an NIR status query if the history is unknown).	Give the appropriate immunisations due and advise when the next immunisation event is due.
Ensure there are age-appropriate distractions available.	For babies, suggest that the mother breastfeeds baby before, during and after immunisation. For children, sit them upright and talk quietly to the child before and during immunisation. Make eye contact and explain what is going to happen. Even when a child is unable to understand the words, an unhurried, quiet approach has a calming effect and reassures the parent/guardian. See also section 2.3.2.
Ensure the relevant immunisation health education resources are available.	Give written and verbal advice to the individual and parent/guardian. The advice should cover what may be expected after immunisation, and what to do in the event of an adverse event, along with advice on when to notify the vaccinator.

Removal of air bubbles

Advice for removal of air in the syringe before vaccine administration is dependent on the vaccine presentation. See Table 2.7.

Table 2.7: Guidelines for management of air bubbles in a vaccine syringe

Vaccine presentation	Management of air bubbles
Vaccines supplied in a prefilled syringe with a fixed needle (eg, Influvac)	Do not expel the air
Vaccines supplied in a prefilled syringe without a fixed needle (eg, Gardasil 9)	Add an appropriate administration needle Do not expel the air
Vaccines supplied diluted in a vial (eg, HBvaxPRO)	Draw up the entire vaccine volume into a syringe Expel the air until the vaccine is at the level of the syringe hub, then change the needle Do not expel the air contained in the new needle
Vaccines supplied as diluent and powder/pellet requiring reconstitution (eg, Infanrix-hexa, Priorix)	Reconstitute the vaccine correctly Draw up the entire vaccine volume into a syringe Expel the air until the vaccine is at the level of the syringe hub, then change the needle Do not expel the air contained in the new needle

Skin preparation

Skin preparation or cleansing when the injection site is clean is not necessary. However, if an alcohol swab is used, it must be allowed to dry for at least two minutes, otherwise alcohol may be tracked into the muscle, causing local irritation. Alcohol may also inactivate a live attenuated vaccine such as MMR.

A dirty injection site may be washed with soap and water and thoroughly dried before the immunisation event.

2.2.3 Route of administration

Needle angle, gauge and length

Where possible, vaccinators should refer to the vaccine data sheet (available on the Medsafe website: www.medsafe.govt.nz) for the route of administration.

Most Schedule vaccines (with the exception of MMR, VV and IPV, which are administered subcutaneously, and rotavirus, which is administered orally) are administered by intramuscular injection. Intramuscular injections should be administered at a 90 degree angle to the skin plane. The needle length used will be determined by the size of the limb and muscle bulk, whether the tissue is bunched or stretched, and the vaccinator's professional judgement. BCG vaccine (which can only be administered by authorised vaccinators with BCG endorsement) is given by intradermal injection. See Table 2.8.

Table 2.8: Needle gauge and length, by site and age

Age	Site	Needle gauge and length	Rationale
Intramuscular (IM) injection			
Birth	Vastus lateralis	23–25 G × 16 mm	
6 weeks	Vastus lateralis	23–25 G × 16 or 25 mm	Choice of needle length will be based on the vaccinator's professional judgement.
3–14 months	Vastus lateralis	23–25 G × 25 mm	A 25 mm needle will ensure deep IM vaccine deposition.
15 months to 3 years	Deltoid or Vastus lateralis	23–25 G × 16 mm 23–25 G × 25 mm	The vastus lateralis site remains an option in young children when the deltoid muscle bulk is small and multiple injections are necessary.

Continued overleaf

Age	Site	Needle gauge and length	Rationale
3–7 years	Deltoid	23–25 G × 16 mm	A 16 mm needle should be sufficient to effect deep IM deposition in the deltoid in most children.
	Vastus lateralis[a]	21–22 G × 25 mm	
Older children (7 years and older), adolescents and adults	Deltoid[b]	23–25 G × 16 mm, or 23–25 G × 25 mm, or 21–22 G × 38 mm	Most adolescents and adults will require a 25 mm needle to effect deep IM deposition.
	Vastus lateralis[a]	21–22 G × 38 mm	
Subcutaneous injection			
Subcutaneous injection	Deltoid region of the upper arm	25–26 G × 16 mm	An insertion angle of 45 degrees is recommended. The needle should never be longer than 16 mm or inadvertent IM administration could result.
Intradermal injection: BCG vaccine – for authorised vaccinators with BCG endorsement			
Intradermal injection	Slightly above the insertion of the deltoid muscle on the lateral surface of the left arm. The arm should be gently but firmly supported.	Drawing-up: Tuberculin syringe (attach a drawing-up needle), or a single-use insulin syringe with a needle attached	
		Administering: If using a tuberculin syringe, change the needle to a sterile 26 G × 13 or 16 mm needle (no needle change required if using an insulin syringe)	The syringe should be held with the bevel uppermost, parallel with the skin of the arm. The bevel should be fully inserted but visible under the skin. Inject the vaccine slowly and gradually to form a white 'bleb' or wheal, then gradually withdraw the needle.

a Consideration may be given to the vastus lateralis as an alternative vaccination site, providing it is not contraindicated by the manufacturer's data sheet.

b For females weighing <60 kg use a 23–25 G × 16 mm needle; for 60–90 kg use a 23–25 G × 25 mm needle; for >90 kg use a 21–22 G × 38 mm needle. For adolescent and adult males, a 23–25 G × 25 mm needle is sufficient.[5, 6]

Intramuscular injection sites

Injectable vaccines should be administered in healthy, well-developed muscle, in a site as free as possible from the risk of local, neural, vascular and tissue injury. Incorrectly administered vaccines (incorrect sites and poor administration techniques) contribute to vaccine failure, injection site nodules or sterile abscesses, and increased local reactions.

> Careful use of a longer needle will cause less damage than a shorter needle.

The recommended sites for intramuscular (IM) vaccines (based on proven uptake and safety data) are:

- the vastus lateralis muscle on the anterolateral thigh for infants aged under 15 months – the vastus lateralis muscle is large, thick and well developed in infants, wrapping slightly onto the anterior thigh
- either the vastus lateralis or deltoid site for children aged 15 months to 3 years – the choice will be based on the vaccinator's professional judgement
- the deltoid muscle for older children, adolescents and adults.

The deltoid muscle is not routinely used in infants and young children aged under 15 months, due to the potential for deltoid or radial nerve injury. However, when there is no access to the vastus lateralis (eg, the infant is in a spica cast), the deltoid muscle is used to administer intramuscular vaccines.

The buttock should not be used for the administration of vaccines in infants or young children, because the buttock region is mostly subcutaneous fat until the child has been walking for at least 9 to 12 months. Use of the buttock is not recommended for adult vaccinations either, because the buttock subcutaneous layer can vary from 1 to 9 cm and IM deposition may not occur.

With older children and adults, consideration may be given to using the vastus lateralis as an alternative site to the deltoid, providing it is not contraindicated by the manufacturer's data sheet.

Subcutaneous injection sites

A subcutaneous (SC) injection should be given into healthy tissue that is away from bony prominences and free of large blood vessels or nerves. The recommended site for subcutaneous vaccine administration is the upper arm (overlying the deltoid muscle).

The principles for locating the upper arm site for an SC injection are the same as for an IM injection. *However, needle length is more critical than angle of insertion for subcutaneous injections*. An insertion angle of 45 degrees is recommended and the needle should never be longer than 16 mm, or inadvertent IM administration could result. The thigh may be used for SC vaccines unless contraindicated by the manufacturer's data sheet. See also Table 2.2 for information about thrombocytopenia and bleeding disorders.

Intradermal injections

The intradermal injection technique for BCG vaccine (see section 2.2.4) requires special training, and should only be performed by an authorised vaccinator with BCG endorsement (see Appendix 4).

Oral vaccine administration

The rotavirus vaccine is administered orally. Administer the entire contents of the oral applicator into the infant's mouth, towards the inner cheek (see section A7.2.4). **Do not inject oral vaccines.**

For specific oral vaccine administration instructions, refer to the vaccine data sheet (available on the Medsafe website: www.medsafe.govt.nz).

2.2.4 Infant vaccination

Infants aged under 6 months do not need to be grasped or restrained as firmly as toddlers or older children. At this age, excessive restraint increases their fear as well as muscle tautness. The recommended positioning for an infant is in a cuddle hold with parent/guardian, breastfeeding as appropriate. The cuddle position offers better psychological support and comfort for both the infant and the parent/guardian,[4] and the parent/guardian should be offered this position as a first choice (Figure 2.1).

If the parent/guardian is helping to hold the infant or child, ensure they understand what is expected of them and what will take place. Most vaccinators choose to administer all the injections due quickly and soothe the infant or child afterwards (see section 2.3.2 for soothing measures).

Figure 2.1: The cuddle position for infants

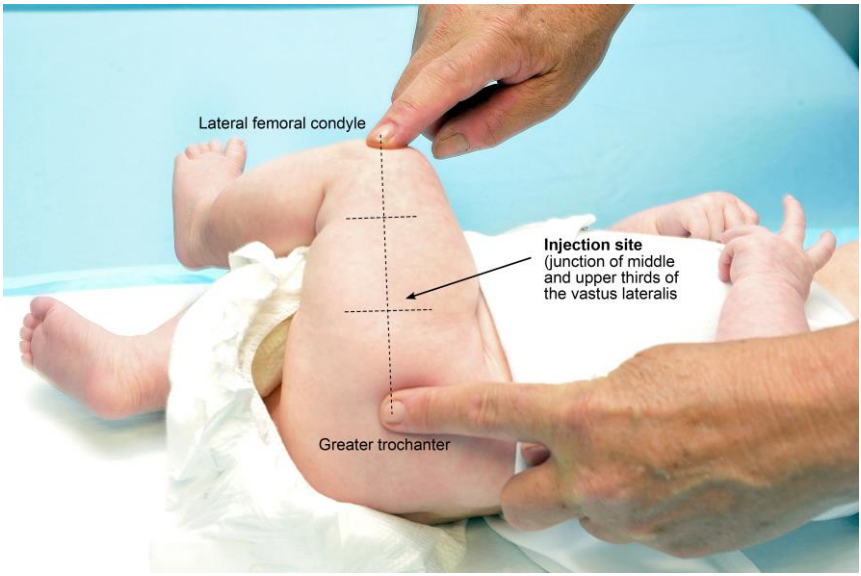
Vastus lateralis

To locate the injection site, undo the nappy, gently adduct the flexed knee and (see Figure 2.2):

1. find the greater trochanter
2. find the lateral femoral condyle
3. section the thigh into thirds and run an imaginary line from the centre of the lower marker to the centre of the upper marker (look for the dimple along the lower portion of the fascia lata).

The injection site is at the junction of the upper and middle thirds and slightly anterior to (above) the imaginary line, in the bulkiest part of the muscle.

Figure 2.2: Photo showing the infant lateral thigh injection site

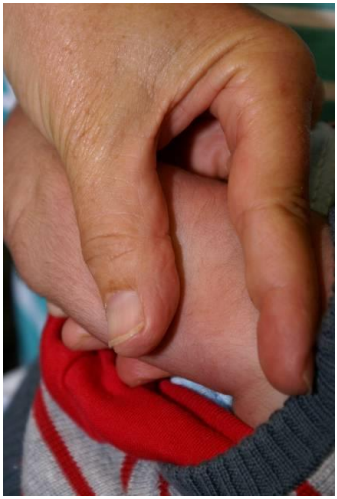


The needle should be directed at a 90 degree angle to the skin surface and inserted at the junction of the upper and middle thirds. Inject the vaccine at a controlled rate. To avoid tracking, make sure all the vaccine has been injected before smoothly withdrawing the needle. Do not massage or rub the injection site afterwards. However, infants with a bleeding disorder may require firm pressure over the injection site without rubbing for at least 10 minutes.

BCG vaccine (administered by authorised vaccinators with BCG endorsement)

The reconstituted BCG vaccine is given by intradermal injection slightly above the insertion of the deltoid muscle on the lateral surface of the left arm. The infant's arm should be gently but firmly supported (see Figure 2.3[a]). The syringe should be held with the bevel uppermost, parallel with the skin of the arm (see Figure 2.3[b]).

Figure 2.3: Photos showing the infant BCG vaccination site, and how to support the infant's arm and hold the syringe

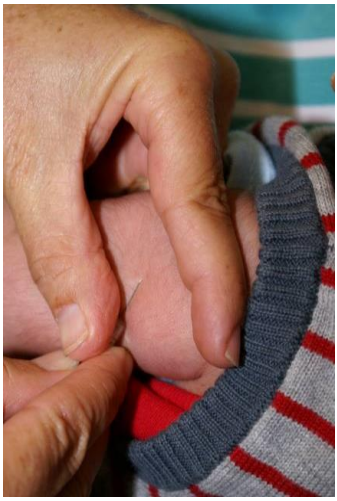


(a)

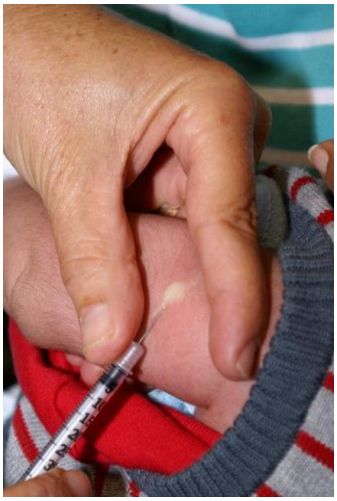
(b)

Inject the vaccine slowly (see Figure 2.4[a]), then gradually withdraw the needle. The injection is given slowly to avoid leakage around the needle or vaccine being squirted. Safety glasses should be used to protect the eyes of those involved. If BCG vaccine is accidentally squirted into the eyes, wash them immediately with water. Following BCG vaccination a white weal should appear (see Figure 2.4[b]), which should subside in approximately 30 minutes. The vaccination site requires no swabbing or dressing.

Figure 2.4: Photos showing the BCG vaccine being slowly injected, and a white weal appearing as the needle is gradually withdrawn



(a)



(b)

2.2.5 Young child vaccination (vastus lateralis or deltoid)

The choice between the two sites for IM injections from 15 months of age will be based on the vaccinator's professional judgement, such as knowledge of the child and ease of restraint. Some vaccinators consider the vastus lateralis preferable for young children when the deltoid muscle bulk is small and because of the superficiality of the radial nerve. Discuss the options with the parent/guardian when making your decision. (See also 'The 15-month event' in section 2.2.7.)

The easiest and safest way to position and restrain a young child for a lateral thigh and/or deltoid injection is to sit the child sideways on their parent's or guardian's lap. The parent's/guardian's hand restrains the child's outer arm and the child's legs are either restrained between the parent's/guardian's legs or by placing a hand on the child's outer knee or lower leg. Alternatively, the child may face their parent/guardian while straddling the parent's/guardian's legs (see Figures 2.5 and 2.6).

Figure 2.5: Photos showing cuddle positions for vastus lateralis or deltoid injections in children

(a)

(b)

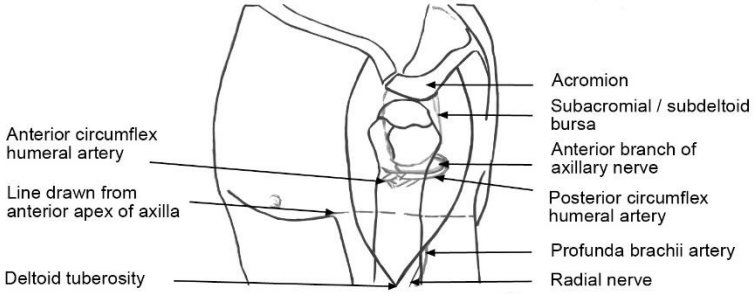
Figure 2.6: Photo showing the straddle position for vastus lateralis or deltoid injections in children

If using the straddle position, both the deltoid and vastus lateralis muscle are likely to be more tense or taut, and the injection may therefore be more painful.

2.2.6 Older child, adolescent and adult vaccination (deltoid)

The deltoid muscle is located in the lateral aspect of the upper arm. The entire deltoid muscle must be exposed to avoid the risk of radial nerve injury (an injection at the junction of the middle and upper thirds of the lateral aspect of the upper arm may damage the nerve) (see Figure 2.7).

Figure 2.7: Surface landmarks and structures potentially damaged by intramuscular injection in the upper limb



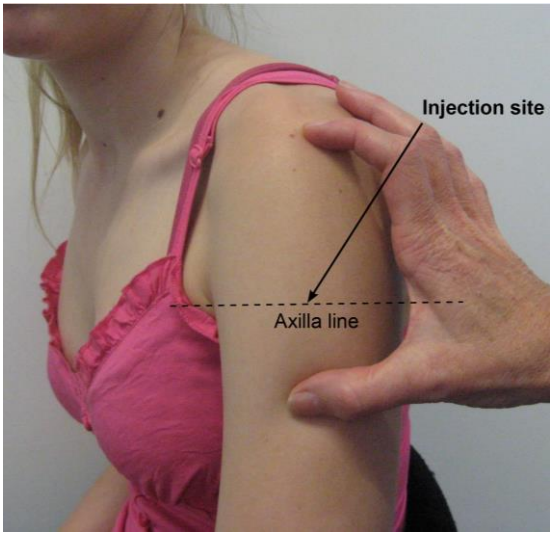
Reproduced with permission: Cook IF. 2011. An evidence based protocol for the prevention of upper arm injury related to vaccine administration (UAIRVA). *Human Vaccines* 7(8): 845–8.

The volume injected into the deltoid should not exceed 0.5 mL in children and 1.0 mL in adults.

The vaccinee should be seated with their arm removed from the garment sleeve and hanging relaxed at their side. The vaccinator places their index finger on the vaccinee's acromion process (the highest point on the shoulder) and their thumb on the vaccinee's deltoid tuberosity (the lower deltoid attachment point).[7]

The injection site is at the axilla line, between these anatomical landmarks. The vaccine should be deposited at the bulkiest part of the muscle (Figure 2.8).

Figure 2.8: How to locate the deltoid site



2.2.7 Multiple injections at the same visit

A well-prepared and confident vaccinator will reassure the parent/ guardian or whānau that giving concurrent vaccines is a safe and appropriate practice, avoiding multiple visits.

When more than one vaccine is scheduled at the same visit, vaccinators are recommended to give all of the scheduled vaccines at that visit. This particularly applies to the 15-month event (see below), when four vaccines are scheduled.

Multiple vaccines should not be mixed in a single syringe unless specifically licensed and labelled for administration in one syringe. A different needle and syringe should be used for each injection.

The 15-month event

MMR, varicella, PCV and Hib vaccines are scheduled at the 15-month event. When giving these vaccines, it is preferable to give the live vaccines (MMR and VV) in separate limbs. The IM injections should be given in the vastus lateralis and the SC injections in the deltoid.

The recommended vaccine administration sequence and location is:

1. Hib: Left vastus (IM)
2. Varicella: Left deltoid (SC)
3. PCV: Right vastus (IM)
4. MMR: Right deltoid (SC).

If parents/guardians request to split the vaccines given at the 15-month event, then providers are advised to give MMR and VV at the first visit, followed by PCV and Hib at the second visit.

Note:

- There is a possible risk of the patient not returning for the second visit when the 15-month vaccines are split.
- If MMR and VV are not given at the same visit (concurrently), then there should be an interval of at least four weeks between them. This interval is to avoid the response to the second vaccine being diminished due to interference from the response to the first vaccine (see section 2.1.5).

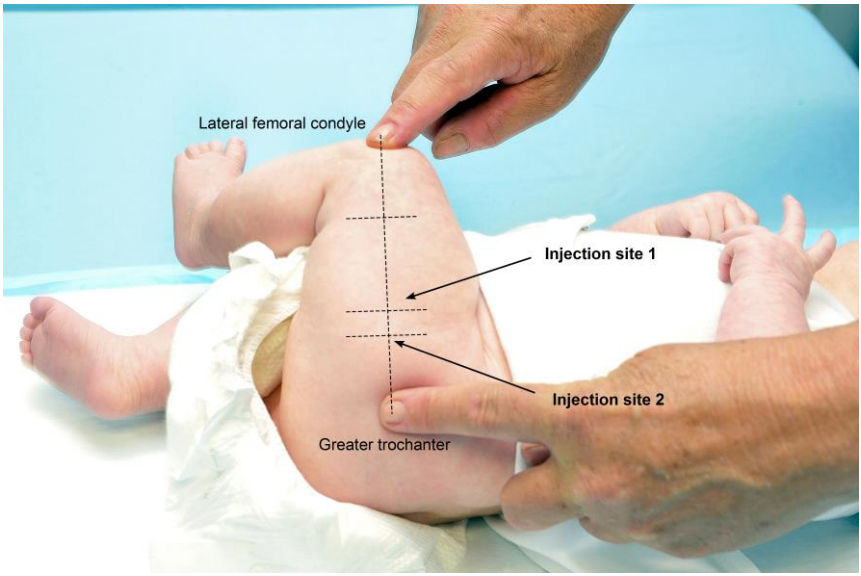
See also the IMAC video 'Four in a row – a best practice guide for multiple vaccinations' (https://vimeo.com/195383691).

Multiple injections in the same muscle

When giving two injections to be given in the same limb, the vastus lateralis is preferred because of its greater muscle mass (see Figure 2.9). The injection sites should be on the long axis of the thigh and *separated by at least 2 cm* so that localised reactions will not overlap.

If multiple injections in the deltoid are required, the sites should be separated by at least 2 cm.[8]

Figure 2.9: Diagram showing suggested sites for multiple injections in the lateral thigh



2.3 Post-vaccination

2.3.1 Post-vaccination advice

Post-vaccination advice should be given both verbally and in writing. The advice should cover:

- which vaccines have been given and the injection sites, and whether the injections were IM or SC
- common vaccine responses following immunisation (see Table 2.9) and what to do if these occur (eg, measures for relieving fever, when to seek medical advice)
- when the individual or parent/guardian should contact the vaccinator if they are worried or concerned
- contact phone numbers (including after-hours phone numbers).

Table 2.9: Expected vaccine responses

Vaccine	Expected vaccine responses
DTaP- or Tdap-containing vaccine	Localised pain, redness and swelling at injection site Mild fever Being grizzly and unsettled Loss of appetite, vomiting, and/or diarrhoea Drowsiness Extensive limb swelling after the 4th or 5th dose of a DTaP-containing vaccine
Hib	Localised pain, redness and swelling at the injection site Mild fever Being grizzly and unsettled
Hepatitis B	Very occasionally pain and redness at the injection site Nausea or diarrhoea
HPV	Fainting, especially adolescents – this is an injection reaction, not a reaction to the vaccine Localised discomfort, pain, redness and swelling at the injection site Mild fever Headache
Influenza	Localised pain, redness and swelling at injection site Headache Fever
MMR	Measles component: Fever which lasts 1–2 days; rash (not infectious) 6–12 days after immunisation Mumps component: Parotid and/or submaxillary swelling 10–14 days after immunisation Rubella component: Mild rash, fever, lymphadenopathy, joint pain 1–3 weeks after immunisation
Pneumococcal	Localised pain, redness and swelling at injection site Mild fever Irritability, sleep changes Loss of appetite
Rotavirus	Diarrhoea and or vomiting may occur after the first dose Mild abdominal pain
Adult Td	Localised discomfort, redness and swelling at the injection site
Varicella	Localised pain, redness and swelling at injection site Mild fever Mild rash, possibly at the injection site (2–5 lesions, appearing 5–26 days after immunisation)

2.3.2 Recommendations for fever and pain management

The use of paracetamol or ibuprofen around the time of immunisation in anticipation of immunisation-related fever or localised pain occurring is not recommended. However, use of these medicines is recommended if the child is distressed due to fever or pain following immunisation.

Paracetamol use may lower the immune response to some vaccines.[9] However, there is no evidence that this results in less protection against disease.

Health care providers are encouraged to discuss with parents possible immunisation responses and non-pharmaceutical management of fever or pain, as well as the role of medicines.

Fever

General fever-relieving measures include:

- giving extra fluids to drink (eg, more breastfeeds or water)
- reducing clothing if the baby is hot.

While a high fever alone does not need treatment, antipyretic analgesics (paracetamol or ibuprofen) may be used for distress or pain in a febrile child who has not responded to the cooling measures described above.

Pain management and soothing measures

For infants aged under 12 months, breastfeeding before, during and after the injection can provide comfort and pain relief.[4, 10]

Give the rotavirus vaccine 1–2 minutes before the other immunisations; rotavirus vaccines contain sucrose that has been shown to reduce pain.[4, 10] The infant can then be breastfed (where possible) or held comfortably while the other immunisations are given.

For infants aged under 6 months the 5 S's (swaddling, side/stomach position, shushing, swinging and sucking) have been found to be effective for soothing and reducing pain after immunisations.[11]

Using age-appropriate distraction has been shown to reduce pain and distress.[4, 10] Examples include showing an interesting or musical toy to an infant, or encouraging an older child to blow using a windmill toy or bubbles. Electronic games/phone games can be useful for older children and teenagers. Do not rub the injection site after the injection as it increases the risk of vaccine reactogenicity.

For infants and children, the use of a topical anaesthetic cream or patch has been found to be effective for immunisation pain management.[4, 10] Parents/guardians and those administering the vaccine should check the manufacturers' recommendations before using topical anaesthetics. The correct dose for infants needs to be followed particularly carefully due to risk of methaemoglobinaemia. Topical anaesthetics may have a role in managing immunisation pain and anxiety, particularly for children who have had previous multiple medical interventions or needle phobias.

Following immunisation, if an infant or child is distressed by pain or swelling at the injection site, placing a cold, wet cloth on the area may help relieve the discomfort. Antipyretic analgesics (paracetamol or ibuprofen) may be used if the above measure does not relieve the child's distress.

2.3.3 Anaphylaxis and emergency management

All vaccinators must be able to distinguish anaphylaxis from fainting, anxiety, breath-holding spells and seizures.

Anaphylaxis is a very rare, unexpected and potentially fatal allergic reaction. It develops over several minutes and usually involves multiple body systems. Unconsciousness is rarely the sole manifestation and only occurs as a late event in severe cases. A strong central pulse (eg, carotid) is maintained during a faint (vasovagal syncope), but not in anaphylaxis.

In general, the more severe the reaction, the more rapid the onset. Most life-threatening adverse events begin within 10 minutes of vaccination. The intensity usually peaks at around one hour after onset. Symptoms limited to only one system can occur, leading to delay in diagnosis. Biphasic reactions, where symptoms recur 8 to 12 hours after onset of the original attack, and prolonged attacks lasting up to 48 hours have been described. All patients with anaphylaxis should be hospitalised.

Signs of anaphylaxis

Anaphylaxis is a severe adverse event of rapid onset, characterised by circulatory collapse. In its less severe (and more common) form, the early signs are generalised erythema and urticaria with upper and/or lower respiratory tract obstruction. In more severe cases, limpness, pallor, loss of consciousness and hypotension become evident, in addition to the early signs. Vaccinators should be able to recognise all of the signs and symptoms of anaphylaxis given in Table 2.10.

Table 2.10: Signs and symptoms of anaphylaxis

	Signs and symptoms	Severity
Early warning signs (within a few minutes)	Dizziness, perineal burning, warmth, pruritus, flushing, urticaria, nasal congestion, sneezing, lacrimation, angioedema	Mild to moderate
	Hoarseness, nausea, vomiting, substernal pressure	Moderate to severe
	Laryngeal oedema, dyspnoea, abdominal pain	Moderate to severe
Life-threatening symptoms (from soon after the injection up to 20 minutes after)	Bronchospasm, stridor, collapse, hypotension, dysrrhythmias	Severe

There is no place for conservative management of anaphylaxis. Early administration of adrenaline is essential (for more details, see Table 2.12).

Misdiagnosis of faints and other common causes of collapse as anaphylaxis may lead to inappropriate use of adrenaline. Misdiagnosis as a faint could also lead to a delay in the administration of adrenaline.

Vaccinators should therefore be able to distinguish anaphylaxis from fainting (vasovagal syncope), anxiety and breath-holding spells (see Table 2.11). Infants and babies rarely faint. Sudden loss of consciousness, limpness, pallor and vomiting (signs of severe anaphylaxis in children) should be presumed to be an anaphylactic reaction.

In adults and older children, the most common adverse event is a syncopal episode (fainting), either immediately or soon after vaccination. During fainting the individual suddenly becomes pale, loses consciousness and if sitting or standing will slump to the ground. Recovery of consciousness occurs within a minute or two. Fainting is sometimes accompanied by brief clonic seizure activity, but this generally requires no specific treatment or investigation if it is a single isolated event.

Table 2.11: Distinguishing anaphylaxis from a faint (vasovagal reaction)

	Faint	Anaphylaxis
Onset	Usually before, at the time, or soon after the injection	Soon after the injection, but there may be a delay of up to 30 minutes
System		
Skin	Pale, sweaty, cold and clammy	Red, raised and itchy rash; swollen eyes and face; generalised rash
Respiratory	Normal to deep breaths	Noisy breathing due to airways obstruction (wheeze or stridor); respiratory arrest
Cardiovascular	Bradycardia; transient hypotension	Tachycardia; hypotension; dysrrhythmias; circulatory arrest
Gastrointestinal	Nausea/vomiting	Abdominal cramps
Neurological	Transient loss of consciousness; good response once supine/flat	Loss of consciousness; little response once supine/flat

Distinguishing a hypotonic-hyporesponsive episode from anaphylaxis

A hypotonic-hyporesponsive episode is a shock-like state defined by the sudden onset of limpness (muscle hypotonia) and decreased responsiveness with pallor or cyanosis in infants and children aged under 2 years after immunisation.

A hypotonic-hyporesponsive episode can occur from immediately to 48 hours after immunisation, typically lasts less than 30 minutes, and resolves spontaneously.[12]

A hypotonic-hyporesponsive episode is a recognised serious reaction to immunisation and should be reported to CARM (see section 1.6.3).

Avoidance of anaphylaxis

Before immunisation:

- ensure there are no known contraindications to immunisation
- if in doubt about administering the vaccine, consult the individual's GP or a paediatrician.

> Individuals should remain under observation for 20 minutes following vaccination in case they experience an immediate adverse event requiring treatment.

Emergency equipment

Vaccinators, providers and quality managers are responsible for:

- ensuring emergency procedures are known by all staff
- practising emergency procedures regularly
- having an emergency kit (see Table 2.12) and adrenaline in every room where vaccinations/medications are given
- checking emergency kits regularly
- not giving vaccines when working alone.

Remember, events happen without warning. Appropriate emergency equipment must be immediately at hand whenever immunisations are given, and all vaccinators must be familiar with the practical steps necessary to save lives following an anaphylactic reaction (see Tables 2.12 and 2.13).

Table 2.12: Emergency equipment

An emergency kit should contain:
• adrenaline* 1:1,000 (3 ampoules) and dosage chart • syringes: 1.0 mL (a minimum of 3) (tuberculin not insulin, as the insulin needle is too short for IM injection) • needles: a range of needle lengths and gauges, including 23 or 25 G × 25 mm, 22 G × 38 mm • a range of airways, including paediatric sizes if vaccinating children.
Other emergency equipment required
It is also necessary to have on hand: • an oxygen cylinder (check that it is filled) • adult and paediatric bag valve mask resuscitator (eg, Ambu bag), oxygen tubing and a range of oxygen masks • access to a telephone.

* The expiry date of the adrenaline and other medicines should be written on the outside of the emergency kit, and the kit should be checked every 4 weeks. Adrenaline is heat and light sensitive and should be stored appropriately. Adrenaline that has a brown tinge must be discarded.

The emergency kit may need to have additional equipment for non-clinical settings (see Appendix 4).

Hydrocortisone injection is used only under the direction of a medical practitioner (available on Medical Practitioner Supply Order).

Emergency management

An IM injection of 1:1,000 adrenaline is the mainstay of the treatment of anaphylaxis, and adrenaline should be universally available when vaccinating. A tuberculin syringe should be used to ensure the accuracy of measurement when drawing up small doses.

In an emergency situation there is no absolute contraindication to the use of adrenaline. It is, however, a very potent agent, and if used when anaphylaxis has not occurred or in excessive doses, adrenaline can cause dysrrhythmias, severe hypertension and left ventricular failure. Tissue necrosis can occur if the same injection site is used repeatedly.

Intravenous adrenaline should be administered by a medical practitioner with extreme caution, in small boluses, and under careful monitoring, and it is not appropriate as the first line of treatment of anaphylaxis.

Table 2.13: Initial anaphylaxis response/management

CALL FOR HELP – send for professional assistance (ambulance, doctor). Never leave the individual alone.

ASSESS – Assess responsiveness, and check Airway, Breathing, Circulation.

- If they are conscious, lie the individual down in the recovery position.
- If they are unconscious and breathing normally, lie the individual down in the recovery position, ensuring that the airway is open.
- If they are unconscious and not breathing normally, institute standard procedures for basic life support. If cardiorespiratory arrest occurs, administer age-appropriate CPR and life-support measures.

ADMINISTER ADRENALINE by deep intramuscular injection – dosage: 1:1,000 (adrenaline 1:1,000 = 1 mg/mL).

Adrenaline dosage for 1:1,000 formulation is 0.01 mL/kg up to a maximum of 0.5 mL.

If the individual's weight is unknown, use the following guidelines:

- Infant aged under 1 year: 0.05–0.1 mL
- Child aged under 2 years: 0.1 mL
- Child 2–4 years: 0.2 mL
- Child 5–10 years: 0.3 mL
- Adolescent ≥11 years: 0.3–0.5 mL
- Adult: 0.5 mL

Route: deep IM. Where possible, administer in a non-injected limb, in either the deltoid or vastus lateralis.

You can expect to see some response to the adrenaline within 1–2 minutes. If necessary, adrenaline can be repeated at 5–15-minute intervals, to a maximum of 3 doses, while waiting for assistance. Use alternate sites/limbs for additional doses.

ADMINISTER OXYGEN at high flow rates where there is respiratory distress, stridor or wheeze.

IF HYPOTENSIVE, ELEVATE LEGS.

IF STRIDOR IS PRESENT, ELEVATE HEAD AND CHEST.

RECORD VITAL SIGNS every 5–10 minutes. All observations and interventions need to be clearly documented in medical notes and should accompany the individual to hospital.

ADMIT TO HOSPITAL – all cases of anaphylaxis should be admitted to hospital for observation. Rebound anaphylaxis can occur 12–24 hours after the initial episode.

Note: Only medical practitioners should administer IV adrenaline.

Ongoing management in hospital or by a medical practitioner

Individuals who experience vaccine-related anaphylaxis should be admitted to hospital. If in an unstable or deteriorating condition, and not being transported by ambulance, the individual must be accompanied by the attending health professional so that treatment can be continued during transfer.

Hydrocortisone may be used as adjunctive medication. Nebulised salbutamol is helpful for bronchospasm. For further information, refer to the product data sheet.

Additional drugs that may be administered under the direction of a medical practitioner include:

- nebulised adrenaline: for laryngeal oedema
- bronchodilators: salbutamol 5 mg nebulised, to help reverse bronchospasm
- corticosteroids: prednisone 2 mg/kg (up to 40 mg) orally, or hydrocortisone 4 mg/kg IV, to help resolve tissue swelling (for young children and infants prednisolone syrup may be more appropriate).

Observation for a period of up to 24 hours after stabilisation of the individual's condition is recommended due to the risk of late deterioration from delayed and biphasic reactions.

All anaphylaxis reactions should be reported to CARM (see section 1.6.3).

2.3.4 Documentation and insurance

Accurate documentation, including information on the NIR, School-Based Vaccination System (SBVS) and practice management system, (PMS) is essential. If the vaccinator has not kept accurate clinical records, it is difficult to prove what action/care was or was not taken/delivered if the patient notes are subject to legal scrutiny.

In addition to the information recorded on the NIR (see section 2.3.5), SBVS or PMS, information that should be collected in the patient's clinical notes includes:

- confirmation that informed consent was given
- confirmation that the individual was observed for the recommended time and no adverse events occurred during the observation period (if an adverse event does occur, it is essential to document the action and treatment given and inform CARM – see section 1.6.3).

The vaccinator should also complete the relevant sections in the *Well Child Tamariki Ora My Health Book* and, where applicable, the child's immunisation certificate (see Appendix 5), the Ministry of Health payment claim form (where applicable), and an NIR notification form if not using a computerised PMS.

Indemnity insurance

All vaccinators should carry indemnity insurance. Most employers have indemnity cover, but vaccinators do not have an automatic right to claim under that cover. Indemnity insurance should cover vaccinators/health professionals for disciplinary proceedings, coroners' inquiries, and claims of negligence or error that may lead to injury, death or damage.

2.3.5 The National Immunisation Register

The National Immunisation Register (NIR) is a computerised information system that has been collecting immunisation information on New Zealand children since 2005 and from 2014 has been collecting some adult immunisation information. The purpose of the NIR is to facilitate immunisation delivery and provide an accurate record of an individual's immunisation history.

The NIR also:

- provides a more accurate record of immunisation coverage rates regionally and nationally – this information assists with better programme planning to improve coverage rates and identify areas with lower immunisation rates
- collects information about the Schedule, HPV immunisations and some targeted programmes (eg, Tdap during pregnancy, BCG vaccine)

- collects information about influenza immunisations and high-risk adolescent and adult immunisations (since July 2014)
- enables health professionals to identify quickly and easily which vaccines an individual has received (especially if they have moved areas or changed health care providers) and any that are due or may have been missed
- enables individuals to have an accurate, up-to-date record of their immunisation history.

Managing the information on the National Immunisation Register

The information held on the NIR (collection, holding, use and disclosure) is governed by the Health Information Privacy Code 1994 and section 22F of the Health Act 1956 (see section 2.1.2).

The NIR's privacy policy can be found on the Ministry of Health website (www.health.govt.nz/nir). The policy sets out the framework for data collection, storage, use and disclosure of health information held about identifiable individuals on the NIR.

Individuals or their parents/guardians may choose at any time not to have any health information collected on the register (ie, they can opt off the further collection of immunisation data). However, the NIR will retain the individual's National Health Index (NHI) number, date of birth, DHB they are resident in, date of opt off, and any immunisation information recorded before opt off. The reason for retaining this information is to provide an accurate denominator for immunisation coverage calculations, and to prevent inappropriate recall and referral.

An individual's immunisation information will be retained on the NIR for their whole life, plus a period of 10 years after their death.

Only authorised users have access to the information held on the NIR. Such a person is authorised to use and disclose NIR information in accordance with their function. Penalties for unauthorised disclosure of information could include the revocation of authorised user privileges, complaints to the Privacy Commissioner, civil proceedings, professional sanctions, and disciplinary action, up to and including termination of employment.

Information collected on the NIR includes:

- date of vaccination
- individual's name
- individual's NHI number
- individual's date of birth
- secondary contact details
- parent/guardian details for children aged under 18 years
- vaccine type and number in the series
- batch number and expiry date
- injection site, injection route and needle length used
- provider name
- vaccinator's name and title
- recall date (when applicable)
- adverse event data, once verified by CARM.

More information about privacy and informed consent can be found in section 2.1.2 and Appendix 3. Further information about the NIR can be found on the Ministry of Health website (www.health.govt.nz/nir).

The SBVS

The SBVS collects and manages the data for school immunisation programmes (eg, where public health nurses deliver the school year 7 and year 8 immunisation programmes). The information collected on the SBVS for the school immunisation programmes is then transferred to the NIR.

Not all DHBs use the SBVS software for managing their school-based programmes; however, all DHBs are required to record school-based vaccination events on the NIR regardless of whether they use the SBVS, another PMS or direct enter on to the NIR.

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3 Vaccination questions and addressing concerns

3.1 Some commonly asked questions

3.1.1 Vaccine scheduling

Which vaccines can be administered at the same visit?

There are no known contraindications to administering registered vaccines at the same visit, provided they are administered in separate syringes at separate sites. If two or more parenterally or intranasally administered *live* vaccines are not given at the same visit, then a minimum interval of four weeks is recommended. The rationale is based on limited data where VV has been given within four weeks of measles-containing vaccine and breakthrough varicella disease (chickenpox) has occurred. Any time interval is acceptable between administering live oral vaccines and all parenteral vaccines (eg, rotavirus and BCG vaccines), live and inactive vaccines, or two inactive vaccines.

What steps are required if the Schedule is interrupted or varied?

Generally, there is no need to repeat prior doses; simply continue the Schedule as if no interruption has occurred (see Appendix 2). Special circumstances where the above does not apply are as follows:

- HepB given at birth to babies born to HBsAg-positive mothers – this dose does not count as part of a catch-up
- the two-dose course of rotavirus vaccine (RV1; Rotarix) should be started before age 15 weeks (ie, the latest is 14 weeks and 6 days) and completed by age 25 weeks (ie, the latest is 24 weeks and 6 days); if an infant reaches age 25 weeks without receiving the second dose, the first dose already given may offer them some protection against disease (see also section 17.5.1 for information about transitioning from RV5 to RV1)

- MMR vaccine given prior to age 12 months – infants who receive MMR vaccine prior to age 12 months still require two further MMR doses at ages 15 months and 4 years
- conjugate vaccine schedule requirements, which are age dependent (eg, children over 12 months of age do not require a full primary course of Hib or PCV vaccine, but do require one or two doses in the second year of life; see Appendix 2)
- when reconciling overseas schedules and the New Zealand Schedule – immigrant children who have commenced vaccine courses (eg, meningococcal C, PCV13) are not funded to complete these vaccine courses once in New Zealand unless they meet the high-risk criteria for these vaccines; however, if the parent or guardian wishes to purchase the vaccines to complete the course, they may do so.

Remember that children who miss one vaccine dose may do so again, so optimising a catch-up schedule is important.

How should the rest of the Schedule be handled when an adverse event has occurred following immunisation?

Proceeding with the Schedule after an AEFI depends on the nature of the event and the likelihood that the vaccine caused it. Most prior adverse events are not contraindications to receiving further immunisations. The only absolute contraindication to receiving a vaccine is an anaphylactic reaction to a prior dose or an ingredient in the vaccine. However, immune dysfunction can be a contraindication to receiving live vaccines (see section 4.3).

Adverse events should be reported to CARM (https://nzphvc.otago.ac.nz/reporting). See section 1.6.3 'AEFI reporting process – notifying CARM'.

Consult the AEFI section in each of the *Handbook* chapters, and seek specialist advice (eg, from the medical officer of health, the Ministry of Health, or IMAC, if required). Other vaccines not related to the AEFI can usually be administered as per the Schedule.

3.1.2 Babies and children

What if a baby had a difficult birth or was premature?

Low birthweight and prematurity are not contraindications to vaccination. The recommended Schedule immunisations should be carried out at the appropriate chronological age. However, if the baby is still in hospital or recently discharged, please seek the advice of the treating specialist (see also section 4.2 on special risk groups and section 8.5.1 on hepatitis B). These babies may be at higher risk of some of these diseases, so vaccinating them on time is particularly important.

Rotavirus vaccine should be given on time to any infant admitted to a general hospital ward (where other patients are not high risk). If standard infection control precautions are maintained, the risk of transmission of vaccine strain rotavirus will be minimal when rotavirus vaccine is administered to hospitalised infants, including hospitalised preterm infants and those in neonatal units.[1] (See also section 4.2.1 and chapter 17.)

What special vaccines are offered to newborn babies?

Babies born to HBsAg-positive mothers should receive:

- 100–110 IU hepatitis B immunoglobulin (HBIG) neonatal, at or as close as possible to birth
- a birth dose of HepB (HBvaxPRO, 5 µg), which should be given at or as close as possible to birth (preferably within 12 hours).

If HBIG and/or HepB is inadvertently omitted, administer as soon as the omission is recognised. HBIG can be administered up to seven days post-delivery. If there is a delay for longer than seven days, seek specialist advice. These babies should then continue as per the Schedule at ages 6 weeks, 3 months and 5 months. Serological testing is required at 9 months of age (see section 8.5.2).

A baby at higher risk of TB is offered a BCG immunisation soon after birth (see section 20.5 for neonatal BCG eligibility and the timing of neonatal BCG). The lead maternity carer will discuss the need for the vaccine with the mother prior to her baby's birth, and the BCG immunisation may be given while the baby is in hospital, or later at a community clinic.

What are the special requirements of immigrant children?

Immigrant children should be immunised according to the New Zealand Schedule with *due account taken of documented prior vaccine administration* and the eligibility criteria defined in the *Health and Disability Services Eligibility Direction 2011*, available on the Ministry of Health website (www.health.govt.nz/eligibility) (see also section 4.4).

It is important to err on the side of giving rather than withholding vaccines if the vaccination history is uncertain (see Appendix 2). The immunisation status of all immigrant children should be checked when they register with a primary health care provider.

Is it possible to boost a child's immune system by other means?

Eating a healthy diet, getting adequate sleep and exercise, having a smokefree environment and minimising high levels of stress will help keep the immune system healthy. However, none of the above confers the disease-specific immunity that vaccination provides (see also section 3.2.4). All children get infections (eg, common colds) but this does not mean the immune system is not working.

3.1.3 Allergies and illnesses

What if the child is unwell on the day of immunisation?

Minor illness or being in the recovery phase of an illness is not a reason to postpone immunisation. Babies and children with a significant acute illness and a temperature >38°C should have immunisation postponed until they are better. This is not because they are at particular risk of vaccine reactions, but because complications of the acute illness may be misinterpreted as a complication of the immunisation, or an AEFI may complicate the clinical picture of the acute illness. (See 'Contraindications' in section 2.1.4, and the contraindications sections in the disease chapters.) If immunisation is postponed, it is important to ensure the child is placed on the recall for the immunisation at a later date.

What if the child is due to have an operation (elective surgery)?

There is no evidence that anaesthetic impairs the immune response to a vaccine or increases the risk of AEFI.

Vaccination with inactive vaccines is preferably avoided for 48 hours prior to an anaesthetic in case post-vaccination symptoms such as fever interfere with preparation for surgery; similarly, live vaccines may induce fever 6–12 days after vaccination. There is no reason to delay surgery following vaccination with a live vaccine if the child is well at the time of immediate pre-operative assessment. There is no reason to delay vaccination after surgery, once the child is well and has recovered from the procedure. See the Association of Paediatric Anaesthetists of Great Britain and Ireland Immunisation guideline (www.apagbi.org.uk/guidelines).

Ideally, individuals scheduled for splenectomy should be immunised at least two weeks before the operation. Pneumococcal, meningococcal, Hib, influenza and varicella vaccines are recommended for these individuals pre- or post-splenectomy (see section 4.3.4 and the relevant disease chapters). Note: If the surgery is an emergency, then the immunisation programme should commence two weeks later.

What if the child has a chronic disease?

Children with chronic diseases should be immunised in the normal way, especially as they may be more at risk from the severe effects of vaccine-preventable diseases. However, if the illness or its treatment results in impaired immunity, immunisation with live vaccines should be considered carefully (see sections 4.2 and 4.3), and the child's GP or paediatrician should be consulted before immunisation.

What if the child has had seizures?

A diagnosed neurological condition is not a contraindication to any vaccine on the Schedule. However, an evolving neurological condition (eg, uncontrolled epilepsy or a deteriorating neurological state) is still considered a contraindication to pertussis immunisation. Until the neurological condition has been diagnosed or stabilised, there is a risk that changes may be attributed to the vaccine. A family history of

seizures or epilepsy of any type is not a contraindication to immunisation.

A febrile reaction may occur after any vaccine and result in a febrile seizure in a susceptible child. Vaccine-related febrile seizures are rare, although the risk is higher following administration of certain vaccines, such as influenza (section 10.7), MMR, and measles, mumps, rubella and varicella (MMRV) (see section 21.7) vaccines. These seizures, although frightening for a parent, are almost always benign, with no associated sequelae.

What if the child is allergic?

Only anaphylaxis to a prior dose of vaccine, or to an ingredient in the vaccine, is considered an absolute contraindication. See the contraindications and precautions section in each disease chapter; in particular, pertussis (section 14.6), measles (section 11.6), influenza (section 10.6) and rotavirus (section 17.6). Children with asthma, eczema, hay fever and other allergies should be immunised in the usual way. Studies have shown that immunised children have slightly lower rates of atopic diseases.[2]

Can children be immunised if they are known to develop a rash with antibiotics?

Yes – but check the vaccine data sheet for the list of components; some vaccines may contain traces of antibiotics.

The only concern is if a child has had a previous anaphylactic reaction (a rash alone is not anaphylaxis) to a component of a vaccine.

Can all children receive all the vaccines?

A child cannot receive a vaccine if they have had an anaphylactic reaction to any component of the vaccine. A child may have an underlying condition that is a contraindication to some vaccines; for example, children with illnesses or treatments that cause immunocompromise may be unable to receive live attenuated vaccines (see sections 4.2 and 4.3 for special risk groups, chapters 11, 13 and 18 for MMR and chapter 21 for varicella).

3.1.4 Parents, guardians and contacts

What if the child's mother or guardian is pregnant or breastfeeding?

This is not a contraindication to giving any of the Schedule vaccines to a child, including live vaccines, such as the MMR vaccine. In addition, consideration should be given to the risks for the mother or guardian and baby from diseases such as pertussis, which can be life-threatening in infants.

Pregnancy is an important opportunity to ensure the infant's siblings have received age-appropriate immunisation.

Pertussis (as Tdap) and influenza vaccines are recommended and funded for pregnant women (see section 4.1).

Are live virus vaccines such as measles, mumps, rubella and varicella transmissible?

These are highly attenuated (weakened) viruses designed specifically to induce an immune response without causing disease. There have been no recorded cases of measles, mumps or rubella disease in individuals who were in contact with a vaccinee. Vaccine-strain varicella transmission to contacts is rare (documented in only 9 immunised people, resulting in 11 secondary cases), and the documented risk of transmission exists only if the immunised person develops a rash[3] (see chapters 11, 13 and 18 for MMR and chapter 21 for varicella).

3.2 Addressing myths and concerns about immunisation

Myths about immunisation have existed since the first use of smallpox vaccine over 200 years ago and have resulted in the loss of confidence in immunisation programmes. Misconceptions about vaccines contribute to vaccine hesitancy, which is an issue of global concern. This section provides information to assist providers with addressing concerns about immunisation.

3.2.1 Background

Concerns about immunisation should be taken seriously and responded to appropriately, with as much information as possible. Individuals have the right to make informed decisions for themselves and those in their care, and to accept responsibility for their decisions. It is important to respect this right.

Globally, including in New Zealand, there are many groups of people and individuals who actively campaign against immunisation. Their reasons for doing so may include personal experience, such as an adverse event they have attributed to immunisation, philosophical beliefs, conspiratorial beliefs or dissatisfaction with inadequate or superficial responses from health professionals, who can seem at times to be dismissive of people's concerns. It is important for all health professionals to be able to provide accurate information about the benefits and risks of immunisation and to respond with as much information as possible to parent/guardian concerns, or refer people appropriately.

It is not always possible to change people's position by way of scientific argument or presentation of evidence. Anti-immunisation arguments are almost exclusively based on fallacies of fact or logic, or on historical information that is no longer applicable in the current context. Often these arguments can be challenging for the health professional, particularly if they are unfamiliar with the particular argument and when they are complicated by logical flaws.

In any discussion, it may help to acknowledge that science does not always have all the answers, but that it provides a tool with which to answer questions and evaluate the evidence. It is important to point out that an event that follows immunisation is not necessarily caused by the immunisation. Finally, it is always helpful to inform parents/guardians about additional sources of information (see section 2.1.2 on informed consent and section 1.6 on the safety monitoring of vaccines in New Zealand).

3.2.2 Understanding anti-immunisation

People tend to take on board information that supports their belief system and to ignore information that does not. The internet makes it very easy to access material that is appealing. Most people usually make logical decisions based on their perception of risk. Therefore, if a person has the perception that the risk of disease is real and that vaccines are reasonably safe and work, then they are more likely to vaccinate. People are unlikely to vaccinate if they perceive that there is little risk of disease and that vaccines are not safe and do not work.[4]

3.2.3 Addressing concerns

If a parent is concerned about immunising their child, determining their concerns and addressing them can be helpful. Most often these concerns are around vaccine safety. As a health professional, you should challenge poor information, in a respectful way.

There are three steps you can take when addressing a parent's or a vaccinee's concerns.[5]

1. Understand the specific concerns.

Not every parent or vaccinee has the same concerns, so it is important to first establish what they are worried about. Ask them. It may be helpful to get them to describe what they know about disease risk and vaccine benefit. If they have misconceptions, you can correct them. Evidence has demonstrated that it can be helpful to relay stories of children harmed by vaccine-preventable diseases. Using a vignette can be powerful. If you have no experience of a particular vaccine-preventable disease, see the IMAC website (www.immune.org.nz), or websites such as the Centers for Disease Control and Prevention, the Immunization Action Coalition and the National Centre for Immunisation Research and Surveillance (see Appendix 9).

2. Stay on message.

Keep your messages clear and focussed on the concern at hand.

3. Discuss the rigours of global vaccine research, such as safety systems.

Many vaccine safety myths focus on the limitations of passive reporting systems for adverse events, such as CARM. The many active safety systems and hypothesis-driven research are overlooked. You can highlight that when studies compare the risk for an adverse event in vaccinated children with the risk in unvaccinated children, they support the safety of vaccines.

3.2.4 Debunking a myth

Debunking myths can be very challenging and can also backfire. When you are addressing a myth, there are three important points to remember.[6]

1. Try not to repeat the myth. Focus on the core facts.

This is because people cannot remember if what they hear was a myth or a fact later on. Debunking can serve to strengthen the myth in people's minds as either familiar or a threat to their world view. Begin with the core facts.

2. Precede a myth with a warning.

Let them know that 'this is untrue', because you often cannot avoid mentioning the myth.

3. Include an alternative explanation that accounts for how the myth misleads.

Do not leave a void but rather replace the myth with accurate information. You can highlight the problems with cherry picking, conspiracy theories and fake experts. If you have them, graphics can be extremely helpful, such as pictures of vaccine-preventable diseases or even a graph showing the impact of vaccination – if you feel it appropriate.

Facts and myths about immunisation

Core fact: Measles and rubella have been eliminated in some countries. The WHO has set targets for global eradication.

Myth: MMR vaccine causes autism.

Explanation: There is no evidence that the MMR vaccine causes autism.[7, 8]

In 1998 a British physician announced he had found an association between the receipt of MMR vaccine and the development of a new disorder that included autism in a study of 12 children. No subsequent studies following his study have been able to reproduce his results.

In 2004 *The Lancet* retracted the original 1998 study from the scientific literature on the grounds that it was the product of dishonest and irresponsible research and the British authorities revoked the doctor's licence to practise medicine.[9] In 2008 a press investigation revealed that the doctor had falsified patient data and relied on laboratory reports that he had been warned were incorrect. Studies exonerating the MMR vaccine continue to be published.

Core fact: The incidence of allergic diseases has been increasing. It is thought that lack of exposure to microbes may play a role.

Myth: Vaccines cause allergic diseases.

Explanation: Extensive research shows that, if anything, vaccines may have a protective effect against allergic disease.

Many studies have explored this issue. A few have shown a positive association, but the majority show no association or a negative association. The international scientific community generally accepts that vaccines do not lead to allergies and in fact have a small protective effect against the development of allergy.[2]

It is especially important that children with asthma be given all recommended vaccines, as catching a disease like pertussis or influenza can worsen asthma.[10] In New Zealand, influenza vaccination is particularly recommended for children with asthma because of this risk.

The 2012 Institute of Medicine review of adverse events rejected any causal relationship between inactivated influenza vaccine and asthma exacerbation or reactive airway disease episodes in children and adults.[8]

Core fact: On-time vaccination is associated with a reduced risk of hospitalisation for diseases such as pertussis and pneumococcal disease in children under 1 year of age.

Myth: Vaccines cause cot death.

Explanation: Vaccines may reduce the risk for cot death.

Sudden unexpected death in infancy (SUDI), also known as cot death, usually occurs in children aged under 12 months and is most common around age 3 months, when many immunisations are given. SUDI may occur by chance within a day or so of immunisation.[11] There is no evidence that vaccination causes SUDI. Despite solid evidence against a link, the claims continue to be made.

There have been many studies that have conclusively shown that SUDI is not caused by immunisation.[11] Some studies, including the New Zealand Cot Death Study, found a lower rate of SUDI in immunised children.[12] This is consistent with a Scandinavian study, which found that some cases of SUDI were probably caused by undiagnosed pertussis.[13] A large case-control study showed no increased risk of SUDI associated with immunisation,[14] and a meta-analysis of nine case-control studies further suggested that immunisation is protective against SUDI.[15] Consistent findings from several studies using a range of methods invalidate claims that associate vaccination with SUDI or cot death.[16]

Core fact: At birth the infant is exposed to thousands of microbes.

Myth: Vaccines 'overload' or 'overwhelm' the infant immune system.

Explanation: It is estimated that the infant immune system could respond to over 10,000 vaccines all at once.

There is no evidence of immune system 'overload', either theoretical or actual. The immune system is able to deal with an extraordinarily large number of different antigens at any one time.

Every day we all come into contact with viruses, bacteria and other agents to which the immune system responds. Any demands placed on the immune system by vaccines are minuscule compared to its ability to respond.

Vaccines have very few antigens in them. The number of immunogenic proteins and polysaccharides in modern vaccines has decreased dramatically compared with early vaccines because of advances in vaccine technology. For example, early whole-cell pertussis vaccines contained around 3,000 immunogenic proteins, compared with two to five in the modern acellular pertussis vaccines. In spite of an increase in the number of vaccines on the Schedule, an infant now receives far fewer immunogenic proteins and polysaccharides than with earlier vaccines.[17] There are considerably more antigens in the organisms that cause disease than in the vaccines.

Explanation: Delaying immunisation for fear that an infant is too young leaves the infant vulnerable to disease, particularly pertussis and pneumococcal diseases. Infants delayed for their pertussis vaccinations are 4–6 times more likely to be hospitalised with the disease.[18] On-time vaccination is important.

Core fact: Vaccines induce immunity through natural processes.

Myth: It is better to get 'natural immunity' than get vaccinated.

Explanation: Some vaccines induce better protection than that resulting from natural disease. Examples are tetanus, HepB and HPV, and protein conjugate polysaccharide vaccines administered to children aged under 2 years (Hib and PCV). There is no evidence that experiencing vaccine-preventable diseases has any benefit on health; on the contrary, these diseases are serious and sometimes fatal. Vaccinated people have fewer diseases than unvaccinated people.

Core fact: The scientific evidence shows there is no association between HPV vaccines and autoimmune conditions.

Myth: HPV vaccines cause autoimmune conditions.

Explanation: Several large cohort studies have been conducted to investigate the link between HPV vaccine and autoimmune conditions.[19, 20, 21, 22, 23] No association has been found in these studies.

Core fact: The quadrivalent human papillomavirus vaccine has reduced cervical disease in countries using the vaccine, and Australia has almost eliminated genital warts.

Myth: HPV vaccines cause postural orthostatic tachycardia syndrome (POTS), complex regional pain syndrome (CRPS) and chronic fatigue syndrome (CFS).

Explanation: There is no scientific evidence that links POTS, CRPS or CFS with HPV vaccination.

POTS is a condition in which tachycardia occurs when a patient moves from a supine position to upright. The condition is associated with a collection of other symptoms, which include palpitations, light-headedness, weakness, blurred vision, headache, extreme fatigue, nausea, syncope and sleep disturbance. Up to 50 percent of people with POTS have an antecedent viral illness and 25 percent have a family history of similar complaints. There is an overlap between POTS and CFS.[24]

CRPS describes a variety of disorders characterised by pain that is disproportional to the inciting event. In children and adolescents it often presents as a painful mottled swollen limb with allodynia and hyperalgesia. Girls are six times more likely to be affected than boys and the peak age of onset is at age 12–13 years. Often minor trauma is the inciting event, but around one-third of people with CRPS are unable to recall an inciting injury or trauma.[25]

CFS is a disorder characterised by extreme fatigue that cannot be explained by an underlying medical condition. The causes are unknown but it has been linked to infection with Epstein–Barr virus and human herpesvirus 6.

Cases of these disorders have been reported in association with HPV vaccination, particularly in the media, and social media. The variable time between vaccination and onset of symptoms, lack of consistent symptoms and a reporting rate that remains below the expected rate for these syndromes all point to HPV vaccine not being the cause of these conditions.[26]

Post-marketing surveillance systems globally continue to monitor the safety of HPV vaccination programmes.[27, 28, 29] The WHO's Global Advisory Committee on Vaccine Safety has systematically reviewed HPV vaccine safety and has not found any safety issue that would alter its recommendations for use.[30] The main challenge with HPV vaccine is communicating its excellent safety profile.[31]

Core fact: Everything is made of chemicals and any chemical can be toxic, even water.

Myth: Vaccines contain toxic chemicals, viruses and cells.

Explanation: Vaccine ingredients are not toxic in the amounts present in a vaccine. It is the dose that differentiates a poison from a harmless substance, essential substance or a medicine.

Most of the ingredients in vaccines are present already in our bodies and we consume them in some way every day. For example, aluminium is the most common metallic element on earth, and the body makes and uses formaldehyde for synthesising deoxyribonucleic acid (DNA).

- There is approximately 60 times more formaldehyde in a pear than a vaccine.
- Polysorbate 80 is used in many foods, including ice cream.
- Vaccines do not contain extraneous cells or viruses.
- Aluminium compounds administered via vaccination do not contribute significantly to the general aluminium exposure and do not raise human serum aluminium levels. Based on 80 years of experience, the use of aluminium adjuvants in vaccines has proven to be extremely safe and effective.[32, 33]

For more information, see the IMAC factsheet *Vaccine Ingredients* (available at www.immune.org.nz/resources/written-resources).

Core fact: *With the exception of safe water, no other modality, not even antibiotics, has had such a major effect on mortality reduction.* – Stanley Plotkin[34]

Myth: Vaccination has played little role in controlling disease.

Explanation: Vaccine programmes have controlled or eliminated polio, tetanus, diphtheria, pertussis, *Haemophilus influenzae* type b, hepatitis B, pneumococcal disease, meningococcal disease, rotavirus, human papillomavirus, varicella, hepatitis, yellow fever, measles, mumps, rubella and others, in populations where vaccines have been used.

Improvements in living conditions and medical care have reduced the chances of dying from infectious disease, but without immunisation most people will still acquire vaccine-preventable infections. For example, measles, which spreads through the air, is largely unaffected by improvements in living conditions other than reduced overcrowding. Indigenous cases of measles, mumps and rubella have been eliminated from Finland over a 12-year period using a two-dose MMR vaccine schedule given between 14 and 16 months and at age 6 years.[35] In September 2016, the Region of the Americas was the first WHO region to be declared free of measles.

Core fact: No vaccine is 100 percent effective and some immunised children will get the disease.

Myth: Vaccines do not work, as most cases of disease are in immunised children.

Explanation: As immunisation coverage increases, the proportion of cases that occur in children who have been immunised compared with those who are unimmunised increases. There is a mathematical relationship between vaccine effectiveness, immunisation coverage and the proportion of cases that are immunised.

To see this clearly, imagine a group of 100 children. If 90 percent of children are given a vaccine with 90 percent efficacy, then:

- 81 of the 100 children will be immune

- 10 children will be susceptible because of not having the vaccine, and another 9 because of vaccine failure.

This means that in the situation of exposure to the infection in a community, we expect that nearly half the cases of disease will be in immunised children, even though only 10 percent of immunised children were susceptible.

Of course, if all 100 children had been vaccinated only 10 would be susceptible to disease. As vaccine uptake rises, the proportion of cases of disease that occur in vaccinated people increases dramatically, but the absolute number of cases of disease falls to very low levels. Failing to provide the denominators (how many vaccinated and how many unvaccinated) can lead to misunderstanding.

For pertussis, where the protection following immunisation lasts only four to six years, immunised children can be infected but the resultant illness is usually milder, with fewer serious consequences and at an older age than if they had not received vaccine. The disease is most severe in infants, but adolescents and adults contribute to the carriage and spread of the disease (see sections 14.2 and 14.3).

For further details on the effectiveness of vaccines, see the 'Written resources' section of the IMAC website (www.immune.org.nz/resources/written-resources).

3.3 Addressing immunisation issues in a constantly changing environment

In the past few years the internet has exploded with a variety of forums that disseminate anti-immunisation material effectively. It is no longer practical to prepare official rebuttals to each new article. Fortunately, the internet also facilitates the rapid communication of scientific commentary on new myths as they appear. There are several scientists who regularly address immunisation myths in the form of regular blogs. In addition, some organisations provide position statements and discussion forums.

Below are some organisations and individuals who write and provide information related to immunisation scares, myths and pseudoscience that can help you to understand the myth. They can be a source of new information that may help to address a concern and ask a question, and may be useful resources for parents.

While the format is often colloquial, the writers are respected scientists who volunteer commentary against the abuse of science and evidence-based medicine.

3.3.1 Science blogs

Below are science blogs that frequently deal with immunisation issues.

- *Respectful Insolence* (http://scienceblogs.com/insolence/) is the blog of ORAC, aka American oncology surgeon Professor David Gorsky, who provides insight into recent vaccine issues, sometimes daily. This blog is hosted by ScienceBlogs, an invitation-only blog set up to enhance public understanding of science.
- *Science-based Medicine* (www.sciencebasedmedicine.org) is a blog site established by scientists and medical professionals to discuss medical treatments and products of public interest in a scientific light. All contributors are medically trained.
- *Diplomatic Immunity* (http://sciblogs.co.nz/diplomaticimmunity/) is a New Zealand Science Media Centre blog dedicated to immunisation issues of particular relevance for New Zealand vaccinators. The contributor is based at the Immunisation Advisory Centre, University of Auckland.

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4 Immunisation of special groups

This chapter discusses the special immunisation requirements of individuals at risk of vaccine-preventable diseases due to certain conditions or underlying disease, or through their occupation or other risk factors. The topics covered are:

- pregnancy and lactation (section 4.1)
- infants with special immunisation considerations (section 4.2)
- immunocompromised individuals of all ages (section 4.3)
- immigrants and refugees (section 4.4)
- travel (section 4.5)
- occupational and other risk factors (section 4.6).

Note: Vaccinators are advised to check the Pharmaceutical Schedule and any online updates (www.pharmac.govt.nz) for changes to funding decisions for special groups.

4.1 Pregnancy and lactation

4.1.1 For women planning pregnancy

Women who are planning pregnancy should know whether they are immune to rubella (see section 18.5.3) and varicella (see section 21.5.4).

MMR

Two doses of MMR vaccine are recommended and funded for women who are susceptible to measles, mumps and/or rubella (see sections 11.5, 13.5 and 18.5). Women who are to receive the rubella vaccine (as MMR) are advised to ensure they are not pregnant at the time of immunisation and for at least four weeks afterwards, although there is no current evidence that rubella vaccine is teratogenic (see

section 18.6.1). If the mother is non-immune, two doses of MMR vaccine, separated by four weeks, should be given after delivery.

Varicella

VV is recommended (but not funded) for adults who are susceptible to varicella. Two doses are given, four to eight weeks apart (see section 21.5 and the manufacturers' data sheets for administration and dosing information). Women who are to receive VV are advised to ensure they are not pregnant at the time of immunisation and for at least four weeks afterwards.

4.1.2 During pregnancy

Inactivated vaccines are considered safe in pregnancy, but because of the theoretical possibility of harm to the fetus, live vaccines should not be administered to a pregnant woman. In some circumstances where there is increased risk of exposure to the microbe, the need for immunisation may outweigh any possible risk to the fetus.

See the relevant disease chapters, particularly rubella (section 18.8.3) and varicella (section 21.8.6), for recommendations on managing exposure to diseases during pregnancy.

Influenza vaccine

The influenza vaccine is recommended and funded for pregnant women, and should be offered to women at any stage of pregnancy, as soon as the annual influenza vaccine becomes available (see section 10.5). Both the pregnant woman and her fetus are at increased risk of influenza complications; influenza immunisation is therefore recommended during pregnancy to reduce this risk.

Maternal influenza immunisation also offers protection to the neonate through maternal antibody transfer.[1] Influenza vaccines are not registered for infants aged under 6 months, therefore immunisation during pregnancy confers protection to newborns and infants who are too young to have received vaccination at the time of exposure.[1, 2] Maternal influenza immunisation is significantly associated with reduced risk of influenza virus infection[3] and hospitalisation for an

influenza-like illness in infants up to 6 months of age,[4, 5] and increased influenza antibody titres are seen in infants through to age 2–3 months.[1]

Influenza immunisation during pregnancy may also reduce the incidence of stillbirth. In an Australian study, stillbirth was 51 percent less likely among vaccinated mothers compared to unvaccinated mothers.[6]

There is no evidence that influenza vaccine prepared from an inactivated virus causes harm to the fetus or to the neonate.[7]

Pertussis vaccine (Tdap)

Pertussis is a severe infection in infants too young to have been immunised. Vaccination with Tdap should be offered in every pregnancy (currently funded between 28 and 38 weeks' gestation, see section 14.5) to protect the mother and so that antibodies can pass to the fetus; post-partum maternal vaccination will reduce the risk of a mother infecting her baby but does not have the added benefit of providing passive antibodies.

In October 2012 the UK introduced a pertussis vaccination programme for pregnant women in response to a nationwide pertussis outbreak. An observational study of the programme in England estimated vaccine effectiveness at 91 percent (95% CI: 84–95) for preventing pertussis in infants aged under 3 months.[8] This high vaccine effectiveness is likely to be a result of protection of infants by both passive antibody transfer and reduced exposure to maternal disease.[8] Three years after the introduction of the programme, vaccine effectiveness in infants was sustained at 90 percent, despite changing to another acellular vaccine with a different antigen composition.[9] Disease incidence in infants aged under 3 months remained low, despite high activity persisting in those aged 1 year and older.[9] Vaccine effectiveness against infant deaths was estimated at 95 percent (95% CI: 79–100).[9]

An observational study of the safety of the UK's maternal pertussis vaccination programme found no evidence of an increased risk of any of the extensive predefined list of adverse events related to pregnancy.[10] In particular, there was no evidence of an increased risk of stillbirth.

Close contacts

The confirmation of pregnancy should act as a trigger to update the pertussis vaccination status of all close contacts. This includes making sure siblings have received their routine scheduled vaccines (funded for children aged under 18 years) and offering Tdap to adults, although this is not currently funded.

4.1.3 Breastfeeding and post-partum

All vaccines on the National Immunisation Schedule and those recommended for special groups are safe for breastfeeding women.

MMR

MMR vaccine (two doses) is recommended (and funded) after delivery for women who are susceptible to any of the three diseases. Breastfeeding is not a contraindication to MMR vaccine.

Pertussis vaccine (Tdap)

To protect the newborn infant, Tdap is recommended (but not funded) for close contacts of newborns, including women who were not vaccinated during pregnancy.

Varicella

VV is recommended (but not funded) for all susceptible adults. Pregnant women who are non-immune can receive VV after delivery.

VV for the mother is recommended (and funded) after delivery if the baby is immunocompromised and the mother is susceptible to varicella (see sections 4.3 and 21.5).

4.2 Infants with special immunisation considerations

4.2.1 Preterm and low birthweight infants

Vaccination as per the Schedule (ie, at the usual chronological age, with the usual vaccine dosage and interval) is recommended for preterm infants and infants with low birthweight. If an infant is in hospital when 6 weeks old, the scheduled vaccines, including rotavirus vaccine, should be given. If standard infection control precautions are maintained, the risk of transmission of vaccine strain rotavirus will be minimal.[11]

Note that there is a potential risk of apnoea in infants born before 28 weeks' gestation. If a preterm infant had apnoeas following immunisation in hospital (6-week and/or 3-month event), readmission for the next infant immunisation and respiratory monitoring for 48 to 72 hours may be warranted,[12] but do not avoid or delay immunisation.

Hepatitis B vaccine

All preterm and low birthweight infants born to HBsAg-positive mothers should be managed the same way as term infants and receive immunoprophylaxis (HBIG and HepB) as soon as possible after birth (see section 8.5.2). They should continue routine immunisation as per the Schedule, starting at age 6 weeks.

Influenza vaccine

Preterm infants who develop chronic lung disease are recommended to receive influenza vaccine once they are aged 6 months or older, and a second dose four weeks later (influenza vaccine is usually available from March each year). Influenza vaccine is recommended (but not funded) for close contacts of preterm infants, including children (see section 10.5).

Pertussis vaccine (for contacts)

It is essential that siblings of preterm infants be up to date with immunisations to reduce the risk of pertussis transmission to vulnerable infants (see section 14.5). Adolescents should have received Tdap in

year 7 as part of the Schedule. Pertussis-containing vaccine is funded for primary and catch-up immunisation of all children aged under 18 years (see Appendix 2 for catch-up schedules).

Tdap is recommended (but not funded) for adult contacts of young infants, with the exception of funded Tdap vaccine for pregnant women from 28 to 38 weeks' gestation.

Pneumococcal vaccines (PCV10, PCV13 and 23PPV)

- PCV10 should be given as per the Schedule at ages 6 weeks, 3, 5 and 15 months.
- For preterm infants who develop chronic lung disease, PCV13 (funded) replaces the scheduled PCV10. Give 23PPV (funded) when the child is aged 2 years or older. There must be a minimum of eight weeks between the last dose of PCV13 and the 23PPV dose. Revaccinate once with 23PPV five years later if still considered at risk.

4.2.2 Infants with congenital heart disease

- Some children with congenital heart disease may have asplenia or polysplenia (functional hyposplenia) (see section 4.3.4).
- Certain conditions such as DiGeorge syndrome may have associated T-cell deficiency (see section 4.3.2).
- Children with complex single ventricle or shunt-dependent lesions (eg, post-Norwood procedure) have an increased risk of deterioration or collapse following immunisation. Discuss with the specialist, as monitoring in hospital may be required for the primary immunisation series.
- Rotavirus vaccine should be given to children with congenital heart disease even if they have received blood products.

4.2.3 Infants with liver and renal disease

Some infants with congenital biliary or renal conditions are likely to need transplantation. An accelerated immunisation schedule for these infants is provided in Table 4.1. The aim of the accelerated schedule is to maximise protection against vaccine-preventable diseases and to deliver live viral vaccines prior to transplantation and immunosuppression.

Infants with biliary atresia may have polysplenia (functional hyposplenia) (see section 4.3.4).

Other chronic kidney diseases also warrant extra immunisations (see section 4.3.3).

Table 4.1: Accelerated immunisation schedule (funded) for infants in whom liver or kidney transplant is likely

Refer to the Pharmaceutical Schedule (www.pharmac.govt.nz) for any changes to funding decisions.

Age	Immunisation/serology	Comments
6 weeks	Usual Schedule, but use PCV13 (Prevenar 13) instead of PCV10 (Synflorix)	Do not start earlier than age 6 weeks.
3 months	Usual Schedule, but use PCV13 instead of PCV10	
	MenCCV (NeisVac-C)	
5 months	Usual Schedule, but use PCV13 instead of PCV10	
	MenCCV (NeisVac-C)	
7 months	MMR (Priorix)	MMR should not be given within 1 month of predicted transplant.
	Varicella (Varilrix)	In general, VV should not be given within 1 month of predicted transplant but may be given closer at the discretion of the specialist.
	Hep A (Havrix Junior)	
	Anti-HBs serology	If anti-HBs is negative, give a further 3 doses of monovalent HepB vaccine, 4 weeks apart (HBvaxPRO 10 µg or Engerix-B 20 µg).
12 months	PCV13 (Prevenar 13)	
	MMR (Priorix)	MMR should not be given within 1 month of predicted transplant.
	Varicella (Varilrix)	In general, VV should not be given within 1 month of predicted transplant but may be given closer at the discretion of the specialist.
	MenCCV (NeisVac-C)	

Continued overleaf

Age	Immunisation/serology	Comments
13 months	DTaP-IPV-HepB/Hib (Infanrix-hexa)	
	MMR (Priorix)	MMR should not be given within 1 month of predicted transplant.
	Hep A (Havrix Junior)	If Hep A and HepB are due at the same time, consider using combined Hep A-HepB vaccine (Twinrix; not funded).
24 months	23PPV (Pneumovax 23)	Revaccinate once after 5 years.
	MCV4-D (Menactra)	2 doses of MCV4-D, 8 weeks apart, and at least 4 weeks after last PCV13.[a] Give a booster after 3 years, then 5-yearly.
4 years	Usual schedule: DTaP-IPV (Infanrix-IPV)	
	MMR (Priorix)	MMR can only be given if pre-transplant. MMR not required if received 2 doses after age 12 months; contraindicated if post-transplant.
From age 9 years	HPV9 vaccine (Gardasil 9)	3 doses at 0, 2 and 6 months.[b] Funded pre- or post-transplant. If given early, they do not require the usual Schedule doses in year 7/8 (age 11/12 years).
11 years	Usual schedule: Tdap (Boostrix)	
6 months post-transplant	HepB (HBvaxPRO or Engerix-B), plus anti-HBs serology before and 1 month after the initial HepB series	3 doses of HepB vaccine (HBvaxPRO 5 µg if available, or Engerix-B 20 µg). If HepB was not previously given, and anti-HBs is negative, give 3 doses of HepB vaccine (HBvaxPRO 10 µg or Engerix-B 20 µg). If there is an inadequate immune response to the initial 3-dose HepB series, give a further 3 doses (HBvaxPRO 10 µg or Engerix-B 20 µg).
	23PPV	If at least 24 months old and not given pre-transplant. Revaccinate once after 5 years.

Continued overleaf

Age	Immunisation/serology	Comments
Annually	Influenza (Fluarix Tetra if aged under 3 years; Influvac Tetra if aged 3 years and older)	Recommended for patients (funded) and all family members (not funded). For patients (from age 6 months) and family members aged under 9 years, give 2 doses 4 weeks apart in the first year, and 1 dose in subsequent years.
Household contacts of transplant patients	National Immunisation Schedule vaccines	Immune-competent siblings and other household contacts may receive all the Schedule vaccines, and should be fully vaccinated for age.
	Varicella (Varilrix)	Two doses of VV are funded for susceptible household contacts of transplant patients.

a Give MCV4-D at least 4 weeks after PCV13[13, 14] (see section 12.4.4).

b Individuals who started with HPV4 may complete their remaining doses with HPV9.

Source: Starship Children's Health.

4.2.4 Asplenic infants

No vaccines are contraindicated for infants with functional or anatomical asplenia. The usual National Immunisation Schedule should be followed (replacing PCV10 with PCV13), with the addition of age-appropriate pneumococcal polysaccharide, meningococcal conjugate and influenza vaccines, as discussed in section 4.3.4.

4.2.5 Infants exposed to hepatitis B, with mothers with chronic HBV infection

Infants exposed to maternal hepatitis B infection require a birth dose of HepB and HBIG (see section 8.5.2).

4.2.6 Immune-deficient infants

Diagnosis of immune deficiency is often not made before children start their immunisation schedules. However, no parenteral live virus vaccines are given on the Schedule in the first year of life.

Rotavirus vaccine

Rotavirus vaccine is an oral, live, attenuated viral vaccine, which should not be given when severe combined immune deficiency (SCID) has been diagnosed. There have been case reports of rotavirus vaccine accidentally administered to infants with SCID, leading to chronic diarrhoea and failure to thrive.[15, 16, 17] In infants with milder immune deficiency, rotavirus vaccine may cause prolonged shedding of the vaccine virus, but it is unlikely to cause harm.

There is little data on rotavirus vaccination in infants born to mothers on immunosuppressive therapies. Certain immunosuppressive medications, such as disease-modifying anti-rheumatic drugs (DMARDs), readily cross the placenta and can be detectable some months later.[11] Infants of mothers who received DMARDs during pregnancy that are monoclonal antibodies (eg, adalimumab/Humira) should not be vaccinated with live rotavirus vaccines until theoretical concerns about safety are clarified.[18] See Table 4.3 for a list of the highly immunosuppressive medications that readily cross the placenta.

BCG vaccine

BCG, being a live bacterial vaccine against TB, can cause disseminated disease in certain rare immune deficiencies. In the past few years, eligibility criteria for neonatal BCG have been restricted (see chapter 20) and universal antenatal human immunodeficiency virus (HIV) screening introduced, thus reducing the risk of BCG being given to a child with an undiagnosed immune deficiency.

For infants whose mothers received DMARDs during pregnancy that are monoclonal antibodies (eg, adalimumab, infliximab; see Table 4.3), BCG vaccination should be delayed until the infant is at least 8 months old.[19]

(See also section 4.3.)

4.2.7 Infants with HIV

Infants with HIV infection who do not have severe immunosuppression should follow the routine Schedule (replacing PCV10 with PCV13) and are eligible to receive funded meningococcal, varicella (two doses) and influenza vaccines, plus pneumococcal polysaccharide vaccine from age 2 years. (See 'HIV infection' in section 4.3.3.)

4.2.8 Other conditions

All infants with the following conditions should receive the routine Schedule vaccines, plus the additional vaccines as described.

- Cystic fibrosis or other chronic lung diseases: influenza vaccine from age 6 months (funded; see section 10.5); PCV13 (funded) replaces PCV10 on the Schedule for these infants, and pneumococcal polysaccharide vaccine is recommended and funded from age 2 years (see section 15.5).
- Metabolic and endocrine disorders (eg, congenital diabetes or adrenal insufficiency).
  - Diabetes: influenza vaccine from age 6 months (funded; see section 10.5); PCV13 (funded) replaces PCV10 on the Schedule for these infants, and pneumococcal polysaccharide vaccine is recommended and funded from age 2 years (see section 15.5).
  - Inborn errors of metabolism at risk of major metabolic decompensation: influenza and varicella (two doses) vaccines (funded; see sections 10.5 and 21.5).
  - Other endocrine disorders: VV is recommended for a variety of endocrine disorders – discuss with the specialist.
- Sickle cell disease (not trait): these infants should be treated as for functional asplenia (see section 4.3.4).
- Other haemoglobinopathies that may result in splenectomy or functional asplenia: influenza vaccine from age 6 months (funded; see section 10.5); pneumococcal polysaccharide vaccine is recommended from age 2 years (see section 15.5).
- Cochlear implants or intracranial shunts, and infants with Down syndrome: influenza vaccine from age 6 months (funded; see section 10.5); PCV13 (funded) replaces PCV10 on the Schedule for these infants, and pneumococcal polysaccharide vaccine is recommended and funded from age 2 years (see section 15.5).
- Infants who may be exposed to TB are eligible for BCG vaccine (see sections 4.4.2 and 20.5). However, if the infant's mother received DMARDs during pregnancy that are monoclonal antibodies (eg, adalimumab, infliximab; see Table 4.3), BCG vaccination of the infant should be delayed until age 8 months (see section 20.6).

4.3 Immunocompromised individuals of all ages

Individuals with chronic conditions, an immune deficiency, or who are immunosuppressed for underlying disease control are at increased risk or severity of infectious diseases. These individuals should be immunised as a matter of priority. Special care is required with some live vaccines. When considering immunising such individuals, seek advice from their specialist. See also the 'Contraindications and precautions' section in each disease chapter and the vaccine data sheets.

The following definitions are used in this *Handbook*:

- **Immunocompromise** – a broad definition for the large group of conditions and their treatments that can reduce the individual's ability to mount an immune response and to fight off infection. A patient may be mildly to severely immunocompromised, and this is often a subjective measure.
- **Immunodeficiency** – refers to specific primary (eg, agammaglobulinaemia) and secondary (eg, HIV) diseases characterised by reduced ability to mount an immune response and fight off infection.
- **Immunosuppression** – refers to treatments such as chemotherapy, immunotherapies and medications that suppress the ability to mount an immune response and fight off infection.

It is important to ensure that the household contacts of these individuals are immune to vaccine-preventable diseases wherever possible.

4.3.1 Introduction

The nature and degree of immunocompromise determines the safety and effectiveness of vaccines. Immune deficiency conditions can be divided into primary and secondary. Primary immune deficiencies that present in childhood are generally inherited, and include antibody deficiency (disorders of B lymphocytes or antibody production), defects of cell-mediated immunity (disorders of T lymphocytes, which most often present as combined defects affecting antibody production as well), and defects of complement and phagocytic function[20] (see

section 4.3.2). Secondary immune deficiencies are acquired, and occur in people with HIV, people with malignant neoplasms, in organ transplant recipients, and in people receiving immunosuppressive treatment, chemotherapy or radiotherapy.[20]

Live parenteral vaccines (these include MMR, varicella, HZV and BCG) should not in general be given to individuals who are severely immunocompromised, because of the risk of disease from vaccine strains. Subunit and inactivated vaccines are safe to administer, although the response of immunocompromised individuals to these inactivated vaccines may be inadequate. For comment on rotavirus vaccine see section 4.2.6 above.

Specific serum antibody titres can be determined to guide immunisation requirements for some vaccines and the future management of disease exposures.

Certain immune deficiencies result in specific disease susceptibility. For example, pneumococcal and meningococcal vaccines are recommended for those with poor or absent splenic function or certain complement deficiencies, because of increased infection risk from encapsulated bacteria. Influenza and varicella vaccines are recommended for individuals with splenic dysfunction, asplenia and phagocyte function deficiencies, both to prevent the diseases and to reduce the risk of secondary bacterial infections. See section 4.3.4 for recommendations for individuals with splenic dysfunction or asplenia.

Household contacts

Immune-competent siblings and household contacts may receive all the Schedule vaccines. It is important to ensure that close household contacts are immune for the added protection of the immunocompromised individual.

Infants in the household should receive rotavirus vaccine at the usual Schedule ages: there are no reported cases of symptomatic infection in immunocompromised contacts.[21] There is no risk of transmission of MMR vaccine viruses to the immunocompromised individual.

VV or age-appropriate HZV can be given safely to the household contacts of immunocompromised individuals. VV is funded for non-immune household contacts of patients who are immunocompromised

or undergoing a procedure or treatment leading to immunocompromise. If the household contact is immune to varicella (previous history of infection or vaccination) and aged 50 years and older, give HZV (funded at age 65 years with a catch-up, until 31 March 2020, for those aged 66–80 years inclusive; unfunded if aged 50–64 years). If a vaccinated person develops a varicella- or zoster-like rash, they should cover the rash and avoid contact with persons who are immunocompromised for the duration of the rash.[22]

4.3.2 Primary immune deficiencies

Live vaccines are contraindicated for all individuals with T lymphocyte-mediated immune deficiencies and combined B- and T-lymphocyte disorders.[20] Most of these individuals will be on intravenous immunoglobulin (IVIG) replacement therapy, which provides passive protection against most vaccine-preventable infections. (See also section 22.6 for contraindications to HZV.)

Hib, PCV13, 23PPV and Td vaccines may be used in testing for primary immune deficiencies, on the recommendation of an internal medicine physician or paediatrician.

Influenza vaccine is funded for all immune-deficient individuals. Regardless of their age, all immune-deficient individuals who receive influenza vaccine for the first time are recommended to receive two vaccine doses at least four weeks apart, and one dose annually after that.[23]

Once an immunodeficiency is recognised, PCV13 should replace PCV10 in the routine schedule (see sections 15.5.2 and 15.5.3).

Below is a summary of the appropriate immunisations for individuals with primary immune deficiencies.[20] Seek specialist advice. (See also Table A6.1 in Appendix 6 of this *Handbook*.)

B lymphocyte deficiencies (humoral)

(Humoral means the development of circulating antibody.)

X-linked, agammaglobulinaemia and common variable immune deficiency

The efficacy of any vaccine that is dependent on a humoral response, such as 23PPV, is doubtful, but all inactivated vaccines are safe.

- Influenza vaccine is recommended.
- BCG and HZV are contraindicated.
- MMR and VV are not required because the individual is on IVIG. IVIG provides passive protection and would interfere with the response to these vaccines.

Selective IgA deficiency

All vaccines are probably effective.

- Influenza vaccine is recommended.
- There are no specific contraindications or precautions.

Lymphocyte deficiencies (cell-mediated and humoral)

Complete defects (eg, SCID) and partial defects (eg, Wiskott–Aldrich syndrome, most patients with DiGeorge syndrome)

The efficacy of any vaccine depends on the degree of immune deficiency.

- Pneumococcal (PCV13 and 23PPV), meningococcal and influenza vaccines are recommended.
- BCG, MMR, VV and HZV are contraindicated.
- Rotavirus vaccine is contraindicated in SCID.

Complement deficiencies

Deficiency of early components (C1, C4, C2, C3)

All routine vaccines are probably effective.

- Influenza, PCV13, 23PPV and meningococcal vaccines are recommended.
- There are no specific contraindications or precautions.

Deficiency of late components (C5–9), properdin, factor B

All routine vaccines are probably effective.

- Influenza, meningococcal and pneumococcal conjugate and polysaccharide vaccines are recommended.
- There are no specific contraindications or precautions.

Phagocytic function deficiencies

Chronic granulomatous disease, leukocyte adhesion defect, myeloperoxidase deficiency

All routine vaccines are probably effective.

- Influenza vaccine is recommended.
- BCG is contraindicated.
- Live viral vaccines are safe in chronic granulomatous disease[9] but discuss individuals with other conditions with specialist.

4.3.3 Secondary (acquired) immune deficiencies

The following sections provide recommendations for individuals with diseases or therapy causing immunocompromise.

The ability of individuals with secondary immune deficiency to develop an adequate immunological response depends on the type of immune deficiency and/or and the intensity of immunosuppressive therapy.

Before commencing a therapy that would be expected to cause significant immunosuppression, a full vaccination history should be obtained. Then, if circumstances permit, such as prior to commencing immunosuppressive therapy for rheumatological disease or prior to solid organ transplant, vaccination should be completed (including HPV from age 9 years) and additional non-routine vaccines (eg, varicella for children or zoster vaccine for certain adults [see section 22.5]; and meningococcal) may be appropriate. Similarly, in diseases such as chronic renal failure, where immune impairment is likely to be progressive, early administration of vaccines may result in better antibody responses. If immediate treatment is required it should not be delayed to allow for vaccination.

Live viral vaccines (MMR and VV) should only be given if the patient is non-immune, is not severely immunocompromised and is four or more weeks prior to commencement of immunosuppressive therapy. VV may be given at a shorter interval at the discretion of the specialist. Checking varicella serostatus is recommended in this situation:[22] if VZV-seronegative, give VV (funded); if VZV-seropositive and aged 50 years and older, give HZV (funded at age 65 years with a catch-up, until 31 March 2020, for those aged 66–80 years inclusive; unfunded if aged 50–64 years).

When immunosuppressive therapy is discontinued, immune recovery usually takes between 3 and 12 months.

Influenza vaccine is funded for immunocompromised individuals before each influenza season, and is recommended three to four weeks after chemotherapy for malignant neoplasm is completed, once both the peripheral granulocyte and lymphocyte counts are $>1.0 \times 10^9$/L. Regardless of their age, all immunocompromised individuals who receive influenza vaccine for the first time are recommended to receive two vaccine doses at least four weeks apart, and one dose annually after that.[23]

Individuals receiving corticosteroids

The minimum amount of corticosteroid administration sufficient to cause immunosuppression is not well defined, and is dependent on dose, duration and the underlying disease. Many clinicians consider a daily dosage equivalent to 2 mg/kg prednisone or greater, or a total daily dosage of 20 mg or greater, particularly when given for 14 days or more, is sufficient to raise concern about the safety of live virus vaccines.

The following guidelines may be used for the safe administration of live virus vaccines to individuals on corticosteroids. Table 4.2 provides a summary of the guidelines for individuals on high-dose corticosteroids (see also Table 22.2 for HZV recommendations).

Live virus vaccines *can be* administered to:

- individuals on topical therapy or local injections of corticosteroids, including on the skin or respiratory tract (by aerosol), or intra-articular, bursal or tendon injections, because such therapies do not usually result in immunosuppression

- individuals on maintenance *physiological* doses of corticosteroids
- individuals on low to moderate doses of systemic steroids given daily or on alternate days (this includes children receiving less than 2 mg/kg per day prednisone, or less than 20 mg/day if they weigh more than 10 kg, or an equivalent dose of another short-acting systemic corticosteroid)
- individuals receiving high-dose corticosteroids for fewer than 14 days (eg, children receiving 2 mg/kg of prednisone, or up to 20 mg if the child weighs more than 10 kg) can receive live virus vaccines immediately on discontinuation of treatment (some experts would delay immunisation for two weeks if possible).

Live virus vaccines *should not* be administered to:

- individuals receiving high-dose corticosteroids daily or on alternate days for more than 14 days (eg, individuals receiving 2 mg/kg of prednisone, or 20 mg or more if the individual weighs more than 10 kg) until the corticosteroid therapy has been discontinued for at least four weeks
- individuals who have a disease process that causes immunosuppression, and who are being treated with either systemic or locally administered corticosteroids, except in special circumstances (discuss with the individual's specialist).

Note: These guidelines are intended to ensure safety of administration of the live virus vaccine; optimal vaccine immunogenicity may not be achieved.

Table 4.2: Guidelines for live virus vaccine administration for individuals on high-dose corticosteroids

	Infants and children <10 kg	Children ≥10 kg and adults	Administration of live viral vaccines after cessation of corticosteroids[24]
High dose <14 days	>2 mg/kg Daily or on alternate days	>20 mg/day	Can be given immediately on discontinuation, but delay 2 weeks if possible
High dose >14 days	>2 mg/kg Daily or on alternate days	>20 mg/day	Delay for 4 weeks

Source: IMAC

Other immunosuppressive agents (eg, for autoimmune diseases, rheumatological diseases, inflammatory bowel disease)

In recent years there has been rapid development of immunosuppressive agents, particularly targeted biological therapies, and an increasing number of patients are receiving such therapies.[18] Table 4.3 lists the categories of agents available, according to their potential for immunosuppression.

As a general guide, low-level immunosuppression includes treatment with prednisone <2 mg/kg with a maximum of 20 mg/day; methotrexate ≤0.4 mg/kg/week; azathioprine ≤3 mg/kg/day; or 6-mercaptopurine ≤1.5 mg/kg/day. High-level immunosuppression regimens include treatment regimens with higher than the above doses, and those on biological agents such as tumour necrosis factor antagonists or rituximab. Combination therapies increase the level of immunosuppression.

See also Table 22.2 for HZV recommendations. For children aged under 18 years, see the Starship Clinical Guideline *Immunosuppression and Infection in Rheumatology Patients* (available at www.starship.org.nz/for-health-professionals/starship-clinical-guidelines/i/immunosuppression-and-infection-in-rheumatology-patients/). For adults, see the IMAC factsheet *Immunisation for adults with immune-mediated inflammatory disease (IMID)* (available for download from: www.immune.org.nz/resources/written-resources).

Table 4.3: Immunotherapy agents for immune-mediated inflammatory disease

Note: This is not an extensive list of immunotherapy agents; new agents are continually being developed. Seek specialist advice. See also 'Oncology patients being treated with immune checkpoint inhibitors (immunostimulants)' below.

Corticosteroids	Immunosuppressive agents Disease modifying anti-rheumatic drugs (DMARDs)		Targeted biological therapies	Cytotoxics
Prednisone Prednisolone Methyl-prednisolone	DMARDs I Hydroxy-chloroquine Leflunomide Methotrexate Sulphasalazine	DMARDs II Azathioprine Cyclosporin Mycophenolate mofetil	Biological DMARDs Abatacept Anakinra Rituximab Tocilizumab Ustekinumab Anti-tumour necrosis factor DMARDs Adalimumab Etanercept Infliximab	Cyclo-phosphamide

When these agents are used singly

Source: IMAC

Oncology patients

This section provides general guidelines for vaccination after cancer treatment. Specific vaccination questions should be discussed with an expert paediatrician, infectious diseases physician or oncologist. With the exception of patients receiving immune checkpoint inhibitors, annual influenza vaccine is recommended and can be given even while a patient is on treatment (two doses four weeks apart in the first year).

Household contacts may be safely given MMR (funded; see section 11.5.3), VV (funded; see section 21.5) or age-appropriate HZV (funded if aged 65 years and older, unfunded if aged 50–64 years; see section 22.5); annual influenza vaccination is also recommended (not funded) for contacts (see section 10.5). See also 'Household contacts' in section 4.3.1.

Note: patients being treated with immune checkpoint inhibitors are the exception to these guidelines, where immunisation is relatively contraindicated. See 'Oncology patients treated with immune checkpoint inhibitors (immunostimulants)' below.

Vaccination after chemotherapy

Booster dose(s) of a diphtheria/tetanus/pertussis-containing vaccine, and hepatitis B, polio (IPV) and pneumococcal vaccines (PCV13 followed by 23PPV) should be given, starting not less than three months after chemotherapy has ended, when the lymphocyte count is >1.0 × 10^9/L.

Parenteral live viral vaccines should be delayed for at least six months after chemotherapy, but MMR and VV or age-appropriate HZV should then be given. Serological confirmation of previous VZV infection is recommended before administering HZV.[22] If VZV-seronegative, give VV (funded); if VZV-seropositive and aged 50 years and older, give HZV (funded at age 65 years with a catch-up, until 31 March 2020, for those aged 66–80 years inclusive; unfunded if aged 50–64 years). The interval may need to be extended according to:

- the intensity and type of therapy
- radiation therapy
- receipt of blood products or IG (see Table A6.1 in Appendix 6)
- underlying disease
- other factors.

For children aged under 18 years, suggested age-appropriate schedules and worksheets are available on the Starship website (www.starship.org.nz/media/199142/immunisation-2018-amended-version.pdf). For adults, see the IMAC factsheet *Immunisation for adults post-chemotherapy who are not taking immunosuppressive disease modifying drugs* (available for download from: www.immune.org.nz/resources/written-resources).

Vaccination after haematopoietic stem cell transplant (HSCT)/bone marrow transplant

Many factors can affect a transplant recipient's immunity to vaccine-preventable diseases following a successful marrow transplant. These include the donor's immunity, the type of transplant and the interval since the transplant, the continuing use of immunosuppressive drugs, and graft versus host disease. Some recipients acquire the immunity of the donor, but others lose all serological evidence of immunity.

Complete re-immunisation is recommended, starting with routine Schedule inactivated vaccines 12 months after bone marrow transplant (use Tdap for tetanus, diphtheria and pertussis immunisation if the child is aged 10 years or older).

Pneumococcal vaccines (PCV13 followed by 23PPV), meningococcal (conjugate C and quadrivalent conjugate), hepatitis B and a booster dose of Hib and IPV are all recommended.

Healthy recipients of bone marrow transplant who are immune competent can be given VV or age-appropriate HZV not less than two years after transplant, with MMR given four weeks later if VV/HZV tolerated. Serological confirmation of previous VZV infection is recommended before administering HZV. If VZV-seronegative, give VV (funded); if VZV-seropositive and aged 50 years and older, give HZV (funded at age 65 years with a catch-up, until 31 March 2020, for those aged 66–80 years inclusive; unfunded if aged 50–64 years). Second doses of MMR and VV should be given four weeks or more after the first doses, unless serological response to measles and varicella is demonstrated after the first dose. The vaccines should not be given to individuals suffering from graft versus host disease because of a risk of a resulting chronic latent virus infection leading to central nervous system sequelae.

For children aged under 18 years, suggested age-appropriate schedules and worksheets are available on the Starship website (www.starship.org.nz/media/199142/immunisation-2018-amended-version.pdf). For adults, see the IMAC factsheet *Immunisation for adults post-haematopoietic stem cell transplantation (HSCT)* (available for download from: www.immune.org.nz/resources/written-resources).

Oncology patients treated with immune checkpoint inhibitors (immunostimulants)

> Specialist advice must be sought before administering any vaccine to patients who are currently being treated with immune checkpoint inhibitors, as well as those who have discontinued treatment within the past 6 months.
>
> As this is a rapidly evolving therapy area, there are currently no international consensus statements on the use of vaccines in patients being treated with immune checkpoint inhibitors. Caution is advised, particularly with live vaccines.

Immune checkpoint inhibitors are immunostimulants, monoclonal antibodies that are used to treat several forms of advanced or metastatic cancer.[25] These medicines include PD-1 inhibitors (eg, pembrolizumab [Keytruda], nivolumab [Opdivo]), PD-L1 inhibitors (eg, atezolizumab [Tecentriq]) and CTLA-4 inhibitors (eg, ipilimumab (Yervoy]). Immune checkpoint inhibitors target proteins ('checkpoints') on T-cells.[26] By blocking these checkpoints, they allow the immune system to boost the immune response against cancer cells. A theoretical side effect of these medicines is an autoimmune-induced condition and, importantly, the autoimmune condition could occur weeks to months after stopping treatment.

While there is currently no clear safety data on the use of vaccines (live or subunit) in patients being treated with one or more immune checkpoint inhibitors, there is a theoretical risk that vaccines may trigger an autoimmune condition in these patients. There have been reports of fatal myositis, myocarditis and rhabdomyolysis in patients being treated with ipilimumab with nivolumab and administered influenza vaccine.[27] A prospective study of patients currently being treated with nivolumab or pembrolizumab and administered trivalent influenza vaccine found an increase in immune-related adverse events compared to unvaccinated patients being treated with these medicines.[28]

The Cancer Institute of New South Wales (Australia) cautions that in patients receiving combination ipilimumab and nivolumab, there have been reported cases of fatal myocarditis, myositis and rhabdomyolysis shortly after administration of the influenza vaccine. Whilst a causative

relationship to the use of influenza vaccine has not been demonstrated, caution is advised.[27]

The British Columbia Cancer Agency (Canada)[29] recommends:

- patients receiving PD-1 or PD-L1 inhibitors may receive the inactivated influenza vaccine. Live attenuated influenza vaccine (not currently available in New Zealand) should not be used in these patients
- patients on ipilimumab monotherapy or combination checkpoint inhibitors (eg, ipilimumab plus nivolumab) should not receive any vaccines within 6–8 weeks of starting treatment or within 6–8 weeks of the last dose
- patients on maintenance nivolumab following combination therapy should discuss the timing of vaccination with their doctor.

Alberta Health Services (Canada)[30] recommends:

- patients currently receiving ipilimumab alone or in combination with other anti-cancer agents, as well as those who have discontinued ipilimumab in the past six months should not receive the influenza vaccine
- patients receiving nivolumab or pembrolizumab alone or in combination with other anti-cancer agents may be immunised with the inactivated influenza vaccine; the timing of the immunisation is not clearly studied in this population, but can be considered one week post-administration of these agents. Patients should be advised to monitor themselves closely, and to report any adverse events to their oncologist.

Chronic kidney disease (CKD)

Immune response and duration of protection after immunisation decrease with advancing kidney disease, so routine Schedule and other recommended vaccines should be given as soon as kidney disease is recognised.

Individuals immunised during the early stages of CKD generally respond to immunisation, but the magnitude of response and/or more rapid waning of immunity have an influence on how well protected they are from infection or severe disease following immunisation. Cases of children developing a disease for which they have serological evidence of immunity have been reported.[31]

Patients should receive routine Schedule vaccines and annual influenza vaccine. Live viral vaccines are considered safe for individuals with CKD and minimal immunocompromise, but they are generally not recommended for individuals on immunosuppressive medicines because of the risk of vaccine virus disease.[32] However, a number of small studies suggest that the risk of disseminated VV-related disease is small and can be managed with antiviral therapy, and that varicella immunisation carries a significantly lower risk for immunosuppressed individuals than wild-type varicella disease.[24]

Individuals with nephrotic syndrome, kidney failure or end-stage kidney disease (CKD stages 4–5) have an increased risk of developing bacterial peritonitis and/or sepsis. Additional pneumococcal vaccines, a Hib booster, conjugate meningococcal vaccines and annual influenza vaccine are recommended. These individuals are also at increased risk of zoster, and may receive HZV upon specialist advice. Serological confirmation of previous VZV infection is recommended before administering HZV. If VZV-seronegative, give VV (funded if prior to transplant); if VZV-seropositive and aged 50 years and older, give HZV (funded at age 65 years with a catch-up, until 31 March 2020, for those aged 66–80 years inclusive; unfunded if aged 50–64 years).

Dialysis patients must be hepatitis B immune, with administration of repeated courses of HepB, of higher strength if required: the higher strength 40 μg HepB (HBvaxPRO) is funded for dialysis patients.

There is no relationship between immunisation and deterioration of renal function or a reduction in the efficacy of dialysis.[31]

A recommended immunisation schedule and worksheet for paediatric CKD stages 4–5 and dialysis patients is available on the Starship website (www.starship.org.nz/media/286703/vaccination-record-for-paediatric-ckd-august-2017-.pdf). For adults, see the IMAC factsheet *Immunisation for adults with end-stage kidney disease, on dialysis, or*

pre-post-kidney transplant (available for download from: www.immune.org.nz/resources/written-resources).

Solid organ transplants

Specialist advice should be sought in these situations.

An accelerated immunisation schedule is recommended for individuals likely to be listed for solid organ transplant. See Table 4.1 for infant recommendations. For adults, see the IMAC factsheet *Immunisation for adults pre-/post-solid organ transplantation (excluding kidney transplantation)* (available for download from: www.immune.org.nz/resources/written-resources).

Individuals older than 12 months who have been scheduled for solid organ transplantation should receive MMR and VV or age-appropriate HZV at least four weeks before the transplant. Serological confirmation of previous VZV infection is recommended before administering HZV.[22] If VZV-seronegative, give VV (funded); if VZV-seropositive and aged 50 years and older, give HZV (funded at age 65 years with a catch-up, until 31 March 2020, for those aged 66–80 years inclusive; unfunded if aged 50–64 years). Measles antibody titres should be measured one to two years after the transplant; immunisation may be repeated if titres are low, but only if the level of immunosuppression permits. It is advisable to check other antibody titres annually and re-immunise where indicated.

The use of passive immunisation with IG after exposure to measles or chickenpox should be based on the documentation of negative antibody titres, or where immune status is unknown. See chapter 15 for further information on pneumococcal immunisation for these individuals. VV is also funded for non-immune household contacts of transplant patients (see section 21.5).

In patients undergoing organ transplantation, pneumococcal vaccine (PCV13 first followed by 23PPV 8 weeks later, both funded) should be given at least two weeks before the transplant. Hepatitis A, hepatitis B, HPV, influenza, meningococcal conjugate and varicella vaccines are funded for transplant patients. (Re-)vaccination with age-appropriate DTaP-IPV-HepB/Hib, DTaP-IPV, Tdap and Hib vaccines is also funded. (See the relevant disease chapters.)

HIV infection

All HIV-positive children, whether symptomatic or asymptomatic, are recommended to receive the routine Schedule vaccines, including MMR (if CD4+ ≥15%), rotavirus (infants only) and HPV (three doses from age 9 years). Asymptomatic children who are not severely immunocompromised are recommended to receive MMR vaccine at age 12 months to provide early protection against the three diseases.

The efficacy of any vaccine may be reduced in HIV-positive individuals, and antibody levels may wane faster than in individuals who are HIV-negative. Although antiretroviral therapy may improve immune responses, it is unlikely these individuals will achieve the levels of antibodies seen in individuals who are HIV-negative. Serological testing and the need for additional doses (eg, of HepB, see section 8.5.7) should be discussed with the individual's specialist.

VV or age-appropriate HZV may be given upon specialist advice to HIV-positive adults (if CD4+ lymphocyte count is ≥200 cells/mm^3). Serological confirmation of previous VZV infection is recommended before administering HZV.[22] If VZV-seronegative, give VV (funded); if VZV-seropositive and aged 50 years and older, give HZV (funded at age 65 years with a catch-up, until 31 March 2020, for those aged 66–80 years inclusive; unfunded if aged 50–64 years).

Passive immunisation with IG may be required for individuals with HIV infection who are exposed to chickenpox or measles.

Tables 4.4 (children aged under 5 years when diagnosed), 4.5 (children aged 5 to under 18 years) and 4.6 (adults aged 18 years and older) summarise the additional vaccine recommendations and schedules for HIV-positive individuals. For adults, see also the IMAC factsheet *Immunisation for adults with HIV infection* (available for download from: www.immune.org.nz/resources/written-resources).

Table 4.4: Children aged under 5 years when diagnosed with HIV: additional vaccine recommendations

Note: HIV-positive children should receive the routine Schedule vaccines, including rotavirus vaccine for infants, but see the MMR recommendations below. BCG should not be given. Vaccinators are advised to refer to the Pharmaceutical Schedule (www.pharmac.govt.nz) for any changes to funding decisions.

Age at diagnosis	Vaccine (trade name)	Recommended vaccine schedule
Infants aged under 12 months when diagnosed	PCV13 (Prevenar 13)	PCV13[a] at ages 6 weeks, 3, 5 and 15 months or age-appropriate catch-up schedule: • if commencing immunisation at ages 7–11 months, give 2 doses of PCV13 at least 4 weeks apart, followed by a booster dose at age 15 months • for children aged 7–11 months who have completed the primary course with PCV10, give 1 dose of PCV13, followed by the scheduled PCV13 booster at age 15 months.
	23PPV (Pneumovax 23)	Following the completion of the PCV course, give 1 dose of 23PPV at age ≥2 years. There must be at least 8 weeks between the last PCV dose and the 23PPV dose. Revaccinate once with 23PPV, 5 years after the first 23PPV.
	Influenza (Fluarix Tetra)	Annual immunisation from age 6 months. In the first year, give 2 doses 4 weeks apart, then 1 dose in each subsequent year.
	MenCCV (NeisVac-C) and MCV4-D (Menactra)	Use the age-appropriate MenCCV schedule: • if aged under 6 months at diagnosis, give 2 doses 8 weeks apart, with a booster at age 12 months • if aged 6–11 months at diagnosis, give 1 dose, with a booster at age 12 months. At age 2 years, give 2 doses of MCV4-D[b] 8 weeks apart, then a booster after 3 years, then 5-yearly.

Continued overleaf

Age at diagnosis	Vaccine (trade name)	Recommended vaccine schedule
Children aged 12 months to under 5 years when diagnosed	PCV13 (Prevenar 13)	The PCV13[a,c] age-appropriate catch-up schedule is: • if commencing immunisation at ages 12 months or older, give 2 doses of PCV13,[c] 8 weeks apart • children aged >17 months who have completed the primary course of PCV10 but not received PCV13, give 1 dose of PCV13.[c,d]
	23PPV (Pneumovax 23)	Following the completion of the PCV course, give 1 dose of 23PPV at age ≥2 years. There must be at least 8 weeks between the last PCV dose and the 23PPV dose. Revaccinate once with 23PPV, 5 years after the 1st 23PPV.
	Influenza (Fluarix Tetra if aged <3 years; Influvac Tetra if aged ≥3 years)	Annual immunisation. In previously unvaccinated children, give 2 doses 4 weeks apart, then 1 dose in each subsequent year.
	MMR[e] (Priorix)	If CD4+ lymphocyte percentage is ≥15%: • give the 1st MMR dose at age 12 months, followed by the 2nd dose 4 weeks later.
	Varicella[e,f] (Varilrix)	If CD4+ lymphocyte percentage is ≥15%: • give 2 doses (starting 4 weeks after the 2nd MMR), at least 3 months apart.
	MenCCV (NeisVac-C) and MCV4-D (Menactra)	If aged 12–23 months at diagnosis, give 1 dose of MenCCV; followed by MCV4-D[b] at age 2 years, 2 doses 8 weeks apart; then a booster of MCV4-D after 3 years; then 5-yearly. If aged ≥2 years at diagnosis, give 2 doses of MCV4-D[b] 8 weeks apart; then a booster of MCV4-D after 3 years; then 5-yearly.

a PCV13 replaces PCV10 (Synflorix) on the Schedule.

b Give MCV4-D at least 4 weeks after PCV13[13, 14] (see section 12.4.4).

c If 23PPV has already been given (prior to any doses of PCV13) to children aged under 18 years, wait at least 8 weeks before administering PCV13.

d There are no safety concerns, regardless of the interval between the last dose of PCV10 and the 1st dose of PCV13.

e Only a single viral vaccine is recommended at each visit for individuals with HIV infection. A minimum interval of 4 weeks is required between live vaccine doses administered at different visits.

f Give VV on the advice of an HIV specialist.

Source: Starship Children's Health.

Table 4.5: Children aged 5 to under 18 years when diagnosed with HIV: additional vaccine recommendations

Note: HIV-positive children should receive the routine Schedule vaccines, but see the MMR recommendations below. BCG should not be given. Vaccinators are advised to refer to the Pharmaceutical Schedule (www.pharmac.govt.nz) for any changes to funding decisions.

Vaccine (trade name)	Recommended vaccine schedule
HPV9 (Gardasil 9)	From age 9 years, give 3 doses of HPV at 0, 2 and 6 months.[a,b]
PCV13 (Prevenar 13)	For children who have not previously received PCV13, give 1 dose of PCV13.[c]
23PPV (Pneumovax 23)	1 dose of 23PPV at least 8 weeks after the PCV13 dose. Revaccinate once with 23PPV, 5 years after the 1st 23PPV.
Influenza (Influvac Tetra)	Annual immunisation. Regardless of age, if previously unvaccinated, give 2 doses[d] 4 weeks apart. Then give 1 dose in each subsequent year.
MMR[e] (Priorix)	If aged ≤13 years and CD4+ lymphocyte percentage is ≥15%, or if aged ≥14 years and CD4+ lymphocyte count is ≥200 cells/mm^3: • give 2 MMR doses at least 4 weeks apart.
Varicella[e,f] (Varilrix)	If no history of varicella disease or immunisation, and if aged ≤13 years and CD4+ lymphocyte percentage is ≥15%, or if aged ≥14 years and CD4+ lymphocyte count is ≥200 cells/mm^3: • give 2 doses (starting 4 weeks after 2nd MMR), at least 3 months apart.
MCV4-D (Menactra)	Give 2 doses of MCV4-D[g] 8 weeks apart, and: • if the 1st MCV4-D dose was given at age <7 years, give a booster after 3 years, then 5-yearly, or • if the 1st MCV4-D dose was given at age ≥7 years, give a booster dose every 5 years.

a Individuals who started with HPV4 may complete their remaining doses with HPV9.

b HPV9 is registered for use from age 9 years.

c If 23PPV has already been given (prior to any doses of PCV13) to children aged under 18 years, wait at least 8 weeks before administering PCV13.

d The 2nd dose of influenza vaccine is not funded for individuals aged 9 years and older.

e Only a single viral vaccine is recommended at each visit for individuals with HIV infection. A minimum interval of 4 weeks is required between live vaccine doses administered at different visits.

f Give VV on the advice of an HIV specialist.

g Give MCV4-D at least 4 weeks after PCV13[13, 14] (see section 12.4.4).

Source: Starship Children's Health.

Table 4.6: Adults aged 18 years and older when diagnosed with HIV: additional vaccine recommendations

Note: HIV-positive individuals should receive the routine Schedule vaccines, but see the MMR and HZV recommendations in the table below. BCG should not be given. Vaccinators are advised to refer to the Pharmaceutical Schedule (www.pharmac.govt.nz) for any changes to funding decisions.

Vaccine (trade name)	Recommended vaccine schedule
HPV9 (Gardasil 9)	For individuals aged 26 years and under: 3 doses of HPV9 at 0, 2 and 6 months.[a]
PCV13 (Prevenar 13)	1 dose of PCV13.[b]
23PPV (Pneumovax 23)	Give a maximum of 3 doses of 23PPV in a lifetime, a minimum of 5 years apart. The 1st 23PPV dose is given at least 8 weeks after PCV13, the 2nd a minimum of 5 years later, the 3rd dose at age ≥65 years.
Influenza (Influvac Tetra)	Annual immunisation. If previously unvaccinated, give 2 doses[c] 4 weeks apart. Then give 1 dose in each subsequent year.
MMR[d] (Priorix)	If born in 1969 or later and has no record of 2 previous MMR doses and CD4+ lymphocyte count is ≥200 cells/mm^3: • give 1 or 2 MMR doses 4 weeks apart (so individual has 2 documented doses of MMR).
Varicella[d,e] (Varilrix) or Herpes zoster[d,e,f] (Zostavax)	If VZV-seronegative and CD4+ lymphocyte count is ≥200 cells/mm^3: • give 2 doses of VV at least 4 weeks apart. If aged 50 years and older[f] and VZV-seropositive and CD4+ lymphocyte count is ≥200 cells/mm^3: • give 1 dose of HZV.[f]
Hepatitis B (HBvaxPRO 10 µg or Engerix-B 20 µg)	If previously unvaccinated, give 4 doses, at 0, 1, 2 and 12 months.[g]
MCV4-D (Menactra)	Give 2 doses of MCV4-D 8 weeks apart, then 1 dose every 5 years.[h,i]

a Individuals who started with HPV4 may complete their remaining doses with HPV9.

b If 23PPV has already been given (prior to any doses of PCV13) to adults aged 18 years and older, wait at least 1 year before administering PCV13.

c The 2nd dose of influenza vaccine is not funded for individuals aged 9 years and older.

d Only a single viral vaccine is recommended at each visit for individuals with HIV infection. A minimum interval of 4 weeks is required between live vaccine doses administered at different visits.

e Give VV or HZV on the advice of an HIV specialist. Serological confirmation of previous VZV infection is recommended before administering HZV.[22]

f HZV is registered for use in adults from age 50 years. Funded for adults at age 65 years (with a catch-up, until 31 March 2020, for ages 66–80 years, inclusive). Unfunded for adults aged 50–64 years.

g Consider screening for seroconversion after vaccination (see section 8.5.7). The 40 µg HepB dose may be recommended but is not funded.

h Give MCV4-D at least 4 weeks after PCV13[13, 14] (see section 12.4.4).

i MCV4-D is registered for individuals aged 9 months to 55 years, but there are not expected to be any safety concerns when administered to adults older than 55 years.

Source: Starship Children's Health.

4.3.4 Asplenia

There are three main reasons why an individual may not have a functioning spleen:

- surgical removal (eg, post-trauma)
- disease (eg, sickle cell disease, thalassaemia)
- congenital asplenia or polysplenia (eg, with congenital heart disease).

All asplenic individuals are at increased risk of fulminant bacteraemia, which is associated with a high mortality rate. The risk is greatest for infants, and probably declines with age and with the number of years since onset of asplenia.

The degree of risk of death from sepsis is also influenced by the nature of the underlying disease: it is increased 50 times (compared with healthy children) in asplenia after trauma and 350 times in asplenia with sickle cell disease, and the risk may be even higher post-splenectomy for thalassaemia.

Streptococcus pneumoniae is the pathogen that most often causes fulminant sepsis in these individuals. Other less frequent pathogens are *Neisseria meningitidis*, *Haemophilus influenzae* type b, other streptococci, *Staphylococcus aureus*, *Escherichia coli* and other gram-negative bacilli (eg, *Klebsiella*, *Salmonella* species and *Pseudomonas aeruginosa*). There is an increased fatality from malaria for asplenic individuals.

More information about asplenia is available on the Starship website (www.starship.org.nz/for-health-professionals/starship-clinical-guidelines/a/asplenia/).

Immunisation of asplenic individuals

No vaccines are contraindicated for individuals with functional or anatomical asplenia. It is important to ensure that the individual is up to date with the routine immunisations according to the National Immunisation Schedule, especially pneumococcal, Hib and MMR.

In addition to the routine Schedule vaccines, including VV at age 15 months or 11 years and HPV vaccine for individuals aged 26 years and under, the following vaccines are funded and/or recommended as soon as the asplenic condition is recognised. The immunisation schedules are age-dependent and are provided in Table 4.7 below.

- Pneumococcal conjugate and polysaccharide vaccines are funded for asplenic children and adults (see also chapter 15). If children have commenced immunisation with PCV10, they can complete it with PCV13, followed by 23PPV at the appropriate age.
- Meningococcal conjugate vaccine is funded for all asplenic individuals (see also chapter 12). Meningococcal C conjugate vaccine (MenCCV; NeisVac-C) is recommended for children aged under 2 years, followed by quadrivalent meningococcal vaccine (MCV4-D; Menactra) at age 2 years. MCV4-D is recommended for individuals aged 2 years and older.
- Hib vaccine – because of an increased risk of infection, it is particularly important that all asplenic individuals receive the Hib vaccine (funded) (see also chapter 6).
- Annual influenza vaccine is recommended for all asplenic individuals from 6 months of age (funded for individuals pre- and post-splenectomy) (see also chapter 10).
- Age-appropriate pertussis-containing vaccine is funded for (re-)vaccination of individuals pre- or post-splenectomy (see chapter 14).

For elective splenectomy, immunisations should be commenced as soon as possible and at least two weeks pre-operatively. For emergency splenectomy, commence immunisations two weeks post-operatively.

Prior to commencing immunisation, discuss with the individual's specialist.

Table 4.7: Additional vaccine recommendations (funded and unfunded) and schedules for individuals with functional or anatomical asplenia

Note: Individuals with functional or anatomical asplenia should receive the routine Schedule vaccines, including varicella at age 15 months or 11 years and HPV for individuals aged 9–26 years, following recommended catch-up schedules if necessary. Funded vaccines are in the shaded rows, however vaccinators are advised to refer to the Pharmaceutical Schedule (www.pharmac.govt.nz) for any changes to funding decisions.

Age at diagnosis	Vaccine (trade name)	Recommended vaccine schedule
Aged under 12 months when diagnosed with functional asplenia or pre-[a] or post-splenectomy	PCV13 (Prevenar 13)	PCV13 at ages 6 weeks and 3, 5 and 15 months. If commencing immunisation at ages 7–11 months, give 2 doses of PCV13 at least 4 weeks apart, followed by a booster dose at age 15 months.
	23PPV (Pneumovax 23)	Following the completion of the PCV course, give 1 dose of 23PPV at age ≥2 years. There must be at least 8 weeks between the last PCV dose and the 23PPV dose. Revaccinate once with 23PPV, 5 years after the 1st 23PPV.
	MenCCV (NeisVac-C) and MCV4-D (Menactra)	Age-appropriate MenCCV schedule: • if aged under 6 months at diagnosis, give 2 doses 8 weeks apart, with a booster at age 12 months • if aged 6–11 months at diagnosis, give 1 dose, with a further dose at age 12 months. At age 2 years, give 2 doses of MCV4-D[b] 8 weeks apart, then a booster dose after 3 years, then 5-yearly.
	Influenza (Fluarix Tetra)	Annual immunisation[c] from age 6 months. In the first year, give 2 doses 4 weeks apart, then 1 dose in each subsequent year.

Continued overleaf

Age at diagnosis	Vaccine (trade name)	Recommended vaccine schedule
Aged 12 months to under 18 years when diagnosed with functional asplenia or pre-[a] or post-splenectomy	PCV13 (Prevenar 13)	PCV13[d] age-appropriate catch-up schedule: • previously unimmunised children aged ≥12 months to under 5 years require 2 doses of PCV13,[d] 8 weeks apart • previously unimmunised children aged 5 years to under 18 years require 1 dose of PCV13[d] • children aged >17 months who have completed the primary course of PCV10 but have not received PCV13, give 1 dose of PCV13.[e]
	23PPV (Pneumovax 23)	Following the completion of the PCV13 course, give 1 dose of 23PPV at age ≥2 years. There must be at least 8 weeks between the last PCV13 dose and the 23PPV dose. Revaccinate once with 23PPV, 5 years after the 1st 23PPV.
	MenCCV (NeisVac-C) and MCV4-D (Menactra)	If aged 12–23 months at diagnosis, give 1 dose of MenCCV, followed by MCV4-D[b] at age 2 years, 2 doses 8 weeks apart; then a booster of MCV4-D after 3 years, then 5-yearly. If aged ≥2 years at diagnosis, give 2 doses of MCV4-D[b] 8 weeks apart, and: • if the 1st MCV4-D dose was given at age <7 years, give a booster after 3 years, then 5-yearly, or • if the 1st MCV4-D dose was given at age ≥7 years, give a booster dose every 5 years.
	Hib (Hiberix)	If aged 12–15 months, give 1 dose at age 15 months as per the National Immunisation Schedule.[f] If aged 16 months to under 5 years and has not received a single Hib dose after age 12 months, give 1 dose.[f] If aged 5 years and older, give 1 dose, even if fully vaccinated.[f]

Continued overleaf

Age at diagnosis	Vaccine (trade name)	Recommended vaccine schedule
Aged 12 months to under 18 years when diagnosed with functional asplenia or pre-[a] or post-splenectomy (continued)	Influenza (Fluarix Tetra if aged under 3 years; Influvac Tetra if aged 3 years and older)	Annual immunisation.[c] In previously unimmunised children aged under 9 years, give 2 doses 4 weeks apart, then 1 dose in each subsequent year.
	Varicella (Varilrix)	Give 1 dose at age 15 months, as per the National Immunisation Schedule.[g,h] If no history of varicella disease or immunisation, give 1 dose at age 11 years.[i]
	Varicella (Varilrix or Varivax)	For susceptible children who do not meet the eligibility criteria for funded vaccine: • if aged under 13 years, give 1 dose[h] • if aged 13 years and older, give 2 doses, at least 6 weeks apart.
Aged ≥18 years when diagnosed with functional asplenia or pre-[a] or post-splenectomy	PCV13 (Prevenar 13)	1 dose of PCV13.[j]
	23PPV (Pneumovax 23)	Give a maximum of 3 doses of 23PPV in a lifetime, a minimum of 5 years apart. The 1st 23PPV dose is given at least 8 weeks after PCV13; the 2nd a minimum of 5 years later; the 3rd dose at age ≥65 years.
	MCV4-D (Menactra)	Give 2 doses of MCV4-D, 8 weeks apart, then 1 dose every 5 years.[b,k]
	Hib (Hiberix)	Give 1 dose of Hib, regardless of previous vaccination history.
	Tdap (Boostrix)	If partially immunised or unimmunised: • give up to 3 doses[l] of Tdap, 4 weeks apart to complete a 3-dose primary course. If fully immunised: • give 1 dose of Tdap.
	Influenza (Influvac Tetra)	Annual immunisation.[c]
	Varicella (Varilrix or Varivax)	If no history of varicella disease or immunisation, give 2 doses, at least 6 weeks apart.

a Where possible, the vaccines should be administered at least 2 weeks before elective splenectomy. For emergency splenectomy, the vaccines should be administered 2 weeks post-operatively.

b Give MCV4-D at least 4 weeks after PCV13[13, 14] (see section 12.4.4).

c Influenza vaccine is recommended but not funded for individuals with functional asplenia.

d If 23PPV has already been given (prior to any doses of PCV13) to children aged under 18 years, wait at least 8 weeks before administering PCV13.

e There are no safety concerns, regardless of the interval between the last dose of PCV10 and the 1st dose of PCV13.

f Hib is not required if the child is being revaccinated with DTaP-IPV-HepB/Hib.

Continued overleaf

g Funded for children who were born on or after 1 April 2016.

h A second VV dose is not currently funded but may be purchased for those who wish to reduce the risk of breakthrough disease.

i Funded for previously unvaccinated children who are turning 11 years old on or after 1 July 2017 who have not previously had a varicella infection.

j If 23PPV has already been given (prior to any doses of PCV13) to adults aged 18 years and older, wait at least 1 year before administering PCV13.

k MCV4-D is registered for individuals aged 9 months to 55 years, but there are not expected to be any safety concerns when administered to adults older than 55 years.

l Although Tdap is not registered for use as a primary course, there are expected to be to be no safety concerns.

Source: Starship Children's Health.

4.3.5 Other high-risk individuals

Individuals with chronic lung diseases should receive influenza and pneumococcal vaccines. See chapters 10 and 15.

4.3.6 (Re-)vaccination following immunosuppression

All vaccines on the National Immunisation Schedule are funded for (re-)vaccination of individuals following immunosuppression. Note that the period of immunosuppression due to steroid or other immunosuppressive therapy must be longer than 28 days. The timing and number of doses should be discussed with the individual's specialist.

See also the individual disease chapters.

4.4 Immigrants and refugees

4.4.1 Introduction

Adults and children who enter New Zealand as refugees or immigrants will need an assessment of their *documented* vaccination status and an appropriate catch-up programme planned.

Regardless of their immigration and citizenship status, all children aged under 18 years are eligible to receive Schedule vaccines, and providers can claim the immunisation benefit for administering the vaccines (see the 'Eligibility for publicly funded vaccines' section in the Introduction to this *Handbook*). All children are also eligible for Well Child Tamariki Ora services, regardless of immigration and citizenship status. For more information about eligibility for publicly funded services, see the Ministry of Health website (www.health.govt.nz/eligibility).

Children who have been previously immunised in low-income country may have received BCG, three doses of DTwP and oral polio vaccine (and/or IPV) in the first six months of life, and a dose of measles vaccine between 9 and 15 months of age. However, they are unlikely to have received Hib, pneumococcal, HepB, MMR or VV. Many countries, including European countries, do not have HepB included in their national childhood immunisation schedule. For immigrant children a catch-up immunisation plan may be needed.

If a refugee or immigrant has no valid documentation of vaccination, an age-appropriate catch-up programme is recommended (see Appendix 2). The programme may require modification for any **documented** doses: only clearly documented doses should be considered as given.

Details of immunisation schedules of other countries can be found on the WHO website (http://apps.who.int/immunization_monitoring/globalsummary/schedules). See also the *Recommendations for Comprehensive Post-Arrival Health Assessment for People from Refugee-like Backgrounds (2016 edition)*, available on the Australasian Society for Infectious Diseases website (www.asid.net.au/resources/clinical-guidelines).

4.4.2 Tuberculosis

TB is an important public health problem for refugees and immigrants. Figures from the US show that approximately 1–2 percent of refugees are suffering from active TB on arrival, and about half have positive tuberculin skin tests. The number who have received BCG immunisation is unknown. In New Zealand there is a significant increasing trend in the number of TB cases in overseas-born people.

Suspected TB must be appropriately investigated. If individuals are known to have been recently exposed but tests are negative, they should be tested again three months later to identify recently acquired infection. Previous BCG immunisation should be considered when interpreting tuberculin skin test results (see chapter 20).

In New Zealand, the policy is to offer BCG vaccination to infants at increased risk of TB who:

- will be living in a house or family/whānau with a person with either current TB or a history of TB
- have one or both parents or household members or carers who within the last five years lived for a period of six months or longer in countries with a rate ≥40 per 100,000
- during their first five years will be living for three months or longer in a country with a rate ≥40 per 100,000 (see Appendix 8 for a list of the high-incidence countries).

4.4.3 Hepatitis B

If a member of an immigrant or refugee family is found to have chronic HBV infection, it is recommended that all the family be screened and immunisation offered to all those who are non-immune. Even if no one in the family has chronic HBV infection, it is recommended that all children aged under 18 years be vaccinated against hepatitis B. See chapter 8 for more information and Appendix 2 for catch-up schedules.

4.4.4 Varicella

People who have grown up in the tropics are less likely to have had chickenpox and may be non-immune adolescents and adults. Because adult chickenpox can be severe, if there is no history of chickenpox, VV should be offered (although it is currently not funded).

4.5 Travel

All travellers should be encouraged to consider vaccination requirements well in advance of overseas travel. For example, information on diphtheria, MMR, influenza and hepatitis A vaccination for adults is included in the appropriate sections of this *Handbook*. Up-to-date information on overseas travel requirements (eg, for typhoid, yellow fever, rabies, Japanese encephalitis) can be obtained from the Centers for Disease Control and Prevention (wwwnc.cdc.gov/travel) or the WHO (www.who.int/ith/en/).

4.6 Occupational and other risk factors

Certain occupations result in increased risk of contracting some vaccine-preventable diseases. Some infected workers, particularly health care workers and those working in early childhood education services, may transmit infections such as influenza, rubella, measles, mumps, varicella and pertussis to susceptible contacts, with the potential for serious outcomes.

Where workers are at significant occupational risk of acquiring a vaccine-preventable disease, the employer should implement a comprehensive occupational immunisation programme, including immunisation policies, staff immunisation records, information about the relevant vaccine-preventable diseases and the management of vaccine refusal. Employers should take all reasonable steps to encourage susceptible workers to be immunised.

The vaccines in Table 4.8 are recommended for certain occupational groups and in Table 4.9 for those with other risk factors. In addition to the vaccines listed below, all adults should be up to date with routinely recommended vaccines, such as MMR (see section 2.1.7 or Appendix 2).

If a non-immune individual is exposed to a vaccine-preventable disease, post-exposure prophylaxis and control measures should be administered where indicated (see the relevant disease chapters and the *Communicable Disease Control Manual 2012*[33]).

Table 4.8: Recommended vaccines, by occupational group

Occupation	Recommended vaccines
Health care workers	
Medical, nursing, lead maternity carers, other health professional staff and students	Hepatitis B (if susceptible) MMR (if susceptible) Influenza, annually Varicella (if susceptible) Hepatitis A (if work with children) Tetanus, diphtheria and pertussis (Tdap) (if work with children)
Individuals who work with children	
Early childhood education services staff	Hepatitis A Hepatitis B (if susceptible) MMR (if susceptible) Influenza, annually Varicella (if susceptible) Tdap
Other individuals working with children, including: • correctional staff working where infants/children live with mothers • school teachers (including student teachers) • outside school hours carers • child counselling services workers • youth services workers	Influenza, annually MMR (if susceptible) Tdap Varicella (if susceptible)
Carers	
Health care assistants, long-term facility carers, nursing home staff	Hepatitis A (if exposed to faeces) Hepatitis B (if susceptible) Influenza, annually MMR (if susceptible) Tdap Varicella (if susceptible)

Continued overleaf

Occupation	Recommended vaccines
Emergency and essential service workers	
Police and emergency workers	Hepatitis B (if susceptible) Influenza, annually Tetanus (Td or Tdap)
Armed forces personnel	Hepatitis B (if susceptible) Influenza, annually MMR (if susceptible) Tetanus (Td or Tdap) Hepatitis A (if deployed to high-risk countries) Meningococcal C conjugate or quadrivalent meningococcal conjugate (if living in close quarters) Quadrivalent meningococcal conjugate, yellow fever, rabies, typhoid, Japanese encephalitis (as appropriate, if deployed to high-risk countries)
Staff of correctional facilities	Hepatitis B (if susceptible) Influenza, annually MMR (if susceptible)
Staff of immigration/refugee centres	Hepatitis B (if susceptible) Influenza, annually MMR (if susceptible)
Laboratory staff	
Laboratory staff	Hepatitis B (if susceptible) MMR (if susceptible) Influenza, annually Hepatitis A (if exposed to faeces) IPV
Laboratory staff regularly working with *Neisseria meningitidis*	Quadrivalent meningococcal conjugate vaccine
Individuals who work with animals	
Veterinarians, veterinary students, veterinary nurses	Influenza, annually BCG (if exposed to infected animals)

Continued overleaf

Occupation	Recommended vaccines
Zoo staff who work with primates	Hepatitis A Influenza, annually
Poultry workers and others handling poultry, including those who may be involved in culling during an outbreak of avian influenza, and swine industry workers	Influenza, annually
Other individuals exposed to human tissue, blood, body fluids or sewage	
Workers who perform skin penetration procedures (eg, tattooists, body-piercers)	Hepatitis B (if susceptible)
Funeral workers, embalmers and other workers who have regular contact with human tissue, blood or body fluids and/or used needles or syringes	Hepatitis B (if susceptible)
Sewage workers, plumbers or other workers in regular contact with untreated sewage	IPV Hepatitis A
Sex workers	Hepatitis B (if susceptible) HPV

Table 4.9: Recommended vaccines for those with other risk factors

Risk factor	Recommended vaccines
Individuals living in hostels or other close quarters (eg, university hostels, boarding schools)	Hepatitis B (if susceptible) MMR (if susceptible) Influenza, annually Meningococcal C conjugate or quadrivalent meningococcal conjugate*
Individuals in correctional facilities	Hepatitis B (if susceptible) MMR (if susceptible) Influenza, annually Meningococcal C conjugate
Men who have sex with men	Hepatitis B (if susceptible) Hepatitis A HPV
Intravenous drug users	Hepatitis B (if susceptible) Hepatitis A Influenza, annually

* Quadrivalent meningococcal conjugate vaccine is recommended if future travel is likely.

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5 Diphtheria

Key information

Mode of transmission	Contact with respiratory droplets or infected skin of a case or carrier or, more rarely, contaminated articles.
Incubation period	Usually 2–5 days, occasionally longer.
Period of communicability	Variable; usually 2 weeks or less, seldom more than 4 weeks. Carriers may shed for longer. Effective antimicrobial therapy promptly terminates shedding.
Funded vaccines	DTaP-IPV-HepB/Hib (Infanrix-hexa). DTaP-IPV (Infanrix-IPV). Tdap (Boostrix). Td (ADT Booster).
Dose, presentation, route	0.5 mL per dose. DTaP-IPV-HepB/Hib: pre-filled syringe and glass vial. The vaccine must be reconstituted prior to injection. DTaP-IPV, Tdap, Td: pre-filled syringe. Intramuscular injection.
Funded vaccine indications and schedule	6 weeks, 3 months and 5 months: DTaP-IPV-HepB/Hib. 4 years: DTaP-IPV. 11 years: Tdap. 45 and 65 years: Td (administration not funded). During pregnancy (from 28 to 38 weeks' gestation): Tdap. For (re-)vaccination of eligible patients: DTaP-IPV-HepB/Hib, DTaP-IPV, Tdap or Td. For testing for primary immune deficiencies: Td.
Dose interval between Td and Tdap	No minimum interval is required between Td and Tdap, unless Tdap is being given as part of a primary immunisation course.
Vaccine efficacy/ effectiveness	87–98 percent protection has been demonstrated using population-based analysis. Immunised cases have been shown to have less severe disease.
Herd immunity	≥70 percent of the childhood population must be immune to diphtheria to prevent major community outbreaks.

5.1 Bacteriology

Diphtheria is a serious, often fatal, toxin-mediated disease caused by *Corynebacterium diphtheriae*, a non-sporulating, non-encapsulated, gram-positive bacillus. Rarely, it may also be caused by other toxin-carrying Corynebacteria species, such as *Corynebacterium ulcerans*.

5.2 Clinical features

Classic diphtheria characteristically involves membranous inflammation of the upper respiratory tract, with involvement of other tissues, especially the myocardium and peripheral nerves. The organism itself is rarely invasive, but a potent exotoxin produced by some strains (toxigenic strains) causes tissue damage through local and systemic actions. There is also a cutaneous form of diphtheria, which is typically less severe. The detection of either *C. diphtheriae* or *C. ulcerans* is notifiable to the medical officer of health, and the isolates should be referred to the Institute of Environmental Science and Research (ESR) for toxin detection. Transmission is by respiratory tract droplets, or by direct contact with skin lesions or contaminated articles. Cutaneous toxigenic diphtheria is more efficiently transmitted than respiratory toxigenic diphtheria.[1, 2] Humans are the only known host for diphtheria, and the disease is usually spread by close personal contact with a case or carrier, or occasionally by fomites or food. The disease remains communicable for up to four weeks after infection, but carriers of *C. diphtheriae* may continue to shed the organism and be a source of infection for much longer.

Diphtheria has a gradual onset after an incubation period of two to five days. Symptoms and signs may be mild at first, but progress over one to two days with the development of a mildly painful tonsillitis or pharyngitis with an associated greyish membrane. Diphtheria should be suspected particularly if the membrane extends to the uvula and soft palate. The nasopharynx may also be obstructed by a greyish membrane, which leaves a bleeding area if disturbed. The breath of a patient with diphtheria has a characteristic mousy smell.

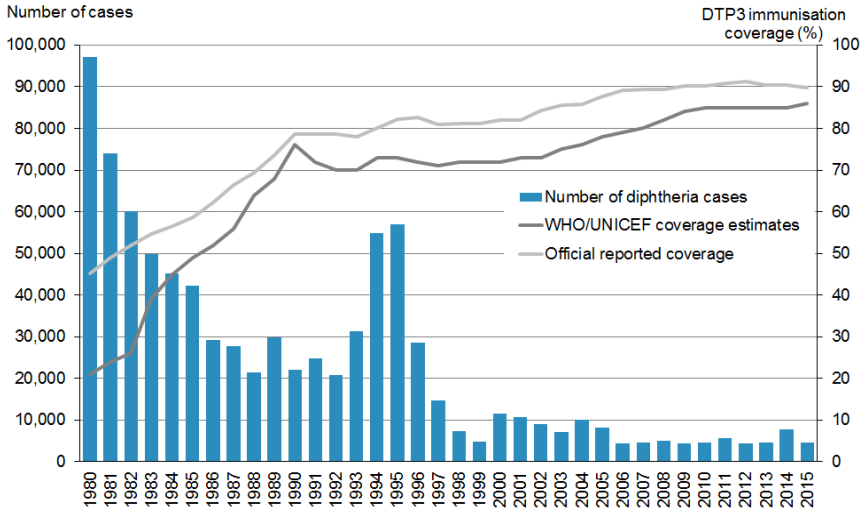
The major complication of diphtheria is respiratory obstruction, although the majority of deaths are due to the effects of diphtheria toxin on various organs. Of particular importance are the effects of the toxin on the myocardium (leading to myocarditis and heart failure), peripheral nerves (resulting in demyelination and paralysis), and the kidneys (resulting in tubular necrosis). The neuropathy begins two to eight weeks after disease onset, while the myocarditis can be early or late.

5.3 Epidemiology

5.3.1 Global burden of disease

In the pre-immunisation era diphtheria was predominantly a disease of children aged under 15 years; most adults acquired immunity without experiencing clinical diphtheria. Asymptomatic carriage was common (3–5 percent) and important in perpetuating both endemic and epidemic diphtheria. The global incidence of diphtheria dropped dramatically during the 20th century. Immunisation played a large part, but may not be wholly responsible for this reduction (see Figure 5.1). The estimated total number of diphtheria cases globally has fallen from just under 100,000 cases in 1980 to 4,530 cases in 2015.[3] Approximately half of the diphtheria cases in 2015 occurred in India.[4]

Figure 5.1: Diphtheria global annual reported cases and DTP3* immunisation coverage, 1980–2015



* DTP3 refers to the third dose of diphtheria, tetanus and pertussis vaccine.

Source: World Health Organization. *Immunization, Vaccines and Biologicals: Monitoring and surveillance – Data, statistics and graphs.* URL: http://www.who.int/immunization/monitoring_surveillance/data/en/ (accessed 13 February 2017).

Immunisation leads to the disappearance of toxigenic strains, but a bacteriophage containing the diphtheria toxin gene can infect and rapidly confer toxigenicity to non-toxigenic strains. This makes the return of epidemic diphtheria a real threat when there is insufficient herd immunity, as happened in the states of the former Soviet Union during 1990–97. Factors contributing to this epidemic included a large population of susceptible adults, decreased childhood immunisation, suboptimal socioeconomic conditions and high population movement.[5] Diphtheria remains endemic in these countries, as well as in countries in Asia and the South Pacific, including Afghanistan, Bangladesh, Cambodia, China, India, Indonesia, Malaysia, Nepal, Pakistan, Papua New Guinea, the Philippines, Thailand, Vietnam and the Pacific Islands.[6,7]

Diphtheria is rare in high-income countries such as New Zealand due to active immunisation with diphtheria toxoid-containing vaccine.

However, continuing endemic cutaneous diphtheria in indigenous communities has been reported from the US, Canada and Australia. Small diphtheria outbreaks still occur in high-income countries.[8] These often appear to be caused by unvaccinated or partially vaccinated individuals travelling to endemic countries.

The overall case fatality rate for clinical diphtheria is 5–10 percent, with higher death rates (up to 20 percent) among persons younger than 5 and older than age 40 years. The case-fatality rate for diphtheria has changed very little during the last 50 years.[9]

5.3.2 New Zealand epidemiology

Diphtheria infection was common in New Zealand until the 1960s. The last case of toxigenic respiratory diphtheria was reported in 1998.[10] Low numbers of cutaneous toxigenic diphtheria are regularly notified in New Zealand: two confirmed cases were notified in 2015 in refugees from Afghanistan, and two cases were notified in 2014.[11] These cases required large-scale public health responses to identify, prophylax and vaccinate local contacts.[7]

Travel to endemic countries is an important risk factor for infection, but transmission within New Zealand can occur to susceptible contacts of cutaneous cases. Tattooing practices in the Pacific Islands have also been implicated in outbreaks in New Zealand.[12]

The 2005–2007 National Serosurvey of Vaccine Preventable Diseases found that 61 percent of 6–10-year-olds, 77 percent of 11–15-year-olds, 71 percent of 16–24-year-olds, 48 percent of 25–44-year-olds and 46 percent of ≥45-year-olds had presumed protective levels of diphtheria antibody.[13] The decline apparent with age suggests there is likely to be a large and increasing pool of adults who may be susceptible to diphtheria in New Zealand, despite the introduction of adult tetanus and diphtheria (Td) vaccination in 1994.

5.4 Vaccines

Diphtheria toxoid is prepared from cell-free purified diphtheria toxin treated with formaldehyde. It is a relatively poor immunogen, which, to improve its efficacy, is usually adsorbed onto an adjuvant, either aluminium phosphate or aluminium hydroxide.

Diphtheria toxoid is only available as a component of combination vaccines (in New Zealand as DTaP-IPV-HepB/Hib, DTaP-IPV, Tdap and Td).

See Appendix 1 for the history of diphtheria toxoid-containing vaccines in New Zealand.

5.4.1 Available vaccines

Funded diphtheria vaccines

The diphtheria toxoid-containing vaccines funded as part of the Schedule are as follows.

DTaP-IPV-HepB/Hib (Infanrix-hexa, GSK): diphtheria, tetanus, acellular pertussis, inactivated polio, hepatitis B and *Haemophilus influenzae* type b vaccine, which contains:

- not less than 30 IU of diphtheria and 40 IU of tetanus toxoids and three purified *Bordetella pertussis* antigens (25 µg of pertussis toxoid; 25 µg of filamentous hemagglutinin; 8 µg of pertactin, a 69 kilodalton outer membrane protein) adsorbed onto aluminium salts
- three types of inactivated polio viruses: 40 D-antigen units of type 1 (Mahoney), 8 D-antigen units of type 2 (MEF-1) and 32 D-antigen units of type 3 (Saukett)
- 10 µg of purified major surface antigen (HBsAg) of the hepatitis B virus (HBV)
- 10 µg of purified polyribosylribitol phosphate (PRP) capsular polysaccharide of *Haemophilus influenzae* type b (Hib), covalently bound to 20–40 µg tetanus toxoid, adsorbed onto aluminium salts

- lactose, sodium chloride, Medium 199, potassium chloride, disodium phosphate, monopotassium phosphate, polysorbate 20 and 80, glycine, formaldehyde, neomycin sulphate and polymyxin B sulphate, which are also present as other components or as trace residuals from the manufacturing process.

DTaP-IPV (Infanrix-IPV, GSK): diphtheria, tetanus, acellular pertussis and inactivated polio vaccine, in the same quantities as for Infanrix-hexa above. Other components and residuals include sodium chloride, aluminium salts, Medium 199, potassium chloride, disodium phosphate, monopotassium phosphate, polysorbate 80, glycine, formaldehyde, neomycin sulphate and polymyxin B sulphate.

Tdap (Boostrix, GSK): a smaller adult dose of diphtheria toxoid and pertussis antigens together with tetanus toxoid. Tdap contains not less than 2 IU of diphtheria toxoid, not less than 20 IU of tetanus toxoid, 8 µg of pertussis toxoid, 8 µg of filamentous hemagglutinin and 2.5 µg of pertactin, adsorbed onto aluminium salts. Other components and trace residuals include sodium chloride, formaldehyde, polysorbate 80 and glycine.

Td (ADT Booster, Seqirus (NZ) Ltd): a smaller adult dose of diphtheria toxoid together with tetanus toxoid. Td contains not less than 2 IU of purified diphtheria toxoid and not less than 20 IU of purified tetanus toxoid. Other components and residuals include aluminium hydroxide, sodium chloride, sodium hydroxide and formaldehyde.

Other vaccines

Other diphtheria toxoid-containing vaccines registered (approved for use) and available (marketed) in New Zealand are:

- Tdap: Adacel (Sanofi)
- Tdap-IPV: Adacel Polio (Sanofi).

5.4.2 Efficacy and effectiveness

Immunity against diphtheria occurs via an antibody-mediated response to the diphtheria toxin and is primarily of the IgG type. Antitoxin antibodies can pass through the placenta to provide passive immunity to the newborn.

Although there are no randomised controlled studies on the efficacy of the vaccine, between 87 and 98 percent protection has been demonstrated using population-based analyses. Immunised cases have been shown to have less severe disease, as highlighted during the outbreak in the former Soviet Union.

Vaccines combining pertussis antigens with diphtheria and tetanus toxoids have been gradually introduced into immunisation schedules throughout the world. Immunogenicity data for these combination vaccines is discussed in section 14.4.2.

Herd immunity

Although immunisation is more effective at preventing disease than preventing infection, it does create herd immunity via reducing carriage and therefore transmission.[14] To prevent major community outbreaks, it has been suggested that 70 percent or more of the childhood population must be immune to diphtheria.[15, 16] This may explain the control of diphtheria in New Zealand despite historically relatively poor coverage.

Duration of immunity

Diphtheria antitoxin levels decline over time in children after they have received a primary series of vaccines and a booster dose is required. In countries where diphtheria immunisation is common practice and high coverage rates are achieved, there will be no natural boosting from circulating disease, and antitoxin levels declining with increasing age may result in a susceptible adult population.[17]

Despite this, there has been minimal disease in high-income countries, suggesting that antibody levels may not be a reliable guide to protection and that other factors may be operating.[18] For example, a high proportion of the adult German population have low antibody levels, indicating susceptibility, yet this has not led to diphtheria outbreaks

despite Germany's relative geographical proximity to the former Soviet Union.[19]

The duration of protection after Tdap boosters is unknown, but the results of an Australian study have shown that five years after the Tdap booster dose, 94.4 percent of adults had seroprotective levels of antibodies against diphtheria, compared with 93.7 percent who received Td vaccine.[20]

5.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.[21] Store at +2°C to +8°C. Do not freeze.

DTaP-IPV-HepB/Hib and Td should be stored in the dark.

> DTaP-IPV-HepB/Hib (Infanrix-hexa) must be reconstituted by adding the entire contents of the supplied container of the DTaP-IPV-HepB vaccine to the vial containing the Hib pellet. After adding the vaccine to the pellet, the mixture should be shaken until the pellet is completely dissolved. Use the reconstituted vaccine as soon as possible. If storage is necessary, the reconstituted vaccine may be kept for up to eight hours at 21°C.

5.4.4 Dosage and administration

The dose of DTaP-IPV-HepB/Hib, DTaP-IPV, Tdap or Td vaccine is 0.5 mL, administered by intramuscular injection (see section 2.2.3).

Co-administration with other vaccines

DTaP-IPV-HepB/Hib, DTaP-IPV, Tdap or Td vaccine can be administered simultaneously (at separate sites) with other vaccines or IGs.

5.5 Recommended immunisation schedule

Table 5.1: Immunisation schedule for diphtheria-containing vaccines (excluding catch-up)

Age	Vaccine	Comment
6 weeks	DTaP-IPV-HepB/Hib	Primary series
3 months	DTaP-IPV-HepB/Hib	Primary series
5 months	DTaP-IPV-HepB/Hib	Primary series
4 years	DTaP-IPV	Booster
11 years	Tdap	Booster
45 years	Td[a]	Booster
65 years	Td[a]	Booster
Pregnant women (weeks 28–38 of each pregnancy)	Tdap	Booster[b]

a The Td vaccine is funded at ages 45 and 65 years, but not the administration.

b The Tdap booster during pregnancy is for protection against pertussis (see section 4.1.2).

5.5.1 Usual childhood schedule

A primary course of diphtheria vaccine is given as DTaP-IPV-HepB/Hib (Infanrix-hexa) at ages 6 weeks, 3 months and 5 months, followed by a dose of DTaP-IPV (Infanrix-IPV) at age 4 years (Table 5.1). A booster is given at age 11 years (school year 7), which includes a pertussis component given as the vaccine Tdap (Boostrix).

If a course of immunisation is late or interrupted for any reason, it may be resumed without repeating prior doses (see Appendix 2).

Alternatives to pertussis-containing vaccines

Some parents or guardians may ask about alternatives to pertussis-containing vaccines. The recommended and funded vaccines for children are those described above. There are no diphtheria-only or tetanus-only vaccines available. The Td vaccine contains half the amount of tetanus toxoid and one-fifteenth the amount of diphtheria toxoid compared to the DTaP-containing vaccines. Td was not clinically designed or tested for use to provide the primary vaccine course in

children and it is not registered for use in children aged under 5 years. Although there are no safety concerns relating to administration of the vaccine, there is no data on the use of this vaccine for a primary course in children and it is not recommended.

5.5.2 Catch-ups for individuals aged 10 years and older

For previously unimmunised individuals aged 10 years and older, a primary immunisation course consists of three doses of a diphtheria toxoid-containing vaccine at intervals of not less than four weeks (see Appendix 2). For children aged under 18 years, a booster dose is recommended at least six months after the third dose.

Children aged under 18 years may receive Tdap (funded from age 7 to under 18 years); adults aged 18 years and older may receive Td (funded) or Tdap (unfunded). Although Tdap and Td are not approved for use (registered) as a primary course, there are expected to be no safety concerns.

Dose intervals between Td and Tdap

When Tdap is to be given to adolescents or adults to protect infants or other vulnerable individuals from pertussis, no minimum interval between Td and Tdap is required[22, 23, 24] – unless Tdap is being given as part of a primary immunisation course.

5.5.3 Booster doses for adults

Studies overseas show that many adults lack protective levels of the antibody, and this has led to concern about waning immunity and recommendations for booster doses beyond childhood (see also section 5.3.2). Most authorities recommend maintaining diphtheria immunity by periodic reinforcement using Td.[8] A single booster dose of Tdap induces seroprotective levels of antibodies to diphtheria and tetanus in virtually all children and adolescents, and in a high proportion of adults and elderly individuals at approximately one month post-vaccination, irrespective of their vaccination history.[25]

In New Zealand, following the dose of Tdap at age 11 years, booster doses of Td are recommended (the vaccine is funded, but not the administration) at ages 45 and 65 years. These age-specific recommendations may facilitate the linkage of adult immunisation to the delivery of other preventive health measures.

Booster doses before travel

If someone is travelling to an area endemic for diphtheria, or there is another reason to ensure immunity, a booster dose is recommended (but not funded) if it is more than 10 years since the last dose. For website sources on travel vaccines, see Appendix 9.

5.5.4 Pregnancy and breastfeeding

Pregnant women should receive a dose of Tdap (funded) from 28 to 38 weeks' gestation. This should be given during each pregnancy[26] to protect the mother against pertussis and so that antibodies can pass to the fetus to protect the newborn (see section 4.1.2).

Td vaccine is not routinely recommended for pregnant women but it can be given under certain circumstances, such as when catch-up is needed for an under-immunised woman, or for management of a tetanus-prone wound[26, 27] (see section 19.5.5).

Td or Tdap vaccines can be given to breastfeeding women.[27]

5.5.5 (Re-)vaccination

Diphtheria toxoid-containing vaccines are funded for (re-)vaccination of eligible patients, as follows. See also sections 4.2 and 4.3.

DTaP-IPV-HepB/Hib (Infanrix-hexa) and DTaP-IPV (Infanrix-IPV)

An additional four doses (as appropriate) of DTaP-IPV-HepB/Hib (for children aged under 10 years) or DTaP-IPV are funded for (re-)vaccination of patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy

- pre- or post-solid organ transplant
- undergoing renal dialysis
- with other severely immunosuppressive regimens.

Up to five doses of DTaP-IPV-HepB/Hib (for children aged under 10 years) or DTaP-IPV are funded for children requiring solid organ transplantation.

Tdap (Boostrix)

An additional four doses (as appropriate) of Tdap (Boostrix) are funded for patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- with other severely immunosuppressive regimens.

Td (ADT Booster)

Td is funded for patients following immunosuppression.

5.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

5.6.1 Contraindications

There are no specific contraindications to diphtheria vaccine (or Td/DT), except for anaphylaxis to a previous dose or any component of the vaccine.

5.6.2 Precautions

See section 14.6.2 for precautions for pertussis-containing vaccines.

5.7 Expected responses and AEFIs

Despite the widespread use of diphtheria toxoid, the 1994 Institute of Medicine review of vaccine reactions did not identify any reaction for which the evidence favoured or established a causal relationship with diphtheria toxoid.[28] However, local and systemic reactions do occur with diphtheria toxoid-containing vaccine, especially when the infant vaccine is used in older children and adults. Mild discomfort or pain at the injection site persisting for up to a few days is common.[29]

See also sections 14.7 and 19.7 for expected responses and AEFIs with DTaP-IPV-HepB/Hib, DTaP-IPV, Tdap and Td.

5.8 Public health measures

It is a legal requirement that all cases of diphtheria be notified immediately on suspicion to the local medical officer of health.

Alert the laboratory that the sample is from a suspected case of diphtheria. All isolates of *C. diphtheriae* and *C. ulcerans* are notifiable until toxigenicity is determined, including cutaneous isolates. If the isolate is determined to be nontoxigenic (does not have the ability to produce diphtheria toxin), the case should be denotified.

All patients with *C. diphtheriae* or *C. ulcerans* isolated from a clinical specimen should be discussed with the medical officer of health urgently.

All contacts should have cultures taken.

5.8.1 Antimicrobial prophylaxis

All close contacts, after cultures have been taken and regardless of immunisation status, should receive:

- a single intramuscular dose of benzathine penicillin (450 mg for children aged under 6 years; 900 mg for contacts aged 6 years or older), or
- 7 to 10 days of oral erythromycin (children: 40 mg/kg/day; adults: 1 g/day, in four divided doses).

Benzathine penicillin is preferred for contacts who cannot be kept under surveillance.

In contacts with a positive culture: two follow-up cultures should be obtained at least 24 hours after completion of therapy. If cultures are still positive, discuss further management with an infectious diseases physician. The primary healthcare practitioner should be kept informed of the management of contacts and laboratory results.

5.8.2 Vaccination of contacts

All close contacts should also be offered a complete course of vaccine or a booster according to the following schedule.

- Fully immunised children aged under 10 years who have only received three doses of diphtheria toxoid-containing vaccine within the last five years: give one injection of a diphtheria toxoid-containing vaccine.
- Fully immunised individuals aged 10 years and older who have not received a booster dose of a diphtheria toxoid-containing vaccine within the last five years: if aged 10–17 years, give one injection of Tdap; if aged 18 years or older, give one injection of Td or Tdap; the latter is not funded (see section 5.5).
- Unimmunised individuals: see Appendix 2.

5.8.3 Exclusion of contacts

Child contacts should be excluded from school, early childhood services and community gatherings until they are known to be culture negative. Adult contacts who are food handlers or who work with children should be excluded from work until known to be culture negative. Cases should be excluded from school until recovery has taken place and two negative throat swabs have been collected one day apart and one day after cessation of antibiotics.

For more details on control measures, refer to the 'Diphtheria' chapter of the *Communicable Disease Control Manual 2012*.[30]

5.9 Variations from the vaccine data sheets

See section 14.9 for variations from the DTaP-IPV-HepB/Hib (Infanrix-hexa), DTaP-IPV (Infanrix-IPV) and Tdap (Boostrix) data sheets.

See section 19.9 for variations from the Td (ADT Booster) data sheet.

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6 *Haemophilus influenzae* type b (Hib) disease

Key information

Mode of transmission	By inhalation of respiratory tract droplets or by direct contact with respiratory tract secretions.
Incubation period	Unknown, but probably 2–4 days.
Period of communicability	May be prolonged. Non-communicable within 24–48 hours after starting effective antimicrobial therapy.
Disease burden	Children aged under 5 years, particularly those aged under 1 year: meningitis, epiglottitis, pneumonia and bacteraemia.
Funded vaccines	DTaP-IPV-HepB/Hib (Infanrix-hexa). Hib-PRP-T (Hiberix).
Dose, presentation, route	DTaP-IPV-HepB/Hib and Hib-PRP-T: • 0.5 mL per dose after reconstitution • pre-filled syringe and glass vial – the vaccines must be reconstituted prior to injection • intramuscular injection.
Funded vaccine indications and schedule	Usual childhood schedule: • at ages 6 weeks, 3 months and 5 months: DTaP-IPV-HepB/Hib • at age 15 months: Hib-PRP-T. For (re-)vaccination of eligible patients: • up to 4 additional doses of DTaP-IPV-HepB/Hib (for eligible children <10 years); or • 1 additional dose of Hib-PRP-T. For children <10 years receiving solid organ transplantation: up to 5 doses of DTaP-IPV-HepB/Hib. For testing for primary immune deficiencies: Hib-PRP-T.
Vaccine efficacy/ effectiveness	Hib disease has been almost eliminated in countries where Hib vaccine is used.
Public health measures	Rifampicin prophylaxis should be administered to contacts as appropriate. All contacts should have their immunisation status assessed and updated as appropriate.

6.1 Bacteriology

Haemophilus influenzae is a gram-negative coccobacillus, which occurs in typeable and non-typeable (NTHi) forms. There are six antigenically distinct capsular types (a–f), of which type b is the most important. Before the introduction of the vaccine, *H. influenzae* type b (Hib) caused 95 percent of *H. influenzae* invasive disease in infants and children.

6.2 Clinical features

Transmission is by inhalation of respiratory tract droplets or by direct contact with respiratory tract secretions. Hib causes meningitis and other focal infections (such as pneumonia, septic arthritis and cellulitis) in children, primarily those aged under 2 years, while epiglottitis was more common in children over 2 years. Invasive Hib disease was rare over the age of 5 years, but could occur in adults. In the absence of vaccination these presentations may still occur. There have always been a small number of cases of *H. influenzae* invasive disease in adults, and these continue to occur. The incubation period of the disease is unknown, but is probably from two to four days.

Immunisation against Hib does not protect against infections due to other *H. influenzae* types or NTHi strains. Non-typeable *H. influenzae* (NTHi) organisms usually cause non-invasive mucosal infections, such as otitis media, sinusitis and bronchitis, but can occasionally cause bloodstream infection, especially in neonates. They are frequently present (60–90 percent) in the normal upper respiratory tract flora.

Young infants (aged under 2 years) do not produce an antibody response following Hib invasive disease, so a course of Hib vaccine is recommended when they have recovered (see section 6.5.3).

Hib and NTHi strains also cause diseases (including pneumonia and septicaemia) in the elderly.

6.3 Epidemiology

6.3.1 Global burden of disease

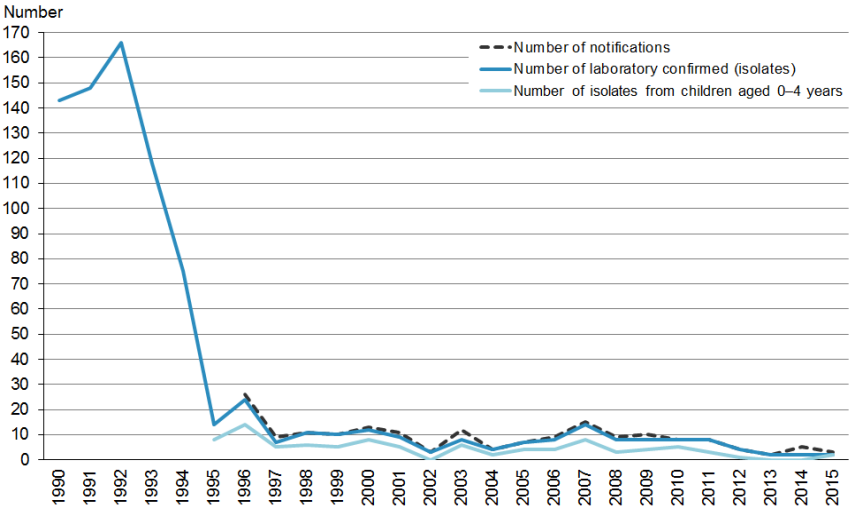
The source of the organism is the upper respiratory tract. Immunisation with a protein conjugate vaccine reduces the frequency of asymptomatic colonisation by Hib. Before the introduction of the vaccine, Hib was the most common cause of bacterial meningitis in children. Worldwide immunisation coverage is increasing, with approximately 191 countries having fully or partially introduced Hib onto their schedules by June 2016 (98 percent of all WHO member states).[1]

6.3.2 New Zealand epidemiology

Hib vaccine was introduced in 1994 (see Appendix 1). In 1993, 101 children aged under 5 years had laboratory-confirmed invasive Hib disease (an age-specific rate of 36.4 per 100,000 population). By 1999 only five children in this age group had laboratory-confirmed disease (1.7 per 100,000) (Figure 6.1).

Three cases of Hib were notified in 2015, of which two were laboratory-confirmed.[2] The third case met the probable case definition. All cases were children aged under 5 years, and none were vaccinated. Two of the cases lived in a communal setting and were part of an outbreak. There have been five deaths from Hib between 1997 and 2015 (ESR, 21 February 2017), the most recent was in 2012 in an adult over 70 years of age.[3]

Figure 6.1: Number of notifications and culture-positive cases of *Haemophilus influenzae* type b invasive disease, 1990–2015



Source: Ministry of Health and ESR

6.4 Vaccines

Antibodies to PRP, a component of the polysaccharide cell capsule of Hib, are protective against invasive Hib disease. To induce a T-cell dependent immune response, the PRP polysaccharide has been linked (conjugated) to a variety of protein carriers. These conjugate Hib vaccines are immunogenic and effective in young infants (see also section 1.4.3). The protein carriers used are either an outer membrane protein of *Neisseria meningitidis* (PRP-OMP Hib vaccine), a mutant diphtheria toxin (Hb-OC Hib vaccine) or a tetanus toxoid (PRP-T Hib vaccine).

Note that the protein conjugates used in Hib vaccines are not themselves expected to be immunogenic and do not give protection against *N. meningitidis,* diphtheria or tetanus.

6.4.1 Available vaccines

Funded vaccines

The Hib vaccines funded as part of the Schedule are:

- Hib-PRP-T, given as the hexavalent vaccine DTaP-IPV-HepB/Hib (Infanrix-hexa, GSK). It contains diphtheria, tetanus, acellular pertussis, inactivated polio, hepatitis B and *Haemophilus influenzae* type b vaccine (see section 5.4 for more information)
- Hib-PRP-T given as monovalent Hib vaccine (Hiberix, GSK). It contains 10 μg of purified Hib capsular polysaccharide conjugated to 25 μg of inactivated tetanus toxoid. Other components (excipients) include lactose in the vaccine and sterile saline solution in the diluent.

Other vaccines

Hib-PRP-T (Act-HIB, Sanofi) was the funded vaccine prior to the 1 July 2017 Schedule change. It contains 10 μg of purified Hib capsular polysaccharide conjugated to 18–30 μg of tetanus protein; other components (excipients) include trometamol, sucrose and sodium chloride.

6.4.2 Efficacy and effectiveness

The high efficacy and effectiveness of Hib vaccines have been clearly demonstrated by the virtual elimination of Hib disease in countries implementing the vaccine,[4, 5, 6] including New Zealand. Hib vaccines are highly effective after a primary course of two or three doses.[7, 8, 9] Disease following a full course of Hib vaccine is rare.

Conjugate vaccines reduce carriage in immunised children and as a result also decrease disease in unimmunised people (herd immunity). These vaccines will not protect against infection with NTHi strains of *H. influenzae*, and therefore do not prevent the great majority of otitis media, recurrent upper respiratory tract infections, sinusitis or bronchitis.

(See also section 14.4.2 for information about the DTaP-IPV-HepB/Hib vaccine.)

Duration of immunity

A primary series followed by a booster dose in the second year of life should provide sufficient antibody levels to protect against invasive Hib disease to at least the age of 5 years.[10]

6.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.[11] Store at +2°C to +8°C. Do not freeze.

DTaP-IPV-HepB/Hib should be stored in the dark.

DTaP-IPV-HepB/Hib vaccine (Infanrix-hexa) must be reconstituted by adding the entire contents of the pre-filled syringe containing DTaP-IPV-HepB vaccine to the vial containing the Hib powder. After adding the vaccine to the powder, the mixture should be shaken until the powder is completely dissolved. Use the reconstituted vaccine as soon as possible. If storage is necessary, the reconstituted vaccine may be kept for up to eight hours at 21°C.

Hib-PRP-T vaccine (Hiberix) must be reconstituted with the supplied diluent and used immediately after reconstitution.

6.4.4 Dosage and administration

The dose of DTaP-IPV-HepB/Hib and Hib-PRP-T vaccines is 0.5 mL administered by intramuscular injection (see section 2.2.3).

Co-administration

DTaP-IPV-HepB/Hib and Hib-PRP-T vaccines can be co-administered with other routine vaccines on the Schedule, in separate syringes and at separate sites.

6.5 Recommended immunisation schedule

6.5.1 Usual childhood schedule

Hib vaccine is funded for all children aged under 5 years. Three doses of DTaP-IPV-HepB/Hib (Infanrix-hexa) vaccine are given as the primary course, with a booster of Hib-PRP-T (Hiberix) at age 15 months (see Table 6.1).

Table 6.1: Usual childhood Hib schedule (excluding catch-up)

Age	Vaccine	Comment
6 weeks	DTaP-IPV-HepB/Hib	Primary series
3 months	DTaP-IPV-HepB/Hib	Primary series
5 months	DTaP-IPV-HepB/Hib	Primary series
15 months	Hib-PRP-T	Booster

For children aged under 5 years who, for whatever reason, have missed out on Hib vaccine in infancy, a catch-up schedule is recommended. The total number of doses of Hib vaccine required is determined by the age at which Hib immunisation commences. Where possible, the combined available vaccines should be used, but individual immunisation schedules based on the recommended national schedule may be required for children who have missed some immunisations (see Appendix 2).

6.5.2 Special groups

Children

Because of an increased risk of infection, it is particularly important that the following groups of children, whatever their age, receive the Hib vaccine as early as possible (see also sections 4.2 and 4.3):

- children with anatomical or functional asplenia, or who are suffering from sickle cell disease (if possible, it is recommended that children be immunised prior to splenectomy)

- children with partial immunoglobulin deficiency, Hodgkin's disease or following chemotherapy (note, however, that response to the vaccine in these children is likely to be suboptimal)
- children with nephrotic syndrome
- HIV-positive children.

Recommendations for Hib vaccine for older children and adults with asplenia

Although there is no strong evidence of an increased risk of invasive Hib disease in asplenic older children and adults, many authorities recommend Hib immunisation for these individuals.[12, 13] The Hib PRP-T vaccine has been shown to be immunogenic in adults.

Hib-PRP-T vaccine (Hiberix) is funded for older children and adults pre- or post-splenectomy or with functional asplenia; one dose of vaccine is recommended (see also section 4.3.4).

(Pneumococcal, meningococcal, influenza, varicella and pertussis-containing vaccines are also recommended for these individuals; see section 4.3.4 and the relevant disease chapters.)

6.5.3 Children who have recovered from invasive Hib disease

Children aged under 2 years with Hib disease do not reliably produce protective antibodies and need to receive a complete course of Hib vaccine. The number of doses required will depend on the age at which the first dose after the illness is given, **ignoring** any doses given before the illness (follow the age-appropriate catch-up schedules in Appendix 2).

Commence immunisation approximately four weeks after the onset of disease.

Any immunised child who develops Hib disease or who experiences recurrent episodes of Hib invasive disease requires immunological investigation by a paediatrician.

6.5.4 (Re-)vaccination

Hib-containing vaccines are funded for (re-)vaccination of eligible patients, as follows. See also sections 4.2 and 4.3.

DTaP-IPV-HepB/Hib (Infanrix-hexa)

An additional four doses (as appropriate) of DTaP-IPV-HepB/Hib are funded for (re-)vaccination of children aged under 10 years:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- with other severely immunosuppressive regimens.

Up to five doses of DTaP-IPV-HepB/Hib are funded for children aged under 10 years receiving solid organ transplantation.

Hib-PRP-T (Hiberix)

One additional dose of Hib-PRP-T (Hiberix) is funded for (re-)vaccination of patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy or with functional asplenia
- pre- or post-solid organ transplant
- pre- or post-cochlear implants
- undergoing renal dialysis
- with other severely immunosuppressive regimens.

6.5.5 Pregnancy and breastfeeding

Hib vaccine is not routinely recommended for pregnant or breastfeeding women. However, for asplenic women refer to 'Recommendations for Hib vaccine for older children and adults with asplenia' in section 6.5.2 above.

6.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general vaccine contraindications. Anaphylaxis to a previous vaccine dose or any component of the vaccine is an absolute contraindication to further vaccination with that vaccine.

See section 14.6 for contraindications and precautions to DTaP-IPV-HepB/Hib vaccine.

Hib-PRP-T vaccines should not be administered to people with a history of an anaphylactic reaction to a prior dose of Hib vaccine or to a vaccine component. Significant hypersensitivity reactions to Hib vaccines appear to be extremely rare.

6.7 Expected responses and AEFIs

See section 14.7.1 for expected responses and AEFIs with DTaP-IPV-HepB/Hib vaccine.

6.7.1 Expected responses

Adverse reactions to Hib conjugate vaccines are uncommon. Pain, redness and swelling at the injection site occur in approximately 25 percent of recipients, but these symptoms typically are mild and last less than 24 hours.[14]

6.7.2 AEFIs

A meta-analysis of trials of Hib vaccination from 1990 to 1997 found that serious adverse events were rare.[15] No serious vaccine-related adverse experiences were observed during clinical trials of Hib vaccine alone. There have been rare reports, not proven to be causally related to Hib vaccine, of erythema multiforme, urticaria, seizures and Guillain–Barré syndrome (GBS).[16]

6.8 Public health measures

It is a legal requirement that all cases of Hib disease be notified immediately on suspicion to the local medical officer of health, who will arrange for contact tracing, immunisation and administration of prophylactic rifampicin, where appropriate (for further information refer to the *Communicable Disease Control Manual 2012*).[17]

6.8.1 Management of contacts

All child contacts should have their immunisation status assessed and updated, as appropriate.

Immunisation reduces – but does not necessarily prevent – the acquisition and carriage of Hib. Therefore, immunised children still need rifampicin prophylaxis, when indicated, to prevent them transmitting infection to their contacts. Careful observation of exposed household and early childhood service contacts is essential. Exposed children who develop a febrile illness should receive prompt medical evaluation.

Rifampicin chemoprophylaxis

To eradicate the carrier state and protect susceptible children, antimicrobial prophylaxis should be given to contacts as soon as possible, and ideally within seven days of the index case developing the disease, irrespective of their own immunisation status. Prophylaxis started after seven days may still be of benefit and is recommended. Note that the prophylaxis for Hib is different from that for meningococcal disease (see chapter 12).

Rifampicin recommendations

Chemoprophylaxis with rifampicin is recommended for the following contacts of an index case of Hib:

- all members of the case's household (including adults) where there is at least one contact aged under 4 years who is either unimmunised or partially immunised

- all members of a household where there is a child aged under 12 months, even if the child has had three doses (primary series) of the Hib vaccine
- all members of a household where there is an immunosuppressed person
- all staff and children at an early childhood service where two or more cases of Hib have occurred within 60 days.

Use oral rifampicin 20 mg/kg (maximum 600 mg) daily for four days. The dose for infants aged under 4 weeks has not been established, but a dose of 10 mg/kg per day is recommended. This is a different regimen to that recommended for prophylaxis from meningococcal disease (see chapter 12).

The index case should also receive rifampicin unless treated with cefotaxime or ceftriaxone.

Rifampicin is not recommended for:

- occupants of households where there are no children aged under 4 years, other than the index case
- occupants of households where all contacts aged 12 months to under 4 years have completed their immunisation series, including the second-year-of-life dose
- pregnant women – rifampicin is contraindicated in pregnant women; pregnant women who are a household contact of an index case should receive ceftriaxone.

For more details on control measures, refer to the '*Haemophilus influenzae* type b invasive disease (Hib)' chapter of the *Communicable Disease Control Manual 2012*.[17]

6.9 Variations from the vaccine data sheets

The Hib-PRP-T (Hiberix) data sheet states that the vaccine is not intended for use in adults. However, the Ministry of Health recommends that asplenic adults (see section 6.5.2) or adults with specified immunocompromised conditions (see section 6.5.4) receive Hib-PRP-T vaccine.[12, 13] There are not expected to be any safety concerns for use in older age groups.

See section 14.9 for variations from the DTaP-IPV-HepB/Hib (Infanrix-hexa) data sheet.

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7 Hepatitis A

Key information

Mode of transmission	Faecal–oral route, either from person-to-person contact or through contaminated food or drink. It is also occasionally spread by injected drug use.
Incubation period	28–30 days average (range 15–50 days).
Period of communicability	The 1–2 weeks before and the first few days after the onset of jaundice.
Burden of disease	Infants and children are usually asymptomatic. Severity in adults increases with age. The disease is more serious in those with chronic liver disease and the immunocompromised. There is no carrier state.
Vaccines (registered and available)	Monovalent inactivated hepatitis A virus (HAV) vaccine (Havrix; Avaxim). Combined inactivated HAV-recombinant HBsAg protein vaccine (Twinrix). Combined HAV-purified *Salmonella typhi* Vi polysaccharide vaccine (Hepatyrix; Vivaxim).
Dose, presentation, route	Havrix, Twinrix, Hepatyrix, Vivaxim: 1.0 mL per dose. Havrix Junior, Twinrix Junior, Avaxim: 0.5 mL per dose. Pre-filled syringe. Intramuscular injection.
Funded vaccine indications	HAV vaccine (Havrix) is recommended and funded for: • transplant patients – 2 doses • children with chronic liver disease – 2 doses • close contacts of hepatitis A cases – 1 dose.
Vaccine efficacy/ effectiveness	High efficacy: HAV infection has been almost eliminated in immunised populations.
Public health measures	In an outbreak (if within 2 weeks of exposure): • age <12 months, human normal immunoglobulin is recommended • ≥12 months, age-appropriate vaccination is recommended.

7.1 Virology

Hepatitis A virus (HAV) is a ribonucleic acid (RNA) virus belonging to the picornavirus group, which also contains enteroviruses and rhinoviruses. The virus is usually transmitted by the faecal–oral route, either from person-to-person contact or through contaminated food or drink.

HAV primarily replicates in the liver and is excreted in large quantities via the biliary tract into the faeces. It is a hardy virus and can survive outside the body for prolonged periods in food and water. It causes a self-limiting illness with no carrier state.

7.2 Clinical features

The incubation period between ingestion of the virus and clinical symptoms is 15 to 50 days, with an average of 28 to 30 days. The virus can be detected in blood and faeces within a few days of ingestion, and it increases to a peak in the two weeks prior to the onset of clinical illness, which is the time that subjects are most likely to spread the infection. Faecal viral shedding continues for one to three weeks in adults, but has been reported to last longer in young children. Virus excretion falls sharply in the week following the onset of hepatitis.

In infants and preschool children, most infections are either asymptomatic or cause only mild, non-specific symptoms without jaundice. Most adults and adolescents develop symptomatic disease, the severity of which generally increases with age. Symptomatic HAV infection is characterised by an acute febrile illness with jaundice, anorexia, nausea, abdominal discomfort, malaise and dark urine. Signs and symptoms usually last less than two months, although 10–15 percent of symptomatic persons have prolonged or relapsing illness lasting up to six months. Liver enzymes almost always return to normal by six months after the illness, and often much sooner. The disease is more serious in people with chronic liver disease or those who are immunocompromised (including people with HIV infection). Chronic carrier states do not occur following hepatitis A infection and persisting liver damage is very rare.

7.3 Epidemiology

7.3.1 Global burden of disease

HAV is common in areas with poor sanitary conditions and limited access to clean water.[1] In highly endemic areas, such as parts of Africa and Asia, the disease is virtually confined to early childhood and is not an important cause of morbidity.[1, 2] Almost all adults in these areas are immune, and hepatitis A epidemics are uncommon. In intermediate endemicity areas, such as Central and South America, Eastern Europe and parts of Asia, children may not be infected in early childhood and reach adulthood without immunity. A high proportion of adolescents and adults are susceptible and large outbreaks are common. In low endemicity areas, such as the US and Western Europe, infection is less common but can occur in high-risk groups. Large outbreaks are usually rare, due to high levels of sanitation that stops person-to-person transmission.

Viral spread occurs readily in households, in early childhood services and in residential facilities that care for the chronically ill, disabled or those with a weakened immune system. In early childhood services, typically the adult guardian develops symptomatic disease while the primary source, the infected young child, is asymptomatic. The risk of spread in early childhood centres is proportional to the number of children aged under 2 years wearing nappies. Infection in these early childhood services is an important source of outbreaks for whole communities.

Other groups at the highest risk of contracting the disease include people in close contact with an infected person, and travellers to areas with high or intermediate rates of hepatitis A infection. Others also at greater risk of contracting HAV are people who have oral–anal sexual contact, illicit drug users, those with chronic liver disease, food handlers, and laboratory workers who handle the virus.

Universal and targeted programmes for childhood immunisation have been introduced in several countries, including Israel, the US and Australia. Acute HAV infection has almost been eradicated in areas with HAV immunisation programmes.

7.3.2 New Zealand epidemiology

The rate of HAV in New Zealand has declined from 145.7 per 100,000 in 1971 to 1.0 per 100,000 in 2015.[3] This fall in rate is attributable to the use of HAV vaccination in travellers and a reduction in HAV prevalence overseas.

In 2015, 47 cases were notified compared with 74 in 2014.[3] Hospitalisation status was recorded for 46 cases, of which, 24 (52.2 percent) were hospitalised.

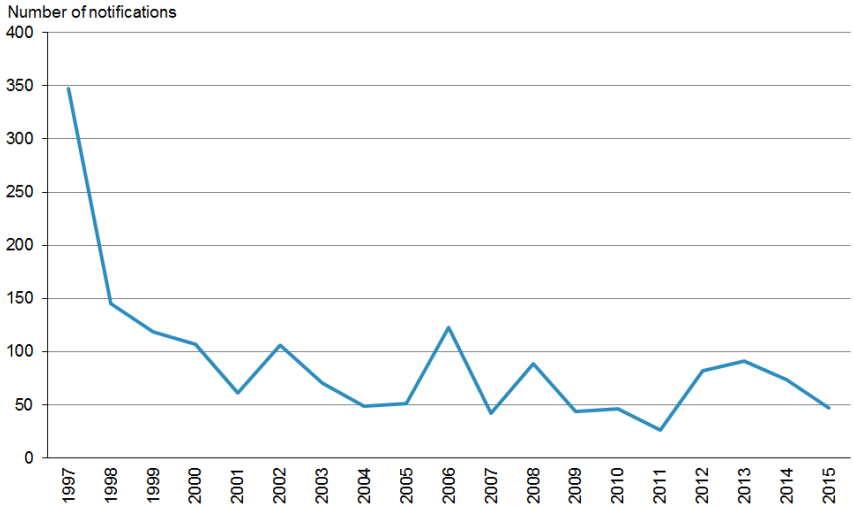
The highest rates occurred in the 20–29 years and 40–49 years age groups (both 1.8 per 100,000), followed by the 15–19 years age group (1.6 per 100,000).[3] Of the 44 cases with ethnicity information recorded, Pacific peoples had the highest notification rate (2.5 per 100,000), followed by the Asian (1.7 per 100,000) and Māori (0.9 per 100,000) ethnic groups.

Travel information was recorded for all cases: 24 cases (51.1 percent) had travelled overseas during the incubation period of the disease.[3] The countries most frequently visited included Samoa (5 cases) and Fiji (4 cases).

Hepatitis A outbreaks continue to occur (see Figure 7.1). There were two outbreaks in 2015, involving nine cases.[3] One outbreak, involving seven cases of hepatitis A reported from five DHBs, was food related.[4] The cases were epidemiologically linked to the consumption of imported frozen berries.

Figure 7.1 illustrates the overall national downward trend since a peak of notifications in 1997.

Figure 7.1: Hepatitis A notifications, by year, 1997–2015



Source: ESR

7.4 Vaccines

7.4.1 Available vaccines

Two inactivated HAV vaccines are currently registered (approved for use) and available (marketed) in New Zealand, as well as a combined HAV and HBV vaccine and two HAV and typhoid combined vaccines.

Funded vaccine

HAV vaccine is not on the Schedule, but is recommended and funded for certain high-risk groups, as shown in Table 7.1.

Each 1.0 mL dose of Havrix (GSK) contains 1,440 EU (enzyme-linked immunosorbent assay [ELISA] units) of inactivated HAV adsorbed onto aluminium hydroxide. Each 0.5 mL dose of Havrix Junior contains 720 EU of inactivated HAV. Other components and residuals include neomycin sulphate, 2-phenoxyethanol, polysorbate 20, amino acid supplement in a phosphate buffered saline solution.

Other vaccines

Inactivated HAV vaccine

- Avaxim (Sanofi) contains 160 antigen units of inactivated HAV in each 0.5 mL dose; other components and residuals include aluminium hydroxide, phenoxyethanol, formaldehyde, Medium 199, neomycin and bovine serum albumin.

Combined HAV and HBV vaccine

- Twinrix (GSK) contains 720 EU of inactivated HAV and 20 µg of recombinant DNA HBsAg vaccine in each 1.0 mL dose. The Twinrix Junior preparation (0.5 mL per dose) contains half these amounts. The vaccines are adsorbed onto aluminium adjuvants. Other components and residuals include aluminium hydroxide, aluminium phosphate, sodium chloride, amino acids, dibasic sodium phosphate, formaldehyde, monobasic sodium phosphate, neomycin sulphate, polysorbate 20 and trometamol.

Combined HAV and typhoid vaccines

The two HAV-typhoid combination vaccines contain inactivated HAV and purified *Salmonella typhi* Vi polysaccharide.

- Hepatyrix (GSK) contains 1,440 EU of HAV and 25 µg of purified *Salmonella typhi* Vi polysaccharide in each 1.0 mL dose; other components and residuals include aluminium hydroxide, sodium chloride, formaldehyde, polysorbate 20, amino acids, trometamol and neomycin.
- Vivaxim (Sanofi) contains 160 antigen units of HAV and 25 µg of purified *Salmonella typhi* Vi polysaccharide in each 1.0 mL dose; other components and residuals include sodium chloride, sodium phosphate, aluminium hydroxide, phenoxyethanol, formaldehyde, Medium 199, neomycin and bovine serum albumin.

7.4.2 Efficacy and effectiveness

After one dose of monovalent HAV vaccine in healthy people, protective levels of antibody have been demonstrated by two weeks, and 94–100 percent of people vaccinated will seroconvert by four weeks.[5]

A second dose 6 to 18 months after the first is thought to be important for long-term protection, particularly in the absence of exposure to HAV.[6, 7] In subjects with an impaired immune system, adequate anti-HAV antibody titres may not be obtained after a single dose.

HAV vaccines have not yet been approved for children aged under 12 months. The limited data on immunogenicity in infants indicates high levels of seroconversion, but those with passively acquired maternal anti-HAV have lower serum antibody titres.

HAV vaccines are highly effective in preventing clinical disease, with recorded efficacy measures of around 94–100 percent from six weeks post-vaccination. Where children, adolescents and young adults have been vaccinated in targeted and/or national programmes, there has been a rapid decline in disease incidence. This decline is through both direct and indirect (herd immunity) effects.[6]

Duration of immunity

Antibodies to two doses of HAV vaccine have been shown to persist in vaccinated adults for at least 17 years after vaccination, and up to 15 years in vaccinated children and adolescents.[8] Mathematical models estimate that following completion of a two-dose series, protective levels of antibody will persist for 25 years or longer in adults and 14–20 years in children.[8] Given that HAV has a long incubation period, it is possible that immune memory with no detectable circulating antibody may be sufficient for protection, as is the case with HBV and HepB.

7.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.[9] Store at +2°C to +8°C. Do not freeze.

7.4.4 Dosage and administration

See Table 7.2 for dosage and scheduling information.

The monovalent HAV and HAV combination vaccines should be administered by intramuscular injection into the deltoid region of the

upper arm in adults and older children, or the anterolateral aspect of the thigh in younger children (see section 2.2.3).

Co-administration with other vaccines

The monovalent HAV and HAV combination vaccines may be administered concurrently with other vaccines.[8, 10] The vaccines should be given in separate syringes and at different injection sites.

Interchangeability of hepatitis A vaccines

The monovalent HAV vaccines may be used interchangeably to complete a two-dose course.[10]

7.5 Recommended immunisation schedule

7.5.1 Recommendations

Hepatitis A vaccines are not on the Schedule, but are recommended and funded for the high-risk groups in the shaded section of Table 7.1 below. They may also be employer-funded or funded during an outbreak (see section 7.8).

Table 7.1: Hepatitis A vaccine recommendations

Note: Funded conditions are in the shaded rows. See the Pharmaceutical Schedule (www.pharmac.govt.nz) for the number of funded doses and any changes to the funding decisions.

Recommended and funded
Transplant patients[a]
Children with chronic liver disease[a]
Close contacts[b] of hepatitis A cases
Recommended but not funded
Adults with chronic liver disease: • chronic hepatitis B or C infection • other chronic liver disease.
Men who have sex with men
Travellers – including occupational[c] and recreational travel.
Occupational groups[c] exposed to faeces, including: • employees of early childhood services, particularly where there are children too young to be toilet trained • health care workers exposed to faeces • sewage workers • those who work with non-human primates (eg, zoos, research laboratories).
Food handlers[c] during community outbreaks.
Military personnel[c] who are likely to be deployed to high-risk areas.

a See also sections 4.2 and 4.3.

b Only one dose is funded for close contacts as protection is only required for the duration of the outbreak. For long-term protection, contacts may seek a second (unfunded) dose, after an interval of at least 6 months. Refer to the *Communicable Disease Control Manual 2012*[11] for a definition of contacts.

c May be employer-funded. See also section 4.6.

Individuals with chronic liver disease

HAV vaccine is recommended and funded for children with chronic liver disease and for children and adults undergoing transplants (see sections 4.2 and 4.3). People with chronic liver disease are not at increased risk for hepatitis A, but acute hepatitis A can have serious or fatal consequences.[6]

Chronic hepatitis B or C infection

Studies have shown that in these individuals, super-infection with HAV leads to increased morbidity and mortality.[6]

Other chronic liver disease

Non-immune individuals who have not been vaccinated should receive HAV vaccine before liver decompensation. It should be given as early as possible before liver transplantation; vaccination may be performed after transplantation, although the response is unlikely to be as good as early in liver disease.[12, 13]

Travellers

The first dose of HAV vaccine should be given as soon as travel is considered.[8] The high and intermediate endemicity areas listed in section 7.3.1 may be used as a guide for recommending hepatitis A vaccination for travel, but there are limits to the data that informs these listings, and variation within countries. Even in low prevalence countries there is a risk of foodborne hepatitis A. In addition, decreasing prevalence in formerly endemic countries leads to large numbers of susceptible people and the risk of large outbreaks, as has recently been reported. The vaccine may be considered for all travellers aged 1 year and older.[1]

Immunoglobulin is not normally available or recommended in New Zealand for pre-travel use.

Certain occupational groups

Immunisation with HAV vaccine is recommended (but not funded) for people in occupational groups exposed to faeces, as listed in Table 7.1 above.

Others at higher risk

Pre-immunisation screening for anti-HAV antibodies is not routinely recommended. There is no danger in vaccinating an already immune person, but some groups with higher probability of prior infection may wish to avoid the expense of vaccination. These include:

- those who are likely to have been exposed as children (born in a country of high endemicity) or in the course of their employment
- those with a history of jaundice.
- Consider HAV vaccine for the following groups:
- intravenous drug users (who account for 30 percent of cases in communities during outbreaks)[6]
- men who have sex with men.

Routine immunisation for children

HAV vaccine is not routinely recommended and is not on the Schedule for children in New Zealand. It should, however, be considered during community outbreaks (see section 7.8).

7.5.2 Immunisation schedule

Immunisation schedules for HAV-containing vaccines are provided in Table 7.2. See the manufacturers' data sheets for more information. For the monovalent HAV vaccines, the first dose is for primary immunisation and the second dose is a booster.

Table 7.2: Hepatitis A-containing vaccines: by age, dose and schedule

Note: Havrix and Havrix Junior are funded for eligible individuals[a] (see Table 7.1).

Age	Vaccine	Dose	Volume (mL)	Number of doses	Schedule
Hepatitis A vaccines					
1–15 years	Havrix Junior	720 EU	0.5	2	0 and 6–12 months[b]
2 years–adult	Avaxim	160 antigen units	0.5	2	0 and 6–36 months
≥16 years	Havrix 1440	1,440 EU	1	2	0 and 6–12 months[b]

Continued overleaf

Age	Vaccine	Dose	Volume (mL)	Number of doses	Schedule
Hepatitis A–Hepatitis B combined vaccine					
1–15 years	Twinrix[c]	720 EU of HAV and 20 µg of HBsAg	1.0	2	0 and 6–12 months
	Twinrix Junior[d]	360 EU of HAV and 10 µg of HBsAg	0.5	3	0, 1 and 6 months
≥16 years	Twinrix	720 EU of HAV and 20 µg of HBsAg	1.0	3	0, 1 and 6 months; or 0, 7, 21 days plus a booster at 1 year
Hepatitis A–Typhoid combined vaccines					
≥15 years	Hepatyrix	1,440 EU of HAV and 25 µg of Vi	1.0	1	At least 14 days before departure; then boost with HAV vaccine at 6–12 months[e]
≥16 years	Vivaxim	160 antigen units of HAV and 25 µg of Vi	1.0	1	At least 14 days before departure; then boost with HAV vaccine at 6–36 months[e]

Key: EU = enzyme-linked immunosorbent assay (ELISA) units of hepatitis A virus protein; HAV = hepatitis A virus; HBsAg = recombinant hepatitis B surface antigen; Vi = *Salmonella typhi* polysaccharide

Notes

a Note that two doses of hepatitis vaccine are funded for transplant patients and children with chronic liver disease; one dose is funded for close contacts of hepatitis A cases.

b Even after a longer interval between the 1st and 2nd doses, there is no need to restart the series. A substantial anamnestic response occurs after a 2nd dose given up to 8 years after the initial dose.[14]

c For children not previously exposed to the hepatitis A or B viruses. Source: GlaxoSmithKline NZ Ltd. 2016. *Twinrix and Twinrix Junior New Zealand Data Sheet*. URL: http://www.medsafe.govt.nz/profs/datasheet/t/Twinrixinj.pdf (accessed 4 December 2016).

d Use when the child is at immediate risk of exposure to hepatitis B (eg, travellers) and did not receive a primary course of HepB as an infant. Source: GlaxoSmithKline NZ Ltd. 2016. *Twinrix and Twinrix Junior New Zealand Data Sheet*. URL: http://www.medsafe.govt.nz/profs/datasheet/t/Twinrixinj.pdf (accessed 4 December 2016).

e If the individual remains at risk from typhoid fever, a single dose of the typhoid vaccine is recommended every 3 years.

7.5.3 Pregnancy and breastfeeding

The safety of HAV vaccine during pregnancy and while breastfeeding has not been determined. However, because HAV vaccine is produced from inactivated HAV, there is not expected to be any risk to the developing fetus and infant. As a precaution, HAV vaccines should be used during pregnancy only when clearly needed, such as when travelling to a country where HAV is endemic.

7.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

7.6.1 Contraindications

Administration of HAV vaccine should be delayed in individuals suffering from acute febrile illness. HAV vaccine should not be administered to people with a history of an anaphylactic reaction to a prior dose of HAV vaccine or to a vaccine component.

7.6.2 Precautions

In individuals with an impaired immune system, adequate anti-HAV antibody titres may not be obtained after a single dose.

Pregnancy is a precaution – see section 7.5.3.

7.7 Expected responses and AEFIs

7.7.1 Expected responses

Soreness, redness and swelling at the injection site, fever, malaise, headache, nausea and loss of appetite have been reported for the monovalent HAV vaccines, but these responses are usually mild and brief.[15] Similar responses are seen with HAV–HBV combination vaccines, and HAV–typhoid combination vaccines.

7.7.2 AEFIs

Review of data from multiple sources has not identified any serious adverse events among children and adults that could be attributed to the HAV vaccine.[15]

7.8 Public health measures

It is a legal requirement that all cases of hepatitis A be notified immediately on suspicion to the local medical officer of health.

7.8.1 Outbreak control

Vaccination

Age-appropriate vaccine is recommended for all close contacts aged older than 1 year. If time allows, consider pre-vaccine serology if there is a history or likelihood of previous HAV vaccination or infection (for example, previous residence in an endemic country). Post-exposure prophylaxis with vaccine should be offered to contacts as soon as possible, and within two weeks of last exposure to an infectious case. The efficacy of vaccine when administered more than two weeks after exposure has not been established.

Immunoglobulin

Where vaccine is contraindicated (or not immediately available), human normal immunoglobulin may be offered to a close contact who may have a reduced response to vaccine or has risk factors for severe disease. The dose is 0.03 mL/kg given by intramuscular injection. Post-exposure prophylaxis should be offered to contacts as soon as possible, and within two weeks of last exposure to an infectious case.

Close contacts aged under 1 year will require human normal immunoglobulin.

Human normal immunoglobulin is available from the New Zealand Blood Service. For further information, refer to the medicine data sheets or the New Zealand Blood Service website (www.nzblood.co.nz).

Early childhood services and other institutional outbreaks

If an outbreak occurs in an early childhood service, vaccination (and/or immunoglobulin if appropriate) may be indicated for all previously unimmunised staff and children at the service and unimmunised new staff and children for up to six weeks after the last case has been identified, including cases in the household of attendees. The number of infected cases should determine the extent of intervention.

Vaccination and/or immunoglobulin may also be indicated for adults and children at a school, hospital or custodial-care institution where an outbreak of hepatitis A is occurring. For sporadic cases in hospitals, schools or work settings, post-exposure prophylaxis is not routinely indicated, but careful hygiene practices should be maintained.

Community-wide outbreaks of hepatitis A infection

HAV vaccine is effective in controlling community-wide epidemics and common-source outbreaks of HAV infection.[16] Before the vaccine is used for outbreak control, consideration should be given to the current epidemiology in the community, the population at risk should be defined, and the feasibility and cost of delivering a programme should be assessed.

For more details on control measures, refer to the 'Hepatitis A' chapter of the *Communicable Disease Control Manual 2012*.[11]

7.9 Variations from the vaccine data sheets

None.

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8 Hepatitis B

Key information

Mode of transmission	Contact with infected blood or body fluids during childbirth (vertical transmission); sexual intercourse, intravenous drug use, or contact with broken skin (horizontal transmission).
Incubation period	45–180 days, commonly 60–90 days.
Period of communicability	Potentially infectious 2–3 weeks before the onset of symptoms, during the clinical disease and usually for 2–3 months after acute hepatitis B illness; as long as HBsAg continues to be present in blood.
Burden of disease	New Zealand is a country with a low overall prevalence of hepatitis B carriage, but it contains certain populations with high prevalence. All pregnant women and high-risk groups should be screened for chronic infection. HBV acquisition in infancy is very likely to lead to chronic infection. Chronic HBV infection can progress to cirrhosis and liver cancer.
Funded vaccines	HepB (HBvaxPRO as 5, 10 and 40 µg presentations. Engerix-B 20 µg is the funded replacement for the HBvaxPRO 5 and 10 µg presentations while supplies are unavailable). DTaP-IPV-HepB/Hib (Infanrix-hexa).
Dose, presentation, route	HepB: • 5 µg presentation – 0.5 mL per dose, single dose vial • 10 and 40 µg presentations – 1.0 mL per dose, single dose vial • 20 µg presentation – 1.0 mL per dose, pre-filled syringe. DTaP-IPV-HepB/Hib: • 0.5 mL per dose • pre-filled syringe and glass vial – the vaccine must be reconstituted prior to injection. Intramuscular injection.

Continued overleaf

Funded vaccine indications and schedule	At ages 6 weeks, 3 months and 5 months: DTaP-IPV-HepB/Hib. Babies born to HBsAg-positive mothers should receive HepB vaccine plus HBIG at birth, then the usual childhood schedule. Serological testing (anti-HBs and HBsAg) at age 9 months. Individuals with eligible conditions: HepB (see section 8.5).
Vaccine efficacy/ effectiveness	In general, efficacy is 85–95 percent, though likely to be lower in older individuals and those with immunocompromise. Protection is expected to be lifelong. Boosters are not recommended.

8.1 Virology

The hepatitis B virus (HBV) is a partially double-stranded DNA virus belonging to the Hepadnaviridae family. Three major subunits make up the structural components:

- the HBV genome, a small, circular, partially double-stranded DNA molecule, in association with a polymerase enzyme
- the nucleocapsid core, which surrounds the genome and consists of core protein (hepatitis B core antigen, HBcAg)
- the outer lipoprotein envelope, which contains the hepatitis B surface antigen (HBsAg).

The genome has four genes (S, C, X and P). Both the core nucleocapsid protein (HBcAg) and the 'early' protein (which makes HBeAg) are translated from the C gene. HBcAg is essential for viral packaging and is an integral part of the nucleocapsid. HBeAg is a soluble protein that is not part of the virus particle. Detection of HBeAg in the serum is correlated with viral replication, and is most commonly found in those with acute hepatitis B and those with chronic HBV infection with high viral load.[1]

8.2 Clinical features

There is a broad spectrum of clinical disease with HBV infection, from subclinical through to fulminant hepatitis. Persistent infection can lead to chronic liver disease, potentially causing cirrhosis or hepatocellular carcinoma.

8.2.1 Serological markers of infection

The HBV antigens and their associated antibodies are serological markers of HBV infection or vaccination (Table 8.1). At least one serological marker is present during the different phases of infection (Table 8.2).

Table 8.1: HBV antigens and their respective antibodies

Antigen	Antibody
HBsAg (hepatitis B surface antigen)	Anti-HBs (antibody to HBsAg), (IgM, IgG, and total)
HBcAg (hepatitis B core antigen)	Anti-HBc (antibody to HBcAg), (IgM, IgG and total)
HBeAg (hepatitis B e antigen)	Anti-HBe (antibody to HBeAg), (IgM, IgG and total)

Table 8.2: Interpretation of serology for HBV infection

Serological marker				Interpretation
HBsAg	Total anti-HBc	IgM anti-HBc	Anti-HBs	
–	–	–	–	Never infected
+	+	+	–	Acute infection
–	+	+	+ or –	Acute resolving infection
–	+	–	+	Recovered from past infection and is immune
+	+	–	–	Chronic infection[a]
–	–	–	+	Immune if ≥10 IU/L.[b] Vaccinated or natural infection.

Key: Anti-HBc = antibody to hepatitis B core antigen; anti-HBs = antibody to hepatitis B surface antigen (HBsAg); IgM = immunoglobulin M; + = positive test result; – = negative test result.

a HBeAg positive (HBeAg+) correlates with high viral load and increased risk of transmission; HBeAg negative (HBeAg–) correlates with lower viral load and reduced risk of developing cirrhosis or cancer.

b Some laboratories may require a higher anti-HBs antibody level for proof of immunity. Please follow the testing laboratory's interpretative comments.

Adapted from: Van Damme P, Ward J, Shouval D, et al. 2013. Hepatitis B vaccines. In: Plotkin SA, Orenstein WA, Offit PA (eds). *Vaccines* (6th edition). Philadelphia, PA: Elsevier Saunders. Table 15.1.

See the 'Hepatitis B' chapter of the *Communicable Disease Control Manual 2012*[2] for recommendations for HBV case and contact management.

8.2.2 Acute hepatitis

The virus preferentially infects liver cells, multiplying there and releasing large amounts of HBsAg, which is present in the blood of people with active infection. The incubation period varies between 45 and 180 days, and is commonly 60 to 90 days.

HBV is not directly cytopathic; it is the host's immune response that leads to death of the infected liver cell. Most infected people mount an effective immune response that leads to eradication of infection over a period of several months. Adults with acute infection may be asymptomatic (approximately 20 percent) or have symptomatic hepatitis (approximately 80 percent, but these proportions vary[3]).

The common symptoms of acute hepatitis B illness are fever, jaundice, malaise, anorexia, nausea, vomiting, myalgia and abdominal pain. Jaundice usually develops within two weeks of onset of the illness, and dark urine and/or clay coloured stools might appear up to five days before clinical jaundice. Clinical signs and symptoms of acute hepatitis B usually resolve one to three months later.[1]

There is a small risk of liver failure (less than 1 percent) with acute infection; almost half will die or require emergency liver transplantation.

8.2.3 Chronic HBV infection

The main burden of HBV disease occurs in people with chronic HBV infection. Chronically infected people are identified by presence and persistence of HBsAg in their serum for at least six months. The age of acquisition of HBV is strongly associated with the risk of developing chronic HBV infection. Approximately 90 percent of those infected perinatally or in infancy develop chronic HBV infection, compared with 30 percent of children infected between ages 1 and 4 years and less than 5 percent of people infected as adults.

Infants seldom mount an immune response to HBV infection, and infection in infancy is often asymptomatic. Asymptomatic chronic infection stimulates persistent immune responses that may eventually lead to cirrhosis (decades later); cirrhosis and chronic infection increase the risk of development of hepatocellular carcinoma.

Chronically infected people who are HBsAg positive can also have HBeAg detectable in the serum, and this combination is considered most infectious. Although recent evidence suggests HBeAg negative patients are less infectious, it is dependent on HBV DNA levels. Whatever the case, both groups can be an ongoing source of infection to susceptible individuals. In the early years of chronic infection, high rates of viral replication are common, and both HBeAg and high levels of HBV DNA are present in the blood. In later years, HBeAg may be absent from the blood, and HBV DNA levels are usually lower, both of which correspond with lower rates of viral replication.

8.2.4 Routes of transmission

HBV is usually transmitted through contact with infected blood or body fluids during childbirth, contact with broken skin, or during sexual intercourse or intravenous drug use. Although HBV can be found in all body fluids, blood has the highest concentration and saliva the lowest. HBV in dried blood remains infective for at least one week.[4]

Perinatal (vertical) transmission

The primary source of HBV infection is perinatal exposure from mothers with chronic HBV infection. Transmission usually occurs at the time of birth. The *in utero* transmission of HBV is relatively rare,[5] accounting for less than 2 percent of infections transmitted from mother to infant.

If no prophylaxis is given to the infant, the baby of an HBeAg positive mother has a 70–90 percent risk of infection, while the baby of an HBeAg negative, HBsAg positive carrier mother has a 5–20 percent risk of infection. Over 90 percent of infants who acquire infection perinatally go on to become chronic carriers.

Person-to-person (horizontal) transmission

Non-sexual person-to-person transmission probably occurs from inadvertent percutaneous or mucosal contact with blood or infectious body fluids amongst people in close daily contact (household members).

The main sources of transmission are:

- sexual contact with an infected individual
- percutaneous exposure to blood or infectious body fluids
- needle-stick injuries or sharing needles
- travelling to high endemic countries (see below).

8.3 Epidemiology

8.3.1 Global burden of disease

Approximately two billion people have been exposed to HBV, and an estimated 240 million people have chronic infection and remain at risk of developing cirrhosis and hepatocellular carcinoma.[6, 7] More than 90 percent of individuals with chronic HBV reside in the Asia–Pacific region, where most countries have high prevalence rates of HBV infection (the population rate of HBsAg positivity is between 5 and 20 percent). More than 99 percent of HBV-infected people in this region acquired infection through vertical transmission from their mother (usually at the time of delivery) or in early childhood. Acquisition of HBV during adulthood (usually via sexual transmission or injecting drug use) is associated with a high rate of symptomatic hepatitis but a low rate of chronic infection.

The introduction of universal childhood HBV immunisation has changed the epidemiology of chronic infection in many countries, but it will be several decades (one to two human generations) before the full benefits are realised. The world can be divided into regions with high (8 percent and over), high-intermediate (5–7 percent), low-intermediate (2–4 percent) and low (less than 2 percent) prevalence of chronic infection, defined as the presence of HBsAg in serum.[8, 9]

In regions with a high prevalence of chronic infection, the lifetime risk of exposure to HBV is almost 80 percent, with most infections occurring in the first decade of life. The Pacific Islands and most of Asia (except Japan and India) are high-prevalence regions. Other high-prevalence regions include Sub-Saharan Africa and Latin America.[8] In contrast, in countries with a low HBsAg prevalence, the lifetime risk of HBV exposure is less than 20 percent, with most infections acquired in adulthood.

New Zealand has a low overall prevalence of hepatitis B carriage but contains certain populations with high prevalence (see section 8.3.2 below).

8.3.2 New Zealand epidemiology

Before the introduction of HBV immunisation in New Zealand, HBV transmission was common among preschool and school-aged children. The exact mode of transmission is uncertain but is thought to be related to close contact. In the eastern Bay of Plenty region almost half of the population were infected by age 15 years.[10, 11] Even after the introduction of universal HepB in 1988 (see Appendix 1), there were regions in New Zealand where children were still at risk of HBV infection due to poor immunisation coverage rates.[12, 13, 14]

Acute HBV infection

Only acute hepatitis B is a notifiable disease in New Zealand. Therefore notification rates do not describe the burden of chronic HBV infections.

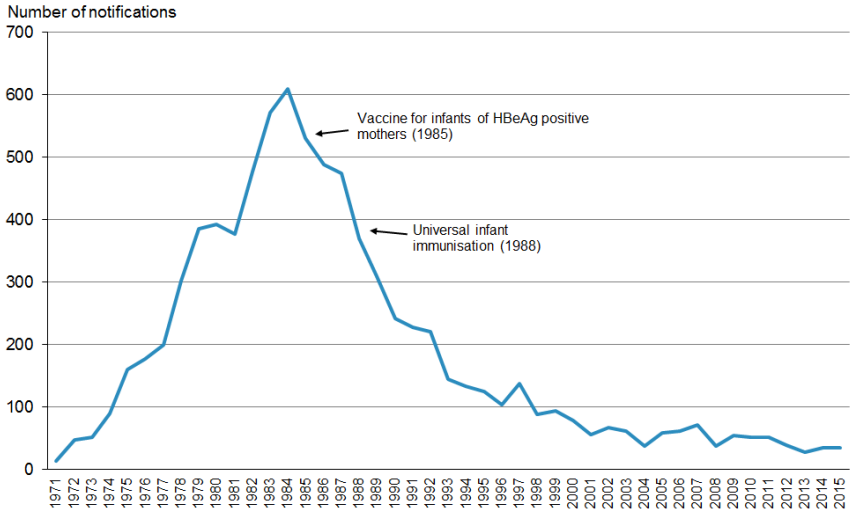
The HBV notification rate in 2015 was 0.7 per 100,000 population (34 cases), similar to the 2014 rate (0.8 per 100,000, 35 cases).[15] The highest notification rate was in the 40–49 and 50–59 years age groups (both 1.3 per 100,000). The notification rate was higher for males (1.1 per 100,000 population) than for females (0.4 per 100,000).

Ethnicity was recorded for 32 cases (94.1 percent).[15] The Māori (0.9 per 100,000) and European/Other (0.6 per 100,000) ethnic groups had the highest hepatitis B notification rates.

The most common risk factors reported in 2015 were overseas travel and sexual contact with a confirmed case or person with chronic HBV infection.

Hepatitis B notifications have declined from 609 cases in 1984 to 34 cases in 2015 (see Figure 8.1). While difficult to quantify accurately, the introduction of universal infant immunisation in 1988 has contributed to the dramatic decline in the number of newly notified cases of HBV infection.

Figure 8.1: Notifications of hepatitis B, 1971–2015



Source: Ministry of Health and ESR

Chronic HBV infection

Approximately 100,000 people in New Zealand are chronically infected with HBV. The National Hepatitis B Screening Programme was a three-year programme that started in 1999 and targeted at-risk populations in the North Island (Māori, Pacific peoples and Asian New Zealanders aged over 15 years). The programme also enrolled people from other ethnic groups and included follow-up of individuals aged under 15 years with chronic HBV.

Approximately one-third of the at-risk populations were screened. Of these, the highest rates were among Chinese (9.1 percent), Pacific peoples (8.5 percent) and Māori (5.8 percent). Although Europeans were not specifically targeted in this screening programme, they have an estimated prevalence rate of 1 percent (higher than in Australia, North

America and Europe), reflecting increased risk of childhood horizontal transmission.[16]

A New Zealand-based modelling study estimated that until the year 2100, people with chronic HBV infection will continue to provide a source of infection to susceptible people.[17] Increased immigration from high-prevalence countries in the Asia–Pacific region is also likely to influence HBV prevalence in New Zealand.

Because people who acquire chronic HBV infection in childhood usually do not develop hepatocellular carcinoma until aged 40 years or older, the introduction of a universal HBV vaccination in 1988 is unlikely to have a significant effect on the incidence of hepatocellular carcinoma until approximately 2030.

A retrospective laboratory data study of antenatal HBsAg tests from the Midlands region (Bay of Plenty, Eastern Bay of Plenty, Waikato and Rotorua) between 1997 and 2009 found a declining prevalence of HBV infection. This decrease was seen across all age groups, but was most marked in the antenatal tests of women aged under 20 years, due to receipt of funded HepB in childhood.[18]

A recent long-term follow-up study in New Zealand has shown horizontally acquired HBV infection during childhood in Māori and Pacific peoples correlates with increased rates of hepatocellular carcinoma and liver-related mortality.[19] This study emphasises the importance of early protection of the infant with vaccination.

Strategy for prevention

In 1988 New Zealand was one of the first countries to introduce universal infant hepatitis B immunisation. At the end of 2016 approximately 93 percent of New Zealand children aged 2 years had completed a primary course of HepB, which confers lifelong immunity in approximately 95 percent of vaccinees.

8.4 Vaccines

8.4.1 Available vaccines

A number of HBV-specific monovalent and combination vaccines that contain recombinant HBsAg (HepB) are licensed (approved for use) and available (marketed) in New Zealand.

Note: In 2018 there is a shortage of the HBvaxPRO 5 µg and HBvaxPRO 10 µg vaccines. If the HBvaxPRO 5 µg or HBvaxPRO 10 µg vaccines are unavailable, the Engerix-B 20 µg vaccine can be used instead. (Supplies of the HBvaxPRO 40 µg vaccine are unaffected.) See also the IMAC factsheet *Engerix-B replaces HBvaxPRO 5 mcg and 10 mcg until 2019* (available for download from: www.immune.org.nz/resources/written-resources).

Funded vaccines

- HepB (HBvaxPRO, MSD): contains either 5 µg, 10 µg or 40 µg of HBsAg per dose; it does not contain a preservative. Other components and residuals include amorphous aluminium hydroxysulphate, sodium borate, sodium chloride and yeast (less than 1 percent of the protein content is from yeast).
- HepB (Engerix-B, GSK): contains 20 µg HBsAg per dose; it does not contain a preservative. Other components and residuals include aluminium hydroxide, sodium chloride, sodium phosphate dehydrate, sodium dihydrogen phosphate and traces of polysorbate 80.
- DTaP-IPV-HepB/Hib (Infanrix-hexa, GSK): diphtheria, tetanus, acellular pertussis, inactivated polio, hepatitis B and *Haemophilus influenzae* type b vaccine (see section 5.4.1 for more information).

Other vaccines

- HepB: Engerix-B (GSK) – paediatric presentation (10 µg HBsAg per dose)
- HAV-HepB (hepatitis A and hepatitis B vaccine): Twinrix and Twinrix Junior (GSK) (see also section 7.4.1).

8.4.2 Efficacy and effectiveness

See also section 14.4.2 for information about the DTaP-IPV-HepB/Hib vaccine.

Immunogenicity

Clinical trials in high-risk groups have shown a vaccine efficacy of 85–95 percent. Serum anti-HBs antibody ≥10 IU/L is the WHO measure of immunity and is considered a correlate of protection. In the primary care setting, individuals who have had a documented seroconversion after three injections are expected to have lifelong immunity with no need for further boosters, even if circulating antibody is subsequently not detectable.

Smoking, obesity, HIV infection and chronic disease (including renal failure) all reduce vaccine efficacy, but age is the primary factor affecting the response. At least 98 percent of infants, 95 percent of children and 90 percent of adolescents develop protective levels of antibody after three doses of vaccine. Some non-responders to the initial vaccination course will not produce adequate antibody levels. These people should be offered a full second course of three injections.

However, some people are persistent non-responders. Persistent non-responders often have an impaired immune system, such as organ transplant recipients and those with HIV infection or chronic disease, including advanced cirrhosis, renal failure or those undergoing haemodialysis (see section 8.5.7).

For babies of HBeAg-positive mothers, controlled trials have shown that vaccine at birth provides 75 percent protection from infection, while administration of HBIG in addition to vaccination provides 85–95 percent protection against transmission.[1, 20] Protection is reduced to less than 80 percent when the mother's HBV DNA level is greater than 10^8 IU/mL (or 10^8 copies/mL). In this situation, administration of tenofovir (an antiviral agent) to the mother during the last trimester is recommended and funded.

Duration of immunity

The development of anti-HBs antibodies after a primary vaccination course (three injections and seroconversion) indicates development of immune memory. The quantity of antibody in serum is thought to determine the length of time the antibody titre can be detected in the blood, although any reading ≥10 IU/L post-vaccination course is considered protective. Once a seroprotective level is reached after the three-dose primary vaccination course, booster doses of vaccine are unnecessary.[21, 22] Children who are given booster doses up to 12 years after the primary series show strong anamnestic (secondary) responses, indicating the boost was unnecessary.

There is evidence from Taiwan,[23] Alaska[24] and Hawaii[25] that boosters of HepB are unnecessary following completion of infant immunisation. This is despite the fact that a large proportion of vaccinees will lose detectable antibodies within seven years of vaccination. Long-term protection from clinical infection despite loss of neutralising antibody is thought to reflect a strong cellular memory immune response following HBV vaccination. Vaccinees who are subsequently infected with HBV do not develop clinical illness but may have anti-HBc present in plasma.

Effects on chronic HBV infection

In all populations where it has been measured, immunisation has led to a dramatic drop in HBV chronic infection.[26] For example, chronic HBV infection dropped from 16 percent to zero in Alaska as a result of 96 percent immunisation coverage. In Taiwan, the incidence of hepatocellular carcinoma also decreased in children as a result of the immunisation programme.[27, 28]

8.4.3 Transport, storage and handling

Transport hepatitis B vaccines according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.[29] Store at +2°C to +8°C. Do not freeze.

DTaP-IPV-HepB/Hib and HepB (Engerix-B) should be stored in the dark.

DTaP-IPV-HepB/Hib (Infanrix-hexa) must be reconstituted by adding the entire contents of the supplied container of the DTaP-IPV-HepB vaccine to the vial containing the Hib pellet. After adding the vaccine to the pellet, the mixture should be shaken until the pellet is completely dissolved. Use the reconstituted vaccine as soon as possible. If storage is necessary, the reconstituted vaccine may be kept for up to eight hours at 21°C.

8.4.4 Dosage and administration

DTaP-IPV-HepB/Hib

Each 0.5 mL dose of DTaP-IPV-HepB/Hib (Infanrix-hexa) vaccine contains 10 µg of HBsAg, and is administered by intramuscular injection (see section 2.2.3).

HepB

The dose of HepB vaccine varies according to the vaccine manufacturer, the age of the individual and/or their health status (see section 8.5 for recommendations):

- HBvaxPRO 5 µg (MSD): 5 µg HBsAg per 0.5 mL
- HBvaxPRO 10 µg (MSD): 10 µg HBsAg per 1.0 mL
- HBvaxPRO 40 µg (MSD): 40 µg HBsAg per 1.0 mL
- Engerix-B 20 µg (GSK): 20 µg HBsAg per 1.0 mL.

HepB vaccine is administered by intramuscular injection.

Co-administration with other vaccines

Hepatitis B vaccines may be given at the same time as all other vaccines on the Schedule, including measles, mumps and rubella (MMR) vaccine.

If a course of vaccine is interrupted, it may be resumed without repeating prior doses (see Appendix 2).

8.5 Recommended immunisation schedule

Table 8.3: Hepatitis B vaccine recommendations, funded and unfunded

Note: Funded conditions are in the shaded rows. See the Pharmaceutical Schedule (www.pharmac.govt.nz) for any changes to the funding decisions.

Recommended and funded
Household or sexual contacts of HBsAg-positive patients (ie, patients with acute or chronic HBV infection)
Babies of HBsAg-positive mothers (ie, mothers with acute or chronic HBV infection) – require a birth dose plus the primary series (HBIG is also given to these babies at birth)
Children and adolescents aged under 18 years who are considered not to have achieved a positive serology and require additional vaccination or require a primary course of vaccination
HIV-positive patients[a]
Hepatitis C-positive patients[b]
Following non-consensual sexual intercourse
Following immunosuppression[a,c]
Solid organ transplant patients[a]
Post-HSCT patients[a]
Following needle-stick injury
Dialysis patients[a,d]
Liver or kidney transplant patients[a,d]

Continued overleaf

Recommended, not funded
Adults at occupational risk (see section 4.6)
Adults at risk of infection by sexual exposure: • people seeking evaluation or treatment for a sexually transmitted infection • people with a high number of sexual partners • people who have sex with commercial sex workers • men who have sex with men
Individuals with haemophilia and other regular recipients of blood products
Prison inmates
Current or recent injecting drug users
Migrants from HBV endemic countries (HBsAg prevalence ≥2%)[e]
Individuals with developmental disabilities
Travellers to HBV endemic regions (HBsAg prevalence ≥2%)[e]

a See also section 4.3.3.

b Hepatitis C patients should also receive hepatitis A vaccine, although this is not currently funded.

c The period of immunosuppression due to steroid or other immunosuppressive therapy must be longer than 28 days.

d The 40 µg dose of HepB is recommended for adult dialysis patients or for adult liver or kidney transplant patients. See Table 8.5.

e See the Centers for Disease Control and Prevention website for countries with HBsAg prevalence ≥2% (https://wwwnc.cdc.gov/travel/yellowbook/2018/infectious-diseases-related-to-travel/hepatitis-b). Consider combined Hep A and B vaccination for travellers to these regions.

8.5.1 Usual childhood schedule

A primary course of hepatitis B vaccination is given as three doses of DTaP-IPV-HepB/Hib at ages 6 weeks, 3 months and 5 months (Table 8.4). If a course of immunisation is interrupted for any reason, it may be resumed without repeating prior doses (see section 8.5.3 and Appendix 2).

Table 8.4: Usual childhood schedule for hepatitis B-containing vaccine (excluding catch-up)

Age	Vaccine	Comment
6 weeks	DTaP-IPV-HepB/Hib	Primary series
3 months	DTaP-IPV-HepB/Hib	Primary series
5 months	DTaP-IPV-HepB/Hib	Primary series

Preterm infants of HBsAg-negative women

Some low birthweight or preterm infants may have a reduced response to HepB at birth.[30] However, by the chronological age of 1 month, all medically stable preterm infants, regardless of initial birthweight or gestational age, respond to HepB as well as term and larger infants.[31] Because New Zealand's Schedule starts at age 6 weeks, low birthweight and preterm infants are expected to respond to HepB. (See also section 4.2.1.)

Infants with liver or renal disease

HepB vaccine is funded for liver or kidney transplant patients and for dialysis patients. For infants requiring transplants, see section 4.2.3. For infants undergoing dialysis, see 'Chronic kidney disease (CKD)' in section 4.3.3.

8.5.2 Babies born to HBsAg-positive mothers

The routine schedule for these infants is a birth dose of 5 μg of HepB (HBvaxPRO 5 μg [use Engerix-B 20 μg if HBvaxPRO 5 μg is not available]) plus HBIG, then three doses of hepatitis B (as DTaP-IPV-HepB/Hib) at ages 6 weeks, 3 months and 5 months.

All pregnant women should receive antenatal screening for hepatitis B infection by testing for HBsAg. Babies of HBsAg-positive mothers are to be notified at birth using the form *HE1446: Consent for hepatitis B vaccine and hepatitis B immunoglobulin and notification to the Medical Officer of Health*, available from www.healthed.govt.nz or the local authorised health education resource provider or public health unit.

Babies born to HBsAg-positive mothers should receive:

- 100–110 IU HBIG neonatal, at or as close as possible to birth
- a birth dose of HepB (HBvaxPRO 5 µg [use Engerix-B 20 µg if HBvaxPRO 5 µg is not available]), which should be given at or as close as possible to birth (preferably within 12 hours).

If HBIG and/or HepB is inadvertently omitted, administer as soon as the omission is recognised. HBIG can be administered up to seven days post-delivery. If there is a delay for longer than seven days, seek specialist advice.

These babies should then continue as per the Schedule at ages 6 weeks, 3 months and 5 months. Serological testing is required at 9 months of age (see below).

The vitamin K injection may also be given at the same time, in the same limb as the HBIG, but not at the same site.

Occasionally women have not been tested for their HBsAg status during the antenatal period. If a woman's HBsAg status is unknown at the time of delivery, the baby should be given HepB at the time of delivery while waiting for the result of an urgent HBsAg test on the mother. If she is found to be HBsAg positive, the baby should be given HBIG as soon as possible, up to seven days post-delivery.[31] Subsequent vaccine doses are given as per the Schedule.

It is essential to take blood to determine whether the baby has seroconverted (anti-HBs positive) or has become infected despite immunoprophylaxis (HBsAg positive), or is neither infected nor immune (ie, HBsAg negative and anti-HBs negative). Testing should not be performed before 9 months of age to avoid detection of anti-HBs from HBIG administered during infancy and to maximise the likelihood of detecting late HBV infections.[31]

Babies of HBsAg-positive mothers should be placed on a practice recall system to have their blood tested at 9 months of age, and should be rechecked at the 15-month immunisation event to ensure that testing has occurred. The serology results should be interpreted as in Figure 8.2.

Figure 8.2: Management of a baby of an HBsAg-positive woman

Screen all women in early pregnancy for hepatitis B carriage

Woman is HBsAg positive **No** ⋯⋯› See section 8.5.1: 'Usual childhood schedule'

Yes

All HBsAg-positive pregnant women should also be tested for HBeAg and should have HBV DNA measured. The results should be discussed with a specialist or the woman should immediately be referred to a specialist for ongoing care.

Give the baby hepatitis B protection as follows.

At age	Action to be taken
Birth	Give HBIG 100–110 IU **and** HepB HBvaxPRO 5 µg (use Engerix-B 20 µg if HBvaxPRO 5 µg is not available)
6 weeks	DTaP-IPV-HepB/Hib
3 months	DTaP-IPV-HepB/Hib
5 months	DTaP-IPV-HepB/Hib
9 months	Take a blood test to check for hepatitis B infection (HBsAg) and for vaccine-induced immunity (anti-HBs). • If HBsAg is negative and anti-HBs level is ≥10 IU/L* at age 9 months, immunity is proven. • If HBsAg is positive, the baby has become infected despite prophylaxis: refer to an appropriate specialist. If HBsAg is negative and anti-HBs level is <10 IU/L* at age 9 months, give a further 3 doses of HepB at least 4 weeks apart. Recheck serology 4 weeks after the last dose. If there is no seroconversion after the third further dose of HepB (ie, if anti-HBs is still <10 IU/L*), discuss with a specialist.

All other vaccines should be administered as per the Schedule.

* Some laboratories may require a higher anti-HBs antibody level for proof of immunity. Please follow the testing laboratory's interpretative comments.

Neonatal HBIG plus vaccine will fail to prevent vertical HBV transmission in more than 20 percent of infants born to HBsAg-positive mothers with serum HBV DNA levels greater than 10^8 IU/mL (or 10^8 copies/mL). These mothers are usually young, with normal alanine transaminase, and are HBeAg positive. If the mother's HBV DNA level is greater than 10^8 IU/mL, administration of tenofovir (an antiviral agent) during the last trimester is recommended and funded.

The number of such high-risk pregnancies appears to be increasing in this country as a result of the immigration of young Asian women of childbearing age, of whom approximately 8 percent are HBsAg positive, with the majority of those also HBeAg positive. In contrast, the number of HBsAg-positive Māori and Pacific women of childbearing age has decreased markedly due to infant vaccination. In addition, most HBsAg-positive Māori and Pacific women are HBeAg negative, with lower HBV DNA levels (below 10^8 IU/mL).

Babies born to mothers who received oral antiviral therapy for chronic HBV must still receive the recommended neonatal HBIG/vaccine schedule. All other vaccines are administered as per the Schedule.

See Appendix 6 and section 8.8.1 for more information about passive immunisation and HBIG.

Preterm and low birthweight infants of HBsAg-positive women

Preterm and low birthweight infants of HBsAg-positive women should be managed as above, regardless of birthweight or gestation.

8.5.3 Catch-ups for children and adolescents

HepB is recommended and funded for everyone aged under 18 years. If the HepB is not given during the first year of life, three doses of vaccine are recommended.

For adolescents aged 11–15 years, an alternative two-dose hepatitis B catch-up schedule may be considered using the monovalent HepB (HBvaxPRO 10 µg), with the second dose given four to six months after the first. If HBvaxPRO 10 µg is not available, use Engerix-B 20 µg instead. (Note: While not approved for a two-dose schedule, there is no reason to expect that two doses of Engerix-B 20 µg, given four to six months apart, would not provide the same level of protection as two doses of HBvaxPRO 10 µg.)

See Appendix 2 for catch-up schedules.

Children and adolescents with liver or kidney disease

HepB vaccine is funded for liver or kidney transplant patients (recommend six months post-transplant) and for dialysis patients.

See Figures 8.3 and 8.4 for serological testing and vaccination recommendations. If non-immune, children aged under 16 years should receive three doses (at 0, 1 and 6 months) of 10 µg HepB (HBvaxPRO 10 µg [use Engerix-B 20 µg if HBvaxPRO 10 µg is not available]), those aged 16 years and older should receive three doses of 40 µg HepB (HBvaxPRO 40 µg). If there is an inadequate immune response to the initial three-dose HepB series (see Figure 8.4), give a further three doses (10 µg, 20 µg or 40 µg, as appropriate).

See also 'Chronic kidney disease (CKD)' and 'Solid organ transplants' in section 4.3.3.

8.5.4 Eligible adults aged 18 years and older

Table 8.5: Hepatitis B vaccine schedules for eligible adults aged 18 years and older

Who	Vaccine	Dose	Volume (mL)	Number of doses	Schedule
Dialysis patients, liver or kidney transplant patients	HepB	40 µg	1.0	3	0, 1, and 6 months[*a]
HIV patients	HepB	10 or 20 µg*	1.0	4	0, 1, 2, and 12 months
Other eligible adults (see Table 8.3)	HepB	10 or 20 µg*	1.0	3	0, 1, and 6 months

* Depending upon supply, HBvaxPRO 10 µg or Engerix-B 20 µg may be used.

Adult dialysis or adult liver or kidney transplant patients

These adults may have a reduced response to HepB,[32] so the higher-dose (40 µg) formulation is recommended and funded. See section 8.5.7 for information about post-vaccination serology.

(See also 'Solid organ transplants' in section 4.3.3.)

Adult HIV patients

Adult HIV patients should receive four doses of HepB (10 μg or 20 μg) at 0, 1, 2 and 12 months.

(See also 'HIV infection' in section 4.3.3.)

Other eligible adults

The optimal dosing regime is three doses of 10 μg or 20 μg HepB given at 0, 1 and 6 months. See the manufacturer's data sheet for sub-optimal accelerated HepB schedules if dosing is time constrained.

8.5.5 Pregnancy and breastfeeding

HepB may be given during pregnancy and while breastfeeding. Acute HBV infection in pregnant women may result in severe acute hepatitis for the mother, with associated increased risk of fetal loss or neonatal infection. Vaccination should not be withheld from a susceptible pregnant woman at increased risk of acquiring hepatitis B (eg, the sexual partner of an injecting drug user, or known infected male).

8.5.6 (Re-)vaccination

Hepatitis B-containing vaccines are funded for (re-)vaccination of eligible children, as follows. See also sections 4.2 and 4.3.

DTaP-IPV-HepB/Hib (Infanrix-hexa)

An additional four doses (as appropriate) of DTaP-IPV-HepB/Hib are funded for (re-)vaccination of children aged under 10 years:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- with other severely immunosuppressive regimens.

Up to five doses of DTaP-IPV-HepB/Hib are funded for children aged under 10 years receiving solid organ transplantation.

HepB (HBvaxPRO or Engerix-B)

HepB is funded for children aged under 18 years who are considered not to have achieved a positive serology and require additional vaccination.

8.5.7 Serological testing

- Globally, pre-vaccination serological testing is NOT recommended as a routine practice in primary care.
- The vast majority of people with documented evidence of three HepB injections will be immune where there is low risk of disease.
- Infants born to HBsAg-positive mothers and some individuals who require protection in relation to their employment, eg, health care professionals, require post-vaccination serology.

Screening for chronic infection

Screening for the antigen (HBsAg) is useful where there is increased likelihood of the individual already being infected.

The Hepatitis Foundation of New Zealand[33] recommends that the following individuals are most at risk of HBV – people who:

- are over age 25 years and of Māori, Pacific or Asian ethnicity
- were born outside of New Zealand (eg, refugees)
- have a mother or a close family member who has HBV infection
- live with someone who has HBV
- have had unprotected sexual contact with an HBV-infected person
- have ever injected drugs
- have received a tattoo using unsterile equipment.

Screening for HBsAg is also part of routine antenatal care (see section 8.5.2).

All HBsAg-positive individuals should be offered follow-up under the Hepatitis Foundation Hepatitis B Follow-up Programme to enable early diagnosis and treatment of the complications of severe liver disease and hepatocellular carcinoma. Vaccination is recommended (and funded)

for household or sexual contacts of HBsAg-positive people (ie, contacts of people with acute or chronic HBV infection).

Serological testing for high-risk groups

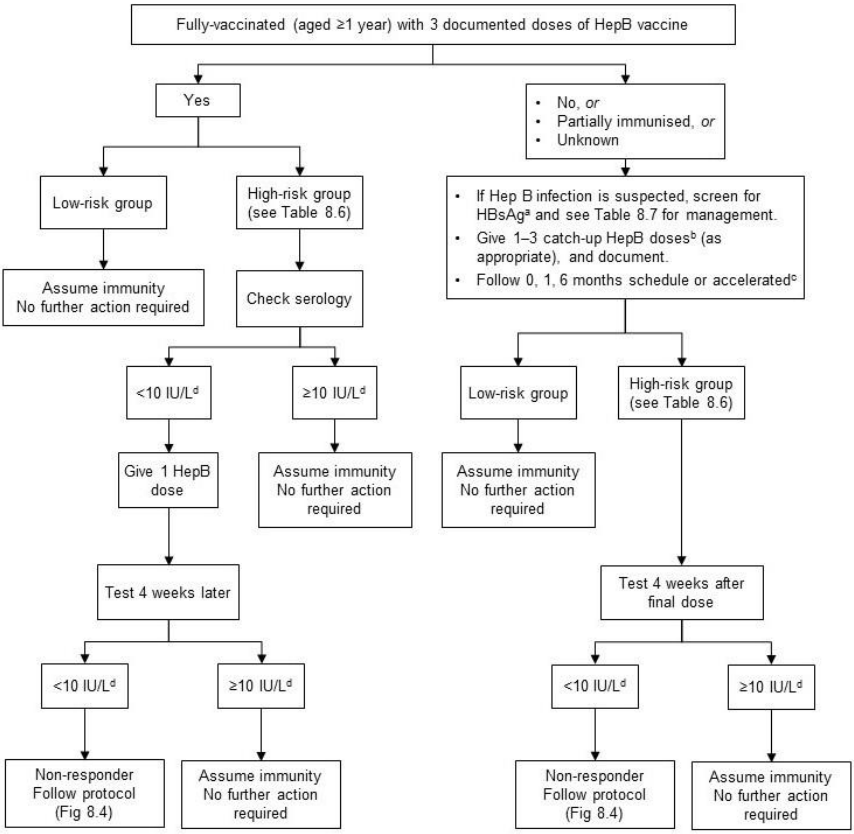
Serological testing is only indicated in high-risk groups (see Table 8.6). These high-risk groups are at higher risk of exposure to HBV, at higher risk of having severe disease or are more susceptible to disease. A flow diagram (Figure 8.3) is included to assist in deciding whether pre- and/or post-vaccination serological testing is indicated. Figure 8.3 may be used for any individual aged 12 months or older, such as for the management of blood and body fluid exposures, or when an adult presents to primary care.

Table 8.6: Individuals at high-risk of hepatitis B infection, for whom serological testing is indicated

Household or sexual contacts of HBsAg-positive patients (ie, patients with acute or chronic HBV infection)
Current or recent injecting drug users
Individuals who change sexual partners frequently (eg, sex workers)
Immunocompromised individuals, including HIV-positive patients
Following non-consensual sexual intercourse
Individuals on immunosuppressive therapies for 28 days or more
Solid organ and post-HSCT patients
Following percutaneous injury (eg, needle-stick injury)
Adults at occupational risk (see section 4.6)
Individuals with haemophilia and other regular recipients of blood products
Inmates of custodial institutions
Individuals with developmental disabilities
People with chronic disease (eg, chronic renal failure requiring haemodialysis, or chronic liver disease)
Migrants from HBV endemic regions (HBsAg prevalence ≥2%)*

* See the Centers for Disease Control and Prevention website for countries with HBsAg prevalence ≥2% (https://wwwnc.cdc.gov/travel/yellowbook/2018/infectious-diseases-related-to-travel/hepatitis-b). Consider combined Hep A and B vaccination for travellers to these regions.

Figure 8.3: Flow diagram for serological testing for hepatitis B



a HBIG may be recommended for non-immune individuals. See Table 8.7.

b Do not count any birth doses of HepB vaccine. See Table 8.3 for the list of funded conditions for HepB vaccine.

c See the manufacturer's data sheet for accelerated HepB schedules.

d Some laboratories may require a higher anti-HBs antibody level for proof of immunity. Please follow the testing laboratory's interpretative comments.

The non-responder protocol

Most vaccinees will develop a high anti-HBs titre, usually greater than 100 IU/L, which usually wanes over time.

Fully vaccinated individuals (ie, three documented doses of HepB) who have at any time had anti-HBs ≥10 IU/L do not need any booster doses, even if antibodies subsequently wane to undetectable levels, which occurs in most individuals by seven years after the last vaccination. If exposed, they will have a secondary anamnestic immune response that will prevent replication of the virus.[1, 34] (Note: Some laboratories may require a higher anti-HBs antibody level for proof of immunity. Please follow the testing laboratory's interpretative comments.)

If a high-risk individual does not achieve a titre of ≥10 IU/L, they should be considered a non-responder and follow the non-responder protocol (Figure 8.4).

Figure 8.4: The non-responder protocol

Individual is high-risk (see Table 8.6), has received three documented doses of HepB and has an anti-HBs <10 IU/L:*

- Complete a second course of three HepB vaccine doses.
- Repeat the serology four weeks after the final HepB vaccine dose.
- If anti-HBs ≥10 IU/L,* then assume immunity. No further action required.
- If, after the second course of three HepB vaccines, they have not achieved anti-HBs ≥10 IU/L,* they should be considered a persistent non-responder to vaccination.
- There is evidence that using a double dose of HAV-HepB (Twinrix) at 0, 1 and 6 months can correct this hyporesponsiveness, using the bystander carrier effect of the HAV component,[35] but this is not funded.
- Persistent non-responders with no immunocompromise who have completed the primary series and a full second course of three vaccine doses should be monitored for wild-type disease, but literature reports of vaccine failures are rare. They should be considered 'unprotected' against hepatitis B and advised to minimise the chance of exposures. Parenteral or mucosal exposure to HBV requires HBIG within 72 hours.

* Some laboratories may require a higher anti-HBs antibody level for proof of immunity. Please follow the testing laboratory's interpretative comments.

Intradermal injections to correct this hyporesponsiveness that have been used in the past, but they are technically difficult and not recommended.

8.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

The only specific contraindication to HepB is anaphylaxis following a previous dose, or individuals with a history of allergic reactions to yeast or any of the vaccine's components. This is uncommon. Immunisation of previously infected subjects is wasteful, but not harmful.

See section 14.6 for contraindications and precautions to DTaP-IPV-HepB/Hib vaccine.

8.7 Expected responses and AEFIs

See section 14.7 for expected responses and AEFIs with DTaP-IPV-HepB/Hib vaccine.

8.7.1 Expected responses

Minor side-effects – including local tenderness and redness, nausea, diarrhoea, general malaise and fever – are more common in adults than in children and, except for local reactions, occur at rates close to those seen with a placebo. Minor reactions reported after receiving the vaccine include a temperature >37.7°C in 1–6 percent, pain in 3–29 percent, and erythema, headache or swelling in 3 percent of vaccinees.

8.7.2 AEFIs

Allergic reactions have been reported but are rare. Anaphylaxis is extremely rare.

A number of studies have examined and failed to find disease events linked to hepatitis B immunisation.[36] These studies have documented no increased risk of multiple sclerosis,[37, 38] diabetes, chronic fatigue syndrome,[39] encephalomyelitis or hair loss.[40] Rarely, transient

thrombocytopenia[41] and myalgia and arthralgia[42, 43] have been reported after HepB vaccination.

8.8 Public health measures

The elimination of HBV transmission is now a realistic public health goal,[7, 44] especially with the proven effectiveness and safety record of HepB.[45]

It is important to ensure vaccination programmes are maintained for the at-risk populations, especially babies of mothers with chronic hepatitis B infection.

> It is a legal requirement that all cases of acute hepatitis B infection be notified to the local medical officer of health.

Babies born to HBsAg-positive mothers should be notified at birth. The prevention of perinatal transmission is covered in section 8.5.2.

8.8.1 Passive immunisation

HBIG is prepared from donated blood plasma and contains high levels of anti-HBs antibody (see Appendix 6). It is given after exposure to HBV and provides passive anti-HBs antibody protection against acute and chronic HBV disease. HBIG prophylaxis should be given in combination with the HepB to confer both passive and active immunity after exposure.

The efficacy of HBIG alone in preventing clinical hepatitis B infection is about 75 percent in adults, but the protection lasts only for a few months.[1]

Whenever immediate protection is required, immunisation with a vaccine should be combined with simultaneous administration of HBIG at a different site. It has been shown that passive immunisation with HBIG does not suppress the active immune response to vaccination. A single dose of HBIG (usually 400 IU for adults, 100–110 IU for the newborn; refer to the 'Hepatitis B' chapter of the *Communicable Disease Control Manual 2012*[2]) is sufficient. If infection has already occurred at the time of the first immunisation, virus replication is unlikely to be inhibited completely, but severe illness and, more importantly, the

development of chronic HBV infection may be prevented, particularly in the infants of HBsAg-positive mothers.

The management of contacts is summarised in Table 8.7.

Table 8.7: Management of contacts of hepatitis B cases

Contact	Serological testing of contact (HBsAg, anti-HBs, anti-HBc, IgM and IgG)	Immunoglobulin (if within 7 days of onset of case's symptoms)	Immunisation
Any sexual contact, including protected sex	Yes	Yes, immediately after blood taken	Yes, immediately after blood taken
Household, mucosal or percutaneous	Yes	Yes, if serology negative	Yes, if serology negative
Other	Yes	No	Yes, if serology negative

Source: Ministry of Health. 2012. *Communicable Disease Control Manual 2012*. URL: http://www.health.govt.nz/publication/communicable-disease-control-manual-2012 (accessed 20 March 2017).

For more details on control measures, refer to the 'Hepatitis B' chapter of the *Communicable Disease Control Manual 2012*.[2]

8.9 Variations from the vaccine data sheet

See section 14.9 for variations from the DTaP-IPV-HepB/Hib (Infanrix-hexa) data sheet.

Two doses Engerix-B 20 µg, given four to six months apart, may be given to adolescents aged 11–15 years if HBvaxPRO 10 µg is not available. While not approved for a two-dose schedule, there is no reason to expect that two doses of Engerix-B 20 µg, given four to six months apart, would not provide the same level of protection as two doses of HBvaxPRO 10 µg.

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9 Human papillomavirus (HPV)

Key information

Mode of transmission	Skin-to-skin contact, predominantly sexual, with a person with HPV infection.
Links to cancer	HPV is linked to almost all cervical cancers and to about 69% of vulvar, 75% of vaginal, 63% of penile, 90% of anal and 70% of oropharyngeal cancers.
Incidence/ prevalence	HPV infection is very common, with initial infection occurring soon after sexual debut and a lifetime risk of over 80%. Recurrent infection and co-infection with multiple types are possible.
Funded vaccine	HPV9 (Gardasil 9) is a recombinant subunit vaccine containing virus-like particles (VLPs). HPV9 contains HPV types 6, 11, 16, 18, 31, 33, 45, 52 and 58.
Dose, presentation, route	0.5 mL per dose. Pre-filled syringe. Intramuscular injection.
Funded indications and recommended schedules	2 doses, at 0 and 6–12 months for children aged 14 years and under. 3 doses, at 0, 2 and 6 months, for individuals: • aged 15–26 years inclusive • aged 9–26 years inclusive: – with confirmed HIV infection OR – who are transplant (including stem cell) patients. An additional dose for individuals aged 9–26 years post-chemotherapy. NB: Individuals who were previously fully vaccinated with HPV4 are not eligible for HPV9.
Vaccine efficacy/ effectiveness	The incidence of HPV infection, precancerous lesions and genital warts is significantly reduced in immunised populations (in women and men). There is evidence for herd immunity (reductions in HPV infection and genital warts in unimmunised populations).

Continued overleaf

Pregnancy	HPV vaccines are not recommended for pregnant women; however, enquiring about the possibility of pregnancy is not necessary before vaccination.
Adverse events to vaccine	Syncope (fainting) is a known injection reaction in adolescents.
Cancer prevention measures	HPV immunisation. Regular cervical screening for women. Safer sex approaches.

9.1 Virology and the causal link to cancer

Human papillomaviruses (HPVs) are small, non-enveloped DNA viruses from the Papillomavirus family. There are about 150 different HPV serotypes. They vary in their preference for infecting squamous epithelium at different sites, thereby causing the various types of HPV infection (eg, common, palmar, plantar or anogenital). More than 40 HPV types can infect the anogenital tract.[1, 2]

Data from the US cancer registry[3] indicates that HPV is causally associated with almost all cervical cancers, about 69 percent of vulvar, 75 percent of vaginal, 63 percent of penile, 90 percent of anal and 70 percent of oropharyngeal cancers (see Table 9.1).

On the basis of their causal link to cancer, HPVs are divided into low-risk and high-risk types. There are approximately 12 high-risk types, which include 16, 18, 31, 33, 45, 52 and 58. Types 16 and 18 are most frequently associated with cervical cancer but are also causally associated with other cancers. In the US, HPV types 16 and 18 are estimated to cause 66 percent of invasive cervical cancers, 80 percent of anal, 49 percent of vulvar, 55 percent of vaginal, 48 percent of penile and 60 percent of oropharyngeal cancers annually[3] (Table 9.1).

Low-risk types are predominantly associated with non-malignant lesions, such as genital warts (especially types 6 and 11), and can also cause recurrent respiratory papillomatosis.

Table 9.1: Average annual percentage of cancer cases attributable to HPV, by anatomic site and sex, United States, 2008–2010

	Cancers attributable to any HPV[a,b]	Cancers attributable to HPV 16, 18[a,b]	Cancers attributable to HPV 31, 33, 45, 52, 58[a,b]
Anatomic site[c]	**%**	**%**	**%**
Cervix	90.6[d]	66.2	14.7
Vulva	68.8	48.6	14.2
Vagina	75.0	55.1	18.3
Penis	63.3	47.9	9.0
Anus			
• women	92.5	79.5	10.8
• men	88.7	79.1	3.8
Oropharyngeal			
• women	63.3	50.8	9.5
• men	72.4	63.4	4.4

a Data is from 2008–2010 diagnosis years from population-based cancer registries that participate in the National Program of Cancer Registries and/or the Surveillance, Epidemiology, and End Results Program.

b These estimates do not take into account future changes in incidence, population structure, or the percentage of cancers that are HPV positive.

c International Classification of Diseases (ICD) codes: Cervix C53; Vulva C51; Vagina C52; Penis C60; Anus C21; Oropharyngeal (includes cancers of the soft palate, walls of pharynx, tonsils and base of tongue) C01.9, C02.4, C02.8, C05.1, C05.2, C05.9, C09.0, C09.1, C09.8, C09.9, C10.0, C10.2, C10.8, C10.9, C14.0, C14.2, and C14.8.

d Although HPV is accepted to be a necessary factor in the causal pathway to invasive cervical cancer, HPV is not always detected in tumour specimens from women who receive a diagnosis of invasive cervical cancer due to a variety of reasons, including misclassification of tissue specimens as cervix, quality of tissue specimens, assay sensitivity, and a small proportion of HPV-negative, cervical cancers.

Adapted from: Saraiya M, Unger ER, Thompson TD, et al. 2015. US Assessment of HPV types in cancers: Implications for current and 9-valent HPV vaccines. *Journal of the National Cancer Institute* 107(6), Table 4. DOI: 10.1093/jnci/djv086 (accessed 14 September 2016).

9.2 Clinical features

9.2.1 Infection

Infection results from skin-to-skin contact, predominantly sexual, with a person with HPV infection. Transmission in the genital region may occur even when condoms are used and does not necessarily require penetrative intercourse. HPV may also be transmitted perinatally, from mother to newborn baby.

Clinically apparent warts are probably more infectious than subclinical infection. The virus penetrates micro-abrasions in the epithelium to reach the basal epithelial cells, where it causes the infected cells to produce proteins that delay cellular maturation. Continued replication of these infected cells in the intermediate epithelial layer, followed by virus replication in the superficial epithelial layer, results in the cellular overgrowth typical of warts.

For most people, HPV infection is transient and becomes undetectable by DNA testing within 6 to 12 months, but in some cases, HPV infection remains latent and may reactivate years later. As it is difficult to detect HPV in its latent stage, it is impossible to know whether in some cases the immune system can completely clear the virus or whether the virus remains latent at undetectable levels, capable of re-emerging later on.

Acquisition of HPV

Infection with oncogenic serotypes of HPV is common, with an estimated 70–80 percent of sexually active individuals becoming infected at some stage during their life. Initial infection occurs soon after sexual debut.

Most episodes of infection become undetectable by DNA testing within two years of acquisition; the average duration of infection is one year. Previous infection does not necessarily create long-term immune memory so does not prevent future re-infection with the same HPV type.

At any one time, approximately 10 percent of women have at least one HPV infection. The HPV serotypes that cause more prolonged infection tend to be those that more frequently result in the development of histological abnormalities.[4, 5]

The rate of acquisition of HPV is similar in men and women; however, there are differences between the sexes in the immune response to HPV. A smaller proportion of men are HPV-seropositive, and men have lower antibody titres than women.[6] In contrast to women, for whom the risk for HPV acquisition increases with age through the early 20s and then decreases, studies have demonstrated HPV prevalence in men seems to peak at slightly older ages and remains constant or decreases slightly with increasing age, suggesting persistent HPV infection or a higher rate of re-infection.[7, 8]

Men who have sex with men, especially those that are HIV-positive, are at higher risk for HPV infection, anal cancer and high-grade anal intraepithelial neoplasia.[9] In teenage men who have sex with men (aged 16–20 years), early and high per-partner HPV transmission occurred between men soon after their first sexual experiences.[10]

Individuals who are immunocompromised (due to medical conditions or treatment) are more likely to develop a persistent HPV infection and to subsequently progress to HPV-related disease.[11, 12] Those with confirmed HIV infection are more at risk of HPV infection.[13] HIV-infected individuals who are co-infected with HPV are less likely to become undetectable.[14, 15] A direct relationship has been identified between low CD4+ cell count and an increased risk of cervical cancer in HIV-infected women.[16]

9.2.2 Cervical cancer

HPV rapidly becomes undetectable in the first 6–12 months of acquisition of infection, with 80–90 percent undetectable by two years. Following this, there is a very small fraction of persistent infection that progresses to cervical intraepithelial neoplasia (CIN); these are non-invasive precancerous lesions, which are categorised as either low or high grade CIN. Invasive cervical cancer occurs when the lesions invade the cervical tissue, and is graded from stage I to IV, depending on how far the cancer has spread beyond the cervix into surrounding tissue or organs.

Cervical cancer does not usually develop until decades after acquisition of infection with an oncogenic (cancer-causing) HPV serotype. Persistent HPV infection is detected in almost all women with cervical cancer.

HPV infection, while essential for the development of cervical cancer, is not, by itself, sufficient. Other factors have been described that may be associated with HPV persistence and high-grade lesions including smoking, early onset sexual activity, older age, contraceptive use, multiple sexual partners and genetic factors.[17, 18]

9.2.3 Other cancers

The clinical features of other HPV-associated cancers and their precancerous lesions in the anogenital and oropharyngeal regions vary, and also depend on the anatomical site.[19] The progression from HPV-associated precancer lesions to cancers in these sites is less well understood than the process in the cervix.

Oropharyngeal cancers

Oropharyngeal cancers include cancers of the soft palate, walls of the pharynx, the tonsils and the base of the tongue. The risk factors for oropharyngeal cancer are similar to those for cervical cancer, including the number of sexual partners, younger age at first sexual intercourse, practice of oral sex, history of genital warts and younger age.[20]

9.2.4 Genital warts

HPV6 and 11 account for around 90 percent of all genital warts cases. The majority of warts cases are self-limited, although some may persist for several years. Persistence is more common in patients with impaired cell-mediated immunity.[1]

9.2.5 Respiratory papillomatosis

Perinatal transmission of HPV virus (usually HPV types 6 or 11) can cause laryngeal infection in infants, which in rare cases can result in recurrent respiratory papillomatosis in children. Respiratory papillomatosis is characterised by multiple warty growths on the mucosal surface of the respiratory tract, which can significantly obstruct the airways.[19]

9.3 Epidemiology

9.3.1 Global burden of disease

HPV is an important international carcinogenic infection. The 12 high-risk types are reported to be the second most common infectious cause of cancer worldwide after *Helicobacter pylori*.[21]

Onset of sexual activity

Most HPV infections occur within the first two years of onset of sexual activity, with more than 40 percent becoming infected during this period. The first sexual relationship carries a substantial risk.[22]

Cervical cancer

Persistent HPV infection can lead to high-grade CIN. A 2010 study reported more than a quarter (26.7 percent; 95% CI: 21.1–31.8) of those with persistent HPV16 and nearly one in five (19.1 percent; 95% CI: 10.4–27.3) of those with persistent HPV18 develop CIN3 or cancer within 12 years.[23] Approximately one-third of CIN3 progresses to invasive cervical cancer within 10 to 20 years.

Cervical cancer is the fourth cause of female cancer in the world. In higher-income countries, it is the second most common cause of female cancer in women aged 15–44 years;[24] with an incidence of approximately 10–15 per 100,000 women aged 20–70 years and an annual mortality of approximately 5–8 per 100,000.

Other HPV-related cancers

HPV types 16, 18, 31, 33, 45, 52 and 58 are linked to other cancers in women and men, including vulval, vaginal, penile, anal and oropharyngeal cancers (see Table 9.1).

Anal cancers

Anal cancer remains relatively rare compared to other cancers but the global incidence has increased among both men and women, particularly in high-income regions (the average worldwide incidence is 1 per 100,000 population).[24] Women have a higher incidence of anal

cancer than men. The incidence is highest among men who have sex with men, women with history of cervical or vulvar cancer, and immunosuppressed populations, including those who are HIV-infected and patients with a history of organ transplantation.[24]

Oropharyngeal cancers

There has been an increase in the incidence of head and neck cancers over the past few decades. This increase is mainly due to an unexpected increase in HPV-related oropharyngeal cancers, primarily in males aged 40 to 55 years with exposure to alcohol and tobacco.[25]

There is wide variability in the reported proportions of oropharyngeal cancers associated with HPV, ranging from 12 to 63 percent, and a lower proportion of oral cancers.[19] Of the oropharyngeal cancers that are HPV-positive, most are associated with HPV types 16 and/or 18 (see Table 9.1).

Genital warts

Genital warts, which are most commonly due to infection with HPV6 or HPV11, have a prevalence of approximately 1 percent of adults in the US.[26, 27] In Scandinavian countries the reported rates are as high as 10 percent.[28]

9.3.2 New Zealand epidemiology

Onset of sexual activity

Data from the Youth'12 survey[29, 30] suggests that approximately 8 percent of New Zealand adolescents may have had sexual intercourse before the age of 13 years. This increases to 24 percent by the age of 15 years and 46 percent by age 17 years.

Compared to 2001, students were more likely to delay sexual debut in 2012 but less likely to use condoms and contraception consistently.[31] Māori (OR 0.7; 95% CIs: 0.6–0.8) and Pacific (OR 0.5; 95% CIs: 0.4–0.7) students used condoms less frequently than NZ European students; those from socioeconomically deprived communities (school decile 1) used condoms less frequently (OR 0.7; 95% CIs: 0.5–0.9) than students from wealthier communities (decile 10).[31]

Cervical cancer

HPV prevalence in precancerous lesions and invasive cervical cancer

The prevalence of HPV infection and distribution of HPV types among New Zealand women with histologically confirmed CIN 2/3 [32, 33] or invasive cervical cancer[34] is broadly consistent with that seen internationally. In women with histologically confirmed CIN 2/3, 97 percent (95% CI: 94–98) were HPV-positive and the prevalence of any high-risk HPV was 96 percent (95% CI: 91–99).[32] In women with histologically confirmed invasive cervical cancer, 88.5 percent (95% CI: 83.7–92.4) were HPV-positive, and the prevalence of any high-risk HPV was 87.2 percent (95% CI: 82.2–91.3).[34] For both CIN 2/3 and invasive cervical cancer, the overall distribution of HPV types was similar in Māori and non-Māori women, with HPV16 being the most commonly detected HPV type in both groups.[32, 34]

Cervical cancer registrations and deaths

In 2015 there were 138 new cervical cancer registrations, down from 143 in 2014 (provisional data).[35] The age-standardised registration rate was 5.3 per 100,000 population, similar to the 2014 rate (5.5 per 100,000). The registration rate for Māori women was 9.7 per 100,000, 2.1 times greater than for non-Māori women (4.7 per 100,000).

The most recent cervical cancer mortality data is from 2014, when there were 46 deaths (1.4 deaths per 100,000 population).[36] The mortality rate for Māori women was 3.0 per 100,000, 2.7 times greater than for non-Māori women (1.1 per 100,000).

Other HPV-related cancers

The most recent New Zealand data available for other HPV-related cancers is from 2014 (see Table 9.2). Note that this data is for new cancer registrations only; the tumours have not been analysed for the presence of HPV.

Table 9.2: Number and age-standardised rate of new registrations for other HPV-related cancers in New Zealand, 2014

Anatomic site*	Number of new registrations	Rate of new registrations (per 100,000)
Vulva	70	2.0
Vagina	20	0.5
Penis	16	0.5
Anus		
• women	54	1.5
• men	32	1.1
Oropharynx		
• women	4	0.1
• men	16	0.6
Tonsils		
• women	13	0.4
• men	57	1.9

* ICD codes: Vulva C51; Vagina C52; Penis C60; Anus C21; Oropharynx C10; Tonsils C09. (Note that in Table 9.1, the US definition for oropharyngeal cancer combines multiple cancers into the definition, using 4-character ICD codes. At the time of writing, New Zealand data for 2014 was only available at the 3-character ICD code level.)

Source: Ministry of Health. 2016. *New cancer registrations 2014*. URL: http://www.health.govt.nz/publication/new-cancer-registrations-2014 (accessed 8 February 2017).

Anal cancers

For the period 2003–2007, the age-standardised rate for anal cancer was 0.5 and 1.1 per 100,000 persons per year among men and women in New Zealand, respectively.[24] In 2015 the rate increased to 1.1 per 100,000 for men and 1.5 for women (see Table 9.2).

Oropharyngeal cancers

A retrospective review of New Zealand cancer registry data for the period 1981–2010 showed a rapid rise in oropharyngeal cancers in men (mainly in those aged 40 years or older), particularly from 2005 onwards.[37] The rate of oropharyngeal cancers was almost four times greater in men (1.87 per 100,000) than in women (0.47 per 100,000). The incidence rates for oral cavity cancer, which is generally associated with alcohol and tobacco consumption, remained relatively stable in

both sexes during that time period. (Note that in this study, oropharyngeal cancers included cancers coded as: C01.9, C02.4, C09.0–C09.9, C14.2 and C10.0–C10.9; oral cavity cancers included: C02.0–C02.3, C02.8, C02.9, C03.0–C03.9, C06.0–C06.2, C04.0–C04.9, C05.0–C05.9, C06.8, C06.9 and C00.3–C00.5).

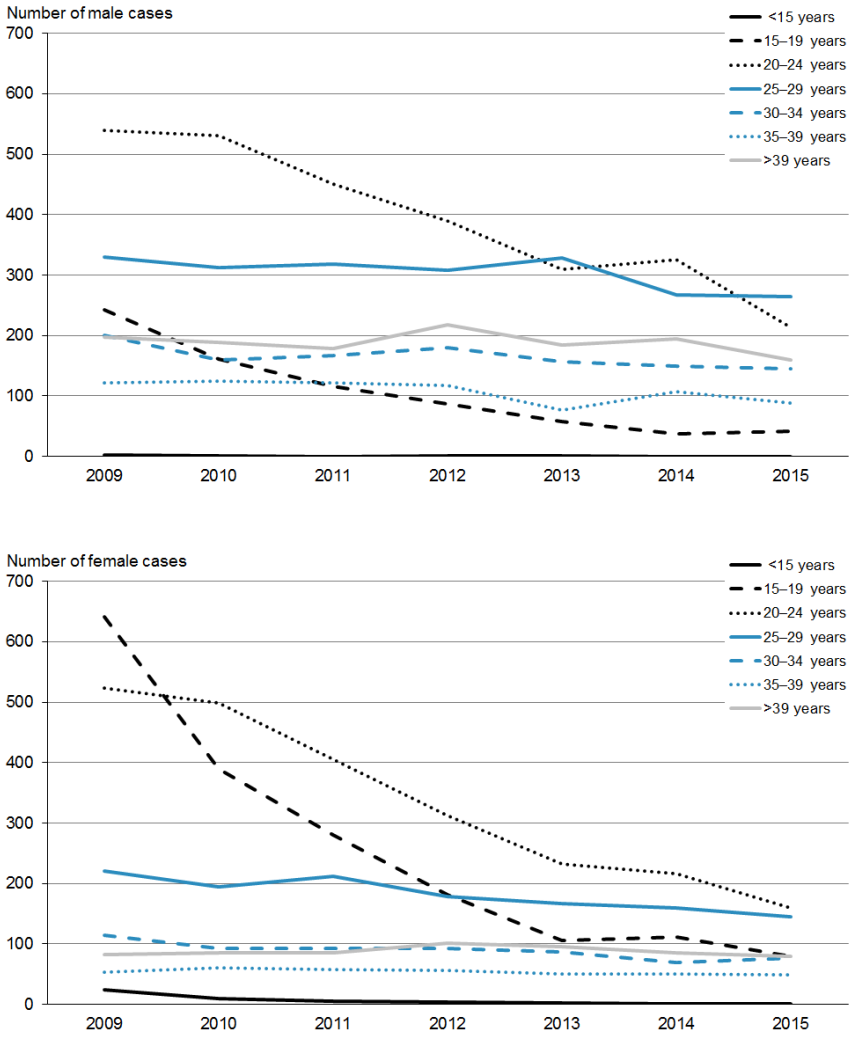
Genital warts

Sexually transmitted infections (STIs) are not notifiable in New Zealand. ESR cautions that the number of cases of STIs reported through the clinic-based surveillance system likely underestimates the true burden of disease in New Zealand because a substantial percentage of STIs are diagnosed by other health care providers.

From 2009[38] to 2015[39] genital warts clinical case counts reported by sexual health clinics decreased by 54.3 percent (from 3,290 to 1,504 cases) and case counts reported by family planning clinics decreased by 65.6 percent (from 546 to 188 cases). In sexual health clinics there was a decrease in diagnoses in all ethnic groups, except 'Other' ethnicity. In family planning clinics, the number of diagnoses decreased in every ethnic group.

In sexual health clinics, the decrease was most notable in the 15–19 years and 20–24 years age groups, and a moderate decrease in the 25–29 years age group, in both sexes (Figure 9.1). The decrease seen in older age groups, and in males, suggests that immunisation is also providing some herd immunity to unvaccinated individuals. A decline in the number of prescriptions for treating genital warts (imiquimod and podophyllum resin-based products) supports this evidence for a herd immunity effect.[40] The largest decline was seen in women aged under 20 years.

Figure 9.1: Number of genital warts (first presentation) in sexual health clinics, by sex and age group, 2009–2015



Source: ESR

9.4 Vaccines

9.4.1 Available vaccines

Two HPV vaccines are approved for use (registered) and are available for distribution (marketed) in New Zealand: HPV9 (Gardasil 9, Seqirus/MSD) and HPV4 (Gardasil, Seqirus/MSD).

Both vaccines are registered for use in females aged 9–45 years and in males aged 9–26 years. HPV9 is registered as a two- or three-dose schedule in individuals aged 14 years and under, and as a three-dose schedule in older individuals. HPV4 is registered as a three-dose schedule for all age groups, but may be used as a two-dose schedule for those aged 9–14 years.

Both vaccines contain HPV virus-like particles (VLPs), which are composed of the L1 protein (a component of the virus outer layer) aggregated into clumps that mimic the outer structure of the HPV virion. The VLPs do not contain viral DNA and are incapable of causing infection. The L1 proteins are produced by genetically engineered yeast cells.

Funded HPV vaccine

Each 0.5 mL dose of HPV9 vaccine (Gardasil 9, Seqirus/MSD) contains:

- 30 µg of HPV6 L1 VLP, 40 µg of HPV11 L1 VLP, 60 µg of HPV16 L1 VLP, 40 µg of HPV18 L1 VLP, 20 µg of HPV31 L1 VLP, 20 µg of HPV33 L1 VLP, 20 µg of HP45 L1 VLP, 20 µg of HPV52 L1 VLP, and 20 µg of HPV58 L1 VLP
- 500 µg of aluminium hydroxyphosphate sulphate.

The vaccine does not contain any preservative or antibiotics.

Other vaccine

HPV4 was the vaccine used prior to the 1 January 2017 introduction of HPV9 (see also section A1.3.4 in Appendix 1 for the history of HPV vaccines in New Zealand).

Each 0.5 mL dose of HPV4 vaccine contains:

- 40 µg of HPV16 L1 VLP, 20 µg of HPV18 L1 VLP, 20 µg of HPV6 L1 VLP and 40 µg of HPV11 L1 VLP
- 225 µg of aluminium hydroxyphosphate sulphate.

The vaccine does not contain any preservative or antibiotics.

9.4.2 Efficacy and effectiveness

The efficacy of HPV vaccines can only be studied in older age groups due to the sexual naivety of the younger age group; protection against persistent HPV infection and related disease is the main target for vaccination. Immunological bridging is therefore used to infer efficacy in the younger age group; that is, by comparing the antibody responses (immunogenicity) between the younger and older age groups. Because the antibody responses are non-inferior to those seen in older age groups, efficacy is inferred for the younger age group.

Immunogenicity

Although there is no known correlate of protection (that is, the antibody level required for protection against HPV-related disease), HPV vaccines generate excellent antibody responses in most recipients.

HPV4

Immunisation with three doses of HPV4 vaccine produces antibody responses against HPV16, HPV18, HPV6 and HPV11 in more than 99 percent of vaccine recipients. The height of the antibody titres following three doses of HPV vaccine is greater than that following natural infection.

Differences in seroconversion rates and antibody titres were seen in immunocompromised individuals. The immune response to HPV4 among immunocompromised children appears adequate,[41, 42] although antibody titres were lower than those in healthy children of the same age groups.[41] Seroconversion among HIV-infected individuals has been demonstrated to be robust and higher among those with lower HIV loads or on antiretroviral therapy.[43, 44, 45]

While some immunosuppression regimes can attenuate the immune response to HPV4, patients with autoimmune diseases generally appear to respond well to the vaccine.[46] In contrast, adult solid organ transplant recipients produce suboptimal responses to HPV4.[47]

The immunogenicity of three doses of HPV4 vaccine has been established to be robust and long-lasting.[48, 49, 50] Anamnestic responses have been demonstrated out to 8.5 years.

Two doses of HPV4 are more immunogenic in recipients aged between 9 and 15 years than in older age groups and comparable to three doses in older recipients.[51] In young females, two doses have been found to be non-inferior to three doses, particularly when the interval between doses is at least six months.[52]

HPV9

The immunogenicity of HPV9 was initially assessed in women aged 16–26 years.[53] Antibody responses generated by the HPV9 vaccine to HPV types 6, 11, 16 and 18 were non-inferior to those generated by the HPV4 vaccine. HPV9 has also demonstrated non-inferiority to HPV4 in girls and boys aged 9–15 years.[54]

Antibody responses to all nine vaccine HPV types in girls and boys aged 9–15 years and men aged 16–26 years were non-inferior to women aged 16–26 years.[55, 56]

Men who have sex with men appear to produce lower antibody titres than heterosexual men (although seroconversion rates to all nine vaccine types were greater than 99 percent in both groups).[55] This lower antibody response is possibly due to greater exposure to the virus, highlighting the importance of vaccination at a young age.

The immunogenicity of two doses of HPV9 in girls and boys aged 9–14 years was compared with three doses in women aged 16–26 years,[57] the age group in which efficacy was demonstrated. Antibody responses in girls and boys after two HPV9 doses were non-inferior to the antibody responses in women who received three doses.

Efficacy

HPV-related cancers

No studies have yet been undertaken to look for protection against invasive cervical cancer because these would require extremely long periods of follow-up and because study participants who develop precancerous lesions (CIN 2/3 or adenocarcinoma *in situ*) require treatment to prevent progression to invasive cancer. However, protection against CIN 2/3 or adenocarcinoma *in situ* is widely accepted as a surrogate for protection against invasive cancer. Bivalent and quadrivalent HPV vaccines have been shown to be highly effective in preventing these HPV16- and HPV18-related precancerous lesions in females.[2, 58] In the pivotal efficacy trial in women aged 15–26 years,[59] HPV4 vaccine efficacy for the prevention of precancerous lesions related to HPV16 or HPV18 was 98 percent (95% CI: 26–58) in the per-protocol susceptible population.

Studies in males, including men who have sex with men, have shown that HPV4 vaccine is efficacious against anal HPV infection and associated precancerous lesions.[6, 60, 61]

HPV9 efficacy was studied in women aged 16–26 years and compared with HPV4.[53] HPV9 prevented cervical, vulvar and vaginal disease and persistent infection related to HPV types 31, 33, 45, 52 and 58 (the five additional serotypes in HPV9). The antibody response and incidence of disease related to HPV types 6, 11, 16 and 18 were similar in the two vaccine groups.

Effectiveness

A 2016 systematic review of published literature[62] summarised the global experiences with HPV4 from 1 January 2007 to 29 February 2016. It assessed the global effect of HPV4 vaccine on HPV infection, genital warts and cervical abnormalities based on 57 publications across nine countries. The greatest impact was seen in countries with high vaccine uptake and among girls vaccinated prior to HPV exposure. Maximal reductions of around 90 percent were reported for vaccine-type HPV infections (6, 11, 16, 18) and genital wart cases.

Duration of protection

As vaccination programmes have only been in place for a maximum of 10 years, the duration of protection is not yet known. Follow-up studies 8–10 years after HPV vaccination have shown no waning of protection.[2] Long-term studies are ongoing to determine the duration of efficacy for all HPV vaccines.

Herd immunity

Australia has seen a reduction in the prevalence of vaccine-type HPV infections (6, 11, 16, 18) in unvaccinated young men after the introduction of the vaccine to young women, supporting the role of herd immunity.[63, 64, 65] There was also a significant decrease in the prevalence of vaccine-type HPV infections in unvaccinated women (aged 25 years or younger).[66]

In a study of data from a sexual health clinic in Melbourne,[65] the researchers noted the near disappearance of genital warts in women and heterosexual men aged under 21 years. In addition, the data indicated that the basic reproductive rate (see section 1.2.1) had fallen below one. This reduction in cases occurred without any corresponding reduction in women aged over 30 years, men who have sex with men, and non-residents. Similar trends were noted in the data from the Australian genital warts national surveillance network.

Previous exposure to HPV

While efficacy is unclear, there are no safety concerns in offering vaccination to women who have had HPV-related disease and would like to use the vaccine to reduce the risk of further disease.

A retrospective analysis of the HPV4 vaccine's pivotal efficacy trial data (Future I and Future II) studied a group of women who were vaccinated before they had their first treatment for HPV-related disease.[67] This showed a reduction in subsequent HPV-related disease in vaccinated women aged 15–26 years who had received treatment for cervical, vulvar or vaginal disease during the trial. The study showed a 46.2 percent reduction (95% CI: 22.5–63.2) after cervical surgery of any HPV-related disease and 35.2 percent reduction (95% CI: 18.8–51.8) after diagnosis of genital warts or vaginal or vulvar disease.

In contrast, a systematic review[68] explored efficacy against CIN3+ precancers in women with evidence of prior vaccine-type HPV exposure in three randomised controlled trials and two post-trial cohort studies and showed no evidence that HPV vaccines were effective in preventing vaccine-type HPV-associated precancer in pre-exposed women. Despite these findings, it was concluded that longer-term benefits in preventing re-infection could not be excluded; ie, the vaccine is not therapeutic but may prevent future infection, emphasising the importance of vaccination prior to sexual debut.

International recommendations

The WHO recommends a two- or three-dose HPV4 schedule for individuals aged under 15 years and a three-dose schedule for older individuals.[69]

HPV9 was registered for use as a two- or three-dose schedule for individuals aged under 15 years and a three-dose schedule for older individuals by the European Medicines Agency[70] in June 2015 and by the New Zealand Medicines and Medical Devices Safety Authority (Medsafe) in July 2016.

Since October 2016, the US Advisory Committee on Immunization Practices has recommended a two-dose HPV schedule for individuals aged 9–14 years and a three-dose schedule for those aged 15–26 years or who are immunocompromised.

9.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.[71] Store in the dark at +2°C to +8°C. Do not freeze.

9.4.4 Dosage and administration

The dose of HPV vaccine is 0.5 mL, administered by intramuscular injection in the deltoid area (see section 2.2.3).

Co-administration with other vaccines

HPV vaccine may be co-administered with any live or inactivated vaccine indicated at the same visit.[2]

Interchangeability

All HPV vaccines may be used interchangeably for completion of a course.[72]

9.5 Recommended immunisation schedule

9.5.1 Recommended and funded

From 1 January 2017 males and females aged 26 years and under become eligible for HPV vaccine. Including males in a routine vaccination programme is expected to increase the benefit to the population in terms of reduction for both HPV-related cancer outcomes and genital warts.

See Table 9.3 for HPV vaccine recommendations and schedules. Children aged 14 years and under receive two doses of HPV vaccine, at 0 and 6–12 months – provided the second dose is administered before their 15th birthday, see Table 9.3 below. However, three doses are required for this age group if they have confirmed HIV infection or are transplant or chemotherapy patients, or if the minimum dosing interval is not met (see below). Older individuals receive three doses of HPV vaccine, at 0, 2 and 6 months.

Table 9.3: HPV vaccine recommendations and schedules

Note: HPV vaccine may be offered from age 9 years, but the usual Schedule will be at age 11/12 years (school years 7/8). Funded recommendations are in the shaded rows. See the Pharmaceutical Schedule (www.pharmac.govt.nz) for any changes to the funding decisions.

Recommended and funded	Doses	HPV Schedule[a]
Children aged 14 years and under	2[b]	0 and 6–12[c] months
Individuals aged 15–26 years[d,e]	3	0, 2 and 6 months[f]
Individuals aged 9–26 years: • with confirmed HIV infection[g] • transplant (including stem cell) patients[g]	3	0, 2 and 6 months
• post-chemotherapy patients[g]	An additional dose	At least 1 month after the last dose
Recommended but not funded	**Doses**	**HPV Schedule**
Individuals aged 27 years and older:[d,e,h] • who have had little previous exposure to HPV and are now likely to be exposed • who are men who have sex with men • with HIV.	3	0, 2 and 6 months[f]

a Individuals who started with HPV4 may complete their remaining doses with HPV9. Those who were fully vaccinated with HPV4 are not eligible for HPV9.

b Regardless of the age at the 1st dose, if the 2nd HPV dose is given at age 15 years or older a 3rd HPV dose is recommended and funded. Give the 3rd HPV dose at least 4 months after the 2nd.

c For children aged 14 years and under, the 2nd dose is preferably given at least 6 months after the 1st. However, if the 2nd dose is given less than 5 months after the 1st, a 3rd HPV dose is recommended and funded. Give the 3rd HPV dose at least 6 months after the 1st.

d The decision to vaccinate older age groups should follow an assessment of the potential benefits of vaccination – based on their likely previous HPV exposure and future risks.

e Individuals who were under age 27 years when they commenced HPV vaccination are currently funded to complete the 3-dose course, even if they are older than 27 years when they complete it.

f If a shortened schedule is required, give the 2nd dose at least 1 month after the 1st dose and the 3rd dose at least 3 months after the 2nd dose.

g See section 4.3.3 for more information.

h HPV vaccines are registered for use in females aged 9–45 years and in males aged 9–26 years. However, there are no theoretical concerns that the efficacy or safety of HPV vaccine in males up to the age of 45 years will differ significantly from females of the same age or younger males.

Immunisation should be completed before the onset of sexual activity. The optimal time for HPV administration is at age 9–13 years, as most males and females in this age group would be naïve to all HPV types. However, individuals who have begun sexual activity may still benefit from vaccination. The decision to vaccinate older age groups should follow an assessment of the potential benefits of vaccination – based on their likely previous HPV exposure and future risks.

Note:

- For the two-dose HPV schedule for children aged 14 years and under:
  - the second dose is preferably given at least 6 months after the first; however, if the second dose is given less than 5 months after the first, a third HPV dose is recommended and funded – give the third HPV dose at least 6 months after the first
  - if the second dose is given at age 15 years or older, a third HPV dose is recommended and funded – give the third HPV dose at least 4 months after the second.
- Individuals who started with HPV4 may complete their remaining doses with HPV9.
- HPV9 is not funded for those individuals who were previously fully vaccinated with HPV4.
- Non-residents who were under age 18 years when they commenced HPV vaccination are currently funded to complete the course, even if they are older than 18 years when they complete it.

9.5.2 Recommended but not funded

Individuals aged 27 years and older

The decision to vaccinate older age groups should follow an assessment of the potential benefits of vaccination – based on their likely previous HPV exposure and future risks.

The data from the pivotal studies for HPV4 has demonstrated potential benefit to some women older than 25 years. HPV4 has been shown to be effective at preventing infection and disease from the vaccine types in women aged 24–45 years who were uninfected at baseline.[73] However, pre-vaccination testing for cervical cytological abnormalities or for HPV infection is not recommended.

HPV9 and HPV4 vaccines are registered for use in females aged 9–45 years and in males aged 9–26 years. However, there are no theoretical concerns that the efficacy or safety of HPV vaccine in males up to the age of 45 years will differ significantly from females of the same age or younger males.

9.5.3 Pregnancy and breastfeeding

HPV vaccines are not recommended for pregnant women; however, enquiring about the possibility of pregnancy is not necessary before vaccination.[74]

Data to date shows no adverse effects of HPV vaccines on pregnancy outcomes.[2, 75] However, if a vaccine dose has been administered around the time of conception or during pregnancy, health professionals are advised to report this to CARM (see section 1.6.3) and the vaccine manufacturer to assist with ongoing safety monitoring. If a woman is found to be pregnant after starting the HPV vaccine schedule, the remaining doses should be delayed until after pregnancy.

HPV vaccines may be given to breastfeeding women.[19]

9.6 Contraindications and precautions

See section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

9.6.1 Contraindications

HPV vaccine should not be administered to people with a history of an anaphylactic reaction to a prior dose of HPV vaccine or to a vaccine component. HPV vaccines contain HPV proteins produced by genetically engineered yeast cells. They should not, therefore, be given to people with a history of an immediate hypersensitivity to yeast.

9.6.2 Precautions

Pregnancy is a precaution – see section 9.5.3.

9.7 Expected responses and AEFIs

HPV vaccines have excellent safety profiles internationally. There have been no safety signals raised since the vaccines were licensed, and a number of large investigations have been carried out to assess specific outcomes, particularly autoimmune conditions.[76, 77, 78, 79, 80] Post-marketing surveillance systems globally continue to monitor the safety of HPV vaccination programmes.[81, 82, 83] The WHO's Global Advisory Committee on Vaccine Safety has systematically reviewed HPV vaccine safety and has not found any safety issue that would alter its recommendations for use.[84] The main challenge with HPV vaccine is communicating its excellent safety profile.[85] (See also the HPV discussion in section 3.2.4.)

Syncope (fainting) occurs frequently in adolescents following vaccination, but this is an injection reaction, not a reaction to the vaccine.[1, 86]

Safety has been evaluated in approximately 15,000 subjects in the HPV9 clinical development programme.[72] The vaccine is well-tolerated, and most adverse events were injection site-related pain, swelling, and erythema that were mild to moderate in intensity. The safety profiles were similar in HPV4 and HPV9 vaccinees. Female HPV9 recipients had more injection site adverse events than female HPV4 recipients, including swelling (40.3 percent compared to 29.1 percent in HPV4 recipients) and erythema (34 percent compared to 25.8 percent in HPV4 recipients). Injection site adverse events were similar in males following either vaccine. Male recipients had fewer injection site adverse events. Rates of injection-site swelling and erythema both increased following each successive dose of HPV9.

In summary, HPV9 is well-tolerated in all age groups, although it is slightly more reactogenic than HPV4.[53, 55, 72] The most common adverse events are pain, swelling, erythema, pruritus, headache and pyrexia.

9.8 Cancer prevention measures

For women, HPV immunisation is part of a three-pronged approach to cervical cancer prevention that also includes regular cervical screening and safer sex approaches. For men, HPV immunisation and safer sex approaches are expected to contribute to the prevention of HPV-related cancers and disease that affect men, as well as cervical cancer prevention in women.

9.8.1 HPV immunisation

A vaccine that can prevent infection with oncogenic HPV types has the potential to reduce the incidence of precursor lesions and cancer. Vaccination needs to be administered before HPV infection occurs in order to prevent atypia and malignancy. Because genital HPVs are so common and so readily transmitted, in practical terms vaccination should be offered before the onset of sexual activity; that is, during early adolescence.

HPV immunisation does not reduce the progression of established disease but can be used in therapeutic situations by preventing the reactivation of latent infection.

9.8.2 Regular cervical screening for women

A successful HPV immunisation programme for men and women will reduce the community prevalence of HPV infection and thus the incidence of cervical cancer in women. However, HPV immunisation will not completely eliminate cervical cancer because some women will not have been vaccinated, a few will not develop immunity despite vaccination, and some will be infected prior to vaccination or with oncogenic types not present in the vaccine.

Consequently, women will need to continue to undergo regular cervical screening to detect those precancerous lesions that occur despite vaccination. Cervical screening programmes are based on regular cytological screening or HPV testing to detect, monitor and treat at an early stage precancerous lesions, or CIN. These programmes have been successful in reducing invasive disease and mortality.

Although the frequency of abnormal cytology is lower in the vaccinated group, women who have received HPV immunisation should still take part in the National Cervical Screening Programme. Three-yearly cervical smears are recommended for women between the ages of 20 and 70 years who have ever been sexually active.

9.8.3 Safer sex approaches

To minimise the risk of HPV infection (plus other sexually transmitted infections), practitioners should remind individuals of safer sex approaches, including sexual abstinence, monogamous relationships, delayed sexual debut, and minimising the number of sexual partners.[2] Consistent and correct use of condoms can decrease the risk of anogenital HPV infection when infected areas are covered or protected by the condom. However, HPV transmission in the genital region may occur even when condoms are used and does not necessarily require penetrative intercourse.

9.9 Variations from the vaccine data sheets

HPV vaccines are registered for use in females aged 9–45 years and in males aged 9–26 years. However, there are no theoretical concerns that the efficacy or safety of HPV vaccine in males up to the age of 45 years will differ significantly from females of the same age or younger males (see section 9.5.2).

For the three-dose schedules, the HPV vaccine data sheets recommend that all three doses are given within a 12-month period. The Ministry of Health recommends that if the three-dose schedule has been interrupted, prior doses do not need to be repeated regardless of how long ago the previous doses were given (see Appendix 2).

The HPV9 data sheet states that there are no studies on the interchangeability of HPV vaccines. The Ministry of Health recommends that all HPV vaccines may be used interchangeably for completion of a course.[72] Those individuals who started with HPV4 may complete their remaining doses with HPV9.

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10 Influenza

Key information

Mode of transmission	Spread by droplets generated by sneezing and coughing, by direct or indirect contact, or by the aerosol route.
Incubation period	Usually 1–3 days (range 1–7 days).
Period of communicability	From 1–2 days before symptoms start until about day 5 of illness; may be longer in young children and if immunocompromised.
Disease burden	Influenza epidemics occur each year. The highest burden of disease is in the very young, the elderly, pregnant women, those with co-morbid conditions, people from low income groups, and in Māori and Pacific ethnic groups.
Funded vaccines	Quadrivalent inactivated split virion vaccine: • children aged 6 months to under 3 years (ie, aged 6–35 months): Fluarix Tetra. • adults and children aged 3 years and older: Influvac Tetra.
Dose, presentation, route	0.5 mL per dose. Pre-filled syringe. Intramuscular injection.
Funded vaccine indications	1 dose is recommended and funded annually for: • pregnant women • individuals aged 65 years and older • individuals aged 6 months to under 65 years with eligible conditions. Children aged under 9 years who have not previously received influenza vaccine require 2 doses 4 weeks apart (funded for children with eligible conditions).
Vaccine efficacy/ effectiveness	Depends on the match of the strains in the vaccine with circulating strains, the age of the individual and whether they have any underlying medical conditions.
Egg allergy	Egg allergy, including anaphylaxis, is **not** a contraindication to influenza vaccination. Influenza vaccine can be safely administered to people with a history of egg allergy, including anaphylaxis, at general practices, pharmacies or at the workplace.

Continued overleaf

Contraindications/ precautions	Seek specialist advice for individuals who are currently being treated with immune checkpoint inhibitors, as well as those who have discontinued treatment within the past 6 months. There may be a small increased risk of fever and febrile convulsions with concomitant delivery of PCV13 and influenza vaccine in children aged 6 months to under 5 years.
Adverse events	Children aged under 5 years are more likely than older children or adults to have a febrile reaction to influenza vaccine.

10.1 Virology

Influenza viruses belong to the Orthomyxoviridiae family, and are classified into influenza virus types A, B and C. Influenza A viruses include a number of subtypes, classified on the basis of two surface antigens:

- haemagglutinin (H), responsible for cell surface attachment during infection
- neuraminidase (N), which potentiates the release of new virions from the cell.

Subtypes which have in the past caused pandemics include the H1N1, H2N2, H3N2 and H1N1pdm09 viruses, while the H3N2 and H1N1pdm09 viruses continue to cause epidemics as seasonal influenza viruses. Influenza B has two lineages of viruses; B/Victoria and B/Yamagata, which are also associated with outbreaks and epidemics, and account for a significant proportion of the overall burden of influenza.[1] Influenza C is associated with mild cases of upper respiratory infection.

10.1.1 Antigenic drift

Influenza A and B viruses undergo frequent small changes (mutations) in their segmented RNA genome. The mutations that occur in the coding regions responsible for H and N surface antigens lead to 'antigenic drift' and the emergence of new antigenic variants or virus strains.

These new strains are described by the geographic site of isolation, laboratory number and year of isolation; for example, A/Hong Kong/4801/2014 (H3N2). Because of this ongoing antigenic drift, seasonal influenza virus vaccine formulations are reviewed by the WHO bi-annually.

10.1.2 Antigenic shift

Novel influenza A virus subtypes have emerged periodically in the past which have caused pandemics in humans. The mixing of the genomic segments of two or more influenza A viruses leads to a new virus subtype with novel H and N surface antigens and is known as 'antigenic shift'. The emergence of novel viruses through the adaptation of avian influenza viruses to humans and the re-assortment of the genomic segments of multiple viruses, ie, human, avian and pig influenza viruses, are also recognised as possible mechanisms.

10.2 Clinical features

Influenza is contagious, with a reproductive number estimated at 1.4–4[2] (see section 1.2.1). The virus is transmitted by respiratory droplets generated by sneezing and coughing that land directly on the respiratory mucous membranes, by direct or indirect contact (contaminated hands or fomites), or by the aerosol route.[3]

The incubation period can range from one to seven days (average one to three days), during which time the virus replicates in the ciliated columnar epithelial cells of the upper and lower respiratory tract. An infected person is contagious from one to two days before symptoms start until about day five of the illness. Peak viral shedding occurs one to three days after the development of symptoms, diminishing to low levels by five days. Children shed more virus and remain infectious for longer than adults.

In older children and adults the illness characteristically begins abruptly with fever and a variety of clinical symptoms, including chills, malaise, headache, myalgia, non-productive cough, rhinitis, sore throat and mild conjunctivitis. Vomiting and diarrhoea may be present. While children aged under 5 years have fever, cough and rhinitis, infants may present with rhinitis only.

There is a wide range of symptoms, from asymptomatic to severe disease. Mild influenza is common and symptoms can be non-specific, resulting in a large proportion of undetected influenza infections.

In the young, influenza virus may cause croup, bronchiolitis and pneumonia. Fever is often less evident in the elderly. Influenza typically resolves after several days in the majority of people, although cough and malaise may persist for two or more weeks.

Infections due to pandemic influenza A strains are more likely to lead to severe morbidity and increased mortality than influenza B or seasonal influenza A strains.

Influenza B infections were previously thought to generally cause more mild illness, but numerous studies indicate that there is little difference between clinical symptoms and outcomes of influenza B compared to influenza A.[1] Influenza B-associated hospitalisations and mortality may have previously been underestimated; studies have reported higher mortality following influenza B infection than A in some years.[1] Influenza B infection is more common in children aged 5–17 years than in other age groups, and disease is more likely to be severe in children than in adults.

In some people, influenza can exacerbate underlying medical conditions, such as pulmonary, cardiac or metabolic disease. Some of the many reported complications associated with influenza include pneumonia, respiratory failure, myositis, encephalopathy, myocarditis, pericarditis, Reye syndrome (associated with aspirin use in children), bronchitis, otitis media and death.

Asymptomatic influenza

The majority of influenza infections are asymptomatic, with most symptomatic cases self-managing without seeking medical help.[4] Results from the 2015 Southern Hemisphere Influenza and Vaccine Effectiveness, Research and Surveillance (SHIVERS) serosurvey showed that around 26 percent of people in New Zealand had contracted influenza over the 2015 season.[5] Approximately 80 percent of infected people (4 in 5 infected) were asymptomatic, with only 2.5 percent of those infected (1 in 40 infected) visiting their GP and 0.2 percent (1 in 560 infected) hospitalised.

10.3 Epidemiology

10.3.1 Global epidemiology

Influenza is an important cause of disease worldwide. Annual epidemics are estimated to result in about 3 to 5 million cases of severe illness, and about 250,000 to 500,000 deaths globally.[6]

In temperate climates, seasonal epidemics occur mainly during winter, while in tropical regions, influenza may occur throughout the year, causing outbreaks more irregularly.[6]

From time to time, pandemics occur when a new virus arises and spreads globally (see section 10.3.3). The last pandemic was caused by the A(H1N1)pdm09 virus. More than 214 countries and overseas territories reported laboratory-confirmed influenza, including over 18,449 deaths.[7]

10.3.2 New Zealand epidemiology

New Zealand experiences the typical temperate climate epidemiology of influenza, with the peak incidence occurring during the winter months, however influenza activity may occur throughout the year.

The impact of influenza in New Zealand is substantial in terms of general practice consultations, hospitalisations and deaths. The highest burden of disease is in the very young, the elderly, pregnant women, those with co-morbid conditions, people from low income groups, and Pacific and Māori ethnic groups.

For detailed information, including influenza surveillance and influenza reports, see the ESR website (www.surv.esr.cri.nz/virology/virology.php).

Influenza surveillance

The New Zealand influenza surveillance system compiles information from a variety of sources, including:

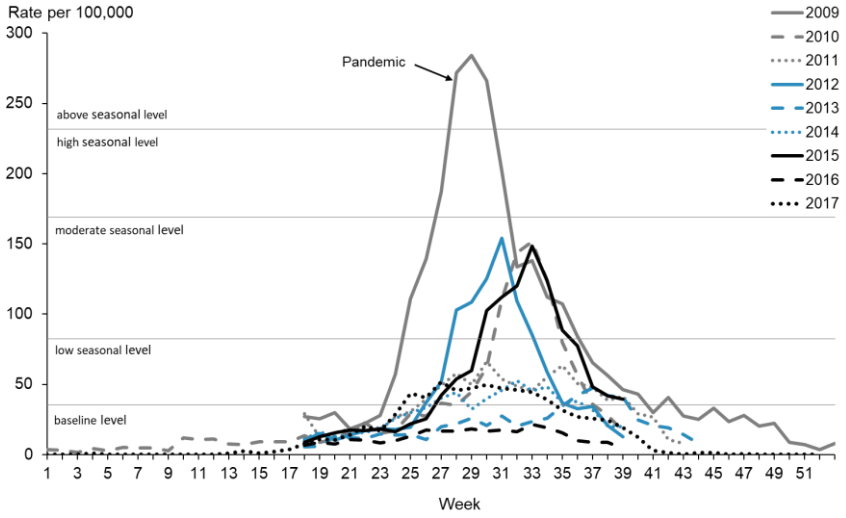
- national sentinel general practice-based influenza-like illness surveillance (part of the WHO's Global Influenza Programme)

- year-round laboratory-based surveillance by the regional virus diagnostic laboratories
- hospital-based severe acute respiratory infection surveillance in Auckland and Counties DHBs
- data from Healthline, HealthStat, publicly funded hospital discharges and the NIR.

At the time of writing, only high-level, provisional surveillance data for 2017 was available.

The national weekly consultation rate is used to describe the overall level of influenza-like illness (ILI) activity presenting to the general practice level, using the moving epidemic method to define the start of and intensity level of the influenza season.[8] Figure 10.1 shows the national weekly ILI consultation rates from 2009 to 2017. Although increased since 2016, the overall ILI activity remained at a low seasonal level (between 35.1 and 82.5 ILI consultations per 100,000 patient population per week).[9] There were 2,977 ILI cases identified in 2017, with an ILI cumulative incidence of 724.1 per 100,000 patient population.[10]

Figure 10.1: Weekly consultation rates for influenza-like illness in New Zealand, 2009–2017



Source: ESR

Influenza-associated severe acute respiratory illness (SARI) hospitalisations were high in 2017 but slightly lower than known high years (2012 and 2014).[9] However, intensive care unit admissions were low or comparable to these years.

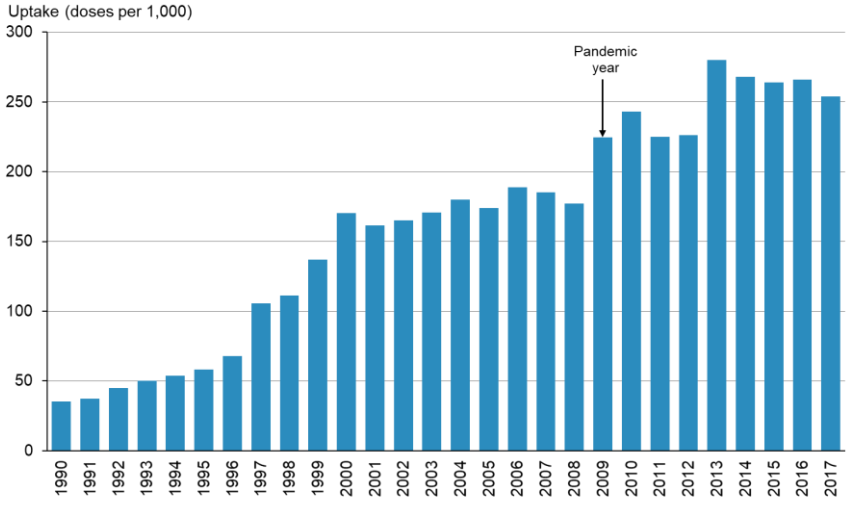
As in 2016,[11] influenza A(H3N2) and B(Yamagata) were the predominant influenza strains circulating in 2017, although influenza B(Victoria) co-circulated with B(Yamagata).[9]

Influenza immunisation uptake

In 2017 more than 1.2 million doses of influenza vaccine were distributed.

The uptake rate of influenza vaccine (both publicly and privately funded), as estimated by vaccine distribution figures, was slightly lower in 2017 (254 doses per 1,000 population) than in the previous three years (see Figure 10.2). Publicly funded uptake for individuals aged 65 years and older was 65 percent. As this is based on immunisation claims data for publicly funded influenza vaccination, it is likely to be an underestimate.

Figure 10.2: Influenza vaccine uptake per 1,000 population, 1990–2017



Vaccine coverage is estimated using vaccine distribution figures.

Funded vaccine was introduced for: individuals aged 65 years and older in 1997; individuals aged under 65 years with certain medical conditions in 1999; pregnant women in 2010; children aged under 5 years with significant respiratory illness in 2013.

Source ESR and Ministry of Health

Since 2010 the Ministry of Health has requested that all DHBs provide influenza immunisation coverage data for their staff at the end of each influenza season. National influenza immunisation coverage for DHB staff is still low, but it has increased from 45 percent in 2010 to 66 percent in 2017.

10.3.3 Pandemic influenza

The natural ecology of influenza type A viruses is among wild aquatic avian species, and from time to time, these viruses spill over into other species including humans. These avian influenza virus infections are usually severe and associated with a high mortality, however, are rarely transmitted from human to human. In the past, avian viruses have become transmissible either through adaptation or the acquisition of swine or human genomic material, and when natural immunity has been lacking in the population, have resulted in a pandemic with global spread.

Pandemics have the potential to result in large numbers of severe infections, but the degree of severity is hard to predict and will depend upon many factors, including whether there is any previous community immunity. The most severe recorded pandemic was the 'Spanish' A(H1N1) pandemic of 1918–1920 which caused an estimated 20–50 million deaths worldwide. The most recent pandemic was the 2009 A(H1N1)pdm09 strain. It was estimated that 10 percent (800,000) of the New Zealand population were infected with the virus during the first wave, including one in every three children.[12] Risk factors for severe outcomes included obesity, pregnancy,[13] diabetes mellitus and Pacific or Māori ethnicity.[12] This strain is now established as a circulating seasonal influenza strain.

Monitoring, surveillance and response for new pandemic strains are in place. See section 10.8.3.

10.4 Vaccines

Annual influenza vaccination is a most important measure for preventing influenza infection and mortality. The National Influenza Specialist Group coordinated by IMAC, is responsible for New Zealand's annual Influenza Communication Campaign (www.influenza.org.nz). This campaign includes an annual influenza kit for health care professionals and a national education and communication programme.

10.4.1 Available vaccines

Funded vaccines

Two quadrivalent inactivated split virion influenza vaccines are funded.

- Fluarix Tetra (GSK) for infants and children aged 6 months to under 3 years (ie, aged 6–35 months). Each 0.5 mL dose contains 15 µg of each of the four recommended influenza strains in phosphate buffered saline; other components and excipients include hydrocortisone, gentamicin sulfate, ovalbumin (≤0.05 µg), formaldehyde, and sodium deoxycholate.
- Influvac Tetra (Mylan New Zealand Ltd) for adults and children aged 3 years and older. Each 0.5 mL dose contains 15 µg of each of the four recommended influenza strains; other components and excipients include potassium chloride, monobasic potassium phosphate, dibasic sodium phosphate, sodium chloride, calcium chloride dihydrate, magnesium chloride hexahydrate. Each 0.5 mL dose contains residual amounts of ovalbumin (≤0.1 µg), formaldehyde, cetrimonium bromide, sodium citrate, sucrose, gentamicin sulfate, and traces of tylosine tartrate, hydrocortisone and polysorbate 80 which are used during the manufacturing process.

Vaccine preparations

Influenza vaccine preparations vary by their type, the number of influenza strains contained in the vaccine and their delivery systems. There are a range of delivery mechanisms available internationally, including intradermal and intranasal mists. Intradermal vaccines are

generally recognised as offering similar immune responses in healthy subjects[14] and possibly more efficient immune responses,[15] particularly in the older adult population.[16] Live attenuated influenza vaccines are delivered by intranasal spray.

The influenza vaccine strains vary each year depending on the prevailing virus viruses. The WHO conducts technical consultations in February/March and September each year to recommend viruses for inclusion in both trivalent and quadrivalent vaccines for the northern and southern hemisphere influenza seasons, respectively. For 2018 the southern hemisphere recommendations include the two influenza type A (H1N1pdm09 and H3N2) and two B (Victoria and Yamagata) strains likely to circulate in New Zealand over the coming influenza season.[17]

Inactivated influenza vaccines (split virion or subunit vaccines)

Trivalent inactivated vaccines (TIVs) are inactivated split virion vaccines prepared from virus grown in the allantoic cavity of embryonated hens' eggs. They contain two influenza type A strains and one type B strain. The virus is purified, disrupted and inactivated with beta-propiolactone or formaldehyde.

Quadrivalent inactivated vaccines (QIVs) contain two type A and two type B influenza strains. Compared to TIVs, QIVs have the potential to offer broader protection against co-circulating B-strains and better effectiveness in seasons of B-strain mismatch.[1]

Live attenuated influenza vaccines (LAIVs)

LAIVs may induce stronger immune responses than TIVs, particularly in children, by mimicking natural influenza infection and evoking both mucosal and systemic immunity, and including broader cellular immune responses.[18] Live attenuated influenza vaccines (LAIVs; trivalent and quadrivalent) are licensed for use in North America for healthy non-pregnant individuals aged 2–49 years and in Europe for children aged 2–18 years.[19] LAIVs have been shown to be effective in children aged 6 months to 7 years.[20]

However, based on recent observational data showing lack of effectiveness in US children aged 2–17 years for the 2013/14 and 2015/16 influenza seasons, the US Advisory Committee on

Immunization Practices (ACIP) has recommended that LAIVs not be used for the 2016/17 influenza season.[19]

In contrast, UK data from the 2015/2016 season has shown a LAIV effectiveness in children aged 2–17 years of 57.6 percent (95% CI: 25.1–76.0) against any influenza, with higher vaccine effectiveness (81.4 percent; 95% CI: 39.6–94.3) against the B strain.[21] It is not currently clear why there are such significant effectiveness differences for different regions, although variations in circulating strain matches, the make-up of the LAIV itself and previous vaccination history may all have some effect.[21]

At the time of writing, LAIVs were not registered in New Zealand.

Adjuvanted vaccines

Adjuvants enhance the immune response to an antigen. There are three adjuvants licensed (internationally) for use in influenza vaccines: two oil-in-water emulsions, and a third that uses immunopotentiating reconstituted influenza virosomes.[22]

Vaccines with these adjuvants show modestly improved immune responses, which may be particularly useful for the elderly, but may also cause more local and systemic reactions than unadjuvanted vaccines.[22] At the time of writing, influenza vaccines containing these adjuvants were not registered and/or available in New Zealand.

10.4.2 Efficacy and effectiveness

International data

The efficacy (prevention of illness among vaccinated individuals in controlled trials) and effectiveness (prevention of illness in vaccinated populations) of influenza vaccine depends on several factors. The age and immune competence of the vaccine recipient are important, as well as the match between the virus strains in the vaccine and those in circulation each year. Previous vaccination history may reduce the vaccine effectiveness in some cases, possibly more so when the previous vaccination was mismatched with the circulating strains at the time.[23]

Two influenza B strains can frequently co-circulate, and due to the complexity involved in predicting which B strains will circulate in the upcoming season, mismatches between the B strain selected for TIVs and the circulating B strains have occurred in up to one-half of influenza seasons. Because QIVs contain two influenza B strains, modelling studies suggest that QIVs are expected to prevent more influenza cases, hospitalisations and deaths than TIVs, due to their capacity to broaden the immune response against B strains and reduce the likelihood of a B-mismatched season.[1]

Data for vaccine efficacy and effectiveness of TIVs is summarised in Table 10.1.

Table 10.1: Current estimates of TIV influenza vaccine efficacy and effectiveness

Population	Type of outcome	Level of protection (95% confidence intervals)
Infants aged under 6 months whose mothers received influenza vaccine	Efficacy against laboratory-confirmed influenza	41–48%[24, 25]
Healthy children aged under 2 years	Efficacy against laboratory-confirmed influenza	Insufficient data[20, 26]
	Effectiveness against laboratory-confirmed influenza	66% (9–88)[27]
Healthy children aged 6–35 months	Effectiveness against laboratory-confirmed influenza	66% (29–84)[27]
Healthy children aged under 16 years	TIV vaccine efficacy in prevention of laboratory-confirmed influenza in randomised controlled trials	59% (41–71)[26]
Healthy adults aged 18–65 years	Effectiveness against influenza-like illness*	30% (17–41)[28]
	Efficacy against influenza symptoms*	73% (54–84)[28]
	Efficacy against laboratory-confirmed influenza	59% (51–67)[20]

Continued overleaf

Population	Type of outcome	Level of protection (95% confidence intervals)
Those aged 65 years and older	Effectiveness in preventing influenza, influenza-like-illness, hospitalisations, complications and mortality	Inconclusive due to poor quality of studies[29]
Those aged 65 years and older	Effectiveness against non-fatal and fatal complications	28% (26–30)[30]
	Effectiveness against influenza-like illness	39% (35–43)[30]
	Effectiveness against laboratory-confirmed influenza	49% (33–62)[30]

* From age 16 years.

Vaccine effectiveness in New Zealand

New Zealand data is consistent with international data. While there is some variability from year to year and with different strains, overall the data shows that TIV influenza vaccine effectiveness is approximately 50 percent overall for preventing both visits to the general practice and hospitalisations, for both influenza type A and B strains.[31, 32, 33, 34] However, estimates for vaccine effectiveness tend to be higher in children and healthy midlife adults, and lower in the elderly.

Pregnant women and neonates

A pregnant woman and her fetus are at increased risk of influenza complications, including hospitalisation from influenza-related cardiorespiratory disorders during the second and third trimesters, and this was especially apparent in the 2009 pandemic.[35] Influenza immunisation is therefore recommended during pregnancy to reduce this risk. Influenza immunisation is expected to have the same efficacy in healthy pregnant women as in other healthy adults.

Maternal influenza immunisation also offers protection to the fetus through maternal antibody transfer.[18, 25, 35, 36] Influenza vaccines are not registered and have not been shown to be effective in infants aged under 6 months, therefore immunisation during pregnancy confers protection to newborns and infants who are too young to have received vaccination at the time of exposure.[24, 37] Maternal influenza immunisation is significantly associated with reduced risk of influenza virus infection

and hospitalisation for an influenza-like illness in infants up to 6 months of age, and increased influenza antibody titres are seen in infants through to age 2–3 months.[24]

Influenza immunisation during pregnancy may also reduce the incidence of stillbirth. In an Australian study, stillbirth was 51 percent less likely among vaccinated mothers compared to unvaccinated mothers.[38]

Children

The evidence for vaccine efficacy and effectiveness in very young children is varied. There is evidence to support moderate effectiveness of TIV in children aged 3 years and older.

Healthy adults

Generally, randomised placebo-controlled trials of TIV in healthy adults support good protection against a variety of outcomes, particularly laboratory-confirmed influenza.

Adults aged over 65 years

Although less effective at preventing clinical illness in older people,[39] influenza vaccination does reduce hospitalisation and deaths. A 1995 meta-analysis of 20 cohort studies in older people estimated that influenza vaccine prevented 56 percent of upper respiratory illnesses, 53 percent of pneumonias, 50 percent of all hospitalisations and 68 percent of deaths.[40]

There is wide variability in the estimates of effectiveness of annual influenza vaccination against influenza-like illness in nursing home residents (0–80 percent).[22] Vaccination has been demonstrated to prevent hospitalisation and death in these groups,[40, 41, 42, 43] but a 2010 Cochrane review concluded that there was insufficient evidence to support influenza vaccine effectiveness in the elderly.[29] However, researchers have more recently re-examined this review and its methodology and argue that there is substantial evidence for the ability of influenza vaccine to reduce the risk of influenza infection and influenza-related disease and death in the elderly.[30]

Adults with co-morbid conditions

Influenza vaccination has been associated with reductions in hospitalisations and deaths among adults with risk factors for influenza complications. Among Danish adults aged under 65 years with underlying medical conditions, vaccination reduced all-cause deaths by 78 percent and hospitalisations attributable to respiratory infections or cardiopulmonary diseases by 87 percent.[44] Benefits from influenza vaccination have been observed for both diabetes[45] and chronic obstructive pulmonary disease.[46] An Australian study of adults aged 40 years and older showed that unvaccinated adults are almost twice as likely as vaccinated adults to have an acute myocardial infarct.[47]

Herd immunity

There is some evidence to suggest that herd immunity can be achieved, particularly by vaccinating children.[48] Some studies suggest that herd immunity may also be achieved in nursing homes if immunisation coverage of residents is greater than 80 percent.[49] Vaccinating health care workers is likely to be an effective strategy, particularly when in contact with high-risk patients such as in nursing homes.[50]

The UK has had three seasons of a progressively rolled-out vaccination programme using LAIV, starting with children aged 2–3 years in 2013/14 and then extended to children aged 4–7 years by 2015/16. There were also school-age pilot programmes in England for older children. Early results show evidence of indirect and overall impact, with decreases in disease incidence and influenza positivity in the school-age pilots versus control areas in vaccinated and non-vaccinated groups.[51]

Duration of immunity

Due to the continual drift of influenza viruses, duration of immunity provided by influenza vaccines is difficult to study. However, when the strains stay the same for consecutive years, vaccination in a previous year appears to confer immunity into the next year for healthy adults and children.[19, 22] However shorter duration of immunity is likely in other groups, particularly the elderly.[19]

Protection due to LAIVs has been demonstrated to persist beyond a year.[52, 53]

10.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.[54] Store in the dark at +2°C to +8°C. Do not freeze.

10.4.4 Dosage and administration

The funded quadrivalent influenza vaccine should be administered by intramuscular or subcutaneous injection (see section 2.2.3). The contents of the syringe must be shaken thoroughly before use.

Individuals aged 9 years and older

Individuals aged 9 years and older receive a single 0.5 mL intramuscular dose of Influvac Tetra vaccine.

Children aged under 9 years

Children aged under 9 years who have not previously received influenza vaccine require two doses of vaccine four weeks apart to produce a satisfactory immune response. Children aged 6 months to under 3 years (ie, aged 6–35 months) receive a 0.5 mL dose of Fluarix Tetra; children aged 3 years and older receive a 0.5 mL dose of Influvac Tetra (see Table 10.2).

Table 10.2: Recommended influenza vaccine doses in children

Age	Vaccine	Dose	Number of doses
6–35 months	Fluarix Tetra	0.5 mL	1 or 2*
3–8 years	Influvac Tetra	0.5 mL	1 or 2*

* Two doses separated by at least four weeks if the vaccine is being used for the first time.

> The recommended dosages for young children at different ages may vary between vaccine manufacturers, so check the manufacturer's data sheet before administering.

Immunocompromised individuals

Regardless of their age, previously unvaccinated immunocompromised individuals are recommended to receive two doses of influenza vaccine, four weeks apart.[55] One dose is then given in each subsequent year. (See section 4.3.)

Co-administration with other vaccines

Influenza vaccine can be administered with other vaccines, such as pneumococcal polysaccharide vaccine, tetanus diphtheria (Td) vaccine, the live attenuated herpes zoster vaccine[56] and the scheduled childhood vaccines. Individuals recommended to receive both influenza vaccine and 13-valent pneumococcal conjugate vaccine (PCV13) have an increased risk of fever following concurrent administration of these vaccines.[57, 58] Separation of the vaccines by two days can be offered, but is not essential. (See also section 15.6.2.)

10.5 Recommended immunisation schedule

The optimal time to vaccinate people in high-risk groups is usually during March and April. This is in advance of the usual May to September period of influenza virus activity. The vaccine can be given even when influenza virus activity has been identified, because protective antibody levels develop from four days after immunisation, with full protection after two weeks.[59] The vaccine should be administered annually to maintain immunity and to provide protection against new strains.

Vaccine effectiveness may be reduced in those at highest risk from influenza. Therefore, it is important to consider not just individual protection but also reducing spread by vaccinating contacts of high-risk individuals, such as family and caregivers, and occupational vaccination. See Table 10.3 for a summary of the funded and unfunded recommendations for influenza immunisation.

Table 10.3: Influenza vaccine recommendations

Note: Funded conditions are in the shaded rows. See the Pharmaceutical Schedule (www.pharmac.govt.nz) for any changes to the funding decisions.

Recommended and funded
All individuals aged 65 years and older.
Individuals aged 6 months to under 65 years who: • have cardiovascular disease (ischaemic heart disease, congestive heart failure, rheumatic heart disease, congenital heart disease or cerebrovascular disease) • have chronic respiratory disease (asthma if on regular preventive therapy; other chronic respiratory disease with impaired lung function) • have diabetes • have chronic renal disease • have any cancer,[a] excluding basal and squamous skin cancers if not invasive • have other conditions (autoimmune disease, immunosuppression or immune deficiency,[a] HIV infection, transplant recipients, neuromuscular and central nervous system diseases/disorders, haemoglobinopathies, children on long-term aspirin, have a cochlear implant, errors of metabolism at risk of major metabolic decompensation, pre- or post-splenectomy, Down syndrome) • are pregnant • are children aged 4 years and under who have been hospitalised for respiratory illness or have a history of significant respiratory illness • are children aged under 18 years living in the Seddon/Ward and rural Eastern Marlborough region (within the Nelson Marlborough District Health Board) and Kaikoura and Hurunui areas (within the Canterbury District Health Board) • are children aged under 18 years who have been displaced from their homes in Edgecumbe and the surrounding region • are patients who are compulsorily detained long-term in a forensic unit within a DHB hospital.[b]
Recommended but not funded
Individuals with asthma not requiring regular preventive therapy
Individuals with functional asplenia
Individuals in essential positions and health care workers
Individuals who may transmit influenza to persons at increased risk of complications from influenza infection
Travellers
Children aged under 5 years
Residents of residential care facilities
The homeless

a Seek specialist advice for individuals who are currently being treated with immune checkpoint inhibitors, as well as those who have discontinued treatment within the past 6 months. See 'Oncology patients treated with immune checkpoint inhibitors' in section 4.3.3.

b This is a Pharmaceutical Schedule Section H – Hospital Medicines List funding restriction.

10.5.1 Pregnancy and breastfeeding

The influenza vaccine is strongly recommended, and funded, for women who will be pregnant while the vaccine is available.

Influenza vaccine is safe to administer during any stage of pregnancy or while breastfeeding. There is no evidence that influenza vaccine prepared from inactivated virus causes damage to the fetus or neonate[60] and some evidence it may be protective against stillbirth.[38]

Pregnant women are at greater risk from complications associated with influenza illness. When pregnancy is superimposed on high-risk conditions such as asthma or diabetes, influenza-related morbidity is three to four times greater than in non-pregnant women with similar high-risk conditions.

Because there is no registered or effective vaccine for children aged under 6 months, vaccination during pregnancy is highly recommended to improve maternal fetal passive antibody transfer.[37] Influenza vaccination of pregnant women has been shown to significantly decrease influenza in their newborn babies.[18, 25, 35, 36] Breastfeeding is also recommended, to deliver passive immunity to the infant.[18] (See also section 4.1.2.)

10.5.2 At-risk children

Influenza vaccine is funded for children aged 6 months and older with chronic illnesses and a history of respiratory disease. Children with the following conditions should be prioritised to receive influenza vaccine due to their increased risk:

- all asthmatics on regular preventive therapy
- other children with chronic respiratory disorders (eg, cystic fibrosis, non-cystic fibrosis bronchiectasis, and chronic lung disease of infancy).

Special considerations apply to children, as follows. (See also section 4.3.)

- In children aged 6–24 months with significant chronic medical conditions, influenza immunisation is occasionally associated with fever between 6 and 24 hours after administration, which may cause an exacerbation of the underlying condition.
- Children receiving cancer chemotherapy may have a weaker response to influenza vaccine. Vaccination is recommended three to four weeks after the last dose of chemotherapy, when the neutrophil and lymphocyte counts are each $\geq 1.0 \times 10^9$/L. Children who are no longer receiving chemotherapy can be expected to show seroconversion three months after the cessation of chemotherapy.

Note: Seek specialist advice for children who are currently being treated with immune checkpoint inhibitors, as well as those who have discontinued treatment within the past 6 months. See 'Oncology patients treated with immune checkpoint inhibitors' in section 4.3.3.

10.5.3 At-risk adults

Adults aged 65 years and older

In adults aged 65 years and older, influenza vaccine has been shown to be effective against non-fatal and fatal influenza complications, influenza-like illness and laboratory-confirmed influenza (see Table 10.1).

Adults with underlying medical conditions

Influenza has been associated with increased morbidity and mortality in adults with underlying medical conditions.

Note: Seek specialist advice for individuals who are currently being treated with immune checkpoint inhibitors, as well as those who have discontinued treatment within the past 6 months. See 'Oncology patients treated with immune checkpoint inhibitors' in section 4.3.3.

10.5.4 Recommended but not funded

Influenza vaccine is recommended, but not funded, for the groups listed in Table 10.3.

Healthy adults

Healthy individuals are encouraged to have the vaccine, especially if they are in close contact with individuals at high risk of complications. Employers are encouraged to provide influenza vaccine to avoid illness in their employees, especially those engaged in health care and other essential community services. Immunising healthy individuals has been shown to be cost-effective.

In order to optimise the protection of high-risk (see Table 10.3) infants and toddlers (including those aged under 6 months) all household and close contacts should receive influenza vaccine (not funded unless eligibility criteria are met).

Health care workers

The Ministry of Health strongly recommends, and expects, that all health care workers will receive annual influenza vaccination for their own protection and the protection of those in their care.

Travellers

People travelling outside New Zealand, especially those who are in the at-risk groups who have not received vaccine during the previous autumn, are recommended to have influenza vaccination depending on the season and their destination. In tropical countries, influenza activity can occur throughout the year but is more likely during the winter (wet) and summer seasons, while in the northern hemisphere activity is commonest between the months of December and March. Outbreaks of influenza among organised tourist groups (eg, on cruise ships) can occur throughout the year.

10.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

Note: Seek specialist advice for individuals who are currently being treated with immune checkpoint inhibitors, as well as those who have discontinued treatment within the past 6 months. See 'Oncology patients treated with immune checkpoint inhibitors' in section 4.3.3.

10.6.1 Contraindications

Influenza vaccine should not be administered to people with a history of an anaphylactic reaction to a prior dose of influenza vaccine or to a vaccine component. Egg allergy, including anaphylaxis, is **not** a contraindication or precaution, see section 10.6.3.

Fluvax is contraindicated for children aged under 5 years (see section 10.7) due to the increased risk of febrile events. The Ministry of Health recommends that Fluvax not be given to children aged under 9 years.

10.6.2 Precautions

History of Guillain–Barré syndrome

There appears to be a small increase in the risk of GBS following influenza vaccination (less than one additional case per million doses administered,[19] substantially less than the risk of developing severe complications from influenza infection[22, 28]). There is also an increased risk of developing GBS following influenza infection, and the magnitude of the risk is several times greater than that following influenza vaccination.[61]

New Zealand hospitalisations for GBS showed no increase during the 1990s despite the marked increase in vaccine use during this period, but did show a marked year-to-year variation. In particular, the doubling of vaccine use in 1997 (with the introduction of funded vaccine) was not associated with any increase in GBS hospitalisations. No excess risk for

GBS following influenza vaccine in children has been documented. No association between influenza vaccines and any other neurological disease has been substantiated.

The risks and benefits of withholding vaccination should be considered on an individual basis, based on the potential morbidity and mortality associated with influenza for that individual, including the potential risk of recurrent GBS following influenza infection.

Co-administration with PCV13

Individuals (or their parents/guardians) who are recommended to receive both influenza vaccine and 13-valent pneumococcal conjugate vaccine (PCV13) should be advised of the increased risk of fever following concomitant administration of these vaccines.[57, 58] Separation of the vaccines by two days can be offered, but is not essential. (See also section 15.6.2.)

10.6.3 Egg allergy

Influenza vaccine can be safely administered to people with a history of egg allergy, including anaphylaxis, at general practices, pharmacies or at the workplace.[62]

Reported cases of anaphylaxis after influenza vaccination in egg-allergic individuals all occurred over 30 years ago, at a time when vaccine egg (ovalbumin) content was much higher than it is now. Recent studies have shown that influenza vaccines containing less than one microgram (<1 µg) of ovalbumin do not trigger anaphylaxis in sensitive individuals.[62] The residual ovalbumin in one dose of Influvac Tetra (≤0.1 µg) or Fluarix Tetra (≤0.05 µg) is significantly below this limit.[63, 64]

10.7 Expected responses and AEFIs

Inactivated influenza vaccines are generally well tolerated. The safety profile of quadrivalent inactivated vaccines is comparable to that of trivalent inactivated vaccines.[19] Placebo-controlled trials of TIVs have shown that influenza vaccine is not associated with systemic reactions (eg, fever, malaise, myalgia) in older persons and healthy young adults.[19] Systemic reactions are more likely in children not previously exposed to the vaccine or virus, these are generally self-limiting and resolve within

one to two days.[19] A large post-licensure study in the US, which reviewed more than 250,000 children aged under 18 years given influenza vaccine, showed no increase in clinically important medically attended events for two weeks after vaccination compared to control periods.[65]

In early 2010 there were reports of children in both Australia and New Zealand who had received the influenza vaccine and experienced febrile seizures. All of the cases were linked to the Fluvax brand of vaccine.

Vaccinators need to emphasise to recipients that:

- it is an inactivated vaccine and cannot cause influenza
- local reaction and mild systemic symptoms may occur within a day or two of immunisation
- respiratory viral infections are common, and many individuals will develop one coincidentally following immunisation, and these should not be falsely attributed to the vaccine.

Local reactions, including redness and induration at the injection site, may persist for one to two days in 10–64 percent of adult recipients, but these effects are usually mild.[19] Passive reporting of local and systemic reactions to influenza vaccines is more frequent for females (both young and older adults) than males.[66]

In 2010 an association was found between one H1N1 pandemic vaccine (an adjuvanted vaccine not licensed or used in New Zealand) and narcolepsy. There is now data from a number of European countries that supports a temporal link.[67, 68, 69] The association may have been related to the adjuvant. However, it is possible that the onset of narcolepsy may be confounded by other factors (such as genetic predisposition, (H1N1)pdm09 influenza and/or other environmental factors).[68, 70, 71] Further data is required to confirm the strength of this association and the size of the risk, and to identify the underlying biological mechanisms.[68, 72]

See section 10.6.3 for information on egg allergy.

Immune checkpoint inhibitors

There have been reports of fatal myositis, myocarditis and rhabdomyolysis in patients being treated with ipilimumab with nivolumab and administered influenza vaccine.[73] A prospective study of

patients currently being treated with nivolumab or pembrolizumab and administered trivalent influenza vaccine found an increase in immune-related adverse events compared to unvaccinated patients being treated with these medicines.[74] See 'Oncology patients treated with immune checkpoint inhibitors' in section 4.3.3.

10.8 Public health measures

Using influenza signs and symptoms to assess the burden of influenza is of limited value. There is also a significant amount of asymptomatic circulation of influenza in the community. The most sensitive diagnostic method is polymerase chain reaction (PCR) of respiratory nasopharyngeal swabs or aspirate samples.

The methods of controlling influenza are:

- immunisation
- hand hygiene (ie, regularly washing hands for at least 20 seconds and drying them for 20 seconds, or regularly using an alcohol-based hand rub)
- respiratory hygiene (ie, cough and sneeze etiquette, and the judicious use of viricidal tissues and wearing of face masks in some settings)
- social distancing (ie, persuading those with symptoms to avoid others in the community by staying away from school and work when sick; in particular, infected individuals should avoid contact with the elderly, the chronically ill, and infants and babies)
- regularly cleaning flat surfaces such as bathroom sinks, bedside cabinets, desks and table tops
- antiviral therapy, but this has a limited role.

10.8.1 Improving vaccine uptake

Studies in New Zealand and overseas have found that provider attitudes and recommendations are key to improving influenza vaccine uptake. Organised registers for recall and opportunistic immunisation are also likely to be important factors in achieving high uptake.

Every effort should be made during March and April to immunise all people at risk, such as those aged 65 years and older, those aged under

65 years (including children) who have certain medical conditions, pregnant women and health care workers. A decision to offer immunisation in winter, during an influenza epidemic, to those who were not immunised in the autumn will depend on the circumstances of the outbreak or epidemic, among other factors. Availability of an appropriate vaccine is the most pertinent of these factors.

Vaccination of healthy adults and children is encouraged but is not funded by the Ministry of Health; adult vaccination may be funded by employers.

10.8.2 Antiviral drugs

Influenza antiviral drugs can be used to treat or to prevent influenza and can be adjuncts to influenza vaccination. Use of antivirals very early in an illness can reduce the duration of symptoms and the risk of complications from influenza. Clinical benefit is greatest if antivirals are used as early as possible, especially within the first 48 hours of the illness.

Meta-analyses of the effectiveness of oseltamivir in treating uncomplicated influenza show a reduction in duration of symptoms for healthy adults and adolescents of around one day,[75] a 63 percent (95% CI: 19–83) decreased risk of hospitalisation for any cause and a 44 percent (95% CI: 25–58) decreased risk of antibiotic prescription use.[76] For use with severe influenza, observational studies show early treatment is critical, and can lead to a decreased risk for death.[77, 78]

Antivirals should be considered for unimmunised or recently immunised contacts who are at high risk of severe disease. When used to limit the size of an institutional outbreak, antiviral drugs are usually given for a period of two weeks after immunisation or until one week after the end of the outbreak. Institutional outbreaks should be notified to the local medical officer of health.[79]

10.8.3 Pandemics

At the time of a pandemic, the public health advice, priority groups and the timing of vaccination may be quite different from those during inter-pandemic periods. The *New Zealand Influenza Pandemic Plan: A framework for action*[80] describes the key phases of a pandemic and the actions and responsibilities within each phase.

10.9 Variations from the vaccine data sheet

The Influvac Tetra data sheet states that hypersensitivity to the residues of eggs is a contraindication to receiving influenza vaccination. The Ministry of Health recommends that individuals with hypersensitivity to eggs, including anaphylaxis, may receive influenza vaccination– see section 10.6.3.

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11 Measles

Key information

Mode of transmission	By direct contact with infectious droplets or by airborne spread. Measles is one of the most highly communicable of all infectious diseases.
Incubation period	About 10 days, but may be 7–18 days from exposure to onset of fever. The incubation period may be longer in those given IG after exposure.
Period of communicability	From 5 days before to 5 days after rash onset, counting the day of rash onset as day 1.
Herd immunity threshold	To prevent recurrent outbreaks of measles, 95 percent of the population must be immune.
Funded vaccine	MMR vaccine (Priorix) is a live attenuated vaccine.
Dose, presentation, route	0.5 mL per dose after reconstitution. Pre-filled syringe and glass vial. The vaccine must be reconstituted prior to injection. Subcutaneous injection.
Funded vaccine indications and schedule	Children at ages 15 months and 4 years. Adults who are susceptible to one or more of measles, mumps and rubella. Susceptible adults are: • individuals born from 1 January 1969 with no documented history of 2 doses of measles-containing vaccine after age 12 months • individuals with no documented measles IgG antibody. For (re-)vaccination following immunosuppression (if the individual is immunocompetent enough to safely receive the vaccine).
Vaccine efficacy/ effectiveness	Measles vaccines are highly efficacious, and immunisation programmes have controlled measles to the point of elimination in many populations.
Egg allergy	Egg allergy, including anaphylaxis, is **not** a contraindication for MMR vaccine.
Adverse events to vaccine	MMR vaccine is generally well tolerated. The risk of adverse reactions to MMR vaccine is low compared to the risk of complications from measles disease.

Continued overleaf

Public health measures	Notify the local medical officer of health immediately on suspicion. Prevent measles transmission through exclusion and use of personal protective equipment. Promote immunisation to susceptible individuals. Management of contacts of measles cases should be discussed with the medical officer of health.

11.1 Virology

The measles virus is an RNA virus, from the genus *Morbillivirus*, in the family Paramyxoviridae. Humans are the only natural host for the measles virus. The virus is rapidly inactivated by sunlight, heat and extremes of pH.[1]

11.2 Clinical features

Measles is transmitted by direct contact with infectious droplets and also by airborne spread. It is one of the most highly communicable of all infectious diseases, with an approximate basic reproductive number of 12–18 in high-income countries[2] (see section 1.2.1). There is a prodromal phase of two to four days with fever, conjunctivitis, coryza and Koplik's spots on the buccal mucosa. The characteristic maculopapular rash classically appears first behind the ears on the third to seventh day, spreads over three to four days from the head and face, over the trunk to the extremities. It lasts for up to one week. The patient is most unwell during the first day or two after the appearance of the rash.

The incubation period is about 10 days, but may be 7 to 18 days from exposure to onset of fever. It may be longer in those given IG after exposure. Measles is highly infectious from five days before to five days after rash onset, counting the day of rash onset as day one.

Complications are common, occurring in 10 percent of cases, and include otitis media, pneumonia, croup and diarrhoea. Encephalitis has been reported in 1 in every 1,000 cases, of whom some 15 percent die and a further 25–35 percent are left with permanent neurological damage. Other complications of measles include bronchiolitis, sinusitis, myocarditis, corneal ulceration, mesenteric adenitis, hepatitis and

idiopathic thrombocytopenic purpura (ITP or immune thrombocytopenia).

Sub-acute sclerosing panencephalitis, a rare degenerative central nervous system disease resulting from persistent measles virus infection, is fatal. Sub-acute sclerosing panencephalitis typically occurs 7 to 11 years after wild-type measles virus infection.[3] This complication has virtually disappeared where there is widespread measles immunisation.

The case fatality rate for reported cases of measles in the US is 1–3 per 1,000.[3] Measles is particularly severe in the malnourished, children with vitamin A deficiency, and in patients with defective cell-mediated immunity, who may develop giant cell pneumonia or encephalitis without evidence of rash, and have a much higher case fatality rate. Measles during pregnancy can cause miscarriage, stillbirth and preterm delivery.[1]

Measles is also serious in healthy children: over half of all the children who died from measles in the UK between 1970 and 1983 were previously healthy.[4] No other conditions were reported as contributing to the death of seven people who died from measles in the 1991 New Zealand epidemic.

11.3 Epidemiology

11.3.1 Global burden of disease

Mortality and morbidity

From 2000 to 2015, the annual reported measles incidence decreased by 75 percent worldwide, from 146 to 36 cases per million population, due to increased vaccine coverage. Annual estimated measles deaths decreased by 79 percent, from 651,600 cases to 134,200.[5]

Although measles mortality rates have fallen significantly,[6] measles remains an important vaccine-preventable cause of death among children throughout the world, particularly in low-income countries. The disease is highly infectious in non-immune communities, with epidemics occurring approximately every second year.

Measles elimination

When a country is verified by the Measles Regional Verification Commission as having eliminated measles, it means that the country interrupted transmission of the endemic strain of circulating measles virus for a period of 36 months. Importations of measles virus may have occurred during this period, but circulation of the imported strains of measles virus was interrupted within 12 months of the importation.[7]

In May 2012 the 194 member states of the World Health Assembly endorsed the *Global Vaccine Action Plan 2011–2020*,[8] which aims to eliminate measles in at least four WHO regions by 2015 and in five WHO regions by 2020. In September 2016, the Region of the Americas was the first WHO region to be declared free of measles. New Zealand has not yet been verified as having eliminated measles.

11.3.2 New Zealand epidemiology

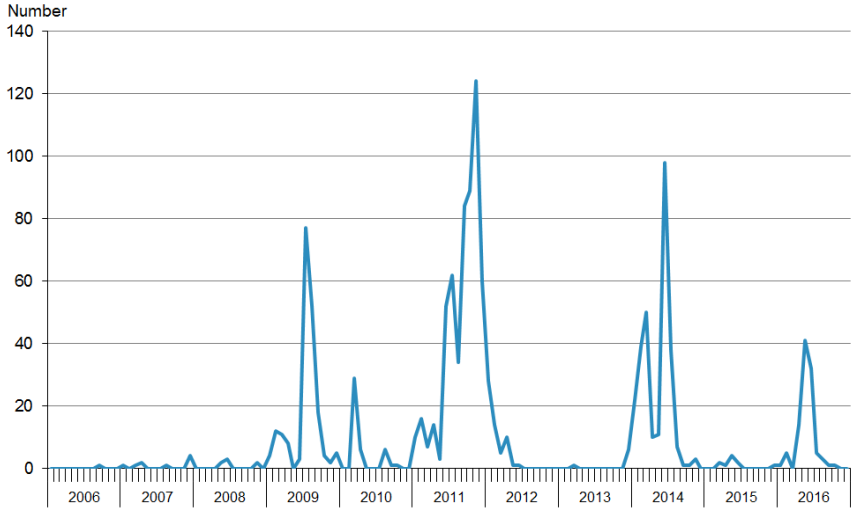
Measles vaccine was introduced in 1969 and moved to a two-dose schedule (as MMR vaccine) in 1992. Measles became a notifiable disease in 1996. The current two-dose schedule at ages 15 months and 4 years was introduced in 2001 (see Appendix 1 for more information about the history of the Schedule).

The most recent measles epidemics occurred in 1991 (the number of cases was estimated to be in the tens of thousands) and 1997 (2,169 cases identified).

Smaller outbreaks occurred in 2009, 2011, 2014 and 2016 (see Figure 11.1). The largest outbreak was in 2011 and mainly affected Auckland, with 489 confirmed or probable cases. It started with an unimmunised child who became infected on a family trip to England, then developed measles when back in Auckland. Many of the secondary cases were in unimmunised high school children and young adults. The outbreak officially ended in July 2012.[9]

Importation of measles by non-immune people who had travelled overseas was also linked to the measles outbreaks in New Zealand in 2014 and 2016 (see also section 11.5.5).

Figure 11.1: Number of measles notifications by month reported, January 2006 to December 2016



Note: 2016 data is provisional.
Source: ESR

To eliminate measles epidemics, modelling suggests that New Zealand needs to achieve a coverage level of greater than 90 percent for both doses of MMR.[10] If this coverage level is achieved and maintained, the length of time between epidemics will increase and may lead to the elimination of measles. As at 31 December 2016, the 5-year-old immunisation coverage rate, which includes two doses of measles-containing vaccine, was 88.6 percent – close to the target. However, previous years of low vaccine coverage have resulted in sufficient numbers of non-immune adolescents and young adults to permit outbreaks to occur.

11.4 Vaccines

11.4.1 Available vaccines

The measles vaccine is only available as one of the components of MMR vaccine. This vaccine is a freeze-dried preparation containing live attenuated measles, mumps and rubella viruses.

Funded vaccine

Each 0.5 mL dose of the reconstituted MMR vaccine (Priorix, GSK) contains:

- not less than $10^{3.0}$ $CCID_{50}$ of the attenuated line of Schwarz strain measles, propagated in chick embryo tissue culture
- not less than $10^{3.7}$ $CCID_{50}$ of RIT 4385 mumps strain, derived from the Jeryl Lynn strain and propagated in chick embryo tissue culture
- not less than $10^{3.0}$ $CCID_{50}$ of the Wistar RA 27/3 rubella strains, propagated in MRC_5 human diploid cells
- lactose, amino acids supplement, mannitol, sorbitol and neomycin sulphate as excipients, and water for injection.

Other vaccines

MMR II (MSD) was the funded vaccine prior to the 1 July 2017 Schedule change. It contains:

- Attenuvax (Measles Virus Vaccine Live, MSD), a more attenuated line of measles virus, derived from Enders' attenuated Edmonston strain and propagated in chick embryo cell culture
- Mumpsvax (Mumps Virus Vaccine Live, MSD), the Jeryl Lynn (B level) strain of mumps virus propagated in chick embryo cell culture
- Meruvax II (Rubella Virus Vaccine Live, MSD), the Wistar RA 27/3 strain of live attenuated rubella virus propagated in WI-38 human diploid lung fibroblasts.

Two quadrivalent measles, mumps, rubella and varicella vaccines (MMRV, see chapter 21) are also registered but not currently available in New Zealand:

- ProQuad (MSD), which contains further attenuated Enders' Edmonston (Moraten) strain measles, RA 27/3 rubella, Jeryl Lynn mumps and Varicella Virus Vaccine Live (Oka/Merck)
- MMRV (Priorix-Tetra, GSK) contains not less than $10^{3.0}$ $CCID_{50}$ of the Schwarz measles, not less than $10^{4.4}$ $CCID_{50}$ of the RIT 4385 mumps, not less than $10^{3.0}$ $CCID_{50}$ of the Wistar RA 27/3 rubella and not less than $10^{3.3}$ PFU of the varicella virus strains.

11.4.2 Efficacy and effectiveness

Measles vaccines are highly efficacious, and immunisation programmes have controlled measles to the point of elimination in many populations.[11] Outbreaks and epidemics continue to occur where low immunisation rates and/or sufficient numbers of susceptible members of communities are present. A 2012 Cochrane review of the safety and effectiveness of MMR vaccine concluded that a single dose of MMR vaccine is at least 95 percent effective in preventing clinical measles and 92 percent effective in preventing secondary cases among household contacts aged 6 months and older.[12] This was a systematic review of clinical trials and studies, which involved approximately 14.7 million children.

Seroconversion to all three viruses of MMR vaccine occurs in 85–100 percent of recipients. 'Primary vaccine failure' refers to the lack of protective immunity despite vaccination. It is due to failure of the vaccine to stimulate an immune response. This occurs in 5–10 percent of recipients after the first dose and is rare after a second dose. More than 99 percent of people who receive two MMR doses (given at least four weeks apart, and the first dose given after age 12 months) develop serologic evidence of immunity to measles.[3] Two doses are required for measles control and elimination in populations.[3] The second MMR dose is not a booster, it is given to address primary vaccine failure.

Measles vaccination may have nonspecific effects, reducing mortality from other infectious diseases. Infection with the measles virus may cause immune memory loss and predispose people to opportunistic infections for up to three years.[13] Population-level data from the UK, US and Denmark indicates that when measles was common, measles virus infections could have been implicated in as many as half of all childhood deaths from infectious disease.[13] The authors suggest that the reduction in measles infections was the main factor in reducing overall childhood infectious disease mortality after the introduction of vaccination.

Duration of immunity

Even though antibody levels decline over time, secondary vaccine failure (ie, vaccine failure due to waning of protective immunity) has only rarely been documented for measles and rubella, but recently there have been outbreaks thought to be due to declining vaccine-induced mumps immunity.[14]

In Finland in 1982 a cohort was recruited at the start of the national MMR vaccination programme to study the persistence of vaccine-induced antibodies. By the mid-1990s Finland had eliminated measles, mumps and rubella, and there was little opportunity for natural boosting to occur. The follow-up of this cohort has shown that while antibodies wane over time, 20 years after the second MMR dose immunity to rubella was secure, 95 percent of people remained sero-positive for measles and immunity to mumps declined, with 74 percent being sero-positive.[15] The antibody avidity also decreased over time, by 8 percent for measles and 24 percent for mumps.[16]

Waning of both the concentration and the avidity of antibodies might contribute to measles and mumps infections occurring in individuals who have received two doses of MMR.

See section 21.4.2 for efficacy and effectiveness data for VV.

11.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.[17] Store at +2°C to +8°C. Do not freeze.

MMR vaccine must be reconstituted only with the diluents supplied by the manufacturer. Use MMR vaccine as soon as possible after reconstitution. If storage is necessary, reconstituted MMR vaccine can be stored at +2°C to +8°C for up to eight hours.

11.4.4 Dosage and administration

The dose of MMR is all of the reconstituted vaccine (approximately 0.5 mL) administered by subcutaneous injection (see section 2.2.3).

Co-administration with other vaccines

MMR vaccine can be given concurrently with other vaccines, as long as separate syringes are used and the injections are given at different sites. If not given concurrently, live vaccines should be given at least four weeks apart. (See also section 2.2.7 for information about multiple injections at the same visit.)

Interchangeability

The two brands of MMR vaccine (Priorix and MMR II) may be used interchangeably for completion of a course.[18]

11.5 Recommended immunisation schedule

Table 11.1: Recommended MMR vaccine schedule

	Schedule
Usual childhood schedule[a]	2 doses: at ages 15 months and 4 years
Catch-up[b] for children, adolescents and adults	2 doses: at least 4 weeks apart

a If MMR is given to children aged 6–12 months for outbreak control, 2 further MMR doses are still required at ages 15 months and 4 years.

b For those born from 1 January 1969 who do not have documented evidence of two doses of an MMR-containing vaccine given after age 1 year, or who do not have serological evidence of protection for measles, mumps and rubella. See section 11.5.2.

11.5.1 Usual childhood schedule

MMR vaccine is recommended irrespective of a history of measles, mumps or rubella infection or measles immunisation. A clinical history does not reliably indicate immunity unless confirmed by serology. There are no known ill effects from vaccinating children, even if they have had serologically confirmed infection with any of the viruses.

Measles vaccine is recommended as MMR at age 15 months and at age 4 years. Two doses of measles vaccine are recommended because nearly all of the 5–10 percent who fail to be protected by the first dose will be protected by the second. The second dose of measles vaccine can be given as soon as four weeks after the first dose.

MMR vaccine may be given to children aged 12 months or older whose parents/guardians request it, and no opportunity should be missed to achieve immunity. If MMR is given early (ie, at 12 months of age), the vaccinator may also give the other scheduled 15-month vaccinations. This would reduce the risk of the child not returning for the other 15-month vaccinations.

MMR vaccine when aged under 12 months

MMR may be recommended for infants aged 6–12 months during measles outbreaks if cases are occurring in the very young (see section 11.8). These children still require a further two doses of MMR at ages 15 months and 4 years because their chance of protection from measles is lower when the vaccine is given when they are aged under 12 months. Any recommendations will be made by the local medical officer of health and the Ministry of Health based on local epidemiology. Note: Some immigrant children may have received a measles-containing vaccine when aged under 12 months.

11.5.2 Catch-up

Two doses of MMR (at least four weeks apart) are recommended and funded for any child, adolescent or adult who is known to be susceptible to one or more of the three diseases.

Adults born in New Zealand before 1969 are considered to be immune to measles as circulating virus and disease was prevalent prior to the introduction of measles vaccine in 1969.

Adults born from 1 January 1969

All individuals born in 1969 or later who do not have documented evidence of two doses of an MMR-containing vaccine given after age 1 year (even if they have received two doses of a measles-containing vaccine) or who do not have serological evidence of protection for measles, mumps and rubella should be considered susceptible.

This particularly applies to:

- a student in post-secondary education
- a health care worker with patient contact
- those in institutional care and those who care for them
- a susceptible international traveller visiting a country in which measles is endemic.

Some adults may have received one dose of measles vaccine and one dose of MMR during one of the catch-up campaigns (eg, the 1997 campaign, when all those aged up to 10 years were offered MMR vaccine). They will have therefore received the recommended two doses of measles, but only one of mumps and rubella. While the main reason for a two-dose MMR schedule is to protect against measles, two doses of all three antigens is recommended and funded. These individuals can receive a second dose of MMR (ie, a third dose of measles vaccine) without any concerns. It is important that women of childbearing age are immune to rubella (see chapter 18).

All persons born from 1 January 1969 with only one documented dose of prior MMR should receive a further dose of MMR; if there are no documented doses of prior MMR, then two doses should be administered, at least four weeks apart.

11.5.3 Immunocompromise

Contacts of immunocompromised individuals

In general, MMR is contraindicated in immunocompromised individuals (see section 4.3). They can be partially protected from exposure to infection by ensuring that all contacts are fully immunised (funded), including hospital staff and family members. There is no risk of transmission of MMR vaccine viruses from a vaccinee to the immunocompromised individual (see section 11.7.2). See also 'Household contacts' in section 4.3.1 for general vaccination information for contacts of immunocompromised individuals.

(Re-)vaccination following immunosuppression

MMR vaccine is funded for (re-)vaccination following immunosuppression. However, it is important to be sure that the individual is immunocompetent enough to safely receive the vaccine.

HIV infection

Discuss vaccination of individuals with HIV infection with their specialist (see 'HIV infection' in section 4.3.3).

MMR vaccine is recommended for all HIV-positive children, whether symptomatic or asymptomatic, if the CD4+ lymphocyte percentage is 15 percent or greater. Asymptomatic children who are not severely immunocompromised are recommended to receive MMR vaccine from age 12 months to provide early protection against the three diseases. Susceptible HIV-positive children and adults aged 14 years and older may receive MMR vaccine if the CD4+ lymphocyte count is 200 cells/mm^3 or greater. Administration of MMR with CD4+ counts below these recommended levels has been associated with vaccine-related pneumonitis (from the measles component).[3]

11.5.4 Pregnancy and breastfeeding

MMR vaccine is contraindicated during pregnancy. Pregnancy should be avoided for four weeks after MMR vaccination.[1, 3]

MMR vaccine can be given to breastfeeding women.

(See also sections 4.1 and 18.5.3.)

11.5.5 Travel

International travel is an important factor in reintroducing measles into New Zealand, and so vaccination with a measles-containing vaccine should be considered for all children and adults travelling overseas if they have not previously been adequately vaccinated.

Measles remains endemic in many countries, including areas in Europe, Asia, the Pacific and Africa. Of the 159 measles cases reported in the US from January to April 2015, 153 (96 percent) were import-associated.[19] Travel was also linked to the measles outbreaks in New Zealand in 2011, 2014 and 2016.

11.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general vaccine contraindications.

11.6.1 Contraindications

The general contraindications that apply to all immunisations are relevant to MMR vaccine (eg, children with an acute febrile illness should have their immunisation deferred).

Anaphylaxis following a previous dose of MMR or any of the vaccine components is a contraindication to a further dose of MMR. Individuals who have anaphylaxis after receiving MMR should be serologically tested for immunity and referred to, or discussed with, a specialist if non-immune to rubella or measles.

MMR is contraindicated for:

- those with proven anaphylaxis (but not contact dermatitis) to neomycin
- immunocompromised individuals (ie, those with significantly impaired cell-mediated immunity, including those with untreated malignancy, altered immunity as a result of drug therapy [including high-dose steroids], or receiving high-dose radiotherapy) (see section 4.3)
- individuals who have received another live vaccine, including BCG, within the previous four weeks (see chapter 20)
- pregnant women – pregnancy should be avoided for four weeks after immunisation
- individuals who have received IG or a blood transfusion during the preceding 11 months (see Table A6.1 in Appendix 6 for the length of time to defer measles vaccine after specific blood products)
- those with severe immune deficiency from HIV, because vaccine-related pneumonitis (from the measles component) has been reported[3] – discuss vaccination of individuals with HIV infection with their specialist.

11.6.2 Precautions

Children with a history of seizures should be given MMR, but the parents/guardians should be warned that there may be a febrile response. Children with current ITP should have the timing of vaccination discussed with the specialist responsible for their care.

Women of childbearing age should be advised to avoid pregnancy for the next four weeks[1, 3] after MMR vaccination (see section 18.5.3).

Measles vaccination may temporarily suppress tuberculin skin test (TST/Mantoux) reactivity, so if required, TST should be placed on the same day as MMR vaccination or postponed for four to six weeks after vaccination.[3] TST is not a prerequisite for measles vaccination. An individual with active TB should be established on treatment before administering MMR vaccine.

11.6.3 Egg allergy

The measles and mumps components of the MMR vaccine are manufactured in chick embryo cell culture, so there may be trace amounts of egg protein in the vaccine. However, egg allergy, including anaphylaxis, is **not** a contraindication to measles-containing vaccines. Various studies have confirmed children with egg allergy can be vaccinated safely.[3, 20, 21] Other components of the vaccine may be responsible for allergic reactions.[22] Individuals with egg allergy may therefore be safely vaccinated in primary care.[23]

11.7 Expected responses and AEFIs

11.7.1 Expected responses

A fever of 39.4°C or more occurs in 5–15 percent of children 6 to 12 days after immunisation and generally lasts one to two days.[3] Rash occurs in approximately 5 percent of children at the same interval post-vaccination: these children are not infectious to others.[3] The majority of these events are coincidental and not caused by the vaccine.[24] Serological tests or PCR can be expected to be positive if performed during this time, so testing should not be routinely performed.

The mumps vaccine may produce parotid and/or submaxillary swelling in about 1 percent of vaccinees, most often 10 to 14 days after immunisation.[25] The rubella vaccine can cause a mild rash, fever, lymphadenopathy and joint pain between one and three weeks after immunisation.[26] There were no persisting sequelae associated with the administration of three million doses of MMR to 1.5 million children in Finland.[24, 27]

11.7.2 AEFIs

Temporally related reactions, including febrile seizures, nerve deafness, aseptic meningitis, encephalitis, rash, pruritus, and purpura, may follow immunisation rarely; however, causality has not been established.[28]

Vaccine virus transmission

MMR vaccine viruses have been regarded as being non-transmissible from vaccinees. There are two poorly documented case reports of transmission: one of rubella and one of a mumps vaccine strain from a vaccine that is no longer in production.[29] Following immunisation with both measles and rubella vaccines, live virus has been isolated rarely from pharyngeal secretions.[30, 31] There have been no confirmed cases of disease transmission from MMR vaccine viruses.

Idiopathic thrombocytopenic purpura (ITP)

MMR vaccine is the only childhood vaccine with an elevated risk of ITP, which occurs in 1 in 22,000 to 40,000 people, 15 to 35 days after immunisation.[3] A review of data from 1.8 million children in the US found 197 cases of ITP, with an incidence risk ratio of 5.48 (95% CI: 1.61–18.64) in the 1 to 42 days after vaccination.[32] If ITP occurs, measles, mumps and rubella serology should be measured, and if the individual is immune to all three infections, a second dose is not required. However, if the individual is susceptible to any of the three infections, a second dose should be administered.[33, 34, 35] The risk of thrombocytopenia is higher after the first dose of vaccine than after the second dose.[3]

11.7.3 Adverse outcomes not linked to MMR

There have been multiple epidemiological studies published from the UK,[36] Finland[37] and elsewhere[38, 39] confirming that there is no link between MMR vaccine and the development of autism in young children (see section 3.2.4 for further discussion on this issue).

11.8 Public health measures

It is a legal requirement that all cases of measles be notified immediately on suspicion to the local medical officer of health – do not wait for a laboratory confirmation.

11.8.1 Diagnosis

A single case of measles should be considered an outbreak and result in a suitable outbreak response. Practitioners should have a low index of suspicion for notification, and all suspected clinical cases should be isolated immediately and notified to the medical officer of health.

The standard clinical case definition for measles is 'an illness characterised by all of the following: generalised maculopapular rash, starting on the head and neck; fever (at least 38°C if measured) present at the time of rash onset; cough or coryza or conjunctivitis or Koplik's spots present at the time of rash onset'.

It is important that the diagnosis be laboratory confirmed, as many viral infections can mimic measles. In the first instance, a nasopharyngeal and throat swab should be taken for viral identification by PCR. Further testing should be discussed with a clinical microbiologist. For instructions on measles specimen collection and transport, see the National Measles Laboratory website (www.measles.co.nz).

11.8.2 Prophylaxis

Management of contacts of a measles case should be discussed with the local medical officer of health.

MMR vaccine

There is evidence that a single dose of MMR vaccine when given to an unvaccinated person within 72 hours of first contact with an infectious person may reduce the risk of developing disease.[1] If there is doubt about vaccination status, MMR should still be given. MMR will not exacerbate the symptoms of measles if a person is already incubating the

disease, but in these situations, any measles-like illness occurring shortly after vaccination is likely to be due to infection.

If MMR vaccine is not given within 72 hours of first exposure, it should still be offered at any interval in order to offer protection from future exposures, unless the vaccine is contraindicated.

In an outbreak affecting infants, the use of MMR vaccine for infants aged 6–14 months should be considered. If MMR vaccine is given to an infant aged under 12 months, two more doses are still required after age 12 months and at least four weeks apart. This is because the seroconversion rate is lower when MMR is administered to an infant aged under 12 months. In an outbreak affecting young children, the second MMR vaccine does not have to be delayed until 4 years of age but can be given at any time from four weeks after the first dose.

Human normal immunoglobulin prophylaxis for contacts

Human normal immunoglobulin is recommended for measles-susceptible individuals in whom the vaccine is contraindicated (see section 11.6) and susceptible pregnant contacts. For these individuals, human normal immunoglobulin is given to attenuate disease and should be given as soon as possible, up to a maximum of six days after exposure. All other susceptible contacts should be offered MMR as post-exposure prophylaxis (as described above). Infants aged under 6 months where there is evidence of maternal immunity do not require any prophylaxis, but will still need the scheduled MMR doses at ages 15 months and 4 years.

Human normal immunoglobulin may be recommended for the following contacts of measles cases as soon as possible and up to six days after exposure:

- immunocompromised or immune-deficient people
- susceptible pregnant women
- immune-competent infants aged under 6 months where there is no evidence of maternal immunity (presence of maternal antibody, or documentation of two MMR doses or previous history of measles infection)
- immune-competent children aged between 6 and 15 months, who are outside the 72-hour exposure window for MMR vaccine.

The recommended doses as follows.

- Immune-competent infants aged under 15 months should receive 0.6 mL/kg intramuscularly, to a maximum volume of 5 mL.
- Pregnant women and immunocompromised or immune-deficient people should receive 0.6 mL/kg intramuscularly, to a maximum dose of 15 mL, recommended as three 5 mL injections.

Prophylaxis with intravenous immunoglobulin

IVIG (Intragam P) can be considered for immunosuppressed and immune-deficient measles contacts (who may, for example, have a central venous catheter), individuals with reduced muscle bulk, or in those people for whom large doses are required (see Appendix 6 for more information about passive immunisation).

The recommended dose of IVIG is 0.15 g/kg. See the guidance from the Health Protection Agency for further information (www.gov.uk/government/publications/measles-post-exposure-prophylaxis).

If there are further queries, these can be directed to the New Zealand Blood Service medical team via the DHB blood bank.

11.8.3 Exclusion

Exclusion of measles cases or contacts should be discussed with the local medical officer of health.

Parents/guardians should be advised that children who are suspected or confirmed measles cases should be excluded from early childhood services, school or community gatherings until at least five days after the appearance of the rash.

Immune contacts (ie, children aged 12 months to under 4 years who have received one dose of measles-containing vaccine after their first birthday and children aged 4 years and older who have received two doses) need not be excluded from these settings. Non-immune (susceptible) contacts should be excluded because of the risk of developing the disease themselves, and the risk of passing on the disease during the prodromal phase to other susceptible children. Advise

susceptible contacts to avoid attending school, early childhood services or community gatherings, and to avoid contact with other susceptible individuals, until 14 days after the last exposure to the infectious case.

Given that post-exposure MMR vaccination cannot guarantee protection, susceptible contacts who have received their first MMR vaccination within the 72-hour period after first exposure should also be excluded for 14 days after the last exposure to the infectious case (unless they subsequently meet the criteria for immunity). Contacts who have previously received one documented dose of MMR and then receive their second dose of MMR within 72 hours after first exposure can go back to school or work. If contacts receive their second MMR more than 72 hours after exposure, they should be excluded for 14 days after the last exposure to a person with measles.

Individuals who have received IG prophylaxis should also be excluded for 14 days after the last exposure to the infectious case.

Acceptable evidence of immunity is:

- anyone born before 1 January 1969
- documentation of previous immunity or previous infection
- children aged 12 months to under 4 years who have documentation of at least one dose of measles-containing vaccine after their first birthday
- individuals aged 4 years and older who have documentation of two doses of measles-containing vaccine, given at least one month apart and given after 12 months of age.

For more details on control measures, refer to the 'Measles' chapter of the *Communicable Disease Control Manual 2012*.[40]

11.9 Variations from the vaccine data sheet

The vaccine data sheet recommends a single dose of MMR vaccine. However, as 5–10 percent of recipients fail to seroconvert after the first dose (see section 11.4.2), the Ministry of Health recommends and funds a second dose of MMR vaccine. Two doses are required for measles control and elimination;[3] the second MMR dose is not a booster.

The vaccine data sheet states that pregnancy should be avoided for three months after vaccination. The Ministry of Health advises that women of childbearing age should avoid pregnancy for the next four weeks[1, 3] after MMR vaccination.

The vaccine data sheet states that individuals who have experienced anaphylaxis after egg ingestion should be vaccinated with extreme caution, with adequate treatment for anaphylaxis on hand should such a reaction occur. However, various studies have confirmed that egg-allergic children can be vaccinated safely.[3, 20, 21] The Ministry of Health recommends that individuals with egg allergy, including anaphylaxis, may be safely vaccinated in primary care (see section 11.6.3).

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12 Meningococcal disease

Key information

Mode of transmission	By respiratory droplets or direct contact with nasopharyngeal secretions from a carrier or case.
Incubation period	2–10 days, commonly 3–4 days.
Period of communicability	Therapy with cefotaxime, ceftriaxone, rifampicin, or ciprofloxacin eradicates *N. meningitidis* from mucosal surfaces within 24 hours, and the case is no longer considered infectious.
Available vaccines	Meningococcal group C conjugate (MenCCV): • NeisVac-C. Quadrivalent meningococcal conjugate (MCV4): • Menactra (MCV4-D) – conjugated to diphtheria toxoid • Nimenrix (MCV4-T) – conjugated to tetanus toxoid.
Dose, presentation, route	0.5 mL per dose. Presentation: • MenCCV: pre-filled syringe • MCV4-D: vial • MCV4-T: vaccine vial and pre-filled syringe. MCV4-T must be reconstituted before use. Intramuscular injection.
Funded vaccine indications	MCV4-D (Menactra) or MenCCV (NeisVac-C) for: • patients pre- or post-splenectomy or with functional asplenia • patients with HIV, complement deficiency (acquired, including monoclonal antibody therapy against C5, or inherited) or pre- or post-solid organ transplant • HSCT (bone marrow transplant) patients • patients following immunosuppression • close contacts of meningococcal cases (of relevant serotype).
Vaccine efficacy/ effectiveness	MenCCV: 83–100% effectiveness. Marked reduction in disease incidence when used in population-wide programmes. Immunity wanes with time. MCV4: 80–85% effectiveness; 2–5 years after vaccination, effectiveness wanes to 50–60%.

Continued overleaf

Public health measures	Cases: must be notified upon suspicion. Administer antibiotics as soon as possible, often prior to transfer to hospital. Contacts: administer antibiotic prophylaxis preferably within 24 hours of the initial diagnosis, but recommended up to 14 days after the diagnosis of illness.

12.1 Bacteriology

Meningococcal disease is caused by *Neisseria meningitidis*, a gram-negative bacterium, and is an important cause of sepsis and meningitis. Worldwide, the most important serogroups of meningococci are groups A, B, C, W135 and Y. Groups B and C are the most important types seen in children and young adults in New Zealand. Group A is an important epidemic strain, particularly in Africa and the Middle East. Serotype distribution patterns differ between countries. W135 and Y group organisms are seen as rare causes of bacteraemia and pneumonia in the elderly.

Spread from person to person is by respiratory droplets or direct contact with nasopharyngeal secretions, from a carrier or case.

12.2 Clinical features

Table 12.1 below describes the symptoms and signs of meningococcal disease – individuals may present with some or all of these. Meningococcal bacteraemia is more common than meningitis, and the illness may be a mild non-specific illness or a rapidly progressive illness with fatal outcome.

Table 12.1: Symptoms and signs of meningococcal disease

Adolescents and adults	Young infants and children
Sepsis syndrome Nausea Vomiting Meningism Rash – petechial or purpuric or maculopapular; a rash may not be present in the early stages of the disease and is absent in about one-third of cases Sleepy, difficult to rouse Arthralgia and myalgia Occasionally in young adults, irrational behaviour	As for adolescents and adults, plus the following: • bulging fontanelle • tachycardia • altered responsiveness • irritability and/or floppiness • refusing drinks or feeds • poor peripheral perfusion
Notify all suspected cases as soon as possible to the local medical officer of health. This includes out-of-hours notification.	

Meningococcal disease covers a spectrum, from chronic septic arthritis and minor rash to fulminant sepsis and meningitis. Classic meningococcal sepsis frequently presents with sudden onset of fever and rash. Septic shock may rapidly ensue. Meningitis can occur with and without signs of sepsis. In fulminant cases, disseminated intravascular coagulation, shock, coma and death can occur within a few hours despite appropriate treatment.

Because of the fulminant nature of meningococcal sepsis, antibiotics (Table 12.2) should be administered as soon as possible, often prior to transfer to hospital. Antibiotics given prior to transfer should be clearly noted on the clinical information that accompanies the patient to hospital.

Table 12.2: Recommended antibiotics for suspected cases

Antibiotic	Dosage
Benzylpenicillin*	Adults: 1.2 g (2 MU) IV (or IM) Children: 50 mg/kg IV (or IM)
Amoxycillin	Adults: 1–2 g IV (or IM) Children 50 mg/kg IV (or IM)

* Patients with a documented history of anaphylaxis to penicillin and who are suspected of suffering from meningococcal disease should be sent immediately to hospital without pre-admission antibiotics.

12.3 Epidemiology

12.3.1 Global burden of disease

Incidence and serotypes

Introduction of a serogroup A conjugate vaccine has had a dramatic impact on disease in sub-Saharan Africa. Before the introduction the vaccine, Group A disease caused massive epidemics in sub-Saharan Africa (the 'meningitis belt'), with incidence ranging from 10 to 25 per 100,000 during non-epidemic periods and up to 1,000 per 100,000 during epidemic years.[1]

The incidence in Canada, the US and Europe varies substantially by country, ranging from 0.18 per 100,000 to 3 per 100,000 persons per year.[1] The serotype distribution varies by age, location and time, with types B, C and Y accounting for most of the reported cases.[2] Group B disease is often the most common serotype causing infection, and can cause epidemics that start slowly and persist for five or more years. Group C meningococci have been associated with small clusters of meningococcal disease cases in schools and universities.

Risk groups

Those particularly at risk of meningococcal disease are children aged under 5 years, although all age groups can be infected. There is a higher case fatality rate in adults. Most infection occurs in healthy people, but those with a deficiency of terminal components of complement (C5–9), properdin deficiency or asplenia are at particular risk of recurrent meningococcal disease. Individuals with infection caused by an uncommon serogroup or recurrent disease should be investigated.

Close contacts of primary cases of meningococcal infection are at increased risk of developing infection, such as within families,[3] early childhood education services, semi-closed communities, schools, correctional facilities and military recruit camps. Students living in hostel accommodation may also be at higher risk.[4, 5, 6] In health care settings, only those with close exposure to oropharyngeal secretions of patients with meningococcal disease (as may occur during intubation or

resuscitation) and microbiology laboratory workers are considered to be at increased risk.

It is not possible to calculate the incubation period for meningococcal disease for sporadic cases. Secondary cases (ie, in contacts of known cases of meningococcal disease) usually occur within four days, but it can be up to 10 days. The infectivity of patients with meningococcal disease is markedly reduced after 24 hours of antibiotic therapy, although treatment with cefotaxime, ceftriaxone, rifampicin or ciprofloxacin is necessary to reliably eradicate nasopharyngeal carriage and hence relax infection prevention and control precautions (see section 12.8.2).

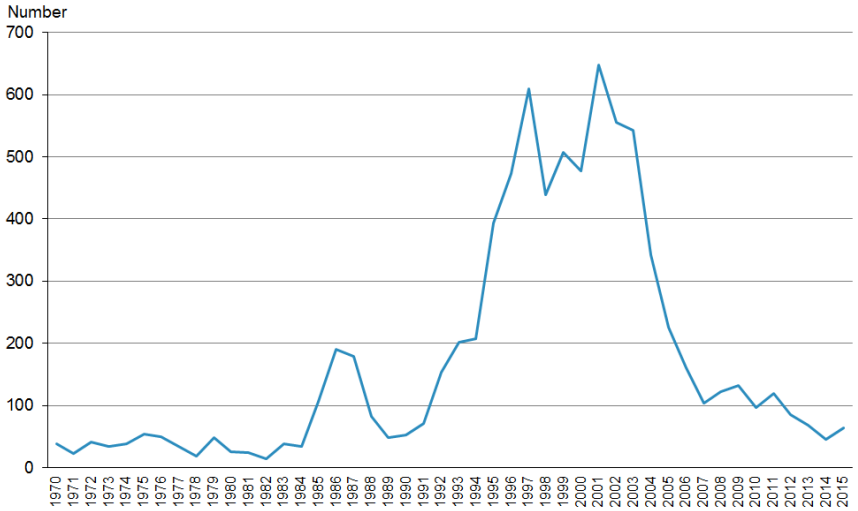
In high-income countries, nasopharyngeal carriage of *N. meningitidis* occurs in approximately 10 percent of the overall population, rising from 2 percent in children aged under 4 years to a peak of 24.5 percent to 32 percent among 15–24-year-olds, then declining with increasing age.[1] The relationship between risk factors for disease and those associated with carriage is incompletely understood.[1] Carriage prevalence does not predict the disease incidence nor the occurrence or severity of outbreaks, as most of the carried strains are non-encapsulated and do not cause disease.[1] Smoking, passive smoking, household crowding and upper respiratory tract infections increase carriage.

12.3.2 New Zealand epidemiology

Incidence and mortality

In 2015 the notification rate for meningococcal disease was 1.4 cases per 100,000 population, with a total of 64 cases notified (61 laboratory-confirmed).[7] This was slightly higher than the 2014 rate (1.0 per 100,000, 45 cases), but significantly lower than the peak rate experienced during the meningococcal disease epidemic (overall 16.7 per 100,000 but 200 per 100,000 in children under 12 months) in 2001. The annual number of notified cases of meningococcal disease in New Zealand since 1970 is shown in Figure 12.1. The epidemic from 1991 to 2007 was largely due to a single Group B subtype (B:4:P1.7b,4).

Figure 12.1: Notified cases of meningococcal disease, 1970–2015



Source: ESR

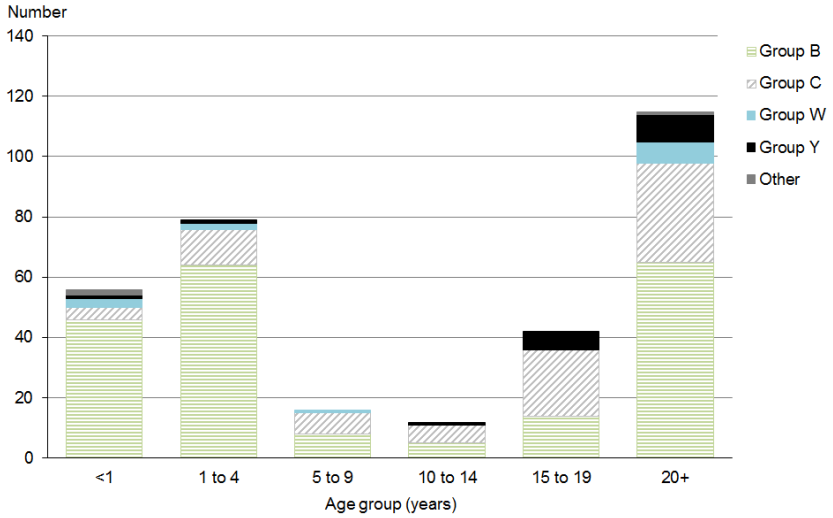
Meningococcal infection rates remain consistently higher in Māori and Pacific peoples compared with the total population. Māori had the highest disease rate in 2015 (2.9 per 100,000, 20 cases), followed by Pacific peoples (2.8 per 100,000, 8 cases).[7]

Household crowding is an important risk factor for meningococcal disease, independent of ethnicity.[8]

In 2015 the highest age-specific disease rates were among those aged under 1 year (22 per 100,000, 13 cases) and 1–4 years (6.9 per 100,000, 17 cases).[7]

Figure 12.2 shows the age distribution of the 320 strain-typed cases from 2011 to 2015. Group B strains were the most prevalent in all age groups except for the age group 15–19 years, in which Group C strains were the most prevalent.

Figure 12.2: Age distribution among strain-typed meningococcal disease cases, 2011–2015 cumulative data



Note: Other includes 2 cases with non-groupable strains (1 each in the <1 and 20+ age groups) and 1 case with a group 29E strain (in the <1 age group).

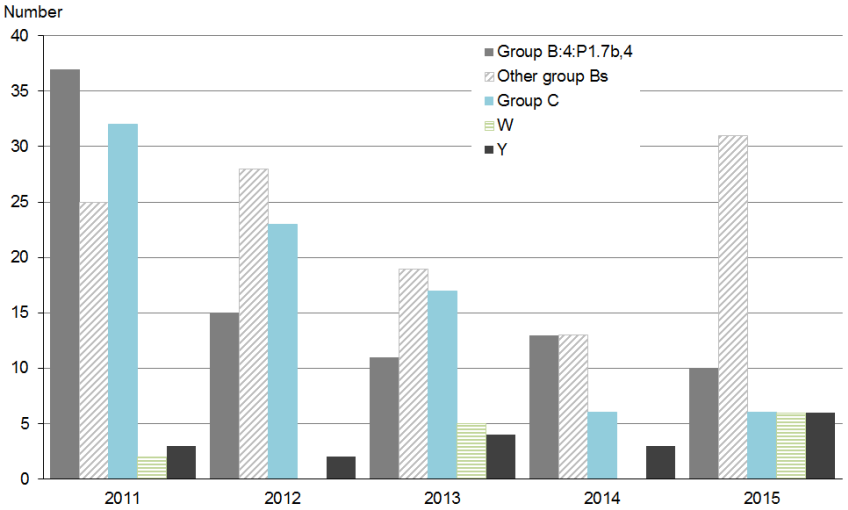
Source: ESR

Almost all cases (62/64) in 2015 were hospitalised. Four deaths were reported, giving a case fatality rate of 6.3 percent.[7]

Strain types

Strain type was determined for 59 of the 61 laboratory-confirmed cases.[7] Group B strains were the most prevalent in 2015, causing 69 percent of the confirmed cases (Figure 12.3). The group B strain (B:4:P1.7b,4) responsible for the epidemic caused 17 percent of all meningococcal disease in 2015 (10 of the 59 typed cases). The number of cases of meningococcal disease caused by group C strains has decreased since 2011 (Figure 12.3).

Figure 12.3: Groups and dominant subtypes among strain-typed meningococcal disease cases, 2011–2015



Note: Not shown in the figure are 2 cases with non-groupable strains (1 each in 2011 and 2013), and 1 case in 2014 with a group 29E strain.

Source: ESR

12.4 Vaccines

12.4.1 Introduction

Internationally, meningococcal vaccination programmes have been revolutionised by the development of conjugate vaccines, which allow vaccination in younger children and are associated with the development of herd immunity when used widely (see section 1.4.3 for more information about conjugate vaccines).

The monovalent (C) and quadrivalent (ACYW135) conjugate vaccines contain CRM_{197} or diphtheria or tetanus toxoid conjugate and are currently the only meningococcal vaccines available in New Zealand that can be effectively used in children aged under 2 years. Polysaccharide vaccines can offer three to five years' protection in adults, but they are generally regarded as inferior to conjugate vaccines. There are no polysaccharide vaccines registered (approved for use) and available (marketed) in New Zealand at the time of writing. Vaccination against

serogroups other than C (except serogroup B, which is not available in a conjugate vaccine) does not really offer much advantage in the New Zealand context, but those travelling to Africa, the Middle East and other areas with different serotype prevalence may benefit from broader protection. The meningococcal vaccines registered and available in New Zealand are summarised in Table 12.3 below.

Table 12.3: Meningococcal vaccines registered and available in New Zealand

Name (manufacturer)	Vaccine type
NeisVac-C (Pfizer NZ Ltd)	Meningococcal group C conjugate (MenCCV)
Menactra (Sanofi)	Quadrivalent meningococcal conjugate (MCV4-D) (contains serogroups A, C, Y, and W135)
Nimenrix (Pfizer NZ Ltd)	Quadrivalent meningococcal conjugate (MCV4-T) (contains serogroups A, C, Y, and W135)

Funded vaccines

No meningococcal vaccines are included on the routine Schedule but meningococcal group C conjugate and quadrivalent meningococcal conjugate vaccines are recommended and funded for certain individuals (see section 12.5).

Two meningococcal conjugate vaccines are funded for certain at-risk groups.

- Meningococcal group C conjugate vaccine MenCCV (NeisVac-C, Pfizer NZ Ltd) contains 10 μg of polysaccharide derived from the group C capsule, conjugated to 10–20 μg of tetanus toxoid. Other components include aluminium hydroxide and sodium chloride.
- Quadrivalent meningococcal conjugate vaccine MCV4-D (Menactra, Sanofi) contains 4 μg of each polysaccharide derived from the capsules of group A, C, Y and W135 *N. meningitidis* strains, each conjugated to diphtheria toxoid. Other components include sodium chloride and sodium phosphate.

Other vaccines

Quadrivalent meningococcal conjugate vaccines

A second quadrivalent meningococcal conjugate vaccine MCV4-T (Nimenrix, Pfizer NZ Ltd) is registered and available in New Zealand for individuals aged 12 months to 55 years.

MCV4-T contains 5 μg of each polysaccharide derived from the capsules of group A, C, Y and W135 *N. meningitidis* strains, conjugated to 44 μg of tetanus toxoid carrier protein. Other components and excipients include sodium chloride, trometamol and sucrose.

Group B meningococcal vaccines

Group B vaccines are not currently registered in New Zealand. A strain-specific group B meningococcal vaccine (MeNZB, Chiron/Novartis) containing outer membrane vesicles derived from the epidemic strain B:4:P1.7b,4 (NZ 98/254) was developed for epidemic control in New Zealand and used between 2004 and 2008. The vaccination programme ceased in 2008 because of a decline in the incidence of group B disease.

The immune response to the vaccine was short lived and it is not expected that anyone previously vaccinated would still have existing immunity to B disease. This programme was covered in previous editions of the *Handbook*.

Since this time there have been major advances in group B vaccine development, and there are now two recombinant group B vaccines (4CMenB and 2CMenB), both of which cover a broad range of group B subtypes. Neither vaccine is currently available in New Zealand.

The 4CMenB recombinant vaccine (Bexsero) contains four components from the group B bacteria: three different group B surface proteins plus detoxified outer membrane vesicles from the New Zealand group B epidemic strain. The 4CMenB vaccine has large-scale clinical trial data to support its use, and licensure has been granted in Europe, Australia, Canada and the US. The 4CMenB vaccine is associated with more local and febrile reactions than some other childhood vaccines. No serious adverse events have been identified; however, febrile seizures have occurred in temporal association with this vaccine.[9]

The 2CMenB recombinant vaccine (Trumenba) contains two group B surface proteins. One protein from each factor H binding protein subfamily (A and B) is included in the vaccine. The immunogenicity and safety of 2CMenB was assessed in individuals aged 10 years and older who received the vaccine in studies conducted in the US, Europe and Australia. The vaccine was licensed in the US in October 2014. The most commonly reported side effects by those who received the 2CMenB vaccine were pain at the injection site, fatigue, headache, joint pain and chills.[10]

In February 2015 the US Advisory Committee on Immunization Practices recommended that individuals aged 10 years or older at increased risk for meningococcal disease should receive meningococcal B vaccine (either 4CMenB or 2CMenB).[10] In June 2015, this recommendation was extended to include all adolescents and young adults aged 16–23 years (with a preferred age of 16–18 years), to provide short-term protection against most strains of serogroup B meningococcal disease.[11] In September 2015 the UK introduced the 4CMenB vaccine as part of a funded schedule for infants.[12] The vaccine is offered to infants at ages 2 and 4 months, with a booster at age 12 months.[13]

12.4.2 Efficacy and effectiveness

Meningococcal group C conjugate vaccines

The first national immunisation programme using a conjugate group C meningococcal vaccine was introduced in the UK in 1999. Group C conjugate vaccine was introduced into the UK infant immunisation schedule at ages 2, 3 and 4 months, as well as via a mass vaccination campaign up to age 20 years. Four years after introduction the overall reported effectiveness was at least 83 percent in children who had received the conjugate vaccine from age 5 months to 18 years.[14] Data from that programme indicates that a booster dose in the second year of life is important for sustained protection following infant vaccination.

The meningococcal C programme introduced in the UK in 1999 was successful in reducing invasive disease meningococcal C to a very small number of cases.[13] The routine schedule for protection against meningococcal C subsequently moved to a primary dose at age

12 months (as combined Hib-meningococcal C) and a booster at age 14 years (as MCV4).

Protective efficacy against carriage by adolescents of group C one year after the UK immunisation campaign was estimated at 69 percent.[15] At the same time there was no increase in colonisation by the other meningococcal groups. Consistent with the reduction in meningococcal carriage rates, there has been a 67 percent reduction in group C disease among unvaccinated children within the target age groups and a reduction of 35 percent of cases in unvaccinated adults older than age 25 years.[16] At the same time there was no evidence of capsular switching or an increase in disease caused by group B strains.[17]

The optimal vaccine schedule for sustained control of group C meningococcal disease by a universal programme has yet to be established. It is now recognised that circulating antibody is probably required for vaccine-induced protection and that antibody decay occurs quite rapidly in young children. Although conjugate vaccines can induce an anamnestic response, invasive disease develops within hours or days of acquisition and colonisation of the nasopharynx. This timeframe is shorter than that required for bactericidal antibodies to develop.

Herd protection, from reduced carriage resulting in reduced exposure to the organism, has an important role in the prevention of meningococcal disease. Consequently, further doses may be needed, possibly in early adolescence and then prior to leaving school. The exact timing will depend on any catch-up vaccination programme undertaken when the vaccine is first introduced, and the country's specific epidemiology.

Quadrivalent meningococcal conjugate vaccines

An estimate of the effectiveness of the diphtheria conjugate quadrivalent meningococcal vaccine (MCV4-D, Menactra) among adolescents in the US was determined as 80–85 percent, which is similar to that reported for the polysaccharide vaccines.[18] Estimates from a large case-control study in the US evaluating one of the two MCV4 vaccines, MCV4-D, suggest high vaccine effectiveness early after vaccination, but two to five years after vaccination, vaccine effectiveness wanes to 50–60 percent.[1]

The MCV4-D vaccine was poorly immunogenic in infants aged under 6 months,[19] and it is currently registered in New Zealand for individuals aged 9 months to 55 years.

The MCV4-T vaccine (Nimenrix) is registered in New Zealand for individuals aged 12 months to 55 years. Clinical trials showed that the vaccine was immunogenic in children above the age of 12 months, adolescents, and adults, and has an acceptable reactogenicity and safety profile.[20]

Although both conjugate quadrivalent meningococcal vaccines available in New Zealand are licensed up to age 55 years, there was no published data for evidence of the effectiveness in older adults identified at the time of writing.

Quadrivalent meningococcal polysaccharide vaccines

These are not currently available in New Zealand. Conjugated quadrivalent vaccines are used in preference to polysaccharide vaccines.

12.4.3 Transport, storage and handling

Transport meningococcal conjugate vaccines according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.[21] Store at +2°C to +8°C. MCV4-D and MCV4-T should be protected from light. Do not freeze.

Reconstitution

MCV4-T (Nimenrix) must be reconstituted with the supplied diluent and used as soon as possible.

12.4.4 Dosage and administration

Meningococcal group C conjugate vaccine (MenCCV)

Each MenCCV (NeisVac-C) dose is 0.5 mL, administered by intramuscular injection (see section 2.2.3).

For healthy infants aged under 12 months, two doses are given at least eight weeks apart, with the first dose given not earlier than age 8 weeks. A booster is given in the second year of life. For healthy children, adolescents and adults, one dose is given. See Table 12.5 for schedules for at-risk individuals.

MenCCV can be administered concurrently with other scheduled vaccines, in separate syringes and at separate sites.

Quadrivalent meningococcal conjugate vaccines (MCV4)

Each MCV4 dose is 0.5 mL, administered by intramuscular injection (see section 2.2.3).

Menactra (MCV4-D)

Menactra is registered in New Zealand for individuals aged 9 months to 55 years. For healthy children aged 9–23 months, two doses are given at least three months apart. For healthy individuals aged 2–55 years, one dose is given. See Table 12.5 for schedules for at-risk individuals.

MCV4-D can be concurrently administered with other vaccines in separate syringes and at separate sites,[22, 23, 24, 25] except for PCV13. MCV4-D should be administered at least four weeks after PCV13. This is because when administered concurrently, there is impairment of the immune response to some of the pneumococcal serotypes.[26, 27]

Nimenrix (MCV4-T)

Nimenrix is registered in New Zealand for individuals aged 12 months to 55 years. One dose is given.

MCV4-T can be concurrently administered with other vaccines in separate syringes and at separate sites; however, there is no data on concurrent administration of MCV4-T and PCV13.

12.5 Recommended immunisation schedule

12.5.1 At-risk individuals

Meningococcal conjugate vaccines are not on the Schedule but are funded in special circumstances, as described in the shaded section of Table 12.4 below, with recommended dosing schedules in Table 12.5.

See sections 4.2 and 4.3 for more information about vaccination of special groups, including recommended immunisation schedules for high-risk individuals with certain medical conditions.

The conjugate vaccines are recommended (but not funded) for other individuals at risk, as described in Table 12.4.

Before travel

There are areas of the world where the risk of acquiring meningococcal infection is increased. Nevertheless, the risk to travellers to the developing world as a whole has been estimated as being less than one in a million per month. Recurrent epidemics of meningococcal disease occur in the sub-Saharan 'meningitis belt', from Senegal in the west to Ethiopia in the east, usually during the dry season (December to June). Epidemics are occasionally identified in other parts of the world and occurred recently in Saudi Arabia (during a Hajj pilgrimage), Kenya, Tanzania, Burundi, Mongolia and Nepal.

MCV4-D or MCV4-T are the preferred vaccines for travel. For website sources for information about meningococcal vaccines for travellers, see the WHO website (www.who.int/ith/en). Quadrivalent meningococcal vaccine is a requirement for pilgrims to the Hajj.

Before moving into communal living situations

Adolescents and young adults living, or planning to live, in communal accommodation such as a hostel, student accommodation, boarding school, in military accommodation, in correctional facilities or in other long-term institutions are likely to be at higher risk of acquiring meningococcal infection. Meningococcal vaccination should be considered.

Table 12.4: Meningococcal group C conjugate (MenCCV) and quadrivalent meningococcal vaccine (MCV4) recommendations

Note: Funded conditions are in the shaded rows. See the Pharmaceutical Schedule (www.pharmac.govt.nz) for any changes to the funding decisions.

Recommended and funded
MenCCV and MCV4-D are recommended and funded for: • patients pre- or post-splenectomy or with functional asplenia[a,b] • patients with HIV, complement deficiency (acquired, including monoclonal antibody therapy against C5, or inherited) or who are pre- or post-solid organ transplant[b] • HSCT (bone marrow transplant) patients[b] • patients following immunosuppression[b,c] • close contacts of meningococcal cases[d]
Recommended but not funded
MenCCV, MCV4-D or MCV4-T are recommended, but not funded, for individuals: • who are laboratory workers regularly handling meningococcal cultures • who are adolescents and young adults living in communal accommodation (eg, in a hostel or at boarding school, in military accommodation, in correctional facilities or in other long-term institutions). MCV4-D or MCV4-T are recommended, but not funded, for individuals: • who are travelling to high-risk countries (see www.who.int/ith/en) or before the Hajj.

a Pneumococcal, Hib, influenza and varicella vaccines are also recommended for individuals pre- or post-splenectomy or with functional asplenia. See section 4.3.4.

b See sections 4.2 and 4.3 for more information.

c The period of immunosuppression due to steroid or other immunosuppressive therapy must be longer than 28 days.

d Only one dose is funded for close contacts of meningococcal cases.

Table 12.5: Recommended meningococcal vaccine schedule for high-risk individuals (funded)

Note: See the Pharmaceutical Schedule (www.pharmac.govt.nz) for any changes to the funding decisions.

Age at diagnosis	Vaccine (trade name)	Recommended vaccine schedule
Infants aged 6 weeks to under 12 months	MenCCV (NeisVac-C) and	Age-appropriate MenCCV schedule: • if aged under 6 months at diagnosis, give 2 doses 8 weeks apart, with a booster at age 12 months • if aged 6–11 months at diagnosis, give 1 dose, with a further dose at age 12 months.
	MCV4-D (Menactra)	At age 2 years, give 2 doses of MCV4-D[a] 8 weeks apart, then a booster dose after 3 years, then 5-yearly.
Children aged 12 months to under 18 years	MenCCV (NeisVac-C) and MCV4-D (Menactra)	If aged 12–23 months at diagnosis, give 1 dose of MenCCV, followed by MCV4-D[a] at age 2 years, 2 doses 8 weeks apart; then a booster of MCV4-D after 3 years, then 5-yearly. If aged ≥2 years at diagnosis, give 2 doses of MCV4-D[a] 8 weeks apart, and: • if the 1st MCV4-D dose was given at age <7 years, give a booster after 3 years, then 5-yearly, or • if the 1st MCV4-D dose was given at age ≥7 years, give a booster dose every 5 years.
Adults aged 18 years and older	MCV4-D (Menactra)	Give 2 doses of MCV4-D, 8 weeks apart, then 1 dose every 5 years.[a,b]

a Give MCV4-D at least 4 weeks after PCV13.[26, 27]

b MCV4-D is registered for individuals aged 9 months to 55 years, but there are not expected to be any safety concerns when administered to adults older than 55 years.

12.5.2 Recommendations for children and adolescents

In the absence of a universal programme, non-high-risk children and adolescents may be offered meningococcal vaccines, but these are not funded. Table 12.6 suggests the most appropriate ages for this, reflecting the known ages of increased risk. The predominant meningococcal strains in New Zealand in childhood are B and C. There is no vaccine currently available in New Zealand for B. Particularly for those who are

likely to travel, the quadrivalent vaccine is preferable because of the differing serotype patterns between countries, for example, the Y serotype is prominent in the US.

Table 12.6: Suggested meningococcal vaccines for children and adolescents (not funded)

Note: Vaccine immunity is not long-lasting. The suggested ages of vaccination are not expected to protect individuals through all of childhood, but are pragmatically focused on offering protection during the ages of highest risk. This does not apply to epidemic situations.

Age	Vaccine options (trade name)	Number of doses
<12 months	MenCCV (NeisVac-C)	2 doses[a] (primary course) plus a booster after 12 months of age
12 months to 2 years	MenCCV (NeisVac-C), or MCV4-D (Menactra) or MCV4-T (Nimenrix)	1 MenCCV, or 2 MCV4-D[a,b] doses or 1 MCV4-T
Early adolescence (<16 years)	MenCCV (NeisVac-C) or MCV4-D (Menactra) or MCV4-T (Nimenrix)	1 dose plus a booster at age 16–18
Late adolescence ≥16 years	MenCCV (NeisVac-C) or MCV4-D (Menactra) or MCV4-T (Nimenrix)	1 dose, no booster required

a Refer to section 12.4.4 and the vaccine data sheets for the intervals between doses.

b MCV4-D should be administered at least 4 weeks after PCV13 (if used).[26, 27]

12.5.3 Pregnancy and breastfeeding

There are no reports of any adverse effects among pregnant women who have been vaccinated during pregnancy.[26] The vaccine may be given to pregnant women if indicated.[26] Meningococcal vaccine may be given to breastfeeding women.[28]

12.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

There are no specific contraindications for meningococcal vaccines, except for anaphylaxis to a previous dose or any component of the vaccine.

12.7 Expected responses and AEFIs

Frequent adverse reactions after meningococcal conjugate vaccines include localised pain, irritability, headache and fatigue.[2, 20] Fever is reported by 2 to 5 percent of adolescents who receive MCV4-D.

12.7.1 Meningococcal group C conjugate vaccine

The most frequent response to MenCCV in the UK school programme was transient headache in 12 percent of students in the first three days after vaccination.[29] This is more commonly reported by secondary students than primary school students. Mild to moderate local reactions at the injection site consisting of pain, tenderness and occasional redness were also reported. These peaked on the third day after the vaccine and resolved within a day.

A Cochrane Review assessed the safety of MenCCVs against group C disease.[30] MenCCVs were shown to have an excellent safety profile in infants. The events more frequently reported in infants were fever (1–5 percent), irritability (38–67 percent), crying more than expected (1–13 percent), redness at the site of vaccination (6–97 percent), tenderness at the site of vaccination (11–13 percent), and swelling at the site of vaccination (6–42 percent).

The adverse events were similar in groups vaccinated with MenCCV and with the hepatitis B control vaccine, but following booster doses they were more frequent in the MenCCV group in one trial. Adverse events were rare. Anaphylaxis was reported at a rate of one per 500,000 doses distributed.[29]

12.7.2 Quadrivalent meningococcal conjugate vaccine

The safety of two doses of MCV4-D was assessed in a phase III trial of infants: dose one was administered at age 9 months and dose two was administered at age 12 months, with or without routine childhood vaccines.[27] The percentage of participants with solicited systemic reactions after MCV4-D administration alone at age 12 months (60.6 percent) was lower than after the vaccination at age 9 months (68.2 percent), lower than the control groups at age 12 months (75.2–84.1 percent, depending upon the control vaccine), and lower than when

MCV4-D was administered concurrently with the routine childhood vaccines (68.3–73.2 percent).

The safety profile of MCV4-T (Nimenrix) is very similar to other meningococcal conjugate vaccines.[20]

Guillain–Barré syndrome

There is no evidence of an association between meningococcal conjugate vaccines and GBS.[28] An early report in the US of a suspected temporal association between MCV4-D (Menactra) and GBS was followed by a large retrospective cohort study in the US that found no evidence of an increased risk of GBS following administration of MCV4-D.[31, 32] If indicated, meningococcal conjugate vaccines may be administered to individuals with a history of GBS.[28]

12.8 Public health measures

Invasive meningococcal disease must be notified on suspicion to the local medical officer of health.

The overall rate of secondary cases in untreated adults is around 1 per 300. Adults and children in close contact with primary cases of invasive meningococcal infection are recommended to receive antibiotic prophylaxis, preferably within 24 hours of the initial diagnosis, but prophylaxis is recommended up to 14 days after diagnosis of illness.

Blood or cerebrospinal fluid culture is the main diagnostic method, but blood PCR may be useful if antibiotics are given without prior access to blood culture. It is recommended that in primary care three to five millilitres of blood should be taken in an ethylenediaminetetraacetic acid (EDTA) anticoagulant tube (usually with a purple top) prior to administration of antibiotics unless blood culture is available. This should accompany the patient to hospital.

12.8.1 Contacts

A contact is anyone who has had unprotected contact with upper respiratory tract or respiratory droplets from the case during the seven days before onset of illness to 24 hours after onset of effective treatment.[33] Contacts at particular risk include:

- those sleeping at least one night in the same household, dormitory, military barrack, student hostel bunkroom (not residents of nursing or residential homes who sleep in separate rooms) as the case, or who have been in a seat adjacent to the case in a plane, bus or train for more than eight hours
- health care workers who have had intensive unprotected contact (not wearing a mask) with a case during intubation, resuscitation or close examination of the oropharynx
- exchange of upper respiratory tract secretions, including intimate kissing
- other contacts as determined by the medical officer of health on a case-by-case basis, such as children and staff attending an early childhood service.

Prophylaxis is not routinely recommended for health care personnel unless there has been intimate contact with oral secretions (eg, as a result of performing mouth-to-mouth resuscitation or suctioning of the case before antibiotic therapy has started).

12.8.2 Chemoprophylaxis for contacts

Recommended antibiotics

The recommended antibiotics are rifampicin, ceftriaxone or ciprofloxacin, preferably given within 24 hours of initial diagnosis, but prophylaxis is recommended up to 14 days after diagnosis of illness.

Rifampicin

The recommended dose of rifampicin is 10 mg/kg (maximum dose 600 mg) every 12 hours for two days. For infants aged under 4 weeks, the recommended dose is 5 mg/kg every 12 hours for two days.

Avoid rifampicin if pregnant or breastfeeding.

Ceftriaxone

A single dose of intramuscular ceftriaxone (125 mg for children aged under 12 years and 250 mg for older children and adults) has been found to have an efficacy equal to that of rifampicin in eradicating the meningococcal group A carrier state. Ceftriaxone is the drug of choice in a pregnant woman because rifampicin is not recommended later in pregnancy. Ceftriaxone may be reconstituted with lignocaine (according to the manufacturer's instructions) to reduce the pain of injection. A New Zealand study demonstrated that ceftriaxone and rifampicin were equivalent in terms of eliminating nasopharyngeal carriage of *N. meningitidis* group B.[34]

Do not use in infants under aged under 4 weeks.

Ciprofloxacin

Ciprofloxacin given as a single oral dose of 500 mg or 750 mg is also effective at eradicating carriage. This is the preferred prophylaxis for women on the oral contraceptive pill and for prophylaxis of large groups.[33]

Ciprofloxacin is not generally recommended for pregnant and lactating women or for children aged under 18 years.[35] Consult the manufacturer's data sheet for appropriate use and dosage of ciprofloxacin in children.

Use of meningococcal conjugate vaccines for close contacts

Close contacts of cases of meningococcal disease may be offered the appropriate meningococcal conjugate vaccine (see section 12.5). See below for the use of the vaccines for the control of outbreaks, as initiated by the local public health service.

12.8.3 Outbreak control

When there is an outbreak of meningococcal disease of a specific vaccine group, an immunisation programme may be recommended and funded for a defined population. The local medical officer of health will determine the necessary action in discussion with the Ministry of Health.

For more details on control measures, refer to the '*Neisseria meningitidis* invasive disease' chapter of the *Communicable Disease Control Manual 2012*.[33]

12.9 Variations from the vaccine data sheets

The MCV4-D data sheet states that the vaccine is indicated for use in individuals aged 9 months to 55 years. The Ministry of Health recommends that this vaccine may be used in adults aged over 55 years.[28]

The data sheet states that MCV4-D should be given as a single dose for individuals aged 2 years and older. The Ministry of Health recommends that two doses are given to individuals at high risk of meningococcal disease (see Table 12.5 and section 4.3), with booster doses every five years (if the first MCV4-D was given before age 7 years, give a booster after three years, then five-yearly).[2]

A history of GBS is listed as a precaution in the MCV4-D data sheet. However, there is no evidence of an association between meningococcal conjugate vaccines and GBS (see section 12.7.2).[28] The Ministry of Health advises that, if indicated, MCV4-D may be administered to individuals with a history of GBS.[28]

The MenCCV data sheet states that the first dose of vaccine should not be given earlier than age 8 weeks. However, the Ministry of Health recommends that MenCCV may be given from age 6 weeks to infants at high risk of meningococcal disease (see Tables 12.4 and 12.5).

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13 Mumps

Key information

Mode of transmission	Airborne droplets or by direct contact with saliva or urine from an infected person.
Incubation period	About 16 to 18 days, ranging from 12 to 25 days.
Period of communicability	For contact tracing purposes, the recommended period of communicability is from 2 days before to 5 days after the onset of parotitis.
Funded vaccine	MMR vaccine (Priorix) is a live attenuated vaccine.
Dose, presentation, route	0.5 mL per dose after reconstitution. Pre-filled syringe and glass vial. The vaccine must be reconstituted prior to injection. Subcutaneous injection.
Funded vaccine indications and schedule	Children at ages 15 months and 4 years. Adults who are susceptible to one or more of measles, mumps and rubella. For (re-)vaccination following immunosuppression (if the individual is immunocompetent enough to safely receive the vaccine).
Vaccine efficacy/ effectiveness	64–66 percent effective against laboratory-confirmed mumps after 1 dose and 83–88 percent after 2 vaccine doses.
Egg allergy	Egg allergy, including anaphylaxis, is **not** a contraindication for MMR vaccine.
Adverse events to vaccine	MMR vaccine is generally well tolerated. The risk of adverse reactions to MMR vaccine is low, compared to the risk of complications from mumps disease.

Continued overleaf

Public health measures	Cases: exclude for 5 days from onset of parotitis. Susceptible contacts working in healthcare settings or living or working with immunocompromised people: • exclude from 12 days after the first exposure to 25 days after last exposure to the infectious case. • vaccinate with 2 documented doses of MMR. Susceptible contacts in other settings (tertiary education, school, early childhood services or work): • if zero MMR doses, consider exclusion from 12 days after the first exposure to 25 days after last exposure to the infectious case, if there is a high risk of mumps transmission. They can be readmitted immediately after receiving the 1st MMR dose. • if a history of 1 MMR dose, they do not need to be excluded but should be offered a 2nd MMR dose.

13.1 Virology

Mumps is a paramyxovirus, genus *Rubulavirus*, with a single-stranded RNA genome. It is rapidly inactivated by heat, formalin, ether, chloroform and light.

13.2 Clinical features

Mumps is transmitted by airborne droplets or direct contact with infected respiratory tract secretions or urine. Humans are the only known host of the virus.

People with mumps are most infectious from two days before to five days after the onset of parotitis.[1] For contact tracing purposes, the recommended period of communicability is also from two days before to five days after the onset of parotitis.[1] However, mumps virus has been isolated in saliva from seven days before to nine days after the onset of parotitis.[1] Asymptomatic cases also can be infectious.[1]

Classic mumps, an acute viral illness, is characterised by fever, headache, and swelling and tenderness of one or more parotid (salivary) glands. Patients may have no involvement of salivary glands but still experience involvement of other organs (eg, orchitis or meningitis). At least 30 percent of mumps infections in children are asymptomatic.

The complications of symptomatic mumps include aseptic meningitis in 15 percent (almost always without sequelae), orchitis (usually unilateral) in up to 20 percent of post-pubertal males, and oophoritis in 5 percent of post-pubertal females. Sterility occurs rarely. Profound unilateral nerve deafness occurs in 1 in 15,000 cases. Encephalitis has been reported to occur at a frequency of between 1 in 400 and 1 in 6,000, the latter being a more realistic estimate. Pancreatitis, neuritis, arthritis, mastitis, nephritis, thyroiditis and pericarditis may also occur.

The case fatality rate for mumps encephalitis is 1.4 percent, while the overall mumps case fatality rate is reported as 1.8 per 10,000 cases. Mumps in the first trimester of pregnancy may increase the rate of spontaneous abortion, but there is no evidence that it causes fetal abnormalities.

13.3 Epidemiology

13.3.1 Global burden of disease

Prior to the introduction of immunisation, approximately 85 percent of adults had evidence of past mumps infection. Most infections in those aged under 2 years were subclinical, while those affected in adulthood are more likely to experience severe disease. The peak incidence was in late winter and spring.

More recently, there have been numerous reports of increasing numbers of mumps cases in the US, UK and elsewhere, thought to be due to a waning of vaccine-induced immunity.[2] Many cases are reported in 18–30 year olds.[3] Outbreaks appear to occur mainly in those in crowded situations such as university students.[4]

13.3.2 New Zealand epidemiology

Mumps vaccine (as MMR) was introduced to the Schedule in 1990 for children aged 12 to 15 months, with a second dose introduced in 1992 for children aged 11 years. The current two-dose schedule at ages 15 months and 4 years was introduced in 2001 (see Appendix 1 for more information). The last mumps epidemic occurred in 1994.

In 2016, 20 cases of mumps were notified (16 were laboratory confirmed), compared to 13 notifications in 2015 (6 were laboratory confirmed). The 2016 mumps notification rate was 0.4 per 100,000 population, similar to the 2015 rate (0.3 per 100,000) (ESR, 14 March 2017).

From 1 September 2016 to 7 March 2017, 45 confirmed and probable cases of mumps have been notified to EpiSurv (provisional data). This is higher than observed for the same period in previous years: 2015/16 (6 cases), 2014/15 (10 cases) and 2013/2014 (10 cases).

13.4 Vaccines

13.4.1 Available vaccines

Mumps vaccine is one of the components of the live attenuated MMR and MMRV vaccines, considered in sections 11.4 and 21.4. Single antigen mumps vaccine is not available in New Zealand.

Funded vaccine

MMR vaccine funded as part of the Schedule is Priorix (GSK), which contains attenuated Schwarz strain measles, RA 27/3 rubella, and Jeryl Lynn mumps. See section 11.4.1 for more information.

Other vaccines

MMR II (MSD) was the funded vaccine prior to the 1 July 2017 Schedule change (see section 11.4.1).

13.4.2 Efficacy and effectiveness

A 2012 Cochrane review of the safety and effectiveness of MMR vaccine estimated that a single dose of MMR vaccine was 69–81 percent effective in preventing clinical mumps. Effectiveness of MMR in preventing laboratory-confirmed mumps cases in children and adolescents was estimated to be between 64 and 66 percent for one dose and between 83 and 88 percent for two vaccine doses.[5]

A two-dose vaccination schedule and high immunisation coverage has been very successful in controlling disease. However, outbreaks can still occur in highly immunised populations because two doses of vaccine are not 100 percent effective. Declining vaccine-induced mumps immunity may also contribute to outbreaks.[2] Data from Finland shows that 20 years after the second MMR dose, immunity to rubella was secure, 95 percent of people remained sero-positive for measles and immunity to mumps declined, with 74 percent being sero-positive.[6] The antibody avidity also decreased over time, by 8 percent for measles and 24 percent for mumps.[7]

A third dose of MMR vaccine has been used safely and effectively during mumps outbreaks in highly immunised populations.[8] Although the mumps vaccine is less effective than measles and rubella vaccines, cases that have been vaccinated are significantly less likely to experience complications from disease such as orchitis, meningitis and hospitalisation.[9]

13.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.[10] Store at +2°C to +8°C. Do not freeze.

MMR vaccine must be reconstituted only with the diluents supplied by the manufacturer. Use MMR vaccine as soon as possible after reconstitution. If storage is necessary, reconstituted MMR vaccine can be stored at +2°C to +8°C for up to eight hours.

13.4.4 Dosage and administration

The dose of MMR is all of the reconstituted vaccine (approximately 0.5 mL) administered by subcutaneous injection (see section 2.2.3).

Co-administration with other vaccines

MMR vaccine can be given concurrently with other vaccines, as long as separate syringes are used and the injections are given at different sites. If not given concurrently, live vaccines should be given at least four weeks apart. (See also section 2.2.7 for information about multiple injections at the same visit.)

Interchangeability

The two brands of MMR vaccine (Priorix and MMR II) may be used interchangeably for completion of a course.[11]

13.5 Recommended immunisation schedule

Table 13.1: Recommended MMR vaccine schedule

	Schedule
Usual childhood schedule[a]	2 doses: at ages 15 months and 4 years
Catch-up[b] for children, adolescents and adults	2 doses: at least 4 weeks apart

a If MMR is given to children aged 6–12 months for outbreak control, 2 further MMR doses are still required at ages 15 months and 4 years.

b MMR vaccine is funded for those who are susceptible to 1 or more of the 3 diseases.

13.5.1 Usual childhood schedule

Two doses of mumps vaccine as MMR are recommended at age 15 months and age 4 years (Table 13.1).

The second dose can be given as soon as four weeks after the first dose.

Children who in an outbreak receive MMR vaccine when aged under 12 months require two further doses administered after age 12 months. The first scheduled MMR vaccine may be given to children from age 12 months whose parents/guardians request it, and no opportunity should be missed to achieve immunity.

13.5.2 Catch-up

MMR is recommended and funded for children, adolescents and adults who are known to be susceptible to one or more of the three diseases (two doses, four weeks apart). See sections 11.5.2 and 18.5.2.

13.5.3 Immunocompromise

Contacts of immunocompromised individuals

In general, MMR is contraindicated in immunocompromised individuals (see section 4.3). They can be partially protected from exposure to infection by ensuring that all contacts are fully immunised (funded), including hospital staff and family members. There is no risk of transmission of MMR vaccine viruses from a vaccinee to the immunocompromised individual (see section 11.7.2). See also 'Household contacts' in section 4.3.1 for general vaccination information for contacts of immunocompromised individuals.

(Re-)vaccination following immunosuppression

MMR vaccine is funded for (re-)vaccination following immunosuppression. However, it is important to be sure that the individual is immunocompetent enough to safely receive the vaccine.

HIV infection

Discuss vaccination of individuals with HIV infection with their specialist (see 'HIV infection' in section 4.3.3).

MMR vaccine is recommended for all HIV-positive children, whether symptomatic or asymptomatic, if the CD4+ lymphocyte percentage is 15 percent or greater. Asymptomatic children who are not severely immunocompromised are recommended to receive MMR vaccine from age 12 months to provide early protection against the three diseases. Susceptible HIV-positive children and adults aged 14 years and older may receive MMR vaccine if the CD4+ lymphocyte count is 200 cells/mm^3 or greater. Administration of MMR with CD4+ counts below these recommended levels has been associated with vaccine-related pneumonitis (from the measles component).[12]

13.5.4 Pregnancy and breastfeeding

MMR vaccine is contraindicated during pregnancy. Pregnancy should be avoided for four weeks after MMR vaccination.[12, 13]

MMR vaccine can be given to breastfeeding women.

13.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general vaccine contraindications.

13.6.1 Contraindications

See section 11.6.1 for specific MMR vaccine contraindications.

Anaphylaxis to a previous dose of MMR or any of the vaccine components (including neomycin) is a contraindication to a further dose of MMR.

MMR vaccine should not be given to women who are pregnant, and pregnancy should be avoided for four weeks after immunisation.[12, 13]

13.6.2 Precautions

Egg allergy, including anaphylaxis, is **not** a contraindication to MMR vaccine. See section 11.6.3 for more information, and section 11.6.2 for further precautions.

13.7 Expected responses and AEFIs

See sections 11.7 and 18.7.

13.8 Public health measures

It is a legal requirement that all cases of mumps be notified immediately on suspicion to the local medical officer of health.

13.8.1 Diagnosis

Except if there is an epidemiological link with a confirmed case, all suspected mumps cases should have diagnostic testing (eg, by buccal swab and PCR) as there are other causes of parotitis other than the mumps virus. See the latest version of the 'Mumps' chapter of the *Communicable Disease Control Manual 2012*[1] for the specimens

required for laboratory confirmation of mumps, or discuss these with the local laboratory.

13.8.2 Susceptible contacts

A susceptible contact is anyone born after 1981 who has not had mumps infection or has not been fully vaccinated for their age.

All susceptible contacts should be offered MMR vaccine. (All vaccinations given should be recorded on the NIR.) There is no increased risk of adverse events after immunisation during the incubation period of mumps or if the recipient is already immune. Immunoglobulin is ineffective after exposure to mumps.

The mumps vaccine given after exposure has not been shown to be effective in preventing infection, but immunisation will provide protection against future exposure and may prevent a third wave of cases from the susceptible contacts.

13.8.3 Exclusion

Cases

Exclude cases from tertiary education, school, sports, early childhood services or health care employment or other work and from close contact with other susceptible people for 5 days from onset of parotitis.[1]

Susceptible contacts

Discuss exclusion of susceptible contacts with the local medical officer of health. Previously immunised (pre-exposure) contacts need not be excluded. Generally, unimmunised contacts who have no previous history of mumps infection should be advised not to attend early childhood services or school because of:

- the risk of catching the disease themselves
- the risk of passing on the disease, when asymptomatic or in the prodromal phase, to other susceptible children.

Health care settings or working or living with immunocompromised people

Advise exclusion of susceptible contacts in health care settings and for those working or living with immunocompromised people from 12 days after the first exposure to 25 days after last exposure to the infectious case.[1] Documented full immunisation with two MMR doses should be required in these situations.[1]

Other settings

Consider advising exclusion of susceptible contacts with zero MMR doses from tertiary education, school, early childhood services or work from 12 days after the first exposure to 25 days after last exposure to the infectious case, if there is a high risk of mumps transmission. [1] Exclusion is more important in secondary and tertiary education settings as these settings are more conducive to outbreaks.[1]

All excluded contacts in settings other than healthcare or with immunocompromised people can be readmitted immediately after they have received the first MMR dose.[1] Those who have a history of one dose of MMR vaccination should be offered their second vaccine dose and be allowed to remain in tertiary education, school, early childhood services or work (except for health care workers or those working or living with immunocompromised people).[1] However, if the contact subsequently develops mumps symptoms they would need to be excluded.

For more details on control measures, refer to the latest version of the 'Mumps' chapter of the *Communicable Disease Control Manual 2012*.[1]

13.9 Variations from the vaccine data sheet

See section 11.9 for variations from the MMR (Priorix) data sheet.

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14 Pertussis (whooping cough)

Key information

Mode of transmission	By aerosolised droplets.
Incubation period	7–10 days (range 5–21 days).
Period of communicability	For control purposes, the communicable stage lasts from the catarrhal stage to 3 weeks after the onset of paroxysmal cough in a case not treated with antimicrobials. When treated with an effective antibiotic (eg, azithromycin), infectivity lasts until 2 days of antibiotics have been taken. This lengthens to 5 days if other antibiotics (eg, erythromycin) are used.
At-risk populations	Infants aged under 12 months, particularly those too young to be immunised.
Funded vaccines	DTaP-IPV-HepB/Hib (Infanrix-hexa). DTaP-IPV (Infanrix-IPV). Tdap (Boostrix).
Dose, presentation, route	0.5 mL per dose. DTaP-IPV-HepB/Hib: pre-filled syringe and glass vial. The vaccine must be reconstituted prior to injection. DTaP-IPV, Tdap: pre-filled syringe. Intramuscular injection.
Funded vaccine indications and schedule	Usual childhood schedule: • at age 6 weeks, 3 months and 5 months: DTaP-IPV-HepB/Hib • at age 4 years: DTaP-IPV • at age 11 years: Tdap During pregnancy (from 28 to 38 weeks' gestation): Tdap. For (re-)vaccination of eligible patients: DTaP-IPV-HepB/Hib, DTaP-IPV or Tdap.
Dose interval between Td and Tdap	No minimum interval is required between Td and Tdap, unless Tdap is being given as part of a primary immunisation course.

Continued overleaf

Vaccine efficacy/ effectiveness	84 percent efficacy after the 3-dose primary course in infants, lasting up to age 6 years. Immunity (whether from natural infection or immunisation) wanes over time.
Precautions	Children with an evolving neurological disorder.
Adverse events from vaccine	Thigh or upper arm swelling occurs in 2–3 percent of children after the fourth and fifth doses.

14.1 Bacteriology

Pertussis (whooping cough) is a bacterial respiratory infection caused by *Bordetella pertussis*, a gram-negative bacillus. The bacillus is fastidious (it requires special media to culture), and will often have cleared or decreased in numbers by the time the typical cough develops, making laboratory confirmation by culture difficult. The development of sensitive and specific PCR and serological assays has improved our ability to demonstrate *B. pertussis* infection (see section 14.8).

14.2 Clinical features

Pertussis is highly transmissible and it is one of the most infectious vaccine-preventable diseases. The expected number of secondary cases caused by an infectious individual with pertussis (R_0) is approximately 14, similar to measles, and several-fold greater than influenza[1] (see section 1.2.1). Transmission occurs by aerosolised droplets, and the incubation period is 7 to 10 days (range 5 to 21 days).

The initial catarrhal stage, during which infectivity is greatest, is of insidious onset with rhinorrhoea and an irritating cough that can progress to severe paroxysms of coughing. In the catarrhal stage, which usually lasts one to two weeks, the only clue to diagnosis may be contact with a known case. This stage is followed by the paroxysmal stage, with coughing episodes characterised by a series of short expiratory bursts, followed by an inspiratory gasp or typical whoop, and/or vomiting. Patients appear relatively well between paroxysms and are usually afebrile.

Clinical presentation varies with age, immunisation status and previous infection. In young infants apnoea and/or cyanosis may precede paroxysmal cough, and it is important they are recognised as presenting symptoms of severe disease. Thus pertussis must be considered in

infants presenting with an acute life-threatening event, or apnoea.[2] In school-aged children immunised in infancy, symptoms that distinguish pertussis from other causes of coughing illnesses are inspiratory whoop, post-tussive vomiting and the absence of wheezing and fever.[3]

Almost all pertussis infections in adolescents and adults occur in the context of previous infection and/or immunisation. Persistent cough, sometimes for more than four weeks, is the cardinal feature in adults.[4] Cough is worse at night and often paroxysmal, the patient waking with a choking sensation. Post-tussive vomiting and whoop are infrequent. A scratchy throat and sweating attacks are common.

Studies performed in several countries during both epidemic and non-epidemic periods have shown that between 12 and 37 percent of school-aged children, adolescents and adults with persistent cough (lasting 14 days or more) have evidence of recent *B. pertussis* infection.[3, 4, 5, 6, 7, 8, 9] A primary care-based study in New Zealand performed during the early phase of the 2011 to 2013 epidemic showed recent *B. pertussis* infection in 17 percent of children aged 5–16 years and 7 percent of adults aged 17–49 years presenting to primary care with a persistent cough of two or more weeks' duration.[10]

The most common complications of pertussis are secondary infections, such as otitis media and pneumonia, and the physical sequelae of paroxysmal coughing (eg, subconjunctival haemorrhages, petechiae, epistaxes, central nervous system haemorrhages, pneumothoraces and herniae). At the peak of the paroxysmal phase, vomiting can lead to weight loss, especially in infants and young children. The disease is most often severe in infants in the first few months of life. Of infants with pertussis sufficiently severe to require intensive care admission, one in six will either die or be left with brain or lung damage.[11]

14.3 Epidemiology

The epidemiology of *B. pertussis* infection and pertussis disease differ. Infection occurs across the age spectrum, and repeated infection without disease is common.[12] The endemic circulation of *B. pertussis* in older children and adults provides a reservoir for spread of the infection and the development of severe disease in incompletely vaccinated infants.

14.3.1 Global burden of disease

Pertussis mortality rates have always been highest in the first year of life.[13, 14] In the US during the 1940s pertussis resulted in more infant deaths than measles, diphtheria, poliomyelitis and scarlet fever combined.[13] Beyond age 3 years mortality rates have always been relatively low. In immunised populations virtually all deaths occur in the first two months of life, and deaths in toddlers and preschool-aged children have largely disappeared. Among infants, younger age, lack of immunisation, low socioeconomic status, premature gestation, low birthweight and female gender are associated with an increased risk of fatal pertussis.[14]

Pertussis mortality and morbidity[15] is under-reported. It is estimated that in high-income countries three times more deaths are due to pertussis than are reported.[15, 16, 17, 18] Infants continue to die from pertussis despite state-of-the-art intensive care.[11, 19, 20, 21, 22]

Since the introduction of mass immunisation, countries with consistently high immunisation coverage rates achieve consistently low pertussis incidence rates.[23, 24] Higher pertussis incidence rates are due primarily to lower immunisation coverage, but also in some instances to lower vaccine efficacy or less-than-optimal immunisation schedules.[25, 26, 27, 28, 29]

The decrease in incidence following the introduction of mass immunisation has been most pronounced in those aged under 10 years. Despite this, the reported pertussis disease rates have remained highest in infants and young children.[30, 31, 32] Infants aged under 3 months have the highest rate of notification and hospitalisation.[33, 34]

Pertussis is an epidemic disease with two- to five-yearly epidemic cycles. Epidemics are frequently sustained over 18 months or more, during which there are dramatic increases in hospital admission rates. Pertussis does not show the seasonal variability that is typical of most respiratory infections.

The epidemic periodicity of pertussis has not lengthened with the introduction of mass immunisation, unlike other epidemic diseases for which mass immunisation is used, such as measles. This lack of lengthening of the pertussis epidemic cycle implies minimal impact of mass immunisation on the circulation of *B. pertussis* in the human population.[12, 35, 36]

14.3.2 New Zealand epidemiology

Pertussis mortality in New Zealand

On average, there are zero to one deaths from pertussis each year in New Zealand. During the most recent pertussis epidemic (see below) there were three deaths in children: two in infants aged under 6 weeks and one in an unimmunised preschooler. There were no deaths from pertussis (as recorded in EpiSurv) in 2014 or 2015.[37]

Pertussis morbidity in New Zealand

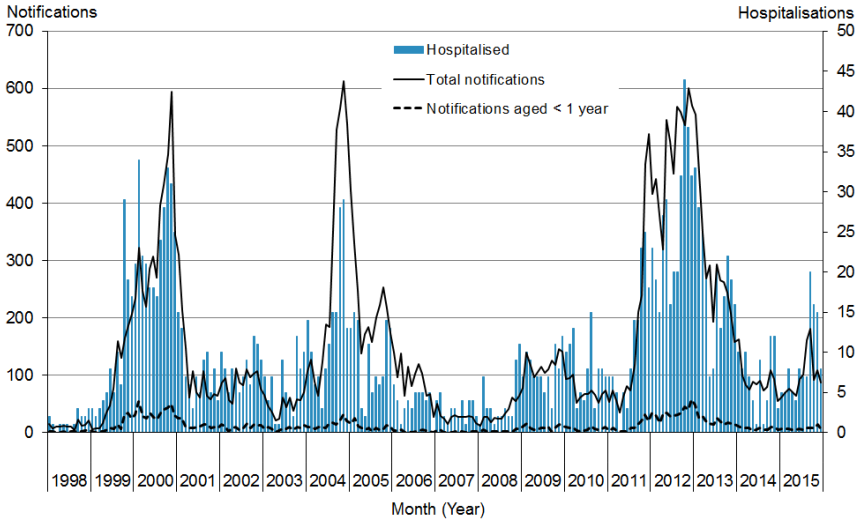
Pertussis morbidity in New Zealand has usually been described using hospital discharge data. National passive surveillance data has been available since 1996, when pertussis became a notifiable disease.

Pertussis morbidity in New Zealand as described by notification data

In 2015, 1,168 cases were notified, of which 650 were laboratory-confirmed.[37] The 2015 notification rate was 25.4 per 100,000 population, similar to the rate in 2014 (24.4 per 100,000, 1,099 cases). Infants had the highest notification rate (152.3 per 100,000, 90 cases), followed by children aged 1–4 years (55.1 per 100,000, 136 cases). By ethnicity, Pacific peoples had the highest notification rate (31.8 per 100,000, 90 cases), followed by European/Other (26.2 per 100,000, 800 cases) and Māori (25.7 per 100,000, 176 cases).

Three epidemics have occurred since pertussis became a notifiable disease, with an epidemic peak annual number of notified cases of 4,140 in 2000, 3,485 in 2004, and 5,897 in 2012 (see Figure 14.1).[37]

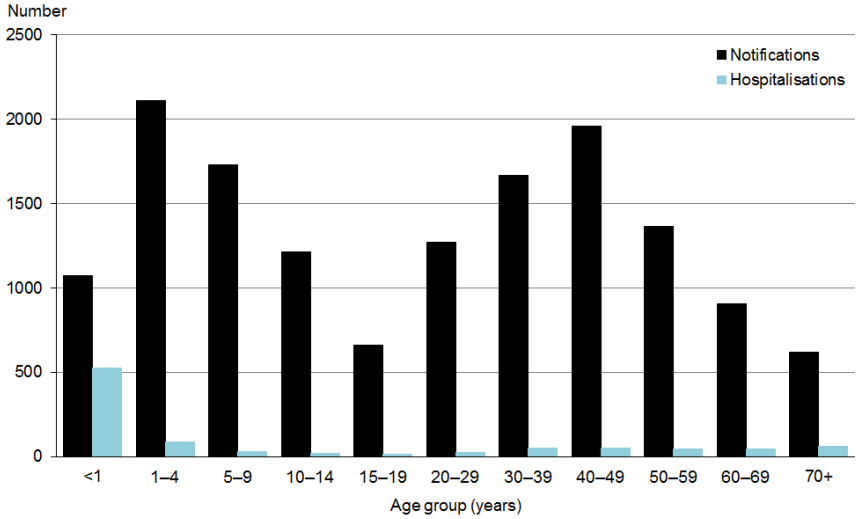
Figure 14.1: Pertussis notifications and hospitalisations, 1998–2015



Note: Includes confirmed, probable and suspect cases, and notifications still under investigation.
Source: ESR

Since pertussis became notifiable, the annual proportion of notified cases aged 30 years or older has increased from 23 percent (in 1997) to 44 percent in 2015.[37] However, the highest proportion of hospitalised cases continues to be in infants. From 2010 to 2015 there were 1,075 notified cases in infants. Hospitalisation status was recorded for 977 of the infant cases; of these, 527 (54 percent) were hospitalised (Figure 14.2).

Figure 14.2: Age distribution of notified and hospitalised pertussis cases, 2010–2015 cumulative data



Source: ESR

Pertussis morbidity in New Zealand, as described by hospital discharge data

Hospitalisation rates for pertussis, as measured by ICD discharge diagnostic codes, provide a measure of severe pertussis disease. The discharge rate in the 2000s was lower than in the 1990s (2000s versus 1990s, relative risk 0.79 [95% CI: 0.74–0.84]). Despite this decrease, the infant hospitalisation rate for pertussis in New Zealand in the 2000s (196 per 100,000) remained three times higher than contemporary rates in Australia (2001 infant rate: 56 per 100,000) and the US (2003 infant rate: 65 per 100,000).[38, 39, 40]

Pertussis hospital admission rates vary with ethnicity and household deprivation. From 2006 to 2010 the infant (aged under 12 months) pertussis hospital discharge rate (per 1,000) was higher for Māori (1.49; relative risk 2.29 [95% CI: 1.77–2.96]) and Pacific peoples (2.03; relative risk 3.11 [95% CI: 2.30–4.22]) and lower for Asian/Indian (0.31; relative risk 0.47 [95% CI: 0.25–0.90]) compared with European/Other people (0.65 per 1,000).[41]

From 2006 to 2010 an infant living in a household in the most deprived quintile was at a four-fold increased risk of being hospitalised with pertussis compared with an infant in the least deprived quintile (1.89 versus 0.39 per 1,000; relative risk 4.81 [95% CI: 2.99–7.75]).[41]

14.4 Vaccines

Whole-cell pertussis vaccine for routine use was introduced in 1960 and was replaced with acellular pertussis vaccine in 2000. The current schedule of three acellular pertussis-containing vaccines in the first year of life plus booster doses at ages 4 and 11 years has been in effect since 2006. See Appendix 1 for more information about the history of pertussis-containing vaccines in New Zealand.

14.4.1 Available vaccines

Funded pertussis vaccines

The acellular pertussis-containing vaccines funded as part of the Schedule are:

- DTaP-IPV-HepB/Hib (Infanrix-hexa, GSK): diphtheria, tetanus, acellular pertussis, inactivated polio, hepatitis B and *Haemophilus influenzae* type b vaccine
- DTaP-IPV (Infanrix-IPV, GSK): diphtheria, tetanus, acellular pertussis and inactivated polio vaccine
- Tdap (Boostrix, GSK): a smaller adult dose of diphtheria and pertussis vaccine, together with tetanus vaccine.

See section 5.4.1 for more information.

Other vaccines

Other acellular pertussis-containing vaccines registered (approved for use) and available (marketed) in New Zealand include:

- Tdap: Adacel (Sanofi)
- Tdap-IPV: Adacel Polio (Sanofi).

14.4.2 Efficacy and effectiveness

Immunogenicity

A review of published data on DTaP-IPV-HepB/Hib found it to be highly immunogenic in infants aged under 2 years for primary and booster vaccination.[42] In clinical studies there was a strong immune response against the vaccine antigens, which persisted for up to approximately six years after vaccination. A review of published clinical trial and post-marketing surveillance data supported the immunogenicity of DTaP-IPV-HepB/Hib across a range of schedules and when administered concurrently with other vaccines.[43]

Efficacy and effectiveness

The acellular pertussis vaccines approved for use in New Zealand have been shown to provide around 81–85 percent efficacy (95% CI: 51–100) after three infant doses, with follow-up studies suggesting sustained efficacy to age 6 years.[44, 45, 46]

Observational study data suggests that acellular pertussis vaccines, while effective, may be less effective than the best performing whole-cell vaccines in preventing whooping cough.[47, 48] Children and adolescents who have received acellular pertussis vaccine for their entire pertussis immunisation series are at greater risk of pertussis than children whose immunisation series included some doses of whole-cell vaccine and some doses of acellular vaccine.[49]

See section 4.1.2 for information about maternal pertussis vaccine effectiveness and safety.

Duration of protection

Protection against pertussis begins to wane within several years of completion of a three-dose primary and two-dose booster dose immunisation series. The US has a pertussis immunisation schedule that includes three doses of acellular vaccine during infancy and booster doses at 15 to 18 months and 4 to 6 years.[50] The risk of pertussis increases in the six years after receipt of the fifth dose of this series, indicating a waning in vaccine-induced immunity over this time interval.

In adults, a trial of a monovalent acellular pertussis vaccine in the US among people aged 15–65 years found an efficacy of 92 percent (95% CI: 32–99) after a median of 22 months of follow-up.[51] Antibodies to pertussis toxoid, filamentous hemagglutinin and pertactin have been shown to persist five years after receipt of Tdap (Boostrix) in a study of Australian adults aged 18 years and older.[52] However, the duration of protection is unknown.

14.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.[53] Store at +2°C to +8°C. Do not freeze.

DTaP-IPV-HepB/Hib should be stored in the dark.

DTaP-IPV-HepB/Hib (Infanrix-hexa) must be reconstituted by adding the entire contents of the supplied container of the DTaP-IPV-HepB vaccine to the vial containing the Hib pellet. After adding the vaccine to the pellet, the mixture should be shaken until the pellet is completely dissolved. Use the reconstituted vaccine as soon as possible. If storage is necessary, the reconstituted vaccine may be kept for up to eight hours at 21°C.

14.4.4 Dosage and administration

The dose of DTaP-IPV-HepB/Hib, DTaP-IPV and Tdap is 0.5 mL, administered by intramuscular injection (see section 2.2.3).

Co-administration with other vaccines

DTaP-IPV-HepB/Hib, DTaP-IPV and Tdap can be administered simultaneously (at separate sites) with other vaccines or IGs.

14.5 Recommended immunisation schedule

Table 14.1: Immunisation schedule for pertussis-containing vaccines (excluding catch-up)

Age	Vaccine	Comment
6 weeks	DTaP-IPV-HepB/Hib	Primary series
3 months	DTaP-IPV-HepB/Hib	Primary series
5 months	DTaP-IPV-HepB/Hib	Primary series
4 years	DTaP-IPV	Booster
11 years	Tdap	Booster
Pregnant women (weeks 28–38 of each pregnancy)	Tdap	Booster

14.5.1 Children

A primary course of pertussis vaccine is given as DTaP-IPV-HepB/Hib (Infanrix-hexa) at ages 6 weeks, 3 months and 5 months, followed by a dose of DTaP-IPV (Infanrix-IPV) at age 4 years (Table 14.1). A further booster is given at age 11 years (school year 7) as Tdap (Boostrix).

Dose intervals

The minimum interval between doses is four weeks, and the first dose should not be given before four weeks of age. If a course of immunisation is interrupted for any reason it may be resumed without repeating prior doses (see Appendix 2). A booster dose should be given no earlier than six months after the primary series.

Catch-up immunisation

See Appendix 2 for detailed catch-up immunisation information.

- DTaP-IPV-HepB/Hib or DTaP-IPV may be used for primary immunisation of children aged under 10 years.
- Tdap may be used for primary immunisation of children aged 7 to under 18 years.

Dose interval between Td and Tdap

When Tdap is to be given to adolescents or adults to protect infants or other vulnerable individuals from pertussis, no minimum interval is required between Td and Tdap,[54, 55, 56] – unless Tdap is being given as part of a primary immunisation course.

14.5.2 Pregnancy and breastfeeding

Pregnant women should receive a dose of Tdap (funded) from 28 to 38 weeks' gestation. This should be given during each pregnancy[57] to protect the mother and so that antibodies can pass to the fetus; post-partum maternal vaccination will reduce the risk of a mother infecting her baby but does not have the added benefit of providing passive antibodies.

See section 4.1.2 for information about maternal pertussis vaccine effectiveness and safety.

Tdap vaccines can be given to breastfeeding women.[58]

14.5.3 (Re-)vaccination

Pertussis-containing vaccines are funded for (re-)vaccination of eligible patients, as follows. See also sections 4.2 and 4.3.

DTaP-IPV-HepB/Hib (Infanrix-hexa) and DTaP-IPV (Infanrix-IPV)

An additional four doses (as appropriate) of DTaP-IPV-HepB/Hib (for children aged under 10 years) or DTaP-IPV are funded for (re-)vaccination of patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- with other severely immunosuppressive regimens.

Up to five doses of DTaP-IPV-HepB/Hib (for children aged under 10 years) or DTaP-IPV are funded for children requiring solid organ transplantation.

Tdap (Boostrix)

An additional four doses (as appropriate) of Tdap (Boostrix) are funded for patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- with other severely immunosuppressive regimens.

14.5.4 Recommended but not funded

Tdap is recommended but not funded for:

- lead maternity carers and other health care personnel who work in neonatal units and other clinical settings (such as GPs and practice nurses), where they are exposed to infants, especially those with respiratory, cardiac, neurological or other co-morbid conditions (with a booster dose at 10-year intervals)
- household contacts of newborns, including adult household and other close contacts (contacts who are aged under 18 years and who are unimmunised or incompletely immunised for their age can receive funded pertussis vaccine; see Appendix 2 for catch-up schedules)
- early childhood workers (with a booster dose at 10-year intervals), although the priority is to ensure all children attending child care have received age-appropriate vaccination
- wound care (see section 19.5.5).

14.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

14.6.1 Contraindications

The only contraindication is an immediate severe anaphylactic reaction to the vaccine, or any component of the vaccine, following a previous dose.

14.6.2 Precautions

For children with an undiagnosed or evolving neurological disorder (eg, uncontrolled epilepsy or deteriorating neurological state), there is the potential for confusion about the role of vaccination in the context of a clinically unstable illness. The risks and benefits of withholding vaccination until the clinical situation has stabilised should be considered on an individual basis.

14.7 Expected responses and AEFIs

Unless the specific contraindications and precautions outlined in section 14.6 above are present, practitioners should have no hesitation in advising the administration of acellular pertussis vaccine. Although whole-cell pertussis vaccine has been associated with febrile seizures, there was never any good-quality evidence that it caused any more significant neurological disorder. Disorders for which any causal association with pertussis vaccine have been disproved include infantile spasms, Reye syndrome and SUDI.[59, 60, 61, 62, 63, 64, 65, 66] Similar to previous studies, the New Zealand Cot Death Study found a lower rate of SUDI in immunised children.[67] Acellular pertussis vaccine has been used in New Zealand since 2000 and is significantly less reactogenic than was the whole-cell pertussis vaccine.

14.7.1 DTaP-containing vaccines

DTaP-containing vaccines (eg, DTaP-IPV-HepB/Hib and DTaP-IPV) are generally well tolerated in children,[68] including preterm (24 to 36 weeks' gestation) and/or low birthweight (820–2,020 grams) infants.[69, 70]

Local reactions commonly include pain, redness, swelling and induration at the injection site.[68] Less common reactions include fretfulness, anorexia, vomiting, crying, and slight to moderate fever.[68] These local and systemic reactions usually occur within several hours of pertussis immunisation and spontaneously resolve within 48 hours without sequelae.[68]

Local reactions increase with age and additional doses of vaccine. The reaction may be due to some of the other vaccine components, such as aluminium. These reactions are usually minor and only last a day or so. In a small percentage of vaccine recipients the reactions will be severe enough to limit movement of the arm and may last for about a week.

14.7.2 Tdap vaccine

The adult reduced-concentration Td and Tdap (Boostrix) vaccines have been found to have no safety concerns in those aged 10–64 years and those aged over 65 years.[71, 72, 73] Administration of Tdap to pregnant women did not identify any concerning patterns in maternal, infant, or fetal outcomes.[74, 75]

Local reactions following immunisation of adolescents with Tdap are common, but are usually mild. They include pain (in 75 percent of recipients), swelling (21 percent) and redness (23 percent) at the injection site.[76]

Expected systemic reactions following immunisation of adolescents with Tdap include fever >38°C (5 percent), headache (16 percent), fatigue (14 percent) and gastrointestinal symptoms (10 percent).[76]

14.7.3 Major adverse events associated with pertussis-containing vaccines

The incidence of major adverse events following primary pertussis immunisation is summarised in Table 14.2.

Table 14.2: Incidence (per 100,000 doses) of major adverse reactions following acellular pertussis vaccine

Event following immunisation	Timing post-vaccination	Incidence per 100,000 doses
Persistent (>3 hours) inconsolable screaming	0–24 hours	44
Seizures	0–2 days	7
Hypotonic-hyporesponsive episode	0–24 hours	0–47 in trials of acellular vaccines
Anaphylaxis	0–1 hour	Very rare

Source: Edwards KM, Decker MD. 2008. Pertussis vaccine. In: Plotkin SA, Orenstein WA, Offit PA (eds). *Vaccines* (5th edition). Philadelphia, PA: WB Saunders Company. Table 21.15.

Swelling involving the entire thigh or upper arm occurs in 2–3 percent of children after administration of the fourth and fifth doses of acellular pertussis vaccine.[68] The pathogenesis is unknown. Resolution occurs without sequelae. Extensive limb swelling after the fourth dose does not predict an increased risk of a similar reaction following the fifth dose of pertussis vaccine and is not a contraindication to receipt of the fifth dose.

Neither a hypotonic-hyporesponsive episode nor seizures are associated with long-term consequences for the child[77, 78, 79] (see section 2.3.3). Children who have febrile seizures after pertussis immunisation do not have an increased risk of subsequent seizures or neurodevelopmental disability.[80] It is safe to give acellular pertussis vaccine after a hypotonic-hyporesponsive episode has occurred following a previous dose.[81]

14.8 Public health measures

14.8.1 Improving pertussis control

The goal of the pertussis immunisation programme is to protect those most at risk of developing severe disease; that is, infants in the first year of life. Two key strategies for reducing the burden of disease in infants are the administration of Tdap vaccination during pregnancy and on-time infant immunisation. Vaccination during pregnancy is recommended and funded for women from 28 to 38 weeks' gestation (see section 14.5.2). More complete and timely delivery of the current

infant immunisation schedule would reduce the infant pertussis disease burden.[82] It is important that all children attending early childhood services should be fully vaccinated for their age.

In October 2012 the UK introduced a pertussis vaccination programme for pregnant women in response to a nationwide pertussis outbreak. The vaccine effectiveness for preventing laboratory-confirmed pertussis in infants aged under 3 months was estimated to be 91 percent (95% CI: 84–95).[83] This high vaccine effectiveness is likely to be a result of protection of infants by both passive antibody transfer and reduced exposure to maternal disease.[83]

Data on the protective effects of indirect strategies is currently incomplete. Infants can be protected by immunisation of others at risk of developing pertussis, with whom the infant may come into contact.[84] The 'cocoon strategy' is the term used to describe the protection of infants by immunising those who are potential sources of *B. pertussis*.[84] This involves the targeted immunisation of adult groups who have the most contact with young and vulnerable infants. Three identified groups are (1) new mothers who have not had recent immunisation, family, and close contacts of newborns; (2) health care workers; and (3) early childhood workers.

Health care workers in particular are at increased risk of pertussis and can transmit pertussis to other health care workers and to patients.[85] Outbreaks in maternity wards, neonatal units and outpatient settings have been described.[86] Fatalities occur as a result of such nosocomial spread.[87]

Immunisation cannot be used to control a community outbreak, although action to update age-appropriate vaccination in institutional settings (schools and early childhood services) is appropriate. When an outbreak occurs, individual immunisation status should be checked and immunisation completed. In an outbreak setting, infants as young as four weeks of age can commence immunisation.

14.8.2 Notification

It is a legal requirement that all cases of pertussis be notified immediately on suspicion to the local medical officer of health.

A suspected pertussis case can be confirmed if a clinically compatible illness is laboratory confirmed, or is epidemiologically linked to a confirmed case. Because transmission is by aerosolised droplets, health care personnel looking after pertussis cases should wear a mask even if vaccinated.

14.8.3 Laboratory diagnosis of *Bordetella pertussis* infection

PCR is the most sensitive method for diagnosing *B. pertussis* infection. In general, *B. pertussis* can be identified by PCR from most upper respiratory tract samples, including throat swabs, for up to four to six weeks after symptom onset. Serology may be useful when symptoms have been present for more than two weeks, at a time when PCR and culture are more likely to be negative.

The local laboratory should be consulted for the specifics of which swabs and transport media to use.

14.8.4 Antimicrobial treatment of case

A number of antibiotics are available for the treatment and prophylaxis of pertussis. Macrolide antibiotics can be used to reduce the severity and duration of clinical disease but only if started during the catarrhal phase. Antibiotics commenced after coughing paroxysms have begun have no effect on the clinical disease but do reduce the risk of spread of disease to others.[68, 88, 89] Antibiotics are of limited value if started after 21 days of illness, but should be considered for high-risk contacts (eg, young infants and pregnant women). To minimise transmission to newborn infants, it is recommended that pregnant women diagnosed with pertussis in the third trimester be treated with appropriate antibiotics (see Table 14.3), even if six to eight weeks have elapsed since the onset of cough.[90]

Macrolide use during pregnancy, lactation and in the neonatal period is associated with an increased risk of infantile pyloric stenosis.[91, 92] With erythromycin, the risk increases with decreasing age and increased duration of treatment.[93] The risk is presumed to be lower with azithromycin, although there are case reports of infantile pyloric stenosis occurring when azithromycin has been used during pregnancy.

Parents should be informed of the risks of this complication and of the symptoms and signs of infantile hypertrophic pyloric stenosis. The infant should be monitored for this complication for four weeks after completion of treatment.[68, 94, 95]

Table 14.3: Recommended antimicrobial therapy and post-exposure prophylaxis for pertussis in infants, children, adolescents and adults

Age	Recommended	Alternative		
	Azithromycin[a]	Erythromycin	Clarithromycin[b]	TMP-SMX[c]
Younger than 4 weeks	Day 1: 10 mg/kg/day in a single daily dose Days 2–5: 5 mg/kg/day in a single daily dose	40 mg/kg/day in 4 divided doses for 14 days	Not recommended	Contraindicated under age 2 months (risk for kernicterus)
1–5 months	Day 1: 10 mg/kg/day in a single daily dose Days 2–5: 5 mg/kg/day in a single daily dose	40 mg/kg/day in 4 divided doses for 14 days	15 mg/kg per day in 2 divided doses for 7 days	Aged 2 months or older: TMP, 8 mg/kg/day; SMX, 40 mg/kg/ day in 2 divided doses for 14 days
6 months or older and children	Day 1: 10 mg/kg/day in a single daily dose (maximum 500 mg) Days 2–5: 5 mg/kg/ day in a single daily dose (max 250 mg per day)	40 mg/kg/day in 4 divided doses for 14 days (maximum 2 g/day)	15 mg/kg/day in 2 divided doses for 7 days (maximum 1 g/day)	Aged 2 months or older: TMP, 8 mg/kg/day; SMX, 40 mg/kg/ day in 2 divided doses for 14 days
Adolescents and adults	Day 1: 500 mg as a single dose Days 2–5: 250 mg once daily	2 g/day in 4 divided doses for 14 days	1 g/day in 2 divided doses for 7 days	TMP, 320 mg/ day; SMX, 1,600 mg/day in 2 divided doses for 14 days

a Preferred macrolide during pregnancy, lactation and in infants <1 month old because of risk of idiopathic hypertrophic pyloric stenosis associated with erythromycin.

b Not funded for treatment or post-exposure prophylaxis in New Zealand.

c TMP = trimethoprim; SMX = sulfamethoxazole. TMP-SMX can be used as an alternative agent to macrolides in patients aged ≥2 months who are allergic to macrolides, who cannot tolerate macrolides, or who are infected with a rare macrolide-resistant strain of *Bordetella pertussis*.

Adapted from: Centers for Disease Control and Prevention. 2005. Recommended antimicrobial agents for treatment and post exposure prophylaxis of pertussis. *Morbidity and Mortality Weekly Report* 54(RR14): 1–16.

Exclusion

Exclude the case from school, early childhood services, other institutions or work until they have received at least two days of an appropriate course of antibiotic treatment (eg, azithromycin; this lengthens to 5 days if other antibiotics [eg, erythromycin] are used), or exclude them for three weeks from the date of onset of typical paroxysms of cough or until the end of the cough, whichever comes first.[96]

Children who have culture-proven pertussis should complete their immunisation series with all of the scheduled doses recommended for their age.

14.8.5 Management of contacts

The local medical officer of health will advise on the management of contacts. For more details on control measures, refer to the latest version of the 'Pertussis' chapter of the *Communicable Disease Control Manual 2012*.[96]

A contact can be defined as someone who has been in close proximity (within one metre)[97] of the index case for one hour or more during the case's infectious period. Contacts include household members, those who have stayed overnight in the same room, and those who have had face-to-face contact with the case.[96]

Those most at risk from pertussis and who are therefore high-priority contacts for public health follow-up are:

- children aged under 12 months
- children and adults who live with, or spend time around, a child aged under 12 months, including health care and education settings
- pregnant women, especially in the last month of pregnancy
- individuals at risk of severe illness or complications (eg, with chronic respiratory conditions, congenital heart disease or immune deficiency).

As the evidence for the effectiveness of chemoprophylaxis of contacts is limited, antibiotics are currently only recommended for high-priority contacts as listed above and if given within three weeks of initial exposure to an infectious case.

Health care workers are frequently exposed to *B. pertussis*. Although the greatest priority is given to protecting young infants and unimmunised children, there are well-documented examples of spread from staff to older adult patients. Pertussis in adults can be debilitating and can cause significant morbidity in those with respiratory disease.

Chemoprophylaxis may therefore be useful for adults exposed to a health care worker with pertussis, and infection control or public health services should normally be involved. Factors to be considered when discussing chemoprophylaxis include whether adult pertussis vaccine has been administered within the last five years, the health status of the individual who has been exposed, how recent the exposure was, and the nature of the health care or special community setting.

Where a case worked in a maternity ward or newborn nursery for more than an hour while infectious, then all babies in that ward and their parents/carers who were exposed to the case (within one metre for more than one hour) should receive antibiotics. Note: If the minimum duration of exposure is uncertain, a neonate exposed to an infectious case for less than one hour may warrant being considered a close contact and receive antibiotics.[98]

Exclusion

Any contacts, high priority or otherwise, should be advised to avoid attending early childhood services, school, work or community gatherings if they become symptomatic. It is important to clearly explain that the early stage of pertussis is catarrhal, with symptoms that are indistinguishable from those of minor respiratory tract infections, and is highly contagious.[96]

In general, susceptible contacts working or living with someone particularly vulnerable to pertussis (in particular: a young child with fewer than three doses of pertussis-containing vaccine; a woman in the last month of pregnancy; a person with a pre-existing health condition that may be exacerbated by a pertussis infection) should be given prophylaxis with antibiotics and not be excluded while taking prophylaxis as long as they don't have any symptoms, or, in the absence of prophylaxis, be excluded/avoid close contact for 14 days after the last exposure to an infectious case.[96] Susceptible contacts are defined as those who are not fully immunised for their age, or if they are over

16 years of age and have not received a booster of pertussis-containing vaccine in the last 5 years. [96]

Additional restrictions may be advised by the local medical officer of health, in particular if there is significant risk of transmission of infection to high-priority individuals.

14.9 Variations from the vaccine data sheets

The DTaP-IPV-HepB/Hib (Infanrix-hexa) and DTaP-IPV (Infanrix-IPV) data sheets state that these vaccines are indicated for primary immunisation of infants and as a booster dose for children. The Ministry of Health recommends that DTaP-IPV-HepB/Hib and DTaP-IPV vaccines may also be used for catch-up of the primary schedule in children aged under 10 years (see Appendix 2).

The data sheets for DTaP-IPV-HepB/Hib, DTaP-IPV and Tdap (Boostrix) state that these vaccines are contraindicated in children with encephalopathy of unknown aetiology or with neurologic complications occurring within seven days following a vaccine dose. The Ministry of Health recommends instead that the only contraindication is a history of anaphylaxis to a previous dose or to any of the vaccine components (see section 14.6.1). The risks and benefits of withholding vaccination until the clinical situation has stabilised should be considered on an individual basis (see section 14.6.2).

Tdap is not approved for use (registered) for primary immunisation. However, the Ministry of Health recommends that children aged 7 to under 18 years may receive Tdap (funded) and adults aged over 18 years may receive Tdap (unfunded) for catch-up of the primary schedule (see Appendix 2).

The Tdap data sheet states that the vaccine may be used during pregnancy when the possible advantages outweigh the possible risks for the fetus. However, the Ministry of Health recommends and funds Tdap vaccine for all pregnant women from 28 to 38 weeks' gestation (see section 14.5.2).

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15 Pneumococcal disease

Key information

Mode of transmission	Contact with respiratory droplets.
Incubation period	Asymptomatic nasopharyngeal carriage is common. The incubation period is variable and may be as short as 1–3 days.
Burden of disease	Particularly the young, the elderly and the immunocompromised.
Funded vaccines	All children aged under 5 years: PCV10 (Synflorix). Children and adults with eligible conditions: • PCV13 (Prevenar 13) • 23PPV (Pneumovax 23).
Dose, presentation and route	All vaccines: • 0.5 mL per dose • pre-filled syringe • intramuscular injection (23PPV may also be given subcutaneously).
Funded vaccine indications and schedule	PCV10 at ages 6 weeks, 3, 5 and 15 months, or age-appropriate catch-up. Children who started with PCV13 can continue with PCV10. PCV13 and 23PPV age-appropriate schedules for (re-)vaccination of children and adults with eligible conditions. PCV13 and 23PPV for testing for primary immune deficiencies.
Vaccine efficacy/ effectiveness	For pneumococcal conjugate vaccines: reductions in pneumococcal disease and carriage of vaccine serotypes in vaccinated populations, plus herd immunity effects reducing pneumococcal disease in other age groups; some increases in disease caused by non-vaccine serotypes.
Precautions	There may be an increased risk of fever and febrile convulsions with concomitant PCV13 and influenza vaccine in children aged 6 months to under 5 years. 23PPV should not be given to children aged under 2 years due to the reduced immune response associated with polysaccharide vaccines.

15.1 Bacteriology

Streptococcus pneumoniae is a gram-positive diplococcus. It is ubiquitous, and many individuals carry the organism asymptomatically in their upper respiratory tract.[1] There are over 90 identifiable serotypes of *S. pneumoniae*. Certain serotypes are more invasive or more associated with antibiotic resistance, and dominant serotypes vary by age and geographical distribution.

Table 15.1 summarises the serotypes contained in the pneumococcal conjugate (PCV) and polysaccharide (PPV) vaccines.

Table 15.1: Summary of pneumococcal vaccine serotype content

Vaccine	Serotypes
PCV7	Serotypes 4, 6B, 9V, 14, 18C, 19F, 23F
PCV10*	Includes: • the serotypes contained in PCV7 • plus serotypes 1, 5, 7F.
PCV13	Includes: • the serotypes contained in PCV10 • plus serotypes 3, 6A, 19A.
23PPV	Includes: • the serotypes contained in PCV13 (except for 6A) • plus serotypes 2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F, 33F.

* PCV10 contains serotype 19F, which elicits cross-reactive antibodies against serotype 19A.[2]

15.2 Clinical features

The human nasopharynx is the only natural reservoir of *S. pneumoniae*. Carriage rates in young children range up to 75 percent.[3] Transmission of *S. pneumoniae* is by contact with respiratory droplets, and although nasopharyngeal colonisation precedes disease, most who are colonised do not develop invasive disease. The nasopharynx is a source of spread between individuals, and reduction of *S. pneumoniae* vaccine serotypes in children by vaccination results in less transmission to, and disease in, adults. Invasive pneumococcal disease (IPD) is the severe end of the pneumococcal disease spectrum and includes cases in which

S. pneumoniae has been isolated from a usually sterile site (such as blood, pleural fluid or cerebrospinal fluid). Major clinical syndromes are bacteraemic pneumonia, bacteraemia without a focus and meningitis; older adults most commonly have bacteraemic pneumonia while young children may have any of the three, with meningitis being the most severe.

Mucosal or non-invasive infection is extremely common, such as acute otitis media (the most common childhood bacterial infection), and sinusitis and pneumonia (without bacteraemia) in all age groups. The incubation period of *S. pneumoniae* infection is variable but may be as short as one to three days.

15.3 Epidemiology

15.3.1 Global burden of disease

Pneumococcal diseases are a common cause of morbidity and mortality worldwide, though rates of disease and death are higher in low-income countries than in high-income countries, with the majority of deaths occurring in sub-Saharan Africa and Asia.[4] Along with the very old and very young, patients with underlying conditions have the highest rates of disease.

The WHO estimates that 476,000 (range 333,000–529,000) children aged under 5 years died from pneumococcal infections in 2008.[4] Five percent of all-cause child mortality in 2008 was due to pneumococcal infections.

Global epidemiology since the introduction of PCV

Herd immunity

There is good evidence for the indirect (herd) effects of infant PCV immunisation on pneumococcal disease due to vaccine serotypes in the non-vaccinated population, especially in adults aged 65 years and older. This includes data showing reductions in the rates of IPD due to PCV7 serotypes in non-vaccinated groups in the US (for both adult pneumonia and IPD in adults),[5, 6, 7] England and Wales,[8] the Netherlands,[9] Norway[10] and Denmark[11] and New Zealand (see Figure 15.1). These herd effects

are due to decreased nasopharyngeal carriage of vaccine types in immunised children resulting in reduced transmission to unimmunised older children and adults. Although most of New Zealand data demonstrates the indirect effect on vaccine-type IPD (see Figure 15.2), there is also evidence of an all-age effect on non-bacteraemic pneumonia.[12] Data from Norway[13] and Canada[14] indicates further decreases in vaccine-type IPD in non-vaccinated populations (aged 5 years and older) after PCV13 replaced PCV7 on the infant immunisation schedule.

Impact of vaccination on non-invasive pneumococcal disease

The impact of pneumococcal conjugate vaccination on the large burden of non-invasive pneumococcal disease has been clearly demonstrated internationally in countries that have introduced these vaccines, particularly through reductions in childhood hospitalisations due to pneumonia.[15, 16] Other impacts, such as on acute otitis media, are less clear and more difficult to measure accurately.[17]

15.3.2 New Zealand epidemiology

Pneumococcal disease occurs throughout the year, but is more common in the autumn and winter months.[18, 19] Historically, the risk of disease is highest in infants and the elderly,[20, 21] especially Māori and Pacific peoples.[18, 20, 22] The introduction of PCV has substantially reduced the risk of IPD in vaccinated infants (see below).

Invasive isolates from cases of IPD are serogrouped and serotyped at ESR. Detailed surveillance information can be found on the ESR Public Health Surveillance website (www.surv.esr.cri.nz/surveillance/IPD.php).

Incidence and mortality

There were 447 IPD cases notified in 2015 (ESR, 1 February 2017). The notification rate was 9.7 cases per 100,000 population, a decrease from 2014 (10.8 cases per 100,000 population; 489 cases) and significantly lower than the 2009 peak rate of 16.2 per 100,000 population (697 cases).

Adults aged 85 years and older (53.7 per 100,000), 75–84 years (35.4 per 100,000), 65–74 years (25.8 per 100,000) and children aged under 1 year (16.9 per 100,000) had the highest rates of IPD (ESR, 1 February 2017). The age-standardised rates of IPD were highest for the Pacific peoples (31.3 per 100,000, 51 cases) and Māori (27.7 per 100,000, 107 cases) ethnic groups. The rates for these ethnic groups were, respectively, 4.3 and 3.8 times higher than the rate for the European/Other ethnic group (7.3 per 100,000, 259 cases).

IPD was recorded as the primary cause of death for 27 cases in 2015 (ESR, 1 February 2017). There were no deaths due to IPD in children aged under 5 years.

In 2015, the most commonly reported risk factor in cases aged under 5 years was premature birth (50.0 percent), and for cases aged 5 years and older it was having a chronic illness (55.2 percent).[23]

New Zealand epidemiology since the introduction of PCV

PCV7 was introduced in June 2008, PCV10 in July 2011 and PCV13 in July 2014. From 1 July 2017, PCV10 will again be used on the routine Schedule (see Appendix 1 for the history of pneumococcal vaccination in New Zealand).

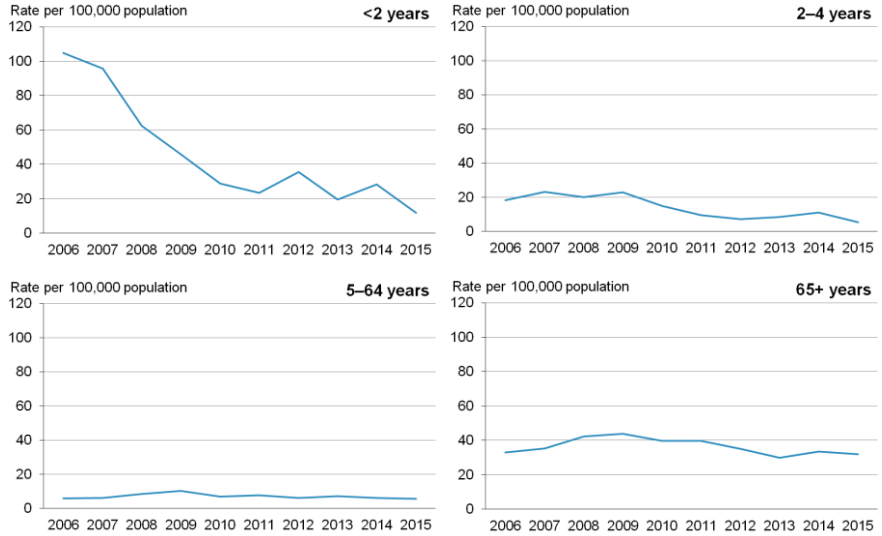
IPD incidence

There have been dramatic reductions in the incidence of IPD in the vaccine-eligible age groups in New Zealand since the introduction of PCV to the Schedule in 2008 (see Figure 15.1).

In New Zealand children aged under 2 years, the rate of IPD has decreased by 88 percent since the introduction of PCV to the Schedule: from an average annual rate of 100.3 per 100,000 for 2006/07[24] to 11.8 per 100,000 in 2015.[23] The impact on IPD caused by PCV7 serotypes in this age group is even greater (see Figure 15.2), with only one case of IPD in a child aged under 2 years due to a PCV7 serotype in 2015 (ESR, 1 February 2017).

Similar reductions were seen for IPD caused by PCV10 and PCV13 serotypes in children aged under 2 years (see Figure 15.2). The rate of IPD has also significantly decreased in children aged 2 to 4 years, for all-cause IPD (Figure 15.1) and IPD caused by PCV serotypes (Figure 15.2).

Figure 15.1: Rate per 100,000 of invasive pneumococcal disease by age group and year, 2006–2015



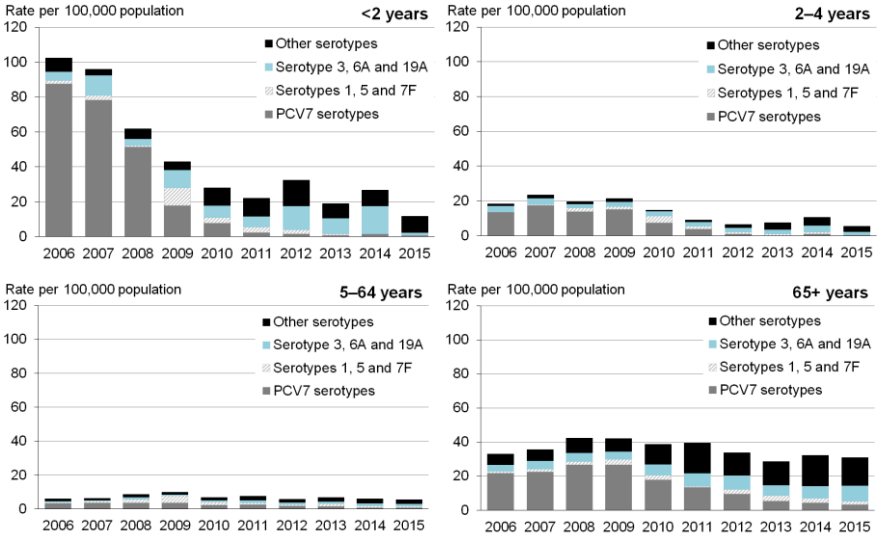
Notes:

PCV7 was introduced in 2008, PCV10 in 2011 and PCV13 in 2014.

IPD became a notifiable disease in 2008. Data presented from 2009 onwards is based on IPD notifications, and data prior to 2009 is from ESR's national laboratory-based surveillance of IPD.

Source: ESR

Figure 15.2: Rate per 100,000 population of invasive pneumococcal disease due to PCV7 serotypes, additional PCV10 types, additional PCV13 types and non-PCV types, by age group and year, 2006–2015



Notes:

PCV7 was introduced in 2008, PCV10 in 2011 and PCV13 in 2014.

'PCV7 serotypes' are cases due to serotypes covered by PCV7 (4, 6B, 9V, 14, 18C, 19F and 23F); 'Serotypes 1, 5 and 7F' are cases due to the additional serotypes contained in PCV10; 'Serotypes 3, 6A and 19A' are cases due to the additional serotypes contained in PCV13; and 'Other serotypes' are all other culture-positive IPD cases.

IPD became a notifiable disease in 2008. Data presented from 2009 onwards is based on IPD notifications, and data prior to 2009 is from ESR's national laboratory-based surveillance of IPD.

Source: ESR

Pneumococcal serotypes

Of the 447 IPD cases notified in 2015, 430 were referred to ESR for serotyping (ESR, 1 February 2017). Just over 90 percent (22/24) of cases in children aged under 5 years were due to serotypes not covered by PCV10, compared with 71.7 percent (142/198) and 83.6 percent (174/208) of cases in the 5–64 years age group and 65 years and older age group, respectively.

Serotype 19A was the most common of all serotypes (90 cases) in 2015 (ESR, 1 February 2017). Three of these 19A cases were in children aged under 5 years (none of whom had received PCV13), down from 17 cases in this age group in 2014.

Serotype 22F was the most common non-vaccine serotype in 2015, although there was little change in cases of 22F disease between 2014 and 2015 (39 to 40 cases) (ESR, 1 February 2017).

Herd immunity

The addition of PCV to the New Zealand schedule in 2008 has seen significant reductions in IPD due to PCV serotypes in age groups not eligible for routine infant immunisation (Figure 15.2). Between 2006/07 and 2015 the rate of IPD due to all vaccine serotypes in the 65 years and older age group decreased 43 percent, from an average of 28.0 per 100,000 population in 2006/07 to 16.0 per 100,000 in 2015, while in the 5–64 years age group there was a 30 percent decrease over the same time period (5.0 to 3.5 per 100,000) (ESR, 1 February 2017). However the overall rate of IPD in these age groups has only marginally decreased due to non-vaccine serotype replacement disease.

Impact of vaccination on non-invasive pneumococcal disease

While hospitalisations for respiratory infections in children aged 5 years and under have been increasing in New Zealand, hospitalisations for all-cause pneumonia have declined significantly since the implementation of the pneumococcal conjugate vaccine programme in 2008. The largest reductions in all-cause pneumonia hospitalisations between 2006 and 2015 were in Māori (a 12 percent reduction) and Pacific children (a 21 percent reduction) and those living in areas of high deprivation.[25] In children aged under 2 years living in Counties Manukau DHB, the introduction of PCV7 was associated with a 70 percent reduction in the risk of pneumonia hospitalisations in Pacific children but there was less impact (a 5 percent risk reduction) for Māori children.[26]

Antimicrobial resistance

As in other countries, there has been concern at the increase in the prevalence of antimicrobial resistance in *S. pneumoniae* in New Zealand. Introduction of pneumococcal conjugate vaccination has reduced the circulation of resistant pneumococcal serotypes elsewhere.[27]

In New Zealand, *S. pneumoniae* resistance to betalactams (penicillin and cefotaxime) has shown little change over the last 10 years; the 2015 rate of penicillin resistance (meningitis interpretation) of 21.9 percent was within the range of rates recorded for other years during the last decade (14.1–22.3 percent) (ESR, 1 February 2017). Similarly, the 2015 rate of cefotaxime resistance of 2.6 percent was within the range recorded for other years during the last decade (1.9–5.1 percent).

In 2015 PCV7 serotypes accounted for a smaller proportion (20.2 percent) of the penicillin-resistant isolates than previous years (92.8 percent in 2006/07), and type 19A accounted for a larger proportion (52.1 percent) (ESR, 1 February 2017). The prevalence of penicillin resistance among serotype 19A isolates has increased significantly in recent years from an average of 15.8 percent in 2006/07 to 54.4 percent in 2015.

15.4 Vaccines

15.4.1 Available vaccines

There are two types of pneumococcal vaccine registered (approved for use) and available (marketed) in New Zealand for use against *S. pneumoniae*: protein conjugate pneumococcal vaccine and unconjugated polysaccharide pneumococcal vaccine. In the protein conjugate vaccines, the pneumococcal surface polysaccharide is coupled to a carrier protein. The protein conjugate induces increased production of antibodies, immunological memory and maturation of the antibody response, enabling an effective immune response in children aged under 2 years (see section 1.4.3).

Funded vaccines

PCV10

Each 0.5 mL dose of PCV10 contains:

- 1 µg of pneumococcal polysaccharide serotypes 1, 5, 6B, 7F, 9V, 14 and 23F and 3 µg of serotype 4, conjugated to a total of 9–16 µg of NTHi protein D carrier protein, 3 µg of serotype 18C conjugated to 5–10 µg of tetanus toxoid carrier protein, and 3 µg of serotype 19F conjugated to 3–6 µg of diphtheria toxoid carrier protein, adsorbed onto 0.5 mg of aluminium phosphate
- 4.3 mg of sodium chloride and water for injection.

PCV10 contains no preservative.

PCV13

Each 0.5 mL dose of PCV13 contains:

- 2.2 µg of pneumococcal purified capsular polysaccharides for serotypes 1, 3, 4, 5, 6A, 7F, 9V, 14, 18C, 19A, 19F and 23F, and 4.4 µg of serotype 6B, conjugated to non-toxic diphtheria CRM_{197} protein and adsorbed onto aluminium phosphate (0.565 mg)
- succinic acid, polysorbate 80, aluminium phosphate, phosphate, and sodium chloride in water for injection.

23PPV

Each 0.5 mL dose of 23PPV contains:

- 25 µg of each capsular polysaccharide antigen (serotypes: 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F and 33F)
- sodium chloride, water for injection, and phenol (0.25 percent) added as a preservative.

15.4.2 Efficacy and effectiveness

10-valent pneumococcal conjugate vaccine (PCV10)

IPD

Two key randomised controlled trials have demonstrated the protective efficacy and effectiveness of PCV10 against pneumococcal disease.[2] The Finnish Invasive Pneumococcal disease (FinIP) study investigated a two- or three-dose infant series plus a toddler booster.[28] Vaccine effectiveness against culture-confirmed vaccine-serotype IPD was shown to be 100 percent (95% CI: 83–100) following the 3+1 schedule and 92 percent (95% CI: 58–100) for the 2+1 schedule. Based on national hospital discharge register data, vaccine effectiveness was 71 percent (95% CI: 52–83) for patient file-verified non-laboratory-confirmed IPD.[29]

In the Clinical Otitis Media and Pneumonia Study (COMPAS) phase III trial in Latin America (Argentina, Colombia and Panama), approximately 24,000 infants received PCV10 or HepB at ages 2, 4 and 6 months with a booster at age 15–18 months.[30] The study showed that the vaccine effectiveness of PCV10 was 100 percent (95% CI: 74.3–100) against pneumococcal vaccine-serotype IPD and 65 percent (95% CI: 11.1–86.2) against any IPD.

A matched case-control study conducted in Brazil found that, following the introduction of PCV10 (as a 3+1 schedule) in 2010, the adjusted effectiveness against vaccine-serotype IPD was 83.8 percent (95% CI: 65.9–92.3) for an age-appropriate PCV10 schedule.[31] The study included 316 cases of IPD and 1,219 neighbourhood age-matched controls. Age-appropriate PCV10 immunisation was up-to-date for 94 (30 percent) cases and 521 (43 percent) of the controls.

Meningitis

A decrease in pneumococcal meningitis morbidity and mortality was observed two years after the introduction of routine PCV10 vaccinations in Brazil in children aged under 2 years, based on data obtained from the Information System on Notifiable Diseases from 2007 to 2012.[32]

Overall, the incidence of pneumococcal meningitis decreased by 50 percent from 3.7 per 100,000 population in 2007 to 1.84 per 100,000 in 2012.[32] Mortality decreased by 69 percent from 1.3 per 100,000 to 0.4 per 100,000.

During the study period, there were 1,311 cases and 430 deaths attributed to laboratory-confirmed pneumococcal meningitis (serotypes not determined).[32] The greatest impact of PCV10 vaccination was seen in the infants aged 6–11 months, with a 73 percent reduction in pneumococcal meningitis incidence (from 7.46 cases per 100,000 in 2007 to 2.02 cases per 100,000 in 2012) and an 85 percent reduction in mortality (from 3.25 deaths per 100,000 in 2007 to 0.49 deaths per 100,000 in 2012).

Pneumonia

The FinIP trial also provided data on the protective effectiveness of PCV10 against hospital-diagnosed pneumonia in Finland. Vaccine effectiveness against all pneumonia episodes was 25.2 percent (95% CI: 2.6–42.6) for the 3+1 PCV10 schedule and 27.6 percent (95% CI: 5.5–44.6) for the 2+1 schedule.[2] A study in children aged under 4 years showed a significant decrease of 12.65 percent ($p<0.001$) in all pneumonia hospitalisations in Brazil when comparing the pre-vaccination (2002–2009) and post-PCV10 vaccination introduction periods (2011–2012).[33] No reduction in non-respiratory-cause hospitalisations were observed for the same time period ($p=0.39$).

Further studies in Brazil have continued to show significant reductions in pneumonia in children aged under 2 years following the introduction of PCV10 to the infant schedule. Active population-based surveillance studies were conducted in Central Brazil (across 17 paediatric hospitals) to investigate pneumonia hospitalisations in children aged under 36 months before and after the introduction of PCV10.[34] The relative rate reduction was 13.1 percent (95% CI: –13.4, –12.9) for clinical and 25.4 percent (95% CI: –26.0, –24.7) for x-ray-confirmed pneumonia in children aged 2–23 months.

Otitis media

A secondary outcome of the COMPAS trial in Latin America was to assess the vaccine effectiveness of PCV10 against clinically confirmed acute otitis media (AOM).[30] At the end of the study, the intent-to-treat analysis found that vaccine effectiveness against AOM was 19.0 percent (95% CI: 4.4–31.4; p=0.007; n=254 vaccinated, 308 controls). When the cause of the AOM was investigated further, vaccine effectiveness was calculated as 55.7 percent (95% CI: 21.5–75.0; n=17 vaccinated, 38 controls) against pneumococcal AOM and 69.9 percent (29.8–87.1; n=7 vaccinated, 23 controls) against vaccine-serotypes. For NTHi confirmed-AOM, vaccine effectiveness was 21.5 percent (95% CI: −43.4, −57.0; n=19 vaccinated, 24 controls).

13-valent pneumococcal conjugate vaccine (PCV13)

Individuals at increased risk of IPD

Few studies have investigated the immunogenicity and effectiveness of PCV13 in individuals at increased risk of IPD. Studies using pneumococcal vaccines with similar but fewer antigens have demonstrated vaccine efficacy in individuals with immunocompromising conditions (eg, HIV, sickle cell disease), but the duration of protection against IPD remains unknown.[35] High IgG titres have been observed following PCV13 vaccination of children with sickle cell disease,[36] HIV infection[37] and nephrotic syndrome.[38]

Oropharyngeal carriage may be a risk factor for IPD in children and adolescents with underlying medical conditions (eg, type 1 diabetes,[39] cancer,[40] cystic fibrosis,[41] asthma[42]). The broader serotype protection provided by PCV13 may be of benefit for these children when oropharyngeal carriage is considered as a risk factor for pneumococcal disease, although booster doses may be necessary.[39]

Use of pneumococcal conjugate vaccines in adults

PCV13 induces robust immune responses in adults,[43, 44, 45, 46] including elderly adults.[47] The antibody titres vary with serotype and between age groups, particularly for those aged over 65 years.[46] However, the clinical significance of this variation was not determined.

There is little data on the effectiveness of pneumococcal conjugate vaccines in adults. A large randomised controlled trial was conducted in the Netherlands to investigate the impact of PCV13 vaccination in reducing vaccine-serotype pneumococcal community-acquired pneumonia (CAP), non-bacteraemic and non-invasive pneumococcal CAP, and IPD in adults aged 65 years and older.[48] PCV13 was effective in preventing vaccine-type pneumococcal CAP (vaccine efficacy 45.6 percent, 95% CI: 21.8–62.5), bacteraemic and non-bacteraemic CAP (vaccine efficacy 45 percent, 95% CI: 14.2–65.3) and vaccine-type IPD (vaccine efficacy 75 percent, 95% CI: 41.4–90.8).

PCV13 is at least as immunogenic as 23PPV in adults. Some studies suggest that 23PPV attenuates the immune response to subsequent doses of PCV13.[47, 49, 50] This attenuation is not seen if PCV13 is given before 23PPV; PCV13 may augment the response to subsequent 23PPV vaccination.[47, 49, 50]

23-valent vaccine pneumococcal polysaccharide (23PPV)

The polysaccharide vaccine (23PPV, Pneumovax 23) is made from the purified capsular polysaccharide antigens of 23 serotypes of *S. pneumoniae*. It is available in New Zealand for adults and children from age 2 years. 23PPV includes the 23 serotypes (see Table 15.1) responsible for about 90 percent or more of cases of invasive disease in high-income countries.

23PPV efficacy

Assessment of the efficacy of pneumococcal vaccination depends on whether immune-competent or immunocompromised patients are studied, and whether the end point is pneumococcal pneumonia or bacteraemia.

The problems with the polysaccharide vaccine have been summarised as:

- reduced efficacy in high-risk individuals
- uncertain efficacy against pneumonia
- only suitable for children aged 2 years and older.

Although it is generally accepted that 23PPV is effective at preventing IPD in immune-competent adults, a 2009 meta-analysis concluded that in trials of high quality, there is no evidence of vaccine protection against IPD and that 23PPV may not be protective against either IPD or pneumonia.[51] A subsequent case-control study in patients aged over 60 years concluded that 23PPV provided a significant protective effect against IPD in elderly immune-competent patients.[52] However, a 2012 review of data from elderly populations concluded that low protection was possible, but differences in study designs prevent definitive conclusions.[53]

15.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.[54] Store at +2°C to +8°C. Do not freeze.

15.4.4 Dosage and administration

The dose of PCV10, PCV13 and 23PPV is 0.5 mL, administered by intramuscular injection (see section 2.2.3). 23PPV can also be administered by subcutaneous injection (see section 2.2.3), but there is an increased likelihood of injection site reactions.[55]

Co-administration with other vaccines

PCV10, PCV13 or 23PPV may be administered at the same time as other routine childhood vaccinations, in a separate syringe at a separate injection site (see section 2.2.7 for information about multiple injections at the same visit). The only exception is PCV13 with the quadrivalent meningococcal conjugate vaccine MCV4-D, which should be given at least four weeks after PCV13. This is because when administered concurrently, there is impairment of the immune response to some of the pneumococcal serotypes.[56, 57]

PCV13 has been associated with increased risk of fever over 39°C and febrile convulsions when co-administered with inactivated influenza vaccine in children aged 6 months to under 5 years. Separation of the vaccines by two days can be offered, but is not essential (see

section 15.6.2). Systemic reactions have been noted in adults aged over 65 years.

Herpes zoster vaccine can be concomitantly delivered with 23PPV (see also section 22.4.4).[58, 59]

15.5 Recommended immunisation schedule

15.5.1 Usual childhood schedule (PCV10)

PCV10 for children aged under 5 years

PCV10 (Synflorix) vaccine is funded for all children aged under 5 years. Three doses of PCV10 are given as the primary course, with a booster at age 15 months (Table 15.2). Children who started their immunisation course with PCV13 can complete it with PCV10.

Table 15.2: Usual childhood PCV10 (Synflorix) schedule

Age	Vaccine	Comment
6 weeks	PCV10	Primary series
3 months	PCV10	Primary series
5 months	PCV10	Primary series
15 months	PCV10	Booster

Where a previously unimmunised child aged under 5 years presents late for pneumococcal vaccination, the age-appropriate catch-up schedules in Appendix 2 should be followed.

15.5.2 PCV13 and 23PPV for eligible individuals

PCV13 and 23PPV are funded for eligible individuals, **as shown in Tables 15.3, 15.4 and 15.5**. Because the recommended schedule depends on the age of the individual at diagnosis, the tables have been organised into age groups (under 5 years, 5–18 years and 18 years and older).

The PCV13 and 23PPV funding restrictions are as follows. See Tables 15.3–15.5 for the eligible conditions.

PCV13

- One dose of PCV13 is funded for high-risk children aged over 17 months and under 18 years who have previously received four doses of PCV10.
- Up to an additional four doses (as appropriate) of PCV13 are funded for (re-)vaccination of high-risk children aged under 5 years.
- Up to an additional four doses (as appropriate) of PCV13 are funded for (re-)vaccination of eligible individuals aged 5 years and older.

23PPV

- Up to three doses (as appropriate) of 23PPV are funded for individuals with eligible conditions.
- Up to two doses of 23PPV are funded for high-risk children aged under 18 years.

See also section 15.5.3 '(Re-)vaccination'. See sections 4.2 and 4.3 for more information about immunocompromised infants, children and adults, including additional vaccine recommendations and schedule tables for certain conditions.

Table 15.3: High-risk children aged under 5 years: funded PCV13 and 23PPV indications and schedules

PCV13 (Prevenar 13) and 23PPV (Pneumovax 23) are funded for children aged under 5 years:

- on immunosuppressive therapy or radiation therapy (vaccinate when there is expected to be a sufficient immune response)
- with primary immune deficiencies
- with HIV infection
- with renal failure or nephrotic syndrome
- who are immune-suppressed following organ transplantation (including HSCT)
- with cochlear implants or intracranial shunts
- with cerebrospinal fluid leaks
- who are receiving corticosteroid therapy for more than 2 weeks, and who are on an equivalent daily dosage of prednisone of 2 mg/kg per day or greater, or children who weigh more than 10 kg on a total daily dosage of 20 mg or greater
- with chronic pulmonary disease (including asthma treated with high-dose corticosteroid therapy)
- who were preterm infants, born before 28 weeks' gestation
- with cardiac disease, with cyanosis or failure
- with diabetes
- with Down syndrome
- who are pre-or post-splenectomy, or with functional asplenia.

Age at diagnosis	Vaccine	Recommended vaccine schedule
<12 months	PCV13	PCV13[a] at ages 6 weeks, 3, 5 and 15 months or age-appropriate catch-up schedule. • If commencing immunisation at ages 7–11 months, give 2 doses of PCV13 at least 4 weeks apart, followed by a booster dose at age 15 months. • For children aged 7–11 months who have completed the primary course with PCV10, give 1 dose of PCV13, followed by the scheduled PCV13 booster at age 15 months.
	23PPV	Following the completion of the PCV course, give 1 dose of 23PPV at age ≥2 years. There must be at least 8 weeks between the last PCV dose and the 23PPV dose. If risk persists, revaccinate once with 23PPV, 5 years after the first 23PPV.

Continued overleaf

Age at diagnosis	Vaccine	Recommended vaccine schedule
12 months to <5 years	PCV13	The PCV13[a,b] age-appropriate catch-up schedule is as follows. • If receiving immunisation for the first time, give 2 doses of PCV13,[b] 8 weeks apart. • Children aged >17 months who have completed the primary course of PCV10 but have not received PCV13, give 1 dose of PCV13.[b,c]
	23PPV	Following the completion of the PCV course, give 1 dose of 23PPV at age ≥2 years. There must be at least 8 weeks between the last PCV dose and the 23PPV dose. If risk persists, revaccinate once with 23PPV, 5 years after the 1st 23PPV.

a PCV13 replaces PCV10 (Synflorix) on the Schedule.

b If 23PPV has already been given (prior to any doses of PCV13) to children aged under 5 years, wait at least 8 weeks before administering PCV13.

c There are no safety concerns, regardless of the interval between the last dose of PCV10 and the 1st dose of PCV13.

Table 15.4: Children aged 5 to under 18 years: funded PCV13 and 23PPV indications and schedules

PCV13 (Prevenar 13) and 23PPV (Pneumovax 23) are funded for children aged 5 to under 18 years:

- with HIV infection
- who are pre- or post-HSCT[a] or chemotherapy[a]
- who are pre- or post-splenectomy or with functional asplenia
- who are pre- or post-solid organ transplant
- undergoing renal dialysis
- with complement deficiency (acquired or inherited)
- with cochlear implants
- with primary immunodeficiency.

For catch-up of high-risk children (see Table 15.3) aged 5 to under 18 years:

- 1 dose of PCV13 is funded for high-risk children who have previously received 4 doses of PCV10
- 2 doses of 23PPV are funded for high-risk children.

Age at diagnosis	Vaccine	Recommended vaccine schedule
5 years to <18 years	PCV13	For children who have not previously received PCV13, give 1 dose of PCV13.[b,c]
	23PPV	1 dose of 23PPV at least 8 weeks after the PCV13 dose. If risk persists, revaccinate once with 23PPV, 5 years after the 1st 23PPV.

a PCV13 is funded pre- or post-HSCT or chemotherapy. 23PPV is only funded post-HSCT or chemotherapy.

b If 23PPV has already been given (prior to any doses of PCV13) to children aged under 18 years, wait at least 8 weeks before administering PCV13.

c There are no safety concerns, regardless of the interval between the last dose of PCV10 and the 1st dose of PCV13.

Table 15.5: Adults aged 18 years and older: funded PCV13 and 23PPV indications and schedules

PCV13 (Prevenar 13) and 23PPV (Pneumovax 23) are funded for (re-)vaccination of patients: • with HIV infection • who are pre- or post-HSCT[a] or chemotherapy[a] • who are pre- or post-splenectomy or with functional asplenia • who are pre- or post-solid organ transplant • undergoing renal dialysis • with complement deficiency (acquired or inherited) • with cochlear implants • with primary immunodeficiency.		
Age at diagnosis	**Vaccine**	**Recommended vaccine schedule**
≥18 years	PCV13	1 dose of PCV13.[b]
	23PPV	Give a maximum of 3 doses of 23PPV in a lifetime, a minimum of 5 years apart. The 1st 23PPV dose is given at least 8 weeks after PCV13, the 2nd a minimum of 5 years later, and the 3rd dose at age ≥65 years.

a PCV13 is funded pre- or post-HSCT or chemotherapy. 23PPV is only funded post-HSCT or chemotherapy.

b If 23PPV has already been given (prior to any doses of PCV13) to adults aged 18 years and older, wait at least 1 year before administering PCV13.

15.5.3 (Re-)vaccination

Up to an additional four doses (as appropriate) of PCV13 are funded for (re-)vaccination of high-risk children aged under 5 years (see Table 15.3) and for (re-)vaccination of children and adults aged 5 years and older:

- with HIV
- who are pre- or post-HSCT or chemotherapy
- who are pre- or post-splenectomy, or with functional asplenia
- who are pre- or post-solid organ transplant
- undergoing renal dialysis
- with complement deficiency (acquired or inherited)
- with cochlear implants
- with primary immune deficiency.

See also sections 4.2 and 4.3.

15.5.4 Recommended but not funded

Two classifications of IPD risk are often identified in the literature: 'high-risk' conditions for which there is significant risk of IPD and 'at-risk' conditions, which on their own may not significantly increase risk, but when combined together or with lifestyle risk factors can increase an individual's risk of IPD. This is described as 'risk stacking' – the risk of IPD substantially increases with the accumulation of concurrent at-risk conditions.[60] The risk of pneumococcal infections in those with two or more at-risk conditions may be as high as the risk for those with a recognised high-risk condition.[61, 62, 63] Therefore, it is not always clear who may benefit from pneumococcal vaccination – the following are some considerations.

Recommendations

PCV13 and 23PPV are recommended but not funded for the following individuals:

- immune-competent adults (aged 18 years and older) at increased risk of pneumococcal disease or its complications because of chronic illness (eg, chronic heart, renal, liver or pulmonary disease, diabetes or alcoholism)
- adults with cerebrospinal fluid leak
- immunocompromised adults at increased risk of pneumococcal disease (eg, those with nephrotic syndrome, multiple myeloma, lymphoma and Hodgkin's disease)
- individuals of any age who have had one episode of IPD
- smokers.

For those individuals who choose to purchase PCV13 and 23PPV vaccines, providers may follow the age-appropriate schedules in Tables 15.4 and 15.5.

Adults aged 65 years and older with no other risk factors

Give one dose of PCV13 followed at least eight weeks later with 23PPV (not funded).

15.5.5 Pregnancy and breastfeeding

Pneumococcal vaccines are not routinely recommended for pregnant women.

Women of child-bearing age who are eligible for funded PCV13 and 23PPV should be vaccinated before a planned pregnancy or as soon as possible after delivery (see Table 15.5). Administration of these vaccines in pregnancy is unlikely to result in serious adverse effects and may be considered in individuals at the highest increased risk of IPD who were not vaccinated prior to pregnancy but require vaccination prior to delivery.[64]

PCV13 and 23PPV may be given to breastfeeding women.[64]

15.6 Contraindications and precautions

See section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

15.6.1 Contraindications

There are no specific contraindications to pneumococcal polysaccharide or conjugate vaccines apart from a severe reaction to a previous dose or known hypersensitivity to any components of either vaccine.

15.6.2 Precautions

- Systemic reactions (chills, rash and myalgia) may occur when PCV13 and influenza vaccine are administered at the same time. PCV13 has been associated with a slightly higher risk of fever over 39°C and febrile convulsions when co-administered with inactivated influenza vaccine in infants and young children, compared to when administered separately.[65] Febrile convulsion history is not a contraindication to PCV13 immunisation. If indicated, PCV13 and influenza vaccines may be given to a child aged under 5 years at the same visit.[64] Parents/guardians should be informed of the small risk of febrile convulsions and separation of vaccines by two days can be offered. If the child has a history of febrile convulsions, separation of the vaccines is recommended.

- 23PPV should not be given to children aged under 2 years due to the reduced immune response associated with polysaccharide vaccines (see section 1.4.3).

15.7 Expected responses and AEFIs

15.7.1 Pneumococcal conjugate vaccines

Pneumococcal conjugate vaccines have excellent safety profiles. A 2016 systematic review found that pneumococcal conjugate vaccines are considered safe for use in children, and serious adverse events are very rarely detected by post-marketing surveillance.[66]

PCV10

Pooled evaluation of data derived from several clinical trials found PCV10 to be very well tolerated and safe with a similar safety profile to other PCVs.[66] After primary immunisation of infants, mild to moderate irritability and injection site redness were most commonly reported, occurring after 55 percent and 41 percent of all doses, respectively. Fever occurred in 30–35 percent of children, regardless of the dose. Injection site pain increased with age, reported by more than 39 percent of younger children and 58 percent of the older subjects. Severe adverse events were exceptionally rare.

When PCV10 was co-administered with DTaP-containing vaccines, fever of 38°C or higher was reported after about one-third of primary or booster vaccine doses.[67] Similar results were seen following co-administration of PCV7 and DTaP-containing vaccines.[67]

PCV13

The most commonly reported adverse reactions are injection-site reactions, fever, irritability, decreased appetite, and increased and/or decreased sleep.[68] An increase in injection site reactions was reported in children older than 12 months compared to rates observed in infants during the primary series with PCV13.

No serious adverse events have been identified for adults, children or associated with underlying disease and immunocompromise.[69, 70, 71]

15.7.2 Pneumococcal polysaccharide vaccine

Local discomfort, erythema and induration lasting a couple of days are expected responses.[72] Local and systemic reactions may occur after revaccination of adults, particularly when the second dose is given within five years of the first dose.[64]

15.8 Public health measures

IPD is a notifiable condition, and if confirmed, the laboratory undertaking the testing must notify the local medical officer of health.

Local public health action is not expected in response to individual notifications of this disease.

Antimicrobial prophylaxis is not indicated for close contacts of cases of IPD. For those at high risk of pneumococcal disease where response to vaccination may be poor, antimicrobial prophylaxis may be indicated. Discuss with an appropriate specialist.

For more details on control measures, refer to the 'Invasive pneumococcal disease' chapter of the *Communicable Disease Control Manual 2012*.[73]

15.9 Variations from the vaccine data sheets

The PCV10 (Synflorix) vaccine data sheet recommends that infants and children who receive a first dose of PCV10 complete the full vaccination course with PCV10. The Ministry of Health recommends that those who started with PCV10 may complete with PCV13 if they are subsequently diagnosed with a PCV13-eligible condition (see section 15.5).

The PCV13 (Prevenar 13) data sheet states that there is no data on the interchangeability of PCV13 with other pneumococcal conjugate vaccines containing a protein carrier different from CRM197. The Ministry of Health recommends that those who started with PCV13 may complete with PCV10 (see section 15.5).

The 23PPV (Pneumovax 23) data sheet states that 23PPV and the herpes zoster vaccine (Zostavax) should not be given concurrently. The Ministry of Health recommends that 23PPV and the herpes zoster vaccine may be given concurrently (see section 22.4.4).[58, 59]

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16 Poliomyelitis

Key information

Mode of transmission	Faecal–oral route or by ingestion of pharyngeal secretions.
Incubation period	Paralytic disease usually 7–14 days, with a reported range of 3–35 days.
Period of communicability	Most infectious in the days immediately before and after the onset of any symptoms. Transmission is possible as long as the virus is shed (can be years in immunocompromised individuals).
Global burden of disease	Endemic in Afghanistan, Nigeria and Pakistan. Outbreaks are still frequent.
Funded vaccines	As inactivated polio vaccine (IPV), in combination with other antigens, or on its own: • DTaP-IPV-HepB/Hib (Infanrix-hexa) • DTaP-IPV (Infanrix-IPV) • IPV (IPOL).
Dose, presentation, route	All 0.5 mL per dose. DTaP-IPV-HepB/Hib: pre-filled syringe and glass vial, the vaccine must be reconstituted prior to intramuscular injection. DTaP-IPV: pre-filled syringe, intramuscular injection IPV: pre-filled syringe, subcutaneous injection
Funded vaccine indications and schedule	Usual childhood schedule: • at age 6 weeks, 3 months and 5 months: DTaP-IPV-HepB/Hib (primary series) • at age 4 years: DTaP-IPV (booster). For non-immune adults, 3 doses of IPV 8 weeks apart (may be shortened to 4-week intervals). For (re-)vaccination of eligible patients: DTaP-IPV-HepB/Hib, DTaP-IPV or IPV.
Vaccine efficacy/ effectiveness	Greater than 90 percent.
Precautions	Non-immune pregnant women may be immunised if they are travelling to a region where polio is endemic.

16.1 Virology

Poliomyelitis (polio) is a highly transmissible infectious disease caused by poliovirus, a small, non-enveloped enterovirus of the family Picornaviridae. There are three serotypes of poliovirus (types 1, 2 and 3), with type 2 now eliminated.

16.2 Clinical features

Poliovirus is transmitted by the faecal–oral route or by ingestion of pharyngeal secretions. The incubation period for poliomyelitis is commonly 7 to 14 days for paralytic disease, with a reported range of 3 to 35 days. The risk of transmission of infection is greatest shortly before to shortly after the onset of symptoms. The virus persists in the pharynx for approximately one week, and in the faeces for three to six weeks or longer, particularly in immunocompromised individuals, where cases have been reported shedding for many years.

The virus is highly neurotropic and its primary effect occurs in the neurones of the spinal anterior horn or the motor ganglia of the brain stem. Infection is clinically inapparent in up to 95 percent of infections, and ranges in severity from a non-paralytic fever to viral meningitis and flaccid paralysis.

Symptoms include fever, headache, gastrointestinal disturbances, malaise, stiffness of the neck and back, and pain in the limbs, back and neck, with or without paralysis. In children who develop paralysis, the illness may be biphasic, the initial phase of one to three days' duration being indistinguishable from that of other viral infections. The patient appears to recover, only to be struck down abruptly two to five days later with meningism, followed by paralysis. In adults and adolescents the illness usually presents with a gradual onset of paralysis and pain without the early symptoms.

Asymptomatic people with the infection will shed the virus in their stool and may spread the infection to others. Infection rates may be as high as 100 percent in households where there are non-immune young children, although paralysis may occur in only 0.1–2 percent of infected individuals. Paralysis is more common in adults, occurring in up to 1 in 75 cases of infection.

Case fatalities from paralytic polio vary from 2–5 percent among children and up to 15–30 percent for adults, increasing to 25–75 percent with bulbar involvement.

The post-polio syndrome may occur some 30 to 40 years after poliomyelitis. The cause is not known, but is probably related to the ageing or death of nerves and muscles that were compensating for the original damage. Patients experience muscle pain and exacerbation of existing muscle weakness. The risk of developing post-polio syndrome is greater in women than in men, and the risk increases with time from the episode of acute polio.

16.3 Epidemiology

16.3.1 Global burden of disease

In the pre-vaccination era, cases of poliomyelitis occurred sporadically and in epidemics in high-income countries in temperate zones. In tropical countries, where the virus still circulates, there is no seasonal pattern.

Classically, poliomyelitis is a disease of young children and adolescents. However, with improvements in living standards, a greater number of cases have occurred in older individuals, with an associated higher frequency of paralytic disease. Paralytic disease is a particular risk in early adult life. In countries where polio was endemic, most children acquired antibodies to all three subtypes by age 5 years and most paralytic disease occurred in children aged under 3 years.

The resurgence of polio in some countries occurred because of the introduction of wild-type polio virus into poorly immunised populations.

Polio remains endemic in Afghanistan, Nigeria and Pakistan, and other countries are vulnerable to international spread. For up-to-date surveillance information, see the 'Polio Now' section of the Global Polio Eradication Initiative website (polioeradication.org/polio-today/polio-now).

The Polio Eradication & Endgame Strategic Plan 2013–2018[1] was developed by the Global Polio Eradication Initiative. Its goal is 'the complete eradication and containment of all wild, vaccine-related and Sabin polioviruses' by 2018. The Americas were certified polio-free in 1994. The Western Pacific, which includes New Zealand, was the second region to be certified polio-free, in October 2000, with no indigenous polio cases reported since March 1997. Vaccination against polio will continue worldwide until the disease has been eradicated.

Vaccine-associated paralytic poliomyelitis (VAPP) with oral polio vaccine (OPV)

After receiving OPV, most infants excrete the polio vaccine virus for about six weeks. Close contacts may acquire then excrete the virus in faeces. There is a small risk that the vaccine virus may revert to neurovirulence and cause VAPP in a vaccine recipient or non-immune contact. VAPP presents with acute flaccid paralysis (AFP) 7 to 30 days after vaccination in the recipient, and from 7 to 60 days in the contact of a vaccine recipient. The immunocompromised are at greater risk of VAPP, either as vaccine recipients or contacts. In New Zealand VAPP can only occur from contact with people vaccinated in countries still using OPV.

Once wild virus became uncommon, the risk of VAPP became higher than the risk of imported wild virus disease. This led New Zealand to change from OPV to IPV in 2002 to eliminate the risk of VAPP (see Appendix 1). The last case of VAPP in New Zealand occurred in 1999.[2]

16.3.2 New Zealand epidemiology

Since 1962 only six polio cases have been reported. Four of these cases were laboratory confirmed as VAPP and two were classified as probable VAPP.

The New Zealand Paediatric Surveillance Unit carries out active surveillance of AFP. In 2015 there were seven notifications: all were reviewed by the New Zealand National Certification Committee for the Eradication of Polio and all were classified as non-polio.[3]

The risk of importing wild-type or neurovirulent oral vaccine-derived strains means that maintaining high IPV coverage in New Zealand is essential.

16.4 Vaccines

New Zealand switched from OPV to IPV in 2002 (see Appendix 1).

16.4.1 Available vaccines

Funded polio vaccines

The polio-containing vaccines funded as part of the Schedule are:

- DTaP-IPV-HepB/Hib (Infanrix-hexa, GSK): diphtheria, tetanus, acellular pertussis, inactivated polio, hepatitis B and *Haemophilus influenzae* type b vaccine (see section 5.4.1 for more information)
- DTaP-IPV (Infanrix-IPV, GSK): diphtheria, tetanus, acellular pertussis and inactivated polio vaccine (see section 5.4.1 for more information)
- IPV (IPOL, Sanofi): contains three strains of poliovirus (40D antigen units of the Mahoney, 8D antigen units of the MEF-1, and 32D antigen units of the Saukett strains), inactivated by formaldehyde and containing phenoxyethanol as a preservative; trace amounts of neomycin, streptomycin, polymyxin B, polysorbate 80 and bovine serum albumin may be present.

Other vaccine

Another polio-containing vaccine registered (approved for use) and available (marketed) in New Zealand is:

- Tdap-IPV: Adacel Polio (Sanofi).

16.4.2 Efficacy and effectiveness

See also section 14.4.2 for information about DTaP-IPV-HepB/Hib vaccine.

Immunogenicity and efficacy

Virtually all infants (99–100 percent) will seroconvert against all three strains after three doses of IPV vaccine, and more than 95 percent will seroconvert after two doses.[4] The efficacy of IPV is greater than 90 percent[5] and immunity is expected to be long lasting.[4] Although antibody may decline over time in some individuals, there is no evidence that this leads to increased susceptibility to poliomyelitis.[6]

The combined IPV-containing vaccines induce immune responses against polioviruses superior to IPV stand-alone vaccines. This is due to the effect of the aluminium adjuvant present in these combination vaccines.[5]

16.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.[7] Store at +2°C to +8°C. Do not freeze.

DTaP-IPV-HepB/Hib vaccine should be stored in the dark.

DTaP-IPV-HepB/Hib (Infanrix-hexa) must be reconstituted by adding the entire contents of the supplied container of the DTaP-IPV-HepB vaccine to the vial containing the Hib pellet. After adding the vaccine to the pellet, the mixture should be shaken until the pellet is completely dissolved. Use the reconstituted vaccine as soon as possible. If storage is necessary, the reconstituted vaccine may be kept for up to eight hours at 21°C.

16.4.4 Dosage and administration

The dose of DTaP-IPV-HepB/Hib (Infanrix-hexa) and DTaP-IPV (Infanrix-IPV) is 0.5 mL, administered by intramuscular injection (see section 2.2.3).

The dose of IPV (IPOL) is 0.5 mL, administered by subcutaneous injection (see section 2.2.3).

Co-administration with other vaccines

DTaP-IPV-HepB/Hib, DTaP-IPV and IPV may be given at the same time as inactivated or live attenuated vaccines, at separate sites and in separate syringes.

16.5 Recommended immunisation schedule

Table 16.1: Immunisation schedule for IPV-containing vaccines (excluding catch-up)

Age	Vaccine	Comment
6 weeks	DTaP-IPV-HepB/Hib	Primary series
3 months	DTaP-IPV-HepB/Hib	Primary series
5 months	DTaP-IPV-HepB/Hib	Primary series
4 years	DTaP-IPV	Booster

16.5.1 Usual childhood schedule

A primary course of poliomyelitis vaccine is given as DTaP-IPV-HepB/Hib at ages 6 weeks, 3 months and 5 months, followed by a booster dose given as DTaP-IPV at age 4 years.

16.5.2 Unimmunised adults and children

For partially immunised or previously unimmunised individuals, a primary immunisation course consists of three doses of IPV-containing vaccine (funded). The recommended interval is eight weeks between doses, but the minimum interval can be as short as four weeks for catch-up of children or adults[8] (see Appendix 2).

If a course of vaccine is interrupted, it may be resumed without repeating prior doses. A booster may be given if 10 years have elapsed since the last dose and exposure is possible (eg, in the case of a traveller to an area where the virus circulates; this is not funded).

If a child who began a course of OPV in another country moves to New Zealand, they can switch to IPV to complete the final doses.

Note: All immunocompromised individuals and their household contacts may receive IPV. OPV was contraindicated in the immunocompromised because of the risk of VAPP (see section 16.3.1). There is no risk of VAPP with IPV.

16.5.3 Pregnancy and breastfeeding

No adverse effects on the fetus have been reported following administration of IPV during pregnancy, but immunisation should not be carried out during the first or second trimester unless there are compelling reasons to do so, such as planned travel to an endemic area. However, bear in mind that pregnant women are particularly susceptible to paralytic polio.

If a previously unvaccinated pregnant woman is travelling to a country where polio is occurring, two doses should be administered four weeks apart prior to departure. If departure cannot be delayed to allow a four-week gap, give two doses at the maximum possible interval, though protection cannot be guaranteed. If the available interval is less than two weeks, a single dose is recommended, with further doses given on arrival where possible.

IPV may be given to breastfeeding women.

16.5.4 (Re-)vaccination

Polio-containing vaccines are funded for (re-)vaccination of eligible patients, as follows. See also sections 4.2 and 4.3.

DTaP-IPV-HepB/Hib (Infanrix-hexa) and DTaP-IPV (Infanrix-IPV)

An additional four doses (as appropriate) of DTaP-IPV-HepB/Hib (for children aged under 10 years) or DTaP-IPV are funded for (re-)vaccination of patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant

- undergoing renal dialysis
- with other severely immunosuppressive regimens.

Up to five doses of DTaP-IPV-HepB/Hib (for children aged under 10 years) or DTaP-IPV are funded for children requiring solid organ transplantation.

IPV (IPOL)

IPV is funded for patients following immunosuppression.

16.5.5 Recommendations for other groups

Booster doses of IPV are recommended (but not funded) for:

- travellers to areas or countries where poliomyelitis remains endemic (see section 16.3.1); a booster of IPV is recommended for these individuals if more than 10 years have elapsed since their last dose (where there is uncertainty about previous immunisation, a full course of IPV is recommended)
- health care workers in direct contact with a case of poliomyelitis
- individuals at particular risk of exposure (eg, laboratory workers routinely handling faecal specimens from persons recently arriving from high-risk countries, which may contain wild or vaccine-derived polioviruses); a booster dose of IPV is recommended every 10 years.

There is no evidence for the need for routine boosters, but they are recommended to reduce any possible risk from waning immunity in situations of increased risk of exposure.

16.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

16.6.1 Contraindications

IPV-containing vaccines are contraindicated if there is a history of an anaphylactic reaction to a previous dose or to any of the vaccine components.

See also section 14.6 for information about DTaP-IPV-HepB/Hib vaccine.

16.6.2 Precautions

Pregnancy is a precaution for IPV-containing vaccines. See section 16.5.3.

16.7 Expected responses and AEFIs

See also section 14.7 for information about DTaP-IPV-HepB/Hib and DTaP-IPV vaccines.

16.7.1 Expected responses

A small proportion of individuals experience mild local symptoms following IPV. Injection site erythema is seen in 1–2 percent of infants, induration in 3–11 percent and pain in 14–29 percent. Similar local reactions are seen with combination vaccines.[5] There is no poliovirus excretion following IPV.

16.7.2 AEFIs

In safety studies of IPV with combined vaccines, symptoms of irritability (14–37 percent), sleepiness (2–23 percent), diarrhoea (2–9 percent), vomiting (1–8 percent) and fever over 39°C (1–3 percent) have been reported after primary immunisation of infants (see the manufacturer's data sheet for IPOL).

Serious adverse events are very rare following administration of the IPV currently manufactured.[4]

16.8 Public health measures

It is a legal requirement that all suspected cases of poliomyelitis be notified immediately on suspicion to the local medical officer of health.

Collect two faecal specimens 24 hours apart, 0 to 14 days after the onset of paralysis and send to the national poliovirus reference laboratory at ESR.

Contact the polio reference laboratory for specific advice on the specimens required, and on packing and transporting the specimens (see also the 'Single human source specimen form', available on the ESR website: www.esr.cri.nz/our-services/testing/test-request-forms/).

Cases of AFP must be investigated as suspected poliomyelitis. All clinicians caring for any person aged under 15 years with AFP must notify the case to the local medical officer of health and report the case to the New Zealand Paediatric Surveillance Unit. If in a hospital, all cases of AFP should also be discussed with a local microbiologist and infection control service.

Case investigation and surveillance for AFP will continue in New Zealand to monitor the successful eradication of polio.[9] The New Zealand Paediatric Surveillance Unit is based at the University of Otago and is responsible for sending case investigation and follow-up forms to clinicians to continue to monitor that New Zealand has eradicated polio and to provide information to the WHO.

Any case of poliomyelitis in New Zealand constitutes a Public Health Emergency of International Concern, and the Director of Public Health at the Ministry of Health should be contacted urgently. The *National Poliomyelitis Response Plan for New Zealand*[9] outlines the actual response and is published on the Ministry of Health website (www.health.govt.nz).

Although polio has been eradicated in the WHO Western Pacific Region, New Zealand will need to continue with high levels of IPV coverage. This is because of the small risk that polio may be imported from another region where polio remains endemic (see section 16.3.1).

For more details on control measures, refer to the 'Poliomyelitis' chapter of the *Communicable Disease Control Manual 2012*.[10]

16.9 Variations from the vaccine data sheets

See section 14.9 for variations from the DTaP-IPV-HepB/Hib (Infanrix-hexa) and DTaP-IPV (Infanrix-IPV) data sheets.

The IPV (IPOL) data sheet recommends three doses of vaccine administered at eight-week intervals. The Ministry of Health recommends that this schedule may be shortened to four-week intervals for catch-up[8] (see Appendix 2).

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17 Rotavirus

Key information

Mode of transmission	Faecal–oral route through close personal contact and fomites.
Incubation period	1–3 days.
Period of communicability	During symptoms and until approximately 8 days after onset of symptoms. Up to 30 days after onset of symptoms in immunocompromised patients.
Burden of disease	All children during infancy or early childhood. Severe disease occurs most often in children aged 3 months to 2 years.
Funded vaccine	RV1 (Rotarix), a live attenuated, orally administered, monovalent vaccine.
Dose, presentation, route	1.5 mL per dose. Oral suspension in an oral applicator Administered orally.
Funded vaccine indications and schedule	2 doses for infants, at ages 6 weeks and 3 months. For catch-up schedules, the 1st dose should be given before age 15 weeks (latest is 14 weeks and 6 days), and the 2nd dose should be given before age 25 weeks (latest is 24 weeks and 6 days).
Vaccine efficacy/ effectiveness	Highly effective against severe rotavirus diarrhoea; some evidence for efficacy against all-cause diarrhoea and herd protection.
Contraindications	Previous intussusception and with conditions that predispose the infant to intussusception. Severe combined immune deficiency.
Precautions	Infants living in households with immunocompromised persons or pregnant women should still be vaccinated. Hand washing and the careful disposal of soiled nappies are likely to minimise any risk of vaccine transmission to household contacts. Immunosuppressed infants including those on immunosuppressive therapy (other than SCID, where it is contraindicated). Infants born to mothers on immunosuppressive therapies (eg, DMARDs) (see section 17.6.2).
Adverse events to vaccine	Potentially a very small risk for intussusception; the benefits of immunisation considerably outweigh this potential risk.

17.1 Virology

The rotaviruses are segmented, double-stranded RNA viruses of the family Reoviridae.[1] They are classified according to two surface proteins on the outer capsid: VP4 protease cleaved 'P' protein and VP7, the 'G' glycoprotein, which allows a binary classification system. The G and P proteins are immunological targets for neutralising antibodies protecting against disease and re-infection.[2] While more than 60 G and P combinations have been found in humans, there are only five strains (P[8]G1, P[4]G2, P[8]G3, P[8]G4, and P[8]G9) that are associated with 80–90 percent of the global burden of disease in children.[3] For simplicity, these strains are commonly referred to by their G serotype as G1, G2, G3, G4 and G9.

17.2 Clinical features

Rotavirus infects almost all children during infancy or early childhood. Transmission occurs through the faecal–oral route through close personal contact and through fomites. Aerosol transmission has been hypothesised but remains unproven.[1]

The incubation period is one to three days, after which illness can begin abruptly, with fever and vomiting often preceding the onset of diarrhoea.[1, 4] Up to one-third of children will develop a fever of greater than 39°C.[5, 6] The illness lasts from three to eight days.

Children with rotavirus are infectious while they have symptoms and until approximately eight days after the onset of symptoms. Immunocompromised patients may be infectious for up to 30 days after the onset of symptoms.[7] Large quantities of rotavirus are shed in the stool, and only a few virions are required to cause infection in a susceptible host.[8]

Rotavirus infection in the first three months of life is frequently mild or asymptomatic. This is possibly due to passive protection from maternally acquired antibodies, being breastfed and the intestinal cell structure of newborn infants.[1, 9]

The burden of severe dehydrating gastroenteritis caused by rotavirus occurs predominantly in infants and children aged 3 months to 2 years.[3]

The clinical spectrum ranges from asymptomatic infection to an acute severe illness with frequent and large-volume diarrhoea and vomiting, leading to dehydration, electrolyte disturbance and their sequelae. The illness spectrum from rotavirus is more severe than from other common causes of diarrhoea in children.[1]

17.3 Epidemiology

17.3.1 Global burden of disease

Rotavirus gastroenteritis is a significant cause of infant diarrhoea worldwide, both in high- and low-income countries. Virtually all children are infected by age 5 years.[1] Each year rotavirus causes the death of approximately 200,000 to 450,000 children aged under 5 years worldwide[10, 11] and results in 2.4 million paediatric hospital admissions.[12] Virtually all of the deaths occur in low-income countries. Prior to the introduction of licensed rotavirus vaccines in high-income countries, more than 220,000 children were hospitalised with rotavirus gastroenteritis every year.[13, 14]

Rates of rotavirus illness in children before the introduction of vaccine were similar in high- and low-income countries, indicating that good hygiene and clean water supplies are unlikely to have a significant impact on disease prevention. As a result, immunisation is the primary public health measure for the reduction of rotavirus disease burden.[1]

In countries with a temperate climate, rotavirus epidemics occur every winter and spring. Factors associated with an increased risk of severe rotavirus gastroenteritis include age under 2 years, low birthweight, premature gestation, lack of breastfeeding, socioeconomic disadvantage, malnutrition and impaired immunity.[1, 15, 16, 17, 18] Rotavirus gastroenteritis is not, however, more severe in HIV-infected children, although viral shedding may be longer.[3]

Rotavirus is an important cause of hospital-acquired infection[19] and can also cause disease in adults, especially those caring for children[20] and those living in aged-care facilities. During outbreaks in early childhood settings, rotavirus has been isolated from telephone receivers, drinking fountains, water-play tables and toilet handles.[21] Outbreaks in elderly populations may be linked to waning immunity, institutional crowding or both.

Children and adults can be infected with rotavirus several times in their lives. After a single natural infection during infancy, approximately one-third are protected against subsequent rotavirus infection, more than three-quarters are protected against subsequent rotavirus gastroenteritis and 85–90 percent against severe rotavirus gastroenteritis.[22] The proportion with protection against both infection and symptomatic rotavirus gastroenteritis increases with successive episodes.[22]

These observations serve as the biological basis for rotavirus vaccines, whereby live attenuated strains are capable of inducing cumulative protective immunity similar to that following natural infection by wild-type rotaviruses. Although the immune mechanism and correlates of protection against rotavirus infection are incompletely understood, it is likely that both mucosal and serum antibodies are associated with protection against rotavirus infection and disease.[23]

Since the introduction of the vaccine in other high-income countries, there have been reductions in all-cause and rotavirus gastroenteritis in age groups not eligible for the vaccine, suggesting herd immunity effects as a result of rotavirus vaccines[24, 25, 26] (see 'Herd immunity in the post-licensure period' in section 17.4.2).

17.3.2 New Zealand epidemiology

Rotavirus vaccine was introduced in July 2014, as a three-dose schedule to infants at ages 6 weeks, 3 months and 5 months, using the RV5 vaccine (RotaTeq) (see Appendix 1).

At present rotavirus is not a notifiable disease, so there is no national surveillance data available. National hospital discharge rates, community and hospital laboratory data plus a sentinel hospital based surveillance system have been used to monitor rotavirus disease since vaccine introduction. The sentinel hospital-based rotavirus surveillance was introduced in December 2014 at Kidz First Children's Hospital in Counties Manukau DHB and extended to Wellington, Hutt and Christchurch hospitals in April 2016.

For detailed information about rotavirus surveillance and rotavirus infections in New Zealand, see the ESR website (https://surv.esr.cri.nz/surveillance/Rotavirus.php).

Pre-vaccine epidemiology

Prior to the introduction of vaccine, by the age of 5 years, it is estimated 1 in 5 children had sought medical advice for rotavirus gastroenteritis and 1 in 43 children had been hospitalised.[13]

From 2010 to 2014, the average annual national hospitalisation rate for rotavirus in children aged under 5 years was 215.4 per 100,000.[27] The highest hospitalisation rates for children aged under 5 years were in those from the Middle Eastern/Latin American/African ethnic group, followed by Pacific and Māori ethnic groups. Hospitalisation rates in children aged under 5 years who reside in the most deprived NZDep2013 quintiles (quintiles 4 and 5) were significantly higher than those who reside in the least deprived quintile. There is a seasonal peak for rotavirus hospitalisations, usually occurring around September each year.

Post-vaccine epidemiology

The introduction of rotavirus vaccination in Australia resulted in a 70 percent decrease in rotavirus hospitalisations in the two and a half years post-vaccine introduction.[28]

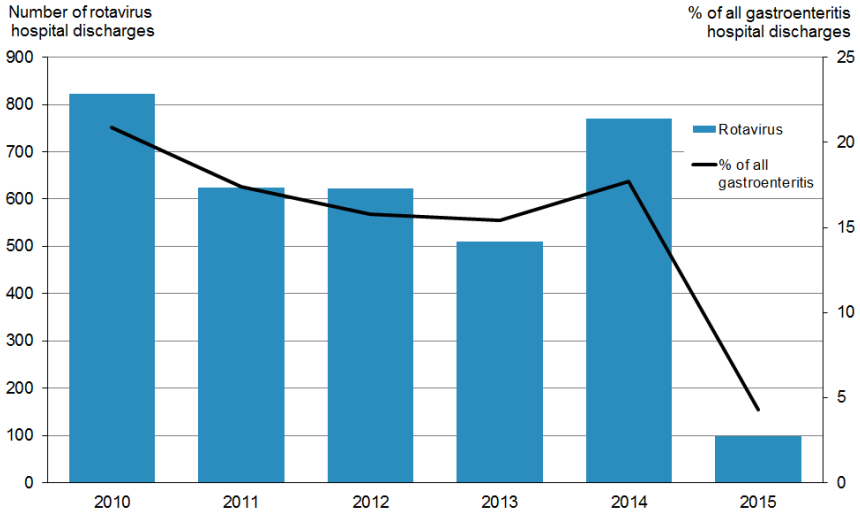
A similar decline has been noted in New Zealand in the first year post-vaccine introduction, where rotavirus hospitalisation rates for children aged under 5 years declined by 85 percent in 2015 compared with the previous five-year average (2010–2014)[27] (Figure 17.1). The vaccine has been effective in decreasing the most severe rotavirus disease. Hospitalisation rates decreased for all ethnic groups and levels of socioeconomic deprivation. Community laboratory data also supports the large decrease in rotavirus infections in the community.

Although only children aged under 1 year were eligible for rotavirus vaccination, hospital discharge rates decreased in all children aged under 5 years in 2015[27] (Figure 17.2). Older children are more likely to have been exposed to rotavirus already, and are less likely to benefit from vaccination.

Hospital discharges for rotavirus ranged from 510 to 822 cases per year in the four years prior to vaccine introduction (2010–2013).[27] There were 99 hospital discharges for rotavirus in children aged under 5 years in New Zealand in 2015, compared with 770 in 2014.

There was a 93.6 percent decrease in rotavirus outbreaks (3 outbreaks reported in 2015 compared with 47 in 2014) after the introduction of vaccine in New Zealand.[27] This demonstrates that universal rotavirus vaccination is an effective public health intervention.

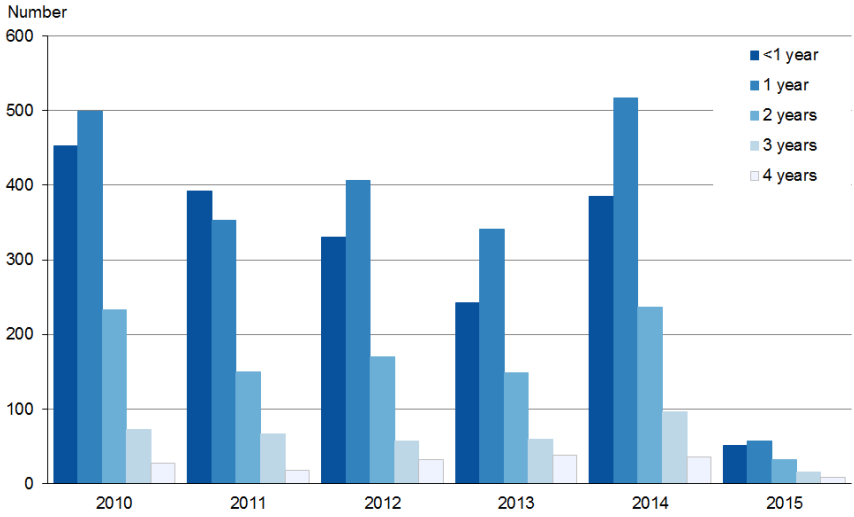
Figure 17.1: Rotavirus hospital discharges and as a percentage of all gastroenteritis discharges for children aged under 5 years, all New Zealand, 2010–2015



Note: Rotavirus vaccine was introduced in July 2014.

Source: ESR

Figure 17.2: Rotavirus hospital discharge rates for children aged under 5 years by age and year, all New Zealand, 2010–2015



Source: ESR

17.4 Vaccines

17.4.1 Available vaccines

The types of virus assessed for use as rotavirus vaccines have included live attenuated virus, both human and animal strains of the virus, and human–animal reassortant viruses. Two rotavirus vaccines have been used in New Zealand. Both are orally administered live attenuated vaccines and have been extensively evaluated.[29, 30] The live attenuated vaccine viruses replicate in the intestinal mucosa and are shed in the stools of vaccine recipients.[29, 31, 32]

Funded vaccine

RV1 (Rotarix, GSK) is a live attenuated monovalent human G1P1A[8] strain rotavirus vaccine. It protects against non-G1 serotypes (these include G2P[4], G3P[8], G8P[4], G9P[8] and G12P[6]) on the basis of other shared epitopes. Each 1.5 mL dose contains:

- at least 10^6 $CCID_{50}$ (cell culture infective dose 50 percent) of the RIX 4414 strain of human rotavirus
- other components and residuals, including sucrose, disodium adipate and culture medium.

Other vaccine

RV5 (RotaTeq, MSD) was the funded vaccine prior to the 1 July 2017 Schedule change. RV5 is a live attenuated pentavalent bovine–human reassortant vaccine representing the common viral protein types G1–4 and P1A[8], and the bovine serotypes G6 and P7. Each 2.0 mL dose contains at least 2.0×10^6 infectious units per dose, depending on serotype. Other components and residuals include sucrose, sodium citrate, sodium phosphate monobasic monohydrate, sodium hydroxide, polysorbate 80 and culture medium. There are no preservatives or thiomersal.

17.4.2 Efficacy and effectiveness

Prevention of disease

A 2012 Cochrane review[33] of the efficacy of rotavirus vaccines for the prevention of rotavirus diarrhoea assessed 41 trials which met the inclusion criteria, involving 186,263 enrolled participants. Of these, 29 trials assessed the monovalent vaccine (RV1; Rotarix) and 12 trials assessed the pentavalent vaccine (RV5; RotaTeq).

For the first two years of life in countries with low mortality rates, both vaccines prevented over 80 percent of cases of severe rotavirus diarrhoea (Table 17.1). Both vaccines have an effect on severe all-cause diarrhoea (moderate to low quality of evidence). See also Figures 17.1 and 17.2 above, which show a reduction in rotavirus hospitalisations in

New Zealand children aged under 5 years after rotavirus vaccine was introduced in 2014.

Table 17.1: Cochrane review: percentage of severe rotavirus and all-cause diarrhoea cases prevented in children by RV1 and RV5, compared to placebo (low mortality rate countries)

Vaccine	Percentage of cases prevented	Risk ratio (95% confidence interval)	Number of participants (number of trials)	Quality of evidence
Severe rotavirus diarrhoea: infants aged under 1 year				
RV1	86	0.14 (0.07–0.26)	40,631 (6)	High
RV5	87	0.13 (0.04–0.45)	2,344 (3)	Moderate
Severe rotavirus diarrhoea: children aged under 2 years				
RV1	85	0.15 (0.12–0.2)	32,854 (8)	High
RV5	82	0.18 (0.07–0.5)	3,190 (3)	Moderate
Severe all-cause diarrhoea: infants aged under 1 year				
RV1	40	0.60 (0.5–0.72)	17,867 (1)	Moderate
RV5	72	0.28 (0.16–0.48)	1,029 (1)	Low
Severe all-cause diarrhoea: children aged under 2 years				
RV1	37	0.63 (0.56–0.71)	39,091 (2)	Moderate
RV5	96	0.04 (0.00–0.70)	5,916 (1)	Low

Adapted from: Soares-Weiser K, MacLehose H, Bergman H, et al. Vaccines for preventing rotavirus diarrhoea: Vaccines in use. *Cochrane Database of Systematic Reviews* 2012, Issue 11, Art. No. CD008521. DOI: 10.1002/14651858.CD008521.pub3 (accessed 12 August 2013).

Effectiveness

In pre-marketing clinical trials, rotavirus vaccination prevented 42–58 percent of all-cause hospital admissions for acute gastroenteritis, suggesting it is responsible for more gastroenteritis than is detected by routine testing.[29, 34, 35]

Post-licensure surveillance studies have demonstrated large reductions in rotavirus-positive stool isolates from children with gastroenteritis (US)[3] and in diarrhoea-related deaths (Mexico).[36, 37] Summarised, post-licensure vaccine effectiveness studies in high-income countries have shown an 89–100 percent reduction in emergency department visits or hospitalisation, a 74–90 percent decline in hospitalisations for rotavirus gastroenteritis in children aged under 2 years, and a 29–50 percent decline in 'all-cause' acute gastroenteritis hospitalisations for children aged under 5 years.[38]

A protective association between rotavirus vaccine and childhood seizures has been reported in the US[39] and Australia.[40] In US children, a full course of rotavirus vaccination was associated with an 18–21 percent reduction in the risk of seizure requiring hospitalisation or emergency department care in the year following vaccination, compared with unvaccinated children.[39] In the Australian state of Queensland, rotavirus vaccine was 35.8 percent effective at preventing emergency department presentation for febrile seizures and 38.0 percent effective at preventing subsequent hospitalisation in children up to two years following vaccination.[40]

Herd immunity in the post-licensure period

Since the beginning of the post-licensure period, over 80 countries have introduced the rotavirus vaccine into their national immunisation programmes.[41] There has been substantial though somewhat variable efficacy data to show a decline in rotavirus infections in the different country environments. In the US, there was a 73 percent reduction in rotavirus infections among infants from 2003 to 2014.[42] The effectiveness tends to wane with age, and rotavirus 'seasons' appear to be longer in the post-licensure period.[42]

While a decline has occurred in rotavirus infection alone, there has also been a reduction in all-cause diarrhoeal illnesses.[41] Furthermore, the protective effect of the vaccine has surpassed the expected level of vaccine efficacy and coverage, resulting in a herd protection. Therefore, the immunised proportion of the population is causing a reduction of infection in the unimmunised portion of the community.[43]

Duration of protection

Prior to the introduction of rotavirus vaccines in Europe, extension studies of the pivotal phase III RV5 trial showed protection lasting up to three years from the last vaccine dose.[44] The duration of protection provided by rotavirus vaccines is difficult to measure because of the herd immunity effect that occurs after the vaccine is implemented. Some studies indicate waning immunity after the first year of life, particularly in low-income countries.[45, 46] In a large multicentre study in the US, both RV1 and RV5 vaccines were found to provide lasting and broadly heterologous protection against infection. Vaccine effectiveness persisted to the seventh year of life for RV5 and through the third year of life for RV1.[47] Note that the differences in duration are because RV1 was licensed in the US approximately two years later than RV5, affecting vaccination coverage and corresponding study power for older age groups for RV1 analyses.[47]

Partial vaccination

Studies in partially vaccinated infants (ie, who have not completed the three-dose course of RV5 or the two-dose course of RV1) found that protection against rotavirus ranged from 51 to 55 percent in low- and middle-income countries, and from 69 to 93 percent in high-income countries.[48]

Cross-protection

Rotavirus vaccine strains vary considerably, and multiple wild-type strains can occur at the same time. In high-income countries, both vaccines appear to provide some cross-protection against non-vaccine serotypes.[49, 50] Vaccine protection against newly emerging genotypes is not well known, and national surveillance of circulating rotavirus types post vaccination is necessary.[51]

17.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.[52]

Store in the dark at +2°C to +8°C. Do not freeze.

17.4.4 Dosage and administration

The dose of RV1 (Rotarix) is 1.5 mL, administered orally (for administration instructions see section A7.2.4 of this *Handbook* or the vaccine data sheet, available at www.medsafe.govt.nz). Do not inject RV1.

Two doses are given, at ages 6 weeks and 3 months. See section 17.5 below for more information.

Co-administration with other vaccines

Rotavirus vaccines can be administered at the same time as other scheduled vaccines. Note that no time interval is required between administration of rotavirus and BCG vaccines; the two live vaccines likely to be administered to infants aged under 6 months.

Interchangeability

A complete course with one vaccine is preferable but, if necessary, a series that contains both vaccines is preferable to an incomplete series.[1] There are not expected to be any safety concerns if an infant starts on one vaccine and completes on another, provided that the upper age limit and inter-vaccine interval, as shown in Table 17.3 below, are met.

If the dose is regurgitated or vomited

If the dose of rotavirus vaccine is regurgitated or vomited during or after administration, a repeat dose *should not be given*.[53] The second dose should be administered as per the schedule. Receptor binding of vaccine is instantaneous making repeat dosing unnecessary.

If the first dose is immediately spat out then a single repeat dose could be given.

17.5 Recommended immunisation schedule

RV1 is recommended and funded for all infants. See section 17.5.2 for RV1 age limit information. For infants who are transitioning from RV5 to RV1, see Table 17.3.

Immunisation is especially encouraged for those who will be attending early childhood education services or where there is an immunocompromised individual living in the household.

Infants who have already had rotavirus gastroenteritis should still receive the full course of immunisation. Initial rotavirus infection only provides partial protection against subsequent infection.[1, 22]

17.5.1 Routine schedule

Two RV1 doses are given orally, at ages 6 weeks and 3 months.

Table 17.2: The infant RV1 (Rotarix) schedule

Dose	Usual scheduled age	Recommended age limits for dosing
Dose 1	6 weeks	6–14 weeks[a]
Dose 2[b]	3 months	10–24 weeks[c]

a The upper age limit for receipt of the 1st dose of RV1 is immediately prior to turning 15 weeks old (14 weeks and 6 days).

b The minimum interval between doses 1 and 2 is 4 weeks.

c The upper age limit for receipt of the 2nd dose of RV1 is immediately prior to turning 25 weeks old (24 weeks and 6 days).

Transitioning from RV5 to RV1

While it is preferable for infants to complete the rotavirus course with the same vaccine, an infant may start with RV5 and finish with RV1, providing the upper age limit and inter-vaccine intervals are met. See Table 17.3.

Table 17.3: Recommendations for infants aged under 25 weeks who are transitioning from RV5 (RotaTeq) to RV1 (Rotarix)

Number of RV5 doses previously received	Number of RV1 doses required
3 RV5	Fully immunised – no RV1 required
2 RV5	1 RV1* at least 4 weeks after the 2nd RV5
1 RV5	2 RV1* at least 4 weeks between each of the doses

* All doses of RV1 must be given prior to turning age 25 weeks (ie, the latest is 24 weeks and 6 days).

17.5.2 Catch-up schedules

The first dose of RV1 should be given before age 15 weeks (ie, 14 weeks and 6 days), with the second dose administered at least four weeks later (see Table 17.2). An infant who has not had the first dose before age 15 weeks will not be able to commence the rotavirus course. Where the first dose is inadvertently given at age 15 weeks or older, the second dose should be given, but both doses should be given before age 25 weeks (ie, the latest is 24 weeks and 6 days).[1] Rotavirus vaccine is not intended for use in older children, adolescents or adults.

The age limits for initiating and completing the vaccine series are recommended because there is insufficient safety data on the use of these vaccines outside this age range. If a partially vaccinated infant reaches age 25 weeks before the second dose is given, the first dose already given will offer them partial protection against disease.

The severity of rotavirus infection decreases with age, so a cost–benefit analysis for vaccinating older children is a low priority and has not been done.

17.5.3 Preterm infants

Vaccination as per the Schedule (ie, at the usual chronological age, with the usual vaccine dosage and interval) is recommended for preterm infants and infants with low birthweight, including those still in hospital (see below). (See also section 4.2.1 for more immunisation recommendations for preterm infants.)

17.5.4 Hospitalised infants

Rotavirus vaccine should be given on time to any infant admitted to a general hospital ward (where other patients are not high risk). If standard infection control precautions are maintained, the risk of transmission of vaccine strain rotavirus will be minimal when rotavirus vaccine is administered to hospitalised infants, including hospitalised preterm infants and those in neonatal units.[54] (See also section 4.2 for more information about infants with special immunisation recommendations.)

17.5.5 Pregnancy and breastfeeding

There is no concern caused by vaccine exposure during pregnancy. There is no restriction for breastfeeding before or after vaccination of the infant (see 'Shedding' in section 17.6.2).

17.6 Contraindications and precautions

See section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

17.6.1 Contraindications

Rotavirus vaccine should not be given to infants with:

- a history of a severe (anaphylactic) allergic reaction after a previous dose or to a vaccine component
- a history of intussusception or an uncorrected congenital malformation of the gastrointestinal tract that would predispose the infant to intussusceptions (see section 17.7.1).
- SCID.[55]

17.6.2 Precautions

Rotavirus vaccine can be administered to infants with a mild illness, including gastroenteritis and upper respiratory tract infections. Infants with moderate to severe gastroenteritis should not be vaccinated until symptoms resolve.

There is very little safety data on infants with predisposing conditions such as metabolic disorders and chronic gastrointestinal diseases (Hirschsprung's, malabsorption syndromes or short gut syndromes). Since there is a greater risk of serious wild-type rotavirus disease, the benefits outweigh the risk, and vaccination is encouraged.[56]

Infants who have received antibody-containing blood products and are the appropriate age should be vaccinated. Rotavirus vaccine and antibody-containing blood products can be administered simultaneously.[53] There is a theoretical risk of interference in the immune response to the vaccine, therefore the interval between

vaccination and receipt of blood products should ideally be as long as possible within the age limits of the vaccine schedule.

Administration of RV1 in immunosuppressed infants, including infants on immunosuppressive therapy, should be based on careful consideration of potential benefits and risks.

Infants born to mothers on immunosuppressive therapies

There is little data on rotavirus vaccination in infants born to mothers on immunosuppressive therapies. Certain immunosuppressive medications, such as DMARDs readily cross the placenta and can be detectable some months later.[54] Infants of mothers who received DMARDs during pregnancy that are monoclonal antibodies (eg, adalimumab/Humira) should not be vaccinated with live rotavirus vaccines until theoretical concerns about safety are clarified.[57] See Table 4.3 for a list of the highly immunosuppressive medications that readily cross the placenta. Each case should be assessed on a risk–benefit basis and with specialist advice.

Shedding

Since rotavirus vaccine virus replicates in the gastrointestinal tract, it can be shed in stools – especially after the first dose.[58] Shedding is also more likely in immunocompromised patients (eg, children with HIV). The vaccine virus could then be transmitted to unvaccinated populations, a feature that is generally beneficial as it promotes herd immunity.

Infants living in households with immunocompromised individuals should be vaccinated. So far there are no safety concerns, but there is also no data to confirm the safety of these vaccines for immunocompromised patients. Infants living in households with pregnant women should also be vaccinated. Hand washing and the careful disposal of soiled nappies are likely to minimise any risk of vaccine transmission to household contacts.[53, 54]

17.7 Expected responses and AEFIs

The 2012 Cochrane review[33] described in section 17.4.2 also reviewed the safety of RV1 and RV5 vaccines. No significant difference was found between children receiving RV1 or RV5 and placebo in the number of serious adverse events, and intussusception in particular (see below). No statistical differences were observed for fever, diarrhoea and vomiting between cases and placebo groups. There was no significant difference between cases and placebos in the number of adverse events leading to discontinuation of the schedule.

In 2010 porcine circovirus or porcine circovirus DNA was detected in both rotavirus vaccines. However, there is no evidence that this virus is a safety risk or causes illness in humans.[53]

17.7.1 Intussusception

Intussusception is a cause of an acute abdomen when one part of the intestine telescopes into another part of the intestine; the mechanism by which these events occur remains uncertain. In 1999 an oral human–rhesus rotavirus quadrivalent vaccine (RotaShield) was licensed in the US and on the infant schedule but was withdrawn later that year after reports of an association with intussusception (a risk of approximately one case in 5,000–10,000 vaccinees).

No increased risk of intussusception was detected in the large phase III pre-licensure clinical trials of RV1 (Rotarix) and RV5 (RotaTeq), despite this being a specifically monitored adverse event. However, post-marketing surveillance of both rotavirus vaccines indicates the possibility of an increased risk of intussusception shortly after the first dose of rotavirus vaccination. Evidence from Australia[59] indicates that after the first dose, RV1 had a relative incidence (relative risk) of 6.8 (95% CI: 2.4–19.0, p<0.001) and 3.5 (95% CI: 1.3–8.9, p=0.01) for the periods of 1 to 7 days and 8 to 21 days after vaccination, respectively. For RV5, the relative incidence was 9.9 (95% CI: 3.7–26.4, p<0.001) and 6.3 (95% CI: 2.8–14.4, p<0.001) for the same time periods.

There was also some elevated risk of intussusception 1 to 7 days after the second dose of both vaccines. The relative incidence for RV1 was 2.8 (95% CI: 1.1–7.3, p=0.03) and for RV5 was 2.8 (95% CI: 1.2–6.8, p=0.02). There was no evidence of increased risk of intussusception

following a third dose of RV5.[59] The increased risk of intussusception following rotavirus vaccination is estimated at approximately 6 additional cases of intussusception among every 100,000 infants vaccinated (approximately 1 in 15,500 vaccinees), or 14 additional cases per year in Australia.[59]

Studies in the post-licensure period continue to show small increases in risk for both RV1 and RV5 and primarily within 7 days of the first dose of vaccine.[60, 61] Recent safety data has continued to emphasise the clear and dramatic benefit of vaccination over the very low risk of vaccine-associated intussusception.[41] For example, a self-controlled case-series study estimated that the RV1 programme in England caused 21 intussusception admissions annually and prevented 25,000 gastrointestinal infection admissions with a clear risk–benefit ratio.[62]

While there appears to be an increased relative risk of intussusception, the condition remains rare, and this risk is outweighed by the benefits of rotavirus vaccination in preventing rotavirus infections, with an estimated 70 percent reduction in hospitalisations in young children after the vaccine's introduction to the Australian schedule.[63] It is uncertain whether rotavirus vaccine administration affects the overall incidence of intussusception: US data suggests no increased overall rate in infants despite a small cluster effect.[64] Both the WHO[65] and the Australian Technical Advisory Group on Immunisation[63] continue to recommend the use of rotavirus vaccine for infants.

Although the risk of intussusception after rotavirus immunisation is very small, it is recommended that parents seek medical advice and health care professionals are attentive if the baby develops intermittent crying or screaming episodes, pulling their knees towards their chest and vomiting, or pink- or red-coloured jelly-like stools.

A recent study has described the epidemiology of intussusception in New Zealand children aged 0–36 months (794 cases) for a 16-year period before the introduction of routine rotavirus vaccination.[66] This study will provide a valuable baseline to determine if the introduction of the vaccine has significant effects on intussusception rates in the New Zealand population.

17.8 Public health measures

Prevention of spread is by contact precautions, including careful handwashing. In an early childhood service setting where there has been a child known to have had a rotavirus infection, the surfaces should be washed with sodium hypochlorite (bleach) and water. Disinfectants inactivate rotavirus and may help to prevent disease transmission resulting from contact with environmental surfaces.[53]

For more details on control measures, refer to the 'Acute gastroenteritis' chapter of the *Communicable Disease Control Manual 2012*.[7]

17.9 Variations from the vaccine data sheet

The RV1 (Rotarix) vaccine data sheet states that if an infant vomits or regurgitates most of the vaccine dose, a single replacement dose may be given at the same vaccination visit. The Ministry of Health does not recommend repeating the dose (see section 17.4.4).[53]

The RV1 data sheet recommends postponing the administration of the vaccine in infants suffering from diarrhoea or vomiting. The Ministry of Health recommends vaccinating infants with mild gastroenteritis, and to wait until symptoms have resolved for infants with moderate to severe gastroenteritis (see section 17.6.2).

The RV1 data sheet states that the vaccine should not be administered to subjects with any chronic gastrointestinal disease. The Ministry of Health recommends instead that pre-existing chronic gastrointestinal disease is not a contraindication to rotavirus vaccination, with the exception of those conditions that may predispose the infant to intussusceptions (see sections 17.6.1 and 17.7.1).[54]

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18 Rubella

Key information

Mode of transmission	By contact with infected nasopharyngeal secretions. Infants with congenital rubella syndrome (CRS) shed rubella virus in their pharyngeal secretions and urine.
Incubation period	14–23 days, usually 16–18 days.
Period of communicability	7 days before until 7 days after the onset of the rash. Infants with CRS may be infectious for months.
Funded vaccine	MMR vaccine (Priorix) is a live attenuated vaccine.
Dose, presentation, route	0.5 mL per dose after reconstitution. Pre-filled syringe and glass vial. The vaccine must be reconstituted prior to injection. Subcutaneous injection.
Funded vaccine indications and schedule	Children at ages 15 months and 4 years. Adults who are susceptible to one or more of measles, mumps and rubella. For (re-)vaccination following immunosuppression (if the individual is immunocompetent enough to safely receive the vaccine).
Pregnancy	All pregnant women and women planning pregnancy should have their immunisation history checked. A woman is considered to be immune to rubella if she has had 2 documented doses of a rubella-containing vaccine given at least 4 weeks apart and given after age 12 months, regardless of serology. Pregnant non-immune women should avoid contact with known cases of rubella, and should receive MMR after delivery.
Vaccine efficacy/ effectiveness	Highly effective with a 2-dose schedule; protection lasts at least 20 years and may be considerably longer.
Egg allergy	Egg allergy, including anaphylaxis, is **not** a contraindication for MMR vaccine.
Adverse events to vaccine	MMR vaccine is generally well tolerated. The risk of adverse reactions to MMR vaccine is low compared to the risk of complications from rubella disease.

18.1 Virology

Rubella is an enveloped RNA virus from the family Togaviridae and the genus *Rubivirus*.

18.2 Clinical features

Clinical features include a transient erythematous rash and lymphadenopathy without respiratory symptoms. Arthritis or arthralgia is relatively common and a classic feature of infection in adults. While usually a mild childhood illness, rubella may also present as a more severe illness, clinically indistinguishable from measles. Encephalitis occurs with a prevalence of approximately 1 in 6,000 cases and may result in residual neurological damage or, occasionally, death. Thrombocytopenia rarely occurs.

Clinical diagnosis is unreliable because the symptoms are often fleeting and can be mimicked by other viruses. In particular, the rash is not diagnostic of rubella. Up to 50 percent of rubella infections are subclinical or asymptomatic. A history of rubella should therefore never be accepted as proof of immunity without laboratory confirmation.

Transmission of rubella is through direct or indirect contact with infected nasopharyngeal secretions and droplets. The incubation period is usually 16 to 18 days (range 14 to 23 days) and infectivity is between seven days before and seven days after the onset of the rash. Infants with congenital rubella syndrome (CRS) shed rubella virus in their pharyngeal secretions and urine for months after birth and should be considered infectious until they are aged 12 months.

Although the vaccine virus is excreted after vaccination, mostly from the pharynx, transmission to susceptible contacts has not been demonstrated (see section 11.7.2). Therefore, a recently immunised contact is not a risk to a pregnant woman.

Rubella infection during pregnancy can result in fetal infection, causing CRS in a high proportion of cases. Rubella infection in the first eight weeks of pregnancy results in fetal damage in up to 85 percent of infants, and multiple defects are common. The risk of damage declines to 10–20 percent by about 16 weeks' gestation, and after this stage of pregnancy fetal abnormalities are rare.

Infants born with CRS may have cataracts, nerve deafness, cardiac malformations, microcephaly, mental retardation and behavioural problems. Inflammatory changes may also be found in the liver, lungs and bone marrow. Some infected infants may appear normal at birth, but have nerve deafness detected later.

The frequency of complications and consequences of rubella infection are best described from the 1963/64 US outbreak, involving 12.5 million cases of rubella and 30,000 infants damaged by intrauterine rubella, an incidence rate of 100 per 10,000 pregnancies (see Table 18.1).

Table 18.1: Estimated morbidity and mortality associated with the 1963/64 US rubella epidemic

Total number of cases of rubella: 12,500,000	
Complications of rubella	**Risk per case**
Arthritis or arthralgia	1.3%
Encephalitis	17 per 100,000
Neonatal deaths	17 per 100,000
Complications caused by congenital rubella syndrome (CRS)	**Numbers of cases (% of CRS cases)**
Total number with CRS	20,000
Deaf children	8,055 (40%)
Deaf–blind children	3,580 (18%)
Intellectually handicapped children	1,790 (9%)

Adapted from: Reef S, Plotkin SA. 2013. Rubella vaccine. In: Plotkin SA, Orenstein WA, Offit PA (eds). *Vaccines* (6th edition). Philadelphia, PA: Elsevier Saunders. Table 31.7.

Rubella infection can occur (very rarely) in individuals with either naturally acquired or vaccine-induced antibody. Rare cases of CRS have been reported after reinfection during pregnancy.

As with measles, public health measures of accurately diagnosing potential cases of rubella with notification and contact tracing are critical (see section 18.8).

18.3 Epidemiology

18.3.1 Global burden of disease

Humans are the only source of rubella infection. Infection is often asymptomatic. In the pre-vaccine era the highest incidence of clinical cases occurred in the spring among 5–9-year-old children, and 80–90 percent of adults were immune to rubella. Extensive outbreaks of rubella occurred every six to nine years, in which many children were affected by CRS. Immunisation against rubella, introduced to prevent the occurrence of CRS, has resulted in a very significant reduction in infection, especially once vaccination was introduced to boys and girls.

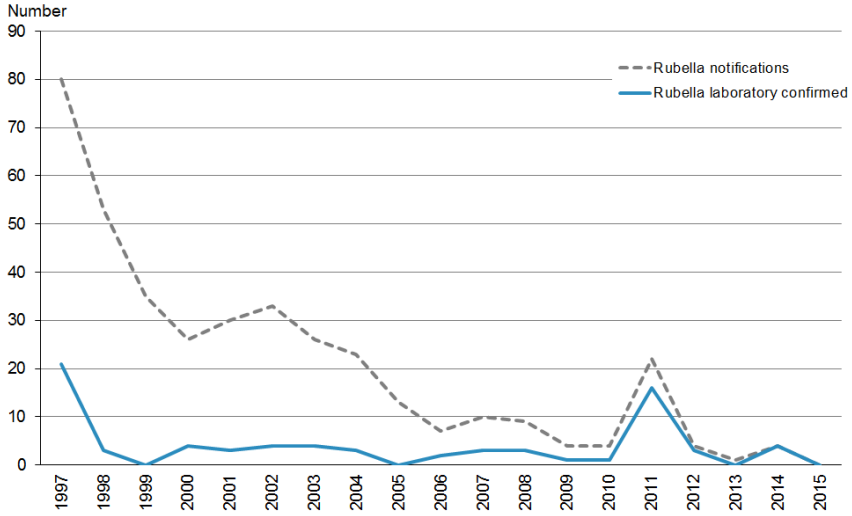
18.3.2 New Zealand epidemiology

Rubella immunisation was introduced in 1970 (see Appendix 1), and rubella has been a notifiable disease since 1996. The last large rubella outbreak in 1995–1996 mostly involved young adult males, who would not have been offered immunisation. This emphasises the need to immunise both boys and girls to reduce the risk of exposure in pregnant women, as well as to reduce illness in men.

Three cases of rubella were notified in 2016, with no notifications in 2015 and four in 2014. All of the 2016 and 2014 cases were imported from overseas (ESR, 14 March 2017).

There have been no reported cases of CRS in New Zealand since 1998.

Figure 18.1: Rubella notifications and laboratory-confirmed cases by year, 1997–2015



Source: ESR

18.4 Vaccines

18.4.1 Available vaccines

Rubella vaccine is one of the components of the live attenuated MMR and MMRV vaccines, considered in sections 11.4.1 and 21.4.1. Single-antigen rubella vaccine is not available in New Zealand.

Funded vaccine

MMR vaccine funded as part of the Schedule is Priorix (GSK), which contains attenuated Schwarz strain measles, RA 27/3 rubella, and Jeryl Lynn mumps. (See section 11.4.1 for more information.)

Other vaccines

MMR II (MSD) was the funded vaccine prior to the 1 July 2017 Schedule change (see section 11.4.1).

18.4.2 Efficacy and effectiveness

The rubella vaccine has been shown to be 90–97 percent effective in an outbreak after a single dose, and this is likely to be higher with a two-dose schedule. One dose of rubella vaccine at 12 months or older induces an antibody response in at least 95 percent of recipients. Studies have found no evidence of waning of protection over decades of follow-up.[1] In 90 percent of recipients, antibodies persisted for at least 16 years; other studies have reported persistence up to 21 years.[1] A few recipients fail to produce antibodies following immunisation, and a small number of individuals lose antibodies, whether derived from natural infection or the vaccine. See also section 11.4.2 for further evidence on the duration of immunity.

18.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.[2] Store at +2°C to +8°C. Do not freeze.

MMR vaccine must be reconstituted only with the diluents supplied by the manufacturer. Use MMR vaccine as soon as possible after reconstitution. If storage is necessary, reconstituted MMR vaccine can be stored at +2°C to +8°C for up to eight hours.

18.4.4 Dosage and administration

The dose of MMR is all of the reconstituted vaccine (approximately 0.5 mL) administered by subcutaneous injection (see section 2.2.3).

Co-administration with other vaccines

MMR vaccine can be given concurrently with other vaccines, as long as separate syringes are used and the injections are given at different sites. If not given concurrently, live vaccines should be given at least four weeks apart. (See also section 2.2.7 for information about multiple injections at the same visit.)

Interchangeability

The two brands of MMR vaccine (Priorix and MMR II) may be used interchangeably for completion of a course.[3]

18.5 Recommended immunisation schedule

As in other high-income countries, New Zealand's primary strategy for preventing and eventually eliminating rubella is to vaccinate both boys and girls with two doses of MMR vaccine (Table 18.2).

It is important for vaccinators to be able to explain why boys need rubella vaccine, given that the aim is to prevent rubella in pregnancy. In New Zealand and the UK, where a targeted approach was used and 11-year-old girls were offered rubella immunisation, even with high coverage there were still women of childbearing age who were susceptible to rubella, either because of failure to be vaccinated or vaccine failure. Rubella continued to circulate in New Zealand because children aged under 11 years and males were not vaccinated, and so CRS continued to occur, albeit at a reduced rate.

To prevent all cases of CRS, rubella must not circulate in the community and therefore males must be immunised. Achieving at least 95 percent coverage of two doses of MMR prevents the circulation of rubella (which is much less infectious than measles) and therefore lead to the elimination of rubella.

Table 18.2: Recommended MMR vaccine schedule

	Schedule
Usual childhood schedule[a]	2 doses: at ages 15 months and 4 years
Catch-up[b] for children adolescents and adults	2 doses: at least 4 weeks apart

a If MMR is given to children aged 6–12 months for outbreak control, 2 further MMR doses are still required at ages 15 months and 4 years.

b MMR vaccine is funded for those who are susceptible to 1 or more of the 3 diseases. See sections 18.5.2 and 18.5.3.

18.5.1 Usual childhood schedule

Two doses of rubella vaccine as MMR are recommended at age 15 months and age 4 years. Over 95 percent of individuals will become immune to rubella after one dose.[4] The second dose is not a booster. Two doses are recommended because the 2–5 percent not protected by the first dose will nearly all be protected by the second. The second dose of vaccine can be given as soon as four weeks after the first dose. (See below for the recommendations for other groups.)

Children who in an outbreak (of measles, mumps or rubella) receive MMR vaccine when aged under 12 months require two further doses administered after age 12 months. MMR vaccine may be given to children aged 12 months or older whose parents/guardians request it, and no opportunity should be missed to achieve immunity.

18.5.2 Catch-up

Any individual born on or after 1 January 1969 (see section 11.5.2) who does not have two documented doses of MMR vaccine, given at least four weeks apart with the first dose given any time after age 12 months, should be offered either one or two doses (four weeks apart) to bring them up to two doses (funded).

Even if the individual has previously received single-antigen measles vaccine, up to two doses of MMR vaccine (ie, additional doses of measles vaccine) may be given to these individuals to ensure rubella and mumps protection. There are no significant adverse effects from further vaccinating individuals who are already immune to measles, mumps and/or rubella, and no reliance can be placed on a prior clinical history of rubella infection.

Immigrants to New Zealand

The vaccination status of immigrants should be checked as a priority group. Anyone who does not have two documented doses of MMR vaccine, given any time after age 12 months, should be offered either one or two doses (four weeks apart) to bring them up to two doses (funded if eligible).

18.5.3 Pregnancy and breastfeeding

Women planning pregnancy

It is particularly important to ensure that women of child-bearing age are immune to rubella.[5] Women who are planning pregnancy should have their immunisation history checked for having received two documented doses of a rubella-containing vaccine given at least four weeks apart and given after age 12 months. Non-immune women may receive MMR vaccine before pregnancy, but pregnancy should be avoided for four weeks after the last MMR vaccination.[6, 7]

Pregnant women

MMR vaccine is contraindicated during pregnancy.

> All pregnant women should have their immunisation history checked. A pregnant woman is considered to be immune to rubella if she has had two documented doses of a rubella-containing vaccine given at least four weeks apart and given after age 12 months, *regardless of serology*. If a pregnant women is non-immune, give one or two doses of MMR vaccine four weeks apart (as appropriate) when not pregnant (funded).

Serological testing for immunity to rubella is not usually performed in New Zealand except as part of routine antenatal care. Improved documentation and effective surveillance showing the rarity of CRS when there is high immunisation coverage has led to some countries, such as England, discontinuing routine antenatal rubella screening.[8] Also, the screening tests used for rubella serology can potentially give inaccurate results and may cause unnecessary stress for women.[8]

In general, it should be remembered that the great majority of New Zealand-born individuals who received all scheduled childhood vaccines will be immune to rubella, and the chance of being exposed in New Zealand to an infectious case is becoming increasingly rare. (If exposure during pregnancy does occur, see the guidelines in section 18.8.3.)

The following groups of women are more likely to be non-immune to rubella:[5]

- women born overseas (especially in Asia, the Pacific Islands, sub-Saharan Africa and South America) who entered New Zealand after the age of routine vaccination
- women over the age of 35 years.

After delivery

If MMR vaccine and Rhesus anti-D IG are required after delivery, both the vaccine and anti-D IG may be given at the same time, in separate sites with separate syringes. The vaccine may be given at any time after the delivery. Anti-D IG does not interfere with the antibody response to the vaccine, but whole blood transfusion does inhibit the response in up to 50 percent of vaccinees (see section A6.4.1).

Breastfeeding

There is no risk to the mother or child in giving MMR to breastfeeding women.[1]

18.5.4 Immunocompromise

Contacts of immunocompromised individuals

MMR vaccine is contraindicated in immunocompromised children (see section 4.3). They can be partially protected from exposure to infection by ensuring that all contacts are fully immunised (funded), including hospital staff and family members. There is no risk of transmission of MMR vaccine viruses from a vaccinee to the immunocompromised individual (see section 11.7.2). See also 'Household contacts' in section 4.3.1 for general vaccination information for contacts of immunocompromised individuals.

(Re-)vaccination following immunosuppression

MMR vaccine is funded for (re-)vaccination following immunosuppression. However, it is important to be sure that the individual is immunocompetent enough to safely receive the vaccine.

HIV infection

Discuss vaccination of individuals with HIV infection with their specialist (see 'HIV infection' in section 4.3.3).

MMR vaccine is recommended for all HIV-positive children, whether symptomatic or asymptomatic, if the CD4+ lymphocyte percentage is 15 percent or greater. Asymptomatic children who are not severely immunocompromised are recommended to receive MMR vaccine from age 12 months to provide early protection against the three diseases. Susceptible HIV-positive children and adults aged 14 years and older may receive MMR vaccine if the CD4+ lymphocyte count is 200 cells/mm^3 or greater. Administration of MMR with CD4+ counts below these recommended levels has been associated with vaccine-related pneumonitis (from the measles component).[6]

18.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general vaccine contraindications.

18.6.1 Contraindications

See section 11.6.1 for specific MMR vaccine contraindications.

The general contraindications that apply to all immunisations are relevant to MMR.

Anaphylaxis to a previous dose of MMR or any of the vaccine components (including neomycin) is a contraindication to a further dose of MMR.

MMR vaccine should not be given to women who are pregnant, and pregnancy should be avoided for four weeks after immunisation.[1, 6] However, inadvertent immunisation with a rubella-containing vaccine in early pregnancy is no longer considered an indication for termination of pregnancy. There have been no cases of teratogenic damage from vaccine virus despite intensive surveillance in the US, the UK and Germany.[1]

18.6.2 Precautions

Egg allergy, including anaphylaxis, is **not** a contraindication for MMR vaccine. See section 11.6.3 for more information, and section 11.6.2 for further precautions.

18.7 Expected responses and AEFIs

See also section 11.7.

18.7.1 Expected responses

A fever of 39.4°C or more occurs in 5–15 percent of children 6 to 12 days after immunisation and generally lasts one to two days.[6] Rash occurs in approximately 5 percent of children at the same interval post-vaccination: these children are not infectious to others.[6] The majority of these events are coincidental and not caused by the vaccine.[9] Serological tests or PCR can be expected to be positive if performed during this time, so testing should not be routinely performed.

Joint symptoms may be reported in 0.5 percent of young children and 10–25 percent of post-pubertal women.[4] Symptoms begin one to three weeks after immunisation and are usually transient. The prevalence of joint symptoms following rubella immunisation is lower than occurs with natural infection at a corresponding age.[4]

It was previously thought that the rubella vaccine might lead to long-term arthritis. A 2012 Institute of Medicine review concluded that the evidence was inadequate to accept or reject a causal relationship between MMR vaccine and chronic arthritis in women.[10]

18.7.2 AEFIs

ITP and, rarely, neurological disturbances have been reported (see section 11.7.2).

18.8 Public health measures

Rubella (including CRS) is a notifiable disease, and suspected cases should be notified by the clinician on suspicion to the local medical officer of health. Accurate diagnosis requires laboratory confirmation.

The preferred method of diagnosis is by PCR or culture (see the 'Rubella' chapter of the *Communicable Disease Control Manual 2012*[11]). Serology may be useful but can be hard to interpret if the person has received rubella vaccine in the past.

The local medical officer of health will arrange contact tracing and alert the contacts or the public of potential exposure, particularly of pregnant women.

18.8.1 Exclusion of cases of rubella infection

Parents/guardians should be advised that children with suspected rubella should be excluded from early childhood services or school until fully recovered and for seven days after the appearance of the rash. Children with CRS should be considered infectious until they are aged 12 months. Adults should be excluded from work until fully recovered and for seven days after the appearance of the rash.

18.8.2 Management of non-pregnant contacts

The local medical officer of health will advise on contact management. Check the immunisation status of all close contacts.

Rubella-containing vaccine does not provide protection if given after exposure to rubella. However, if the exposure did not result in infection, the vaccine would induce protection against subsequent infection. Human normal immunoglobulin does not prevent rubella infection after exposure and should not be used for that purpose.[12]

18.8.3 Management of pregnant contacts

It is critical to accurately document the rubella status of all people who may have rubella and potentially exposed a pregnant woman to the virus. Such people will have travelled overseas or had contact with an infected returned traveller. As described in section 18.3.2, rubella virus does not circulate in New Zealand. Rubella infection in the first half of pregnancy is potentially devastating, and every possible exposure of a pregnant woman should be discussed with the local medical officer of health, obstetrician and microbiologist or infectious diseases physician.

Pregnant contacts with confirmed immunity can be reassured that the likelihood of rubella infection is remote.[11] This applies if:

- she has received at least two documented doses of rubella-containing vaccine, OR
- a previous antibody screening test has detected a protective level of antibodies, and this has been documented, OR
- one dose of vaccine followed by a rubella antibody screening test showing a protective level of antibodies has been documented.[11]

Coordinated care and management

Coordinated care and management are essential (Table 18.3). An obstetrician (or a maternal fetal medicine specialist) and an infectious diseases specialist/microbiologist should be consulted when the diagnosis of possible rubella infection in a pregnant woman is first considered. The clinical picture and all test results should be discussed by all involved in the care of the woman, to enable an accurate interpretation of the serological results before advising the woman about the risk to her fetus and options regarding the continuation of pregnancy.

Pregnant women whose immunity to rubella has not been confirmed for the current pregnancy, **and who have been exposed to rubella in the first half of pregnancy**, must be investigated serologically and virologically, irrespective of immunisation history or history of previous clinical rubella. Serum should be obtained as soon as possible, with the clinical details included on the request form. The laboratory should be asked to store an aliquot of serum for later testing in tandem with a

follow-up sample. These results must be interpreted in conjunction with the time period since exposure, to determine whether or not acute infection has occurred.

It is essential to discuss testing with the local clinical microbiologist before taking samples, to ensure that the right samples are obtained and the best tests performed expeditiously. All requests to laboratories must state the:

- duration of pregnancy and last menstrual period
- date of exposure to possible rubella
- date of blood specimen
- name of the index case who is thought to have rubella.

The use of IG is not recommended for post-exposure prophylaxis of rubella in early pregnancy or any other circumstance. However, IG may be considered if termination of the pregnancy is not an option, but termination must be discussed when maternal infection is confirmed. Although IG has been shown to reduce clinically apparent infection in the mother, there is no guarantee that fetal infection will be prevented.

> It is a legal requirement that all cases of CRS and rubella be notified immediately on suspicion to the local medical officer of health.

For more details on control measures, refer to the 'Rubella' chapter of the *Communicable Disease Control Manual 2012*.[11]

Table 18.3: Suggested roles of health professionals

	Lead maternity carer	Medical officer of health	GP	Obstetrician/ infectious diseases specialist/ maternal fetal medicine specialist
Check rubella status in every pregnancy (2 documented doses of rubella-containing vaccine)	✓			
Investigate initial suspected rubella case and trace contacts		✓		
Coordinate care of exposed non-immune pregnant woman		✓	✓	
Review clinical and laboratory results, and discuss options with the pregnant woman if rubella is confirmed				✓
AFTER delivery – vaccinate any woman who is not immune	✓		✓	

18.9 Variations from the vaccine data sheet

See section 11.9 for variations from the MMR (Priorix) data sheet.

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19 Tetanus

Key information

Mode of transmission	Environmental exposure to the bacillus, usually through contaminated wounds. The disease is not directly transmitted from person to person.
Incubation period	Between 3 and 21 days, commonly about 10 days; may vary from 1 day to several months.
Period of communicability	A person with tetanus is not infectious to others.
Burden of disease	In older individuals, usually women, who are less likely to have received a primary series of tetanus vaccine.
Funded vaccines	DTaP-IPV-HepB/Hib (Infanrix-hexa). DTaP-IPV (Infanrix-IPV). Tdap (Boostrix). Td (ADT Booster).
Dose, presentation, route	0.5 mL per dose. DTaP-IPV-HepB/Hib: pre-filled syringe and glass vial. The vaccine must be reconstituted prior to injection. DTaP-IPV, Tdap, Td: pre-filled syringe. Intramuscular injection.
Funded vaccine indications and schedule	6 weeks, 3 months and 5 months: DTaP-IPV-HepB/Hib. 4 years: DTaP-IPV. 11 years: Tdap. 45 and 65 years: Td. During each pregnancy (from 28 to 38 weeks' gestation): Tdap. For individuals with tetanus-prone wounds. For (re-)vaccination of eligible patients: DTaP-IPV-HepB/Hib, DTaP-IPV, Tdap or Td. For testing for primary immune deficiencies: Td.
Dose interval between Td and Tdap	No minimum interval is required between Td and Tdap, unless Tdap is being given as part of the primary immunisation course.
Wound control	If an injury is considered to be tetanus prone *and* there is any doubt about previous tetanus immunisation, the individual must be given tetanus immunoglobulin (TIG) and a 3-dose primary immunisation course.

19.1 Bacteriology

Tetanus is caused by the action of tetanus toxin released by *Clostridium tetani*, a spore-forming gram-positive, motile, anaerobic bacillus. The most common source of environmental exposure to *C. tetani* spores and bacilli is soil. However, soil is not the only reservoir of the organism. Animals, both herbivores and omnivores, can carry *C. tetani* bacilli and spores in their intestines, and the organism is readily disseminated in their faeces. Once introduced into the relatively anaerobic conditions found in wound tissue, they germinate and produce toxin.

Tetanus spores or bacilli can easily be introduced into a wound at the time of injury, even when the injury is quite trivial. Contaminated wounds, especially wounds with devitalised tissue and deep-puncture trauma, are at greatest risk.

19.2 Clinical features

Tetanus is a clinical diagnosis, and is characterised by muscular rigidity and very painful contraction spasms. When severe, it is associated with a characteristic facial grimace (risus sardonicus) and arching of the back (opisthotonus). The patient suffering from tetanus remains alert unless they become severely hypoxic.

The *C. tetani* toxin reaches the central nervous system via the axons and irreversibly binds to nerve terminals at the neuromuscular junction, blocking the release of inhibitory neurotransmitters and leading to the tetanic muscle spasms.

The incubation period is between 3 and 21 days, commonly about 10 days, but it has been reported to vary from one day to several months. The bacteria need an anaerobic environment in which to grow, and this is often found in damaged and necrotic tissue, although the inoculation site may appear insignificant. Initial symptoms include weakness, stiffness or cramps, and difficulty chewing or swallowing food. Reflex muscle spasms usually occur within one to four days of the initial symptoms, the interval being called the onset period. The shorter the incubation and onset periods, the more severe the disease. Even with modern intensive care, tetanus mortality is about 10 percent overall, and much higher in older people.

Neonatal tetanus, from infection of the umbilical stump, is the commonest form of the disease in some low-income countries, particularly where births take place at home without adequate sterile procedures.[1]

A person with tetanus is not infectious to others, and vaccination provides individual protection only, with no herd immunity. Suffering tetanus does not confer immunity. See section 19.5.2.

19.3 Epidemiology

19.3.1 Global burden of disease

The estimated total number of tetanus cases (including neonatal cases) globally has fallen from more than 110,000 in 1980 to 10,000 in 2015.[2] India, Uganda, Nepal, the Philippines and Pakistan had the highest number of cases in 2015, representing more than 60 percent of the cases worldwide.[3] Of the estimated 3,500 cases of neonatal tetanus worldwide in 2015, half of them occurred in Pakistan, India, the Democratic Republic of Congo and China.[4]

Worldwide, all countries are committed to 'elimination' of maternal and neonatal tetanus; that is, a reduction of neonatal tetanus incidence to below one case per 1,000 live births per year in every district.[1] However, the goal of eliminating maternal and neonatal tetanus by 2015 has not been reached.

The incidence of tetanus reflects the effectiveness of the local immunisation programme, with low incidence in regions with high immunisation coverage. In 2015, 126 countries (65 percent of the 194 WHO member states) had immunisation coverage rates of 90 percent or more for three doses of a diphtheria, tetanus, and pertussis-containing vaccine (DTP) given in the first year of life.[5] Almost 40 percent of the 19.4 million children worldwide who did not receive three doses of DTP vaccine lived in India, Nigeria and Pakistan.

19.3.2 New Zealand epidemiology

One case of tetanus was notified in New Zealand in 2015.[6] The case was a female in the 70 years and older age group (the vaccination status was not known). No cases were reported in 2014.

There were 32 tetanus cases notified between 1997 and 2015.[6] Immunisation status was recorded for 21 of the 32 notified cases (ESR data, 9 February 2017). There were four cases in unvaccinated children (aged under 10 years), 14 cases in unvaccinated adults and three cases in vaccinated adults (the time since vaccination is not known). Two females in the 70 years and older age group died (one was not vaccinated and the vaccination status of the other was unknown).[6]

19.4 Vaccines

Tetanus immunisation protects by stimulating the production of antitoxin, providing immunity against the effects of the toxin. It does not prevent *C. tetani* growing in a contaminated wound. The tetanus vaccine is prepared from cell-free toxin treated with formaldehyde to produce a toxoid. The toxoid is adsorbed onto an aluminium salt adjuvant to improve immunogenicity.

19.4.1 Available vaccines

Funded vaccines

Tetanus vaccine as a single antigen is no longer available in New Zealand. It is only available in combination with other vaccines.

The tetanus toxoid-containing vaccines funded as part of the Schedule are:

- DTaP-IPV-HepB/Hib (Infanrix-hexa, GSK): diphtheria, tetanus, acellular pertussis, inactivated polio, hepatitis B and *Haemophilus influenzae* type b vaccine
- DTaP-IPV (Infanrix-IPV, GSK): diphtheria, tetanus, acellular pertussis and inactivated polio vaccine
- Tdap (Boostrix, GSK): a smaller adult dose of diphtheria and pertussis vaccine, together with tetanus vaccine
- Td (ADT Booster, Seqirus (NZ) Ltd): a smaller adult dose of diphtheria vaccine together with tetanus vaccine.

See section 5.4.1 for more detailed vaccine information.

Other vaccines

Other tetanus toxoid-containing vaccines registered (approved for use) and available (marketed) in New Zealand are:

- Tdap: Adacel (Sanofi)
- Tdap-IPV: Adacel Polio (Sanofi).

19.4.2 Efficacy and effectiveness

Efficacy and effectiveness

Tetanus toxoid vaccine administered to pregnant women can prevent tetanus in their newborns (neonatal tetanus). Subsequent field assessments of the efficacy of two or more tetanus toxoid doses using data collected during neonatal tetanus mortality surveys demonstrated effectiveness of 70–100 percent.

A systematic review and meta-analysis concluded that immunisation of pregnant or childbearing-age women with two or more doses of tetanus toxoid reduces neonatal tetanus mortality by 94 percent (95% CI: 80–98).[7]

Tetanus in adults is too rare for vaccine efficacy to be tested in a clinical trial. However, the effectiveness of tetanus vaccine was clearly demonstrated in World War II, when only 12 cases of tetanus occurred among the 2.7 million wounded US army personnel (0.44 per 100,000), compared to 70 cases out of 520,000 wounded in World War I (13.4 per 100,000).[7] Of the 12 cases, only four had completed primary immunisation. Immunised cases have less severe disease and a lower case fatality.

Duration of protection

In most studies, 100 percent of infants have protective levels of tetanus antibody after three doses of vaccine given at intervals of four weeks or longer. The duration of antibody persistence depends on the initial antibody level. Calculations of tetanus antibody decay have shown that a three-dose primary schedule in infancy will provide protection for at least five years, and a booster at five years will provide protection for at least another 21 years.[8] By mid-life, around 50 percent of vaccinated people have low or undetectable antibody levels;[9, 10, 11, 12] a single dose of tetanus toxoid produces a rapid anamnestic response.[13, 14, 15, 16]

(See also sections 5.4.2 and 14.4.2.)

19.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.[17] Store at +2°C to +8°C. Do not freeze.

DTaP-IPV-HepB/Hib and Td should be stored in the dark.

DTaP-IPV-HepB/Hib (Infanrix-hexa) must be reconstituted by adding the entire contents of the supplied container of the DTaP-IPV-HepB vaccine to the vial containing the Hib pellet. After adding the vaccine to the pellet, the mixture should be shaken until the pellet is completely dissolved. Use the reconstituted vaccine as soon as possible. If storage is necessary, the reconstituted vaccine may be kept for up to eight hours at 21°C.

19.4.4 Dosage and administration

The dose of DTaP-IPV-HepB/Hib, DTaP-IPV, Tdap and Td is 0.5 mL administered by intramuscular injection (see section 2.2.3).

Co-administration with other vaccines

DTaP-IPV-HepB/Hib, DTaP-IPV, Tdap and Td can be administered simultaneously (at separate sites) with other vaccines or IGs.

19.5 Recommended immunisation schedule

Table 19.1: Immunisation schedule for tetanus-containing vaccines (excluding catch-up)

Age	Vaccine	Comment
6 weeks	DTaP-IPV-HepB/Hib	Primary series
3 months	DTaP-IPV-HepB/Hib	Primary series
5 months	DTaP-IPV-HepB/Hib	Primary series
4 years	DTaP-IPV	Booster
11 years	Tdap	Booster
45 years	Td[a]	Booster
65 years	Td[a]	Booster
Pregnant women (weeks 28–38 of each pregnancy)	Tdap	Booster[b]

a The Td vaccine is funded at ages 45 and 65 years, but not the administration.

b The Tdap booster during pregnancy is for protection against pertussis (see section 4.1.2).

19.5.1 Usual childhood schedule

A primary course of tetanus vaccine is given as DTaP-IPV-HepB/Hib (Infanrix-hexa) at ages 6 weeks, 3 months and 5 months, followed by a dose of DTaP-IPV (Infanrix-IPV) at age 4 years (Table 19.1). A booster is given at age 11 years (school year 7), which includes a pertussis component, given as the vaccine Tdap (Boostrix).

If a course of immunisation is late or interrupted for any reason, it may be resumed without repeating prior doses (see Appendix 2).

Alternatives to combination pertussis-containing vaccines

Some parents or guardians may ask about alternatives to pertussis-containing vaccines. The recommended and funded vaccines for children are those described above. There are no diphtheria-only or tetanus-only vaccines available. The Td vaccine contains half the amount of tetanus toxoid and one-fifteenth the amount of diphtheria toxoid compared to the DTaP-containing vaccines. Td was not clinically designed or tested for use to provide the primary vaccine course in children and it is not registered for use in children aged under 5 years. Although there are no safety concerns relating to administration of the vaccine, there is no data on the use of this vaccine for a primary course in children and it is not recommended.

19.5.2 Catch-ups for individuals aged 10 years and older

For adults and children who present with a tetanus-prone wound, boosters are recommended in accordance with the guidelines in the following sections and Table 19.2.

For partially immunised or previously unimmunised individuals aged 10 years and older, a primary immunisation course consists of three doses of a tetanus toxoid-containing vaccine at intervals of not less than four weeks (see Appendix 2). For children aged under 18 years, a booster dose is recommended at least six months after the third dose (which, depending on the age of the child, may be given as the scheduled Tdap vaccine at age 11 years).

Children aged under 18 years may receive Tdap (funded from age 7 to under 18 years); adults aged 18 years and older may receive Td (funded) or Tdap (unfunded). Although Tdap and Td are not approved for use (registered) as a primary course, there are expected to be no safety concerns.

Prior clinical tetanus does not usually confer immunity, and immunisation is required. In 1995 a 40-year-old man developed tetanus for a second time because he failed to complete the recommended course of immunisation after the first episode of tetanus.[18]

Dose intervals between Td and Tdap

When Tdap is to be given to adolescents or adults to protect infants or other vulnerable individuals from pertussis, no minimum interval between Td and Tdap is required,[19, 20, 21] – unless Tdap is being given as part of a primary immunisation course.

19.5.3 Booster doses for adults

Adults are recommended to have their tetanus immunisation status assessed at ages 45 and 65 years, and either given a booster dose of tetanus toxoid-containing vaccine if more than 10 years has elapsed since the previous dose, or a primary course if there is any doubt about the adequacy of previous tetanus immunisation (uncertain or no history of a prior primary course).

Protection against tetanus is expected to last at least 20 years following a booster dose after the primary series. The recommendation for a booster dose at ages 45 and 65 years is intended to ensure ongoing protection, and to facilitate delivery by recommending the booster during routine preventive care for adults.

Offer a booster dose of Td for someone travelling overseas if it has been more than 10 years since the last dose (not funded) (see section 5.5.3).

19.5.4 Pregnancy and breastfeeding

Pregnant women should receive a dose of Tdap (funded) from 28 to 38 weeks' gestation. This should be given during each pregnancy[22] to protect the mother against pertussis and so that antibodies can pass to the fetus (see section 4.1.2).

Td vaccine is not routinely recommended for pregnant women but it can be given under certain circumstances, such as when catch-up is needed for an under-immunised woman, or for management of a tetanus-prone wound[12, 22] (see section 19.5.5). However, Tdap is the preferred vaccine in pregnancy.

Td or Tdap vaccines can be given to breastfeeding women.[12]

19.5.5 Prevention of tetanus following injury

Following injury, it is essential that all wounds be adequately cleaned and devitalised tissue removed. Further treatment depends on the circumstances of each case.

If the injury is considered to be tetanus-prone and there is any doubt about the adequacy of previous tetanus immunisation, the individual must have tetanus immunoglobulin (TIG) and the recommended primary course of three doses of a tetanus toxoid-containing vaccine (Td or Tdap – the latter is not funded for adults aged 18 years and older).

The definition of a tetanus-prone injury is not straightforward, because tetanus can occur after apparently trivial injury, such as from a rose thorn, or with no history of injury. However, there are certain types of wounds likely to favour the growth of tetanus organisms. These include:

- compound fractures
- bite wounds
- deep, penetrating wounds
- wounds containing foreign bodies (especially wood splinters)
- wounds complicated by pyogenic (pus-forming) infections
- wounds with extensive tissue damage (eg, crush injuries, avulsions, contusions or burns)
- any superficial wound obviously contaminated with soil, dust or horse manure (especially if topical disinfection is delayed more than four hours)
- re-implantation of an avulsed tooth – minimal washing and cleaning of the tooth is conducted to increase the likelihood of successful re-implantation.

General measures for the treatment of tetanus-prone wounds

Wounds or injuries should be classified as tetanus-prone or non-tetanus-prone as follows (see Table 19.2):

- non-tetanus-prone wounds – clean, minor wounds that are less than six hours old, non-penetrating and with negligible tissue damage

- tetanus-prone wounds – all wounds that may be contaminated or infected, and are penetrating, more than six hours old and with tissue damage.

Immunised individuals respond rapidly to a booster injection of tetanus toxoid-containing vaccine, even after a prolonged interval. Tetanus toxoid-containing vaccine and TIG should be given at the same time, but into different limbs and using separate syringes.

See also the IMAC factsheet *Guidelines for the management of tetanus-prone wounds* (available for download from: www.immune.org.nz/resources/written-resources).

Table 19.2: Guide to tetanus prophylaxis in wound management

History of tetanus vaccination[a]	Time since last dose	Type of wound	Td or Tdap as appropriate[b,c]	TIG[d]
≥3 doses	<5 years	Tetanus-prone wounds	No	No
≥3 doses	5–10 years	Clean minor wounds	No	No
≥3 doses	5–10 years	Tetanus-prone wounds	Booster dose[e]	No
≥3 doses	>10 years	Tetanus-prone wounds	Booster dose[e]	No
≥3 doses	>10 years	Clean minor wounds	Booster dose[e]	No
<3 doses or uncertain		Clean minor wounds	Complete the course[f]	No
<3 doses or uncertain		Tetanus-prone wounds	Complete the course[f]	Yes

a People who have experienced Arthus-type hypersensitivity reactions (see section 19.7.2) or temperature >39.4°C after a previous dose of a tetanus toxoid-containing preparation should not receive tetanus toxoid-containing preparation more frequently than every 10 years, even if they have a wound that is neither clean nor minor.

b See Appendix 2 for catch-up schedules for previously unimmunised children. DTaP-containing vaccine may be used in children aged under 10 years.

c Td is funded. Tdap may be given to, but is not funded for, individuals aged 18 years and older.

d TIG = tetanus immunoglobulin. The recommended dose is 250 IU given by IM injection as soon as practicable after injury. If more than 24 hours has elapsed, 500 IU is recommended.

e If appropriate, this may count as the age 45 or 65 years booster dose.

f To complete the 3-dose primary immunisation course, give 1 to 3 doses at not less than 4-weekly intervals.

Tetanus immunoglobulin (TIG) availability and storage

TIG is issued in ampoules, each containing 250 IU of human tetanus antitoxin. (Ampoules of 2,000 IU are used for treatment and not for prophylaxis.) These should be protected from light and stored in a refrigerator at +2°C to +8°C. They must never be frozen. TIG is given intramuscularly.

TIG dose

The recommended dose to prevent tetanus is 250 IU of TIG for recent injuries, but this should be increased to 500 IU if more than 24 hours has elapsed since injury, or if there is a risk of heavy contamination or following burns.

There is no need to test the patient's sensitivity before administering TIG, but caution is necessary if the patient is known to suffer complete immunoglobulin A (IgA) deficiency. In this situation, specialist help should be sought (see section 4.3).

Patients with impaired immunity who suffer a tetanus-prone wound may have failed to respond to prior vaccination and may therefore require TIG.

19.5.6 (Re-)vaccination

Tetanus toxoid-containing vaccines are funded for (re-)vaccination of eligible patients, as follows. See also sections 4.2 and 4.3.

DTaP-IPV-HepB/Hib (Infanrix-hexa) and DTaP-IPV (Infanrix-IPV)

An additional four doses (as appropriate) of DTaP-IPV-HepB/Hib (for children aged under 10 years) or DTaP-IPV are funded for (re-)vaccination of patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- with other severely immunosuppressive regimens.

Up to five doses of DTaP-IPV-HepB/Hib (for children aged under 10 years) or DTaP-IPV are funded for children requiring solid organ transplantation.

Tdap (Boostrix)

An additional four doses (as appropriate) of Tdap (Boostrix) are funded for patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- with other severely immunosuppressive regimens.

Td (ADT Booster)

Td is funded for patients following immunosuppression.

19.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

19.6.1 Contraindications

Immunisation with Td, Tdap or another tetanus toxoid-containing vaccine should not be repeated in individuals who have had previous severe hypersensitivity reactions to the vaccine or a vaccine component. Most cases of hypersensitivity have been reported in individuals who have had an excessive number of booster injections outside the guidelines noted above.

19.6.2 Precautions

Protection against the risk of tetanus is paramount if the wound is thought to be tetanus-prone. Immunisation should not be postponed because the patient has a minor infection.

People who have experienced Arthus-type hypersensitivity reactions (see section 19.7.2) or temperature greater than 39.4°C after a previous dose of a tetanus toxoid-containing preparation should not receive tetanus toxoid-containing preparation more frequently than every 10 years, even if they have a wound that is neither clean nor minor.[23]

GBS within six weeks of a tetanus toxoid-containing vaccine weeks is a precaution to receiving a further dose[24] (see section 19.7.2).

See section 14.6.2 for precautions to pertussis-containing vaccines, including DTaP-IPV-HepB/Hib.

19.7 Expected responses and AEFIs

See also sections 5.7 and 14.7 for expected responses and AEFIs with Td, DTaP-IPV-HepB/Hib, DTaP-IPV and Tdap vaccines.

19.7.1 Expected responses

Tetanus toxoid combination vaccines have not been associated with any safety concerns. Sterile abscesses and persistent nodules at the injection site may develop if the injection is not given deeply enough into the muscle.[25] Mild discomfort or pain at the injection site persisting for up to a few days is common.[12]

Tdap has a safety profile similar to Td and both vaccines are generally well tolerated.[26, 27]

19.7.2 AEFIs

Anaphylaxis was reported at a rate of 1.6 per million doses of Td in the US from 1991 to 1995.

The 1994 US Institute of Medicine review of adverse events from tetanus vaccine concluded that the evidence supported a link with brachial plexus neuropathy at a rate of 0.5 to 1 per 100,000 doses within four weeks of immunisation.[28]

Severe local reactions (including large injection site swelling, called Arthus reactions, which are presumed to be immune-complex mediated reactions) are hypersensitivity reactions that have been associated with vaccines containing tetanus and diphtheria toxoids. Historical data on multiple doses of Td and tetanus toxoid vaccines indicate that hypersensitivity was associated with higher levels of pre-existing antibody.[7, 29] People who have experienced Arthus-type hypersensitivity reactions or temperature greater than 39.4°C after a previous dose of a tetanus toxoid-containing preparation usually have very high serum tetanus antibody concentrations and should not receive tetanus toxoid-containing preparation more frequently than every 10 years, even if they have a wound that is neither clean nor minor.[23]

No increased risk of GBS has been observed with use of tetanus toxoid-containing vaccines, and therefore a history of GBS is not a contraindication to receiving a tetanus toxoid-containing vaccine. However, out of prudence, it is recommended that having GBS within six weeks of a tetanus toxoid-containing vaccine is a precaution to receiving a further dose.[24]

19.8 Public health measures

All cases of tetanus must be notified immediately on suspicion to the local medical officer of health, who should be provided with as accurate an immunisation history as possible.

See section 19.5.5 'Prevention of tetanus following injury'. See also the 'Tetanus' chapter of the *Communicable Disease Control Manual 2012*.[30]

19.9 Variations from the vaccine data sheets

Td (ADT Booster) vaccine is not approved for use (registered) for primary immunisation. However, adults aged over 18 years may receive Td (funded) for catch-up of the primary schedule (see Appendix 2).

See section 14.9 for variations from the DTaP-IPV-HepB/Hib (Infanrix-hexa), DTaP-IPV (Infanrix-IPV) and Tdap (Boostrix) data sheets.

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20 Tuberculosis

Key information

Mode of transmission	Inhalation of airborne droplets produced by people with pulmonary or laryngeal tuberculosis (TB). People with latent TB infection and non-pulmonary TB disease are not infectious.
Incubation period	Between 2 and 10 weeks from infection to primary lesion or significant tuberculin skin test (Mantoux) reaction.
Period of communicability	May be years with untreated pulmonary TB. Refer to the *Guidelines for Tuberculosis Control in New Zealand 2010*[1] (or current edition).
Burden of disease	Disseminated and meningeal TB are more common in very young children. The immunocompromised, particularly HIV-infected individuals, are more at risk of disease and complications. In New Zealand, TB is highest in those born in high prevalence countries.
Vaccine	Bacillus Calmette-Guérin (BCG) vaccine can only be administered by an authorised vaccinator with BCG endorsement. Live attenuated vaccine, which must be reconstituted. At the time of writing, BCG supply to New Zealand was interrupted by a global shortage.
Recommendations	Neonatal BCG vaccine should be offered to infants at increased risk of TB, defined as those who: • will be living in a house or family/whānau with a person with either current TB or a history of TB • have one or both parents or household members or carers who, within the last 5 years, lived for a period of 6 months or longer in countries with a TB rate ≥40 per 100,000 • during their first 5 years will be living for 3 months or longer in a country with a TB rate ≥40 per 100,000. (See Appendix 8 for a list of countries with a TB rate ≥40 per 100,000.)

Continued overleaf

Contraindications	Individuals receiving corticosteroids or other immunosuppressive treatment. Individuals suffering from malignant conditions such as lymphoma, leukaemia, Hodgkin's disease or other tumours of the reticulo-endothelial system. HIV-positive or potentially HIV-positive individuals. Infants of mothers who received DMARDs during pregnancy that are monoclonal antibodies (eg, adalimumab, infliximab). Generalised infected skin conditions. Other individuals in whom immunocompromise is known or suspected (see section 20.6.1).
Expected responses	90–95% of people develop a local reaction, which may scar within 3 months. A minor degree of adenitis is normal, not a complication. Suppurative adenitis may take months to resolve; usually no treatment is required.

20.1 Bacteriology

Human TB is caused by infection with *Mycobacterium tuberculosis* or *Mycobacterium bovis*.

20.2 Clinical features

M. tuberculosis or *M. bovis* infection most commonly causes disease in the lungs, but any part of the body can be affected.

The initial infection with *M. tuberculosis* usually goes unnoticed. Early infections can be cleared, progress rapidly to primary TB, or be contained in a latent phase (LTBI) – see Figure 20.1.

Primary TB occurs most commonly in young children aged under 5 years, individuals with immunocompromise or those infected by particularly transmissible isolates of TB.

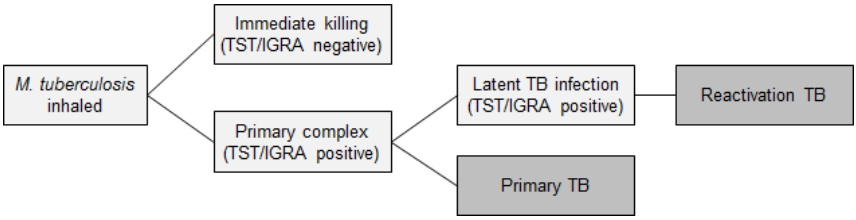
Latent TB infection has no symptoms and is diagnosed by a positive tuberculin skin test or interferon gamma release assay after the exclusion of active TB. Latent infection progressing to active TB is also called reactivation TB.

The lifetime risk for infected people progressing from this latent phase to active TB disease may be as high as 20 percent, but this risk is strongly affected by infecting dose, the age of the person, the presence of healed lesions on chest X-ray and immunocompromise.[2, 3]

The time from infection to clinical manifestations of primary TB varies, from one to six months after infection. Reactivation TB can occur at any time thereafter, even decades after infection. The most common site of infection is the lung (pulmonary TB), where TB infection classically causes an asymmetrical pulmonary infiltrate. The 'classic' TB pathology of caseation, cavity formation and fibrosis occurs late and in a minority of cases. Young children with active TB disease may be asymptomatic or present with symptoms of fever, lassitude and failure to thrive. Older children and adults with active TB disease may present with symptoms of anorexia, fatigue, weight loss, chills, night sweats, cough, haemoptysis and chest pain.

Any organ can be affected by extrapulmonary TB, causing meningitis, pleurisy, pericarditis, bone or joint infection, renal infection, gastrointestinal tract infection, peritonitis or lymphadenitis, or disseminating via the bloodstream and affecting multiple organs (disseminated TB). Disseminated and meningeal TB are more common in very young children. Immunocompromise, like HIV, is associated with higher rates of disseminated TB and less specific clinical features.[4]

Figure 20.1: Stages in the natural history of tuberculosis



Key: TST = tuberculin skin test; IGRA = interferon gamma release assay; TB = tuberculosis.

20.3 Epidemiology

20.3.1 Global epidemiology

Worldwide, the incidence rate of TB is slowly falling by about 1.5 percent per year, but TB remains a major global health problem. The majority of the TB burden exists in 30 high-burden countries. In 2015, TB was one of the top 10 causes of death worldwide and caused more deaths than HIV/AIDS. The WHO estimates there were 10.4 million new TB cases in 2015 and 1.4 million deaths.[5] People living with HIV accounted for 11 percent of all new TB cases (1.2 million) in 2015, and there were an additional 400,000 deaths resulting from TB disease among people living with HIV. There has been an increasing burden of multidrug-resistant TB (defined as resistance to at least isoniazid and rifampicin) with an estimated 480,000 new cases of multidrug-resistant TB in 2015.

In low-burden countries, such as New Zealand, the peak age for TB is in older adults, reflecting their exposure to TB in the past when incidence was higher. In high-burden countries TB is most common in children and young adults. The risk of TB in people who emigrate from high-burden countries is proportionate to the incidence in their country of origin.[6]

20.3.2 New Zealand epidemiology

For detailed TB information, see the *Tuberculosis in New Zealand: Annual Report*, available on the ESR website (https://surv.esr.cri.nz/surveillance/AnnualTBReports.php).

Notifications and rates

TB remains one of the most common notifiable infectious diseases in New Zealand. Cases of TB declined substantially between 1980 and 2007, but they have remained relatively stable since then.[7]

In 2015 there were 300 notifications, corresponding to a notification rate of 6.5 per 100,000, similar to the rate in 2014 (6.7 per 100,000).[7] Notification rates were highest in adults aged 20–29 years (12.3 per 100,000) and 30–39 years (10.2 per 100,000).

Asian ethnic groups had the highest notification rate in 2015 (35.9 per 100,000), followed by Pacific peoples (19.5 per 100,000) and Middle Eastern/Latin American/African (15.8 per 100,000).[7] The notification rate for Māori was considerably lower (3.9 per 100,000) and even lower for European/Other (0.6 per 100,000) groups. There is substantial regional variation in TB notification rates, with higher rates in Auckland and Wellington; cities where many new arrivals to New Zealand have settled.

Risk factors and transmission

Of the 286 new TB cases in 2015, 237 were born overseas (ESR, 9 February 2017). The highest disease rate was among those born in Southern and Central Asia (125.2 per 100,000), followed by those born in South-East Asia (45.6 per 100,000), the Pacific Islands (33.7 per 100,000) and North-East Asia (16.9 per 100,000).

The date of arrival was recorded for 208 of the 237 new TB cases who were born outside of New Zealand (ESR, 9 February 2017). The median interval between the date of arrival and the TB notification was 6 years.

Three children under 5 years of age were notified with TB in 2015, and none were BCG vaccinated.[7] One had miliary and renal tract TB.

Multidrug-resistant TB

Multidrug-resistant TB is rare but does occur in New Zealand. Between 2006 and 2015, on average, 1.2 percent (28 cases) of culture-positive cases were resistant (ESR, 9 February 2017); 26 of these multidrug-resistant TB cases were born overseas (23 in an Asian country) and are assumed to have acquired their resistant organisms overseas.

20.4 Vaccine

Note: Depending on world supply, BCG vaccine may not be available in New Zealand.

BCG vaccine types vary widely, with different strains. The incidence of side-effects with BCG vaccination differs between strains that are considered more reactogenic (ie, those that elicit stronger immune responses in animal models) and strains that are considered less

reactogenic.[8] The more reactogenic strains have also been associated with a higher rate of lymphadenitis and osteitis, especially among neonates. Reducing the vaccination dosage for the more reactogenic strains also reduces the incidence of lymphadenitis.

20.4.1 Licensed vaccine

BCG Vaccine SSI (Seqirus (NZ) Ltd) is a live attenuated vaccine, containing the less reactogenic Danish 1331 strain of *M. bovis*. The 0.1 mL dose for adults and children aged 12 months and older contains 2–8 × 10^5 colony-forming units of *M. bovis*, and the 0.05 mL dose for infants contains 1–4 × 10^5 colony-forming units. Other components and residuals include sodium glutamate, magnesium sulphate heptahydrate, dipotassium phosphate, citric acid, L-asparagine monohydrate, ferric ammonium citrate and glycerol.

20.4.2 Efficacy and effectiveness

The exact immune response elicited by BCG vaccination and the mechanism of action in the host are still not well understood. There is no reliable established laboratory correlate for immunity to *M. tuberculosis*,[9] though this remains an active area of study.[10]

BCG protection is partial and varies according to the age at which vaccination is administered and the disease phenotype in question. A meta-analysis of randomised controlled trials showed neonatal BCG had 59 percent efficacy against pulmonary TB (95% CI: 0.42–0.71) and 90 percent efficacy against meningeal TB (95% CI: 0.23–0.99).[11] Studies conducted since the advent of interferon gamma release assays suggest BCG may also be effective against *M. tuberculosis* infection. A meta-analysis has estimated BCG effectiveness against *M. tuberculosis* infection at 20 percent, though different methods in the included studies each had a wide range of estimates.[12] Thus, the principal role of BCG in New Zealand is to protect young children who are at greatest risk of disease, particularly miliary and meningeal disease.[8] BCG is less effective in adults and older children, particularly if they already have latent infection.

As BCG has been propagated *in vitro* for over 40 years, there are now several strains being manufactured.[13] Immunological responses vary considerably across vaccine strains, but the data to date cannot differentiate which strains, if any, are overall more effective.[14, 15]

In low-income countries, a birth dose of BCG significantly reduces overall infant mortality.[16]

BCG has had little effect in reducing the population rate and transmission of TB,[17] so there are no herd immunity effects. Duration of protection is unknown, possibly 10 to 15 years, but it may be much longer in some populations.[8]

There have been a number of different approaches to using BCG in the control of TB in middle- and high-income countries.[18] For example, the US has not had a BCG programme, whereas New Zealand (see Appendix 1) and the UK had programmes until 1990 and 2005, respectively. The WHO recommends that countries with low rates of active TB, such as New Zealand, target BCG vaccination at children who are at significantly increased risk of TB exposure through household contact.[19] New Zealand (see section 20.5) and the UK now only offer BCG vaccine to high-risk individuals. A study from the Netherlands suggests that around 9,000 children from countries with rates greater than 50 per 100,000 population would have to be given BCG to prevent a severe case.[20]

The current recommendation to use neonatal BCG vaccination in populations with high rates of active TB is part of a control and treatment programme for TB in New Zealand, which includes active contact tracing and treatment of latent TB infection.

There are large international efforts working to improve BCG vaccines and develop new, more effective vaccines.[21]

20.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.[22] Store in the dark at +2°C to +8°C. Do not freeze.

There are variances in strain potency between brands of BCG vaccine so vaccinators should always follow the instructions in the vaccine data sheet (available on www.medsafe.govt.nz).

BCG vaccine requires reconstitution before administration. It is presented as freeze-dried vaccine in a multi-dose vial with diluent in a separate vial. The diluent must be added to the freeze-dried vaccine vial and mixed gently (do not shake vigorously). Protect the vial from light. Leave the reconstituted vaccine to stand for one minute until it forms an opalescent liquid. Reconstituted vaccine should be stored at 4°C, protected from sunlight and used within four hours.

20.4.4 Dosage and administration

Only authorised vaccinators with BCG endorsement are able to administer BCG vaccine (see Appendix 4).

Administer a dose of:

- 0.05 mL to infants aged under 12 months
- 0.1 mL to children aged 12 months or older and adults.

The vaccine is administered by intradermal injection over the point of insertion of the left deltoid muscle (see sections 2.2.3 and 2.2.4).

No follow-up tuberculin skin testing is required.

Repeat BCG vaccination is not recommended.

BCG immunisation given in other countries

BCG is one of the vaccines that are part of the WHO Expanded Programme on Immunization. It is given at birth in most low-income countries.

The following Pacific Island countries[23] recommend BCG vaccination at birth: Cook Islands, Fiji, Kiribati, Nauru, Niue, Papua New Guinea, Samoa, Solomon Islands, Tonga, Tuvalu and Vanuatu.

Usually BCG vaccine is administered in the left deltoid area, but other sites of administration have also (although uncommonly) been used, such as the right deltoid. Revaccination with BCG is not recommended by the WHO.[19]

Co-administration with other vaccines

BCG can be given simultaneously with any other vaccine. However, it must be administered into a separate site in a separate syringe. Because of the risk of local lymphadenitis, no further vaccinations should be given into the arm used for BCG for at least three months. If not given concurrently, BCG should be given at least four weeks after MMR or VV. Note that no time interval is required between administration of BCG and rotavirus vaccines.

HBIG (given at birth to babies of mothers with chronic HBV infection) or human normal immunoglobulin is thought not to reduce the effectiveness of BCG immunisation, which principally acts through cell-mediated immunity.

20.5 Recommended immunisation schedule

20.5.1 Tuberculin skin testing (Mantoux) before BCG vaccination

Tuberculin skin testing is not needed if BCG is given before age 6 months unless a history of contact with a known or possible case of TB is obtained. Although the tuberculin skin test is usually positive in the year following BCG vaccination, at least 50 percent of children will be negative beyond that time, so tuberculin skin testing still has utility for diagnosing TB infection.

20.5.2 BCG eligibility criteria

TB is more common in migrants or families of migrants from high-incidence countries. However, all pregnant women should have a discussion with their lead maternity carer about the risk of TB for their baby.

Neonatal BCG is recommended and funded for infants at increased risk of TB, as defined in Table 20.1.

Table 20.1: Neonatal BCG eligibility criteria

Neonatal BCG is recommended and funded for infants at increased risk of TB, defined as those who:
• will be living in a house or family/whānau with a person with either current TB or a history of TB
• have one or both parents or household members or carers who within the last five years lived for a period of six months or longer in countries with a TB rate ≥40 per 100,000*
• during their first five years will be living for three months or longer in a country with a TB rate ≥40 per 100,000.*

* A list of high-incidence countries and their TB rates is available in Appendix 8.

As a general indication, the following global areas have TB rates ≥40 per 100,000:

- most of Africa
- much of South America
- Russia and the former Soviet states
- the Indian subcontinent
- China (including Hong Kong) and Taiwan
- South East Asia
- some parts of the Pacific (Kiribati and Papua New Guinea have consistently high rates; see Appendix 8 for a list of the high-incidence countries).

Neonates at risk should be identified antenatally by lead maternity care providers and antenatal referral made to the neonatal BCG service. Health care providers can also identify and refer neonates at risk. Immunisation is desirable before infants leave hospital. If this does not happen, immunisation should be arranged through the local medical officer of health.

Children who have missed vaccination at birth may be vaccinated at any time up to age 5 years. If the child is 6 months or older they should have a pre-vaccination tuberculin skin test to detect whether they have already been infected, with vaccination only being given if the child is uninfected.

Infants born before 34 weeks' gestation should have their BCG vaccination delayed until 34 weeks' post-conceptual age.[24] Babies born after this or with low birthweight appear to produce an adequate response, based on tuberculin skin test responses.[25, 26, 27]

If the baby has not been vaccinated before leaving hospital, and if there is a history of *current* TB in a relative who has had contact with the baby, *do not vaccinate immediately*. Withhold vaccination, conduct tuberculin skin testing, seek paediatric advice and vaccinate only after the possibility of infection in the baby has been excluded. Vaccination may not protect the baby who is incubating disease, and may prevent the tuberculin test from assisting with the diagnosis of disease.

A parent's/guardian's request in itself should not be accepted as an indication for immunisation. Parents/guardians seeking vaccination of children who do not meet the above criteria should be referred to the local medical officer of health to discuss the risks and benefits of immunisation before a final decision is made.

The NIR collects information on neonatal BCG immunisation, unless the individual or their parent/guardian has opted off the NIR (see section 2.3.5). The BCG vaccinator usually documents the immunisation data on a paper form, which is then sent to the DHB NIR Administrator to enter onto the NIR.

BCG vaccine information for parents

Information about the BCG vaccine is available in English and other languages from the HealthEd website (www.healthed.govt.nz). This includes information for parents on why the vaccine is recommended, what to expect and how to care for the vaccination site.

20.5.3 Other high-risk individuals or groups

Repeat BCG vaccination is not recommended.

Funded BCG may be offered to the following at-risk people if they are tuberculin skin test- or interferon gamma release assay-negative:

- contacts of active TB cases aged under 5 years (note that a contact exposed to TB in the preceding three months will need two negative tuberculin skin tests, 8 to 12 weeks apart, before vaccination)
- immigrants aged under 5 years from countries with a rate ≥40 per 100,000
- health care workers and laboratory staff, depending on their risk of exposure (refer to the *Guidelines for Tuberculosis Control in New Zealand 2010*,[1] or the current edition)
- people exposed to animals that are likely to be infected.

Vaccination in New Zealand for overseas travel is not available.

20.5.4 Pregnancy and breastfeeding

BCG vaccine is not routinely recommended for pregnant or breastfeeding women.

BCG is a live vaccine, therefore its use in pregnancy is not recommended (see section 20.6.2). If indicated, BCG vaccine may be given to breastfeeding women.[28]

20.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

20.6.1 Contraindications

BCG vaccine should not be given to individuals:

- known to be hypersensitive to any component of the vaccine
- receiving corticosteroids or other immunosuppressive treatment, including radiotherapy (see section 4.3.3)
- suffering from malignant conditions such as lymphoma, leukaemia, Hodgkin's disease or other tumours of the reticulo-endothelial system
- in whom immunocompromise is known or suspected, such as individuals with hypogammaglobulinaemia – primary immune deficiencies in children are often not detected until after the first few weeks of life (ie, after BCG vaccine is given), so a family history of immune deficiency should be sought and, if present, discussed with a paediatrician before vaccination
- known to be infected with HIV, including neonates where the mother's HIV status is unknown – maternal HIV infection should be excluded prior to neonatal vaccination; testing should have been offered as part of the National Antenatal HIV Screening Programme, and infants born to HIV-infected mothers should be under the care of a paediatrician
- aged under 8 months whose mothers received DMARDs during pregnancy that are monoclonal antibodies (eg, adalimumab, infliximab; see Table 4.3) – BCG vaccination should be delayed until the infant is at least 8 months old;[29] these drugs may cross the placenta and cause immunosuppression in the infant
- with generalised infected skin conditions.

20.6.2 Precautions

- BCG vaccine should be avoided in those who are pregnant (this is a counsel of caution, as no harmful effects to the fetus have been observed following accidental immunisation of the mother during pregnancy).
- In the case of eczema, an immunisation site should be chosen that is free of skin lesions.

- Infants born before 34 weeks' gestation should have their BCG vaccination delayed until 34 weeks post-conceptual age.[24]
- Avoid or defer immunisation in a child born with a condition that may require immunosuppressive therapy in future.

20.7 Expected responses and AEFIs

20.7.1 Expected responses

Following the BCG injection, a white weal should appear. This should subside in approximately 30 minutes. The site requires no swabbing or dressing.

Ninety to ninety-five percent of people vaccinated with BCG develop a local reaction, which may include shallow ulceration, followed by healing and scar formation within three months. A minor degree of adenitis developing in the weeks following immunisation should be regarded as normal, not a complication. It may take months to resolve. Suppurative adenitis may also take months to resolve; usually no treatment is required.

20.7.2 AEFIs

AEFIs with BCG vary with age and vaccine strain and are summarised in Table 20.2.

Table 20.2: Age-specific estimated risks for complications after administration of BCG vaccine

Complication	Incidence per 1 million vaccinations	
	Age <1 year	Age 1–20 years
Local subcutaneous abscess; regional lymphadenopathy	387	25
Musculoskeletal lesions	0.39–0.89	0.06
Multiple lymphadenitis; non-fatal disseminated lesions	0.31–0.39	0.36
Fatal disseminated lesions	0.19–1.56	0.06–0.72

The risk of BCG adverse reactions depends on many factors, including strain type, route of administration and the underlying immune state of the patient. Severe injection site reactions, large ulcers and abscesses can occur in individuals who are tuberculin positive. Special care is needed both in interpreting initial tuberculin skin results and in delivering the BCG vaccine.

Rarely, osteitis and osteomyelitis, lupoid and other types of skin disorders, and neurological disorders have been reported following BCG vaccination. Although rare, disseminated BCG disease is the most severe BCG vaccine complication occurring in immunocompromised people, such as children with primary immune deficiency. This needs rapid and aggressive treatment and has a high mortality.

Keloid scars at the injection site, although not uncommon, are largely avoidable. Some sites are more prone to keloid formation than others and vaccinators should adhere to the site recommended (mid-upper arm). Most experience has been with the upper arm site, and it is known that the risk of keloid formation increases greatly if the injection is given higher than the insertion of the deltoid muscle into the humerus.

Every effort should be made to recover and identify the causative organism from any lesions that constitute a serious complication.

Most local and regional adenopathy resulting from BCG vaccination will resolve spontaneously, and there is rarely a need for medical or surgical intervention. Treatment recommendations for local abscess formation and suppurative lymphadenitis remain controversial.[30] If suppurative adenitis reactions persist for longer than three months, seek specialist opinion. However, anyone presenting with more widespread or distant disease needs referral to a specialist.

Abscesses and more serious complications should be reported to CARM (see 'AEFI reporting process – notifying CARM' in section 1.6.3), and also reported to the local medical officer of health in the interests of quality control of the BCG vaccination technique.

20.8 Public health measures

It is a legal requirement that all cases of active TB be notified to the local medical officer of health. While there is no legal requirement to notify cases of latent TB infection that are being treated, for surveillance purposes and with the patient's consent they should be reported to the local medical officer of health.

Under the Health (Protection) Amendment Act 2016, the medical officer of health is given wide powers to investigate and control all TB cases and their contacts, while DHBs are required to make provision for the treatment and supervision of patients and their contacts.

The primary purpose of neonatal BCG vaccination is to protect child case contacts from TB disease and its most devastating consequences. Screening of certain risk groups and case contact management are other elements of TB control in New Zealand. These programmes do not obviate the need for BCG vaccination, as screening coverage is partial and contact tracing may not occur in time to prevent illness in child contacts. The local medical officer of health can advise on local TB control policies, including issues in BCG immunisation.

Both TB infection and BCG immunisation lead to the development of a cellular immune response, which can be detected by measuring dermal induration after the injection of tuberculin-purified protein derivative (eg, via the tuberculin skin test). A positive response to a tuberculin skin test may be an indication of current infection, previous natural infection or prior BCG immunisation. However, the false positive effect after vaccination will wane, rapidly in all individuals who receive the vaccine in the neonatal period and more slowly in those who are vaccinated at an older age such as during the primary-school years.[31]

In vitro tests have been developed to measure the release of interferon-gamma from host lymphocytes in response to well-defined antigens. The antigens used are not present in BCG strains of *M. bovis* or most non-tuberculous mycobacteria. Interferon gamma release assay has the advantage of greater specificity and convenience, but it is more expensive.[32] For more information, refer to the 'Tuberculosis' page of the Ministry of Health website (www.health.govt.nz/our-work/diseases-and-conditions/tuberculosis) and the 'Tuberculosis' chapter of the *Communicable Disease Control Manual 2012*.[33]

20.9 Variations from the vaccine data sheet

The data sheet states that BCG vaccine should not be given to infants born to HIV-positive mothers. The Ministry of Health recommends that BCG may be given to HIV-negative infants born to HIV-positive mothers – providing that the infant is confirmed to be HIV negative by appropriately-timed PCR tests before the vaccine is given.[28, 34] Seek specialist advice.

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21 Varicella (chickenpox)

Key information

Mode of transmission	Airborne droplets from, or contact with, vesicular lesions or possibly respiratory secretions.
Incubation period	Usually 14–16 days (range 10–21 days).
Period of communicability	From 2 days before onset of the rash until all lesions have crusted.
Burden of disease	Without immunisation, most people have infection during childhood. Groups at risk of severe complications include pregnant women and their unborn babies, and immunocompromised individuals.
Funded vaccine	VV (Varilrix) is a live attenuated vaccine.
Dose, presentation, route	0.5 mL per dose after reconstitution. Pre-filled syringe and glass vial. The vaccine must be reconstituted prior to injection. Subcutaneous injection.
Vaccine indications and schedule	1 dose is funded for: • children at age 15 months (for those who were born on or after 1 April 2016); or • previously unvaccinated children turning 11 years old on or after 1 July 2017 who have not previously had a varicella infection (as determined by clinical history). Up to 2 doses are funded for certain special groups and their contacts. Recommended but not funded for: • susceptible children who are not eligible by age for funded vaccine • susceptible adolescents and adults.
Vaccine efficacy/ effectiveness	1 dose confers approximately 99% protection against severe disease and 80% protection against varicella disease of any severity. Breakthrough disease is usually mild.

Continued overleaf

Contraindications	Certain immune deficiency states – consult the child's paediatrician for advice. High-dose steroids. Known systemic hypersensitivity to neomycin. Active untreated TB. Pregnancy.
Adverse events to vaccine	Generally mild and self-limiting, and include local reactions, fever and mild papulo-vesicular rash in normal healthy individuals.
Post-exposure prophylaxis	Zoster immunoglobulin (ZIG) is most effective if given as soon as possible after exposure but may be given up to 10 days post-exposure. VV may be used for post-exposure prophylaxis for immune-competent people if given within 5 days of exposure.

21.1 Virology

Varicella (chickenpox) is a highly infectious disease caused by human herpes virus type 3 (varicella zoster virus or VZV). Reactivation of latent VZV results in herpes zoster (HZ) (shingles), a disease with considerable morbidity (see chapter 22).

21.2 Clinical features

Varicella is one of the most infectious diseases known (along with pertussis and measles). Transmission occurs via airborne droplets from, or contact with, vesicular lesions and possibly respiratory tract secretions. The incubation period is usually 14 to 16 days (range 10 to 21 days, but can be longer in immunocompromised individuals and those who have received ZIG), and cases are infectious from 2 days before the onset of the rash until all the lesions have crusted. A maculopapular rash, which becomes vesicular, appears in crops over several days, first on the face and scalp, later spreading to the trunk and then the limbs. Vesicles, ranging in number from few to many hundred, dry and crust after three to four days. A hallmark of the rash is lesions in varying stages of development; those on mucosal surfaces (mouth, vagina) can cause considerable distress. The rash is pruritic and is usually associated with mild fever, malaise, anorexia and listlessness.

In the majority of children, varicella is a mild disease, but complications requiring hospitalisation and fatalities do occur. Secondary bacterial skin infections are common. Serious complications include central nervous system involvement (encephalitis, cerebellar ataxia, stroke), pneumonia, secondary invasive bacterial infections, and even death. Adults are 25 times more likely to develop severe disease than children, with pneumonia being the most common complication, often requiring mechanical ventilation. VZV pneumonia carries an overall mortality rate of 10–30 percent.

Maternal varicella occurring in the first half of pregnancy can cause the rare but devastating congenital varicella syndrome (see Table 21.4), whereas disease very late in pregnancy (from five days before to two days after delivery) may cause severe neonatal varicella infection. Pregnant women who contract varicella have an estimated 10–20 percent risk of developing VZV pneumonia.

Others vulnerable to both VZV and HZ are those who are immunocompromised, such as people taking immunosuppressive medications (eg, cancer treatment or organ transplant patients) and those with HIV infection. Varicella can be a fatal disease in immunocompromised individuals.

VZV infection is followed by the production of VZV-specific T-cell mediated immunity, necessary to maintain the latency of VZV in the ganglia and prevent reactivation as shingles (HZ). The immune response is boosted by subclinical reactivation of latent virus. The incidence of HZ increases with age as VZV-specific T cell-mediated immunity declines (see chapter 22).

21.3 Epidemiology

21.3.1 Global burden of disease

In temperate climates, winter-spring epidemics occur with peak incidence in preschool and early primary school ages (1–9 years). Around 90 percent of individuals have been infected by adolescence and fewer than 5 percent of adults are susceptible. The annual number of infections therefore approximates the birth cohort.[1, 2]

Transmission of the virus is less efficient in tropical climates. Adolescent and adult immigrants to New Zealand from such countries are more likely to be susceptible, placing them at risk of contracting chickenpox in their new environment. Being older, they are more likely to suffer severe disease.

The long incubation and high transmissibility of VZV conspire to maximise disruption to families: by the time the rash occurs a child will have been infectious for two days; any susceptible household contacts will then become unwell just as the first child recovers. This results not only in morbidity but also in financial consequences for parents missing work.

Crude hospitalisation admission rates in high-income countries range from around 2–6 per 100,000 population-year. Most of these admissions are children, consistent with the high incidence of varicella in children. Crude mortality rates ranged from 0.3–0.5 per million population-year with overall case fatality ratios of around 2–4 per 100,000 cases. Almost 90 percent of varicella hospital admissions occur in otherwise healthy and immunocompetent individuals.[1, 2]

VV has been introduced into childhood immunisation programmes overseas, including the US from 1995 and Australia from 2005 with dramatic reductions in varicella morbidity, hospitalisations and mortality.[3, 4, 5] By 2005 in the US, vaccine coverage was approximately 90 percent and varicella incidence had declined by more than 90 percent. Herd immunity was observed outside of age groups targeted for vaccination.[1]

Following the introduction of VV onto the childhood schedule, exposure to wild-type virus decreases. It has been theorised that a lack of boosting may lead to an increase in HZ in older adults. However, studies that have investigated this issue have been unable to attribute any increase in incidence of HZ to the childhood VZV vaccine programme.[6, 7] Studies from the UK and Canada reported increases in HZ not associated with a vaccination programme, and some US data showed HZ rates were increasing prior to the initiation of their varicella vaccination programme.[8, 9]

21.3.2 New Zealand epidemiology

Varicella is not a notifiable disease, so data is limited for uncomplicated varicella, but the epidemiology is likely to be as described above for temperate climates. With increasing participation in early childhood services, a greater proportion of infections may now be occurring in preschool-aged children. It is expected that HZ numbers will rise in New Zealand as the population ages.

Prospective nationwide surveillance of varicella in New Zealand children found that the incidence of varicella-related hospitalisation was 8.3 per 100,000 children per year – although this is likely to be a significant underestimate.[10] Māori and Pacific children were disproportionately affected, with an almost three- and four-fold increase in the relative risk of hospitalisation for varicella or its complications, respectively. Nine percent of hospitalised children required ICU admission and the majority of them were previously healthy. Almost one-third of hospitalised children had multiple complications from varicella, and those with neurological complications were more likely to have ongoing problems at discharge.

A retrospective survey of admissions to the paediatric intensive care unit (PICU) at Auckland's Starship Hospital (2001–2011) found 26 children admitted for varicella or its secondary complications.[11] The main PICU admission reasons were neurological (38.5 percent) and secondary bacterial sepsis or shock (26.9 percent). Four children died (15 percent), three of whom were immunocompromised. A further eight children (31 percent) had ongoing disability at discharge, most having had no prior medical condition.

Based on overseas rates, it is estimated that up to one case of congenital varicella syndrome may be expected in New Zealand each year, although few have been reported.

Adults (aged 20 years and older) account for 20–24 percent of VZV-related hospital admissions;[12] approximately one person per year dies from VZV, and most of the VZV-related deaths occur in adults.[13]

21.4 Vaccines

21.4.1 Available vaccines

There are two live attenuated monovalent VVs registered (approved for use) and available (marketed) in New Zealand. Two quadrivalent live attenuated MMRV vaccines are registered but not currently available in New Zealand.

Funded vaccine

Each 0.5 mL dose of monovalent VV (Varilrix, GSK) contains no less than $10^{3.3}$ PFU (plaque-forming units) of the varicella virus (Oka strain). Other components and residuals include amino acids, lactose, neomycin sulphate and polyalcohols (mannitol and sorbitol).

Other vaccines

Monovalent VV

- Monovalent VV (Varivax, MSD) contains not less than 1,350 PFU of the varicella virus (Oka/Merck strain). Other components and residuals include sucrose, gelatin, urea, sodium chloride, monosodium L-glutamate, potassium chloride, MRC-5 cells, neomycin and bovine calf serum.

Quadrivalent MMRV

- MMRV (ProQuad, MSD) contains not less than 3.00 $\log_{10}$ $TCID_{50}$ (50 percent tissue culture infectious dose) of Enders' attenuated Edmonston strain measles virus; 4.30 $\log_{10}$ $TCID_{50}$ of Jeryl Lynn strain mumps virus; 3.00 $\log_{10}$ $TCID_{50}$ of Wistar RA 27/3 rubella virus; and a minimum of 3.99 $\log_{10}$ PFU of Oka/Merck varicella virus. Other components and residuals include sucrose, gelatin, urea, sodium chloride, sorbitol, monosodium L-glutamate, sodium phosphate, human albumin, sodium bicarbonate, potassium phosphate, potassium chloride, neomycin, bovine serum albumin, and residual components of MRC-5 cells, including DNA and protein.

- MMRV (Priorix-Tetra, GSK) contains not less than $10^{3.0}$ $CCID_{50}$ of the Schwarz measles, not less than $10^{4.4}$ $CCID_{50}$ of the RIT 4385 mumps, not less than $10^{3.0}$ $CCID_{50}$ of the Wistar RA 27/3 rubella and not less than $10^{3.3}$ PFU of the varicella virus strains. Excipients and residuals include lactose, amino acids, mannitol, sorbitol, neomycin sulphate (residual), and water for injections.

See also section 11.4.1 for more information about MMR vaccines. Note that MMRV vaccines are not currently available in New Zealand.

21.4.2 Efficacy and effectiveness

Single-dose varicella vaccination programmes have had a dramatic impact on the incidence of VZV infections,[14, 15, 16] hospitalisations[3, 4, 17] and serious outcomes,[5] particularly when high coverage rates are achieved. Indirect effects are also apparent. A 2014 systematic review of varicella vaccines found that a single dose of VV is moderately effective for preventing any severity of varicella (approximately 80 percent) in immune-competent individuals, highly effective for preventing moderate-severe disease (approximately 95 percent) and highly effective in preventing severe disease only (approximately 99 percent).[18] However, single-dose programmes are associated with outbreaks even among highly vaccinated groups.[19] The use of a second dose during outbreaks has been an effective strategy to prevent further cases; catch-ups in non-immunised groups without a previous history of varicella are also important.

There is a significant reduction in breakthrough disease when two doses are given. After a second dose in children the immune response is markedly enhanced, with over 99 percent of children attaining an immune response thought to provide protection, and the geometric mean antibody titre is also significantly increased.

Over a 10-year period the estimated vaccine efficacy of two doses for prevention of any varicella disease is 98 percent (compared to 94 percent for a single dose), with 100 percent efficacy for the prevention of severe varicella. The likelihood of breakthrough varicella is reduced by a factor of 3.3.[20, 21] Because of this data, in 2006 the US authorities recommended a two-dose strategy for varicella prevention, with the first dose at age 12–15 months and the second at age 4–6 years, as for MMR.[19, 20]

The antigenic components of MMRV vaccines are non-inferior compared with simultaneous administration of MMR and VV,[22, 23] for both the first and second doses.

Herd immunity

In regions where universal varicella vaccination programmes have been implemented, significant declines in varicella cases and hospitalisation have been observed. These programmes also reduce circulating VZV and provide protection through herd immunity for those who are unable to be immunised, such as infants and immunocompromised individuals.

In the US, the annual average age-adjusted mortality rate for varicella was 0.05 per million population during 2008–2011, an 87 percent reduction from the pre-vaccine years.[24] In Canada between 2000 and 2007, a single dose of VV was introduced to the immunisation schedules of different provinces at 12 months of age; most provinces also included catch-ups for susceptible children at preschool or school. An ecological study of varicella-related hospitalisations in Canada between 1990 and 2010 found that hospitalisation rates decreased in all age groups, including infants and those aged 20–39 years.[25] Similar herd effects were seen in Germany, with declines in varicella cases and hospitalisations in infants and adolescents who were not eligible for VV.[26]

Duration of immunity

Varicella vaccination provides long-term but probably not lifelong immunity against VZV, in contrast to VZV natural infection. The duration of protection after a single dose of vaccine is difficult to study – especially if wild-type varicella continues to circulate liberally in the community, providing natural boosting and prolonging the duration of protection.[18] Many countries that initially introduced a single-dose vaccination programme have subsequently changed to a two-dose programme as the epidemiology of the disease has changed over time.

21.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.[27]

VV requires reconstitution before administration.

Varilrix is presented as a lyophilised powder for reconstitution with the supplied diluent. The vaccine should be stored in the refrigerator at +2°C to +8°C, although the diluent may be stored at room temperature (to a maximum of 25°C). Reconstituted vaccine should be used immediately. However, if this is not possible, it may be kept for up to 90 minutes at room temperature (to a maximum of 25°C) and up to eight hours in the refrigerator (+2°C to +8°C).

21.4.4 Dosage and administration

The dose of monovalent VV is 0.5 mL, administered by subcutaneous injection in the deltoid area (see section 2.2.3).

Co-administration with other vaccines

Monovalent VV can be administered concurrently with other vaccines, but in a separate syringe and at a different site. If not administered concurrently, the vaccine must be separated from other live vaccines (eg, MMR, BCG) by at least four weeks.

21.5 Recommended immunisation schedule

Recommendations for VV are summarised in Table 21.1 and discussed below.

VV can be administered at age 15 months with MMR, Hib and PCV10 vaccines. Because the risk of febrile seizures for those aged 12–23 months is higher following MMRV than MMR+VV (see section 21.7), this dose should be administered as monovalent VV. (This requires four injections at the 15-month visit; see section 2.2.7.) For a second (currently unfunded) dose of VV, or first doses after age 4 years, either VV or MMRV (when available) can be used.

Table 21.1: Varicella vaccine recommendations and schedule

Recommended and funded

1 dose of VV for:

- children at age 15 months (who were born on or after 1 April 2016); or
- previously unvaccinated children turning 11 years old on or after 1 July 2017 who have not previously had a varicella infection.

2 doses of VV, at least 6 weeks apart, for the following special groups:[a]

- non-immune patients:
  - with chronic liver disease who may in future be candidates for transplantation[b]
  - with deteriorating renal function before transplantation[b]
  - prior to solid organ transplant
  - prior to any elective immunosuppression[c]
  - for post-exposure prophylaxis of immune-competent in-patients
- patients at least 2 years after bone marrow transplantation, on the advice of their specialist
- patients at least 6 months after completion of chemotherapy, on the advice of their specialist
- HIV-positive patients who are non-immune to varicella, with mild or moderate immunosuppression, on the advice of an HIV specialist
- patients with inborn errors of metabolism at risk of major metabolic decompensation, with no clinical history of varicella
- household contacts of paediatric patients who are immunocompromised or undergoing a procedure leading to immunocompromise, where the household contact has no clinical history of varicella
- household contacts of adult patients who have no clinical history of varicella and who are severely immunocompromised or undergoing a procedure leading to immunocompromise, where the household contact has no clinical history of varicella.

Recommended, not funded

1 dose for all susceptible healthy children aged under 13 years who do not meet the eligibility criteria for the funded dose.

2 doses, at least 6 weeks apart, for all susceptible adolescents and adults.

a See chapter 4 'Immunisation of special groups' for more information.

b See Table 4.1 for an accelerated immunisation schedule for infants in whom liver or kidney transplant is likely.

c Note that immunosuppression due to steroid or other immunosuppressive therapy must be for a treatment period of greater than 28 days.

21.5.1 Usual childhood schedule

From 1 July 2017, one dose of VV (Varilrix) is funded for children at age 15 months (who were born on or after 1 April 2016). A second VV dose is not currently funded but may be purchased for those who wish to reduce the risk of breakthrough disease.

A catch-up dose of VV is funded for previously unvaccinated children turning 11 years old on or after 1 July 2017 who have not previously had a varicella infection (as determined by clinical history). This dose aims to protect those who have not become immune to varicella before adolescence, as disease in adolescents and adults can be more severe.

21.5.2 Special groups

Two doses of VV (Varilrix), at least six weeks apart, are recommended and funded for the special groups listed in Table 21.1 above.

Immunocompromised (including immunosuppressed) individuals

The vaccine should not be given to immunocompromised individuals except under the direction and care of a specialist, following a suitable protocol[19] (see sections 4.2 and 4.3). Immunocompromised individuals are at highest risk of severe varicella and zoster infections. The original vaccine formulations, in particular Varivax, have been studied in immunocompromised children (most of whom were children with leukaemia in remission). Approximately 20 percent of these vaccine recipients required acyclovir because of a rash developing up to four weeks after vaccination. Despite this, the study concluded that the vaccine Varivax was safe, immunogenic and effective in these children.[28, 29] The combination MMRV vaccine should not be used in immunocompromised individuals.

Household contacts of immunocompromised individuals

Where such individuals cannot be vaccinated, it is important to vaccinate the household members and other close contacts (funded for household contacts) to provide 'ring fence' protection (see sections 4.2, 4.3 and 21.7.1). Immunisation of children with congenital T-cell immune deficiency syndromes is generally contraindicated, but those with

impaired humoral immunity may be immunised (see section 21.6.1 for further contraindications).

21.5.3 Recommended but not funded

A single dose of VV is recommended for susceptible children who do not meet the eligibility criteria for funded vaccine (Table 21.1). A second dose may also be purchased for those who wish to reduce the risk of breakthrough disease.

VV in a two-dose schedule is recommended but not funded for the following groups:

- adults and adolescents who were born and resided in tropical countries, if they have no history of varicella infection
- susceptible adults and adolescents (ie, those who have no prior history of chickenpox)[19]
- susceptible individuals who live or work in environments where transmission of VZV is likely (eg, staff in early childhood education services, residents and staff members in institutional settings)[19]
- susceptible individuals who live and work in environments where transmission can occur (eg, college students, inmates and staff members of correctional institutions, and military personnel)[19]
- susceptible non-pregnant women of childbearing age[19]
- susceptible international travellers[19]
- health care workers (see below)
- susceptible individuals who have been exposed to varicella (see section 21.8.3).

See section 21.8.1 for information about assessing susceptibility.

Health care workers

All health care workers on obstetric, paediatric and neonatal units, and those caring for immunocompromised children and adults, should be immunised with VV (not funded) if they are susceptible to varicella. When a health care worker has a good history of prior varicella infection,[30] no blood test is required. If there is not a good history of varicella infection, a blood test to assess susceptibility will be necessary,

as many individuals with no clinical history of varicella are immune (see section 21.8).

If a health care worker who has clinical contact with patients develops a rash as a result of the vaccine (around 5 percent), they must be excluded from contact with immunocompromised or other at-risk patients and allocated other duties, or excluded from their place of work, for the duration of the rash.

21.5.4 Pregnancy and breastfeeding

Varicella vaccines are contraindicated in pregnant women. Pregnancy should be avoided for at least four weeks after vaccination.[31] The vaccine's safety for the fetus has not yet been demonstrated, although no congenital defects have been described following inadvertent administration to pregnant women.

A pregnant woman is not a contraindication for immunisation of a child in the household, and the vaccine can be administered to non-immune mothers who are breastfeeding.

21.6 Contraindications and precautions

See section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

21.6.1 Contraindications

Monovalent VV is contraindicated for the following people:

- individuals with primary or acquired T-cell immune deficiency states – consult the child's paediatrician for advice[31]
- individuals on high-dose steroids for more than two weeks (ie, children on 2 mg/kg per day or more of prednisone or its equivalent, or 20 mg per day if their weight is over 10 kg)
- individuals with a history of an anaphylactic reaction to a prior dose of VV or with known systemic hypersensitivity to neomycin or to any other component of the vaccine
- individuals with active untreated TB

- pregnant women – women should avoid pregnancy for at least four weeks after vaccination[31] (see section 21.5.4).

21.6.2 Precautions

Because of the association between Reye syndrome, natural varicella infection and salicylates, the vaccine manufacturers advise against the use of salicylates for six weeks after VV is given. There has been no reported association between the vaccine and Reye syndrome, but avoidance of salicylates is recommended as a precaution,[31] and physicians need to weigh the theoretical risk of Reye syndrome from the vaccine against the known risk from varicella disease in children receiving long-term salicylate therapy. Children on low-dose aspirin following cardiac surgery would be more at risk of thrombosis from stopping their aspirin[32] than from the theoretical risk of Reye's with VV.

If tuberculin testing has to be done, it should be carried out before or simultaneously with vaccination because it has been reported that live viral vaccines may cause a temporary depression (anergy) of tuberculin skin sensitivity.[33] As this anergy may last up to a maximum of six weeks, tuberculin testing should not be performed within that period after vaccination to avoid false negative results.

On the advice of their specialist, VV may be administered to:

- patients at least two years after bone marrow transplantation
- patients at least six months after completion of chemotherapy
- HIV-positive patients who are non-immune to varicella, with mild or moderate immunosuppression.

For suggested intervals between receipt of human normal immunoglobulin or other blood products and VV, see Table A6.1 in Appendix 6.

21.7 Expected responses and AEFIs

21.7.1 Expected responses

A 2013 systematic review of varicella vaccines found that mild adverse events were the most frequently reported AEFIs.[34] This includes

injection site reactions such as pain, swelling and redness, which occurred in up to 28 percent of recipients. There was no increased risk of cerebellar ataxia, encephalitis or ischaemic stroke following vaccination. Post-marketing surveillance in the US found the rate of AEFIs to be 30 per 100,000 doses of VV, and the rate of serious AEFIs was less than 4 per 100,000 doses. Fever has been reported in 15 percent of healthy children following VV and 10 percent of adults.[31, 35]

Post-VV rash

In approximately 1–3 percent of immunised children, a localised rash develops, and in an additional 3–5 percent a generalised varicella-like rash develops.[31] These rashes typically consist of two to five lesions and may be maculopapular rather than vesicular; lesions usually appear 5 to 26 days after immunisation. Not all rashes can be attributable to the vaccine,[31] some may be due to exposure to wild-type virus, prior to vaccination.

Transmission of vaccine virus to contacts of vaccinated individuals

In healthy vaccinees, transmission of vaccine virus to contacts is exceedingly rare, documented in nine immunised people and resulting in 11 secondary cases. The documented risk exists only if the immunised person develops a rash.[31] Err on the side of caution and isolate the vaccinee if they are a household contact of an immunocompromised individual and a post-immunisation rash occurs. If an immunocompromised individual inadvertently comes in contact with a vaccinee who has a varicella-like rash, the administration of zoster immunoglobulin (ZIG) and/or acyclovir should be considered (see below).[31] Intravenous acyclovir may be required if symptoms develop.

21.7.2 AEFIs

Vaccine virus shingles

The Oka strain of varicella used in the available vaccines can establish latent ganglionic infection in vaccinees and later reactivate to produce clinical zoster (shingles). The risk of zoster is lower, and the clinical severity milder, in healthy vaccinees than in naturally infected children.

A cohort study in children with acute lymphoblastic leukaemia (who have a high rate of zoster in childhood) showed that vaccinees had less than one-fifth the zoster rate of their naturally infected counterparts.[28, 36]

Febrile seizures with MMRV vaccine

Compared with the use of MMR and VV at the same visit, use of MMRV vaccine requires one fewer injection but is associated with a higher risk of fever and febrile seizures 5 to 12 days after the first dose among children aged 12–23 months (approximately one extra febrile seizure for every 2,300–2,600 MMRV vaccine doses).[37] After the second dose, there are no differences in incidence of fever, rash or febrile seizures among recipients of MMRV vaccine compared with recipients of MMR and VV.

This is why MMRV vaccine is not recommended in New Zealand as a first dose for children prior to their fourth birthday (approximately 97 percent of febrile seizures occur in children before age 4 years). MMRV vaccine can be given as a first dose to children after their fourth birthday, and as a second dose to children of any age (15 months to 12 years).

21.8 Public health measures

At present, VZV is not a notifiable disease in New Zealand.

21.8.1 Susceptibility

In general, a positive past history of chickenpox can be taken as indicating immunity, provided there has not been an intervening bone marrow transplant or other immunosuppressive therapy. Recall of varicella or characteristic rash is reliable evidence of immunity. In people with no history or recall of the rash, 70–90 percent are found to be immune.[31] Consult with the local laboratory about the availability and interpretation of varicella serology.

21.8.2 Post-exposure prophylaxis with zoster immunoglobulin (ZIG)

ZIG is a high-titre immunoglobulin available from the New Zealand Blood Service for passive immunisation of varicella in high-risk

individuals. It is most effective if given as soon as possible after exposure, but may be given up to 10 days post-exposure.[38, 39] Intravenous immunoglobulin (IVIG) can be given when ZIG is unavailable.

The decision whether to offer ZIG depends on:[40]

- the likelihood that the exposed person is susceptible to varicella
- the likelihood that infection will result from a given contact
- the likelihood that an individual will develop serious complications if infected.

Contact (exposure) can be defined as follows:[40]

- household contact – infection is very likely to occur in a susceptible individual living with an infected contact
- playmate contact – more than one hour of play indoors with infected individual
- newborn infant contact – this occurs when the mother of a newborn infant develops chickenpox (but not shingles) from seven days before to seven days after delivery
- hospital contact – in the same two-bed room or face-to-face contact for longer than 5 minutes.

Provided exposure has occurred and susceptibility is likely, **ZIG is recommended for**:

- pregnant non-immune women (see section 21.8.6 below and discuss with an infectious diseases physician)
- newborn infants whose mother had onset of chickenpox (but not shingles) within seven days before or after delivery (see section 21.8.6)
- hospitalised premature infants whose mothers have no history of chickenpox, or who were born at less than 28 weeks' gestation, or with birthweight less than 1,000 g, irrespective of maternal history
- immunocompromised individuals – discuss the use of ZIG with their specialist, as appropriate.

Dosage of ZIG

The ZIG prepared by CSL Behring in Melbourne, from New Zealand donors, is available in single vials containing 200 IU varicella-zoster antibody. The actual volume in the vial is stated on the label. The recommended dose is based on body weight and is shown in Table 21.2 below. ZIG should be given intramuscularly, not intravenously.

Table 21.2: Dose of ZIG based on body weight

Weight of patient (kg)	Dose (IU)	Number of vials
0–10	125	1
10.1–20	250	2
20.1–30	375	2
30.1–40	500	3
over 40	600	3

Source: CSL Behring. 2014. *Zoster Immunoglobulin-VF Product Data Sheet*. URL: www.nzblood.co.nz/Clinical-information/Transfusion-medicine/Health-professionals-medicine-datasheets/Immunoglobulins (accessed 24 June 2015).

If ZIG is not available, IVIG can be used. The titre of anti-varicella antibody will vary between lots, and the blood transfusion centre haematologist needs to be contacted to confirm the appropriate dose when IVIG is used.

21.8.3 Post-exposure vaccination and outbreak control

VV may be used for post-exposure prophylaxis of susceptible individuals aged 9 months or older, if there are no contraindications to vaccine use[31] – see Table 21.3. Data from the US and Japan from household, hospital and community settings indicates that VV is effective in preventing illness or modifying varicella severity if used within three days, and possibly up to five days, of exposure.

Table 21.3: Post-exposure varicella vaccination recommendations

Note: Funded groups are in the shaded rows below. See the Pharmaceutical Schedule (www.pharmac.govt.nz) for any changes to the funding decisions.

	Number of doses	Schedule
Immune-competent hospital in-patients who are susceptible to varicella	2 doses	1st dose within 3 days of exposure (up to a maximum of 5 days) 2nd dose at least 6 weeks later
Susceptible children aged 9–15 months*	1 dose	Give within 3 days of exposure (up to a maximum of 5 days)
Susceptible children aged under 13 years – who are not eligible for age-appropriate funded vaccine	1 dose	Give within 3 days of exposure (up to a maximum of 5 days)
Susceptible adolescents (aged 13 years and older) and adults	2 doses	1st dose within 3 days of exposure (up to a maximum of 5 days) 2nd dose at least 6 weeks later

* Children who were under age 15 months when they received VV for post-exposure prophylaxis will still be eligible for the age 15-month dose, providing they were born on or after 1 April 2016. Ensure there are at least 6 weeks between doses.

VV may not prevent disease in all cases because some individuals may have been exposed to the same source as the index case.[31] If exposure to varicella does not result in infection, post-exposure vaccination should induce protection against subsequent exposure. If the exposure results in infection, no evidence indicates that administration of VV during the pre-symptomatic or prodromal stage of illness increases the risk for AEFIs. Note that although this method of immunisation may be successful, it is not necessarily reliable. Immunisation before exposure is therefore recommended as the preferred method of preventing outbreaks.

21.8.4 In-hospital exposure

In the event of an exposure:

- susceptible staff should be excluded from contact with high-risk patients from day 8 to day 21 after exposure to varicella (or shingles in an immunocompromised patient)

- hospital staff who have no history of chickenpox and who will be in contact with pregnant women or high-risk patients should be tested for varicella zoster antibodies; vaccination is recommended for those who are not immune or whose serostatus cannot be promptly determined.

Two doses of VV are funded for post-exposure prophylaxis of immune-competent in-patients who are susceptible to varicella (see section 21.8.3).

21.8.5 Exclusion from school or early childhood education services

Parents/guardians should be advised that:

- infected children should be excluded from early childhood education services or school until fully recovered, or all lesions have crusted. Mild breakthrough disease in immunised children may not crust but they should be excluded until no new lesions appear for 24 hours.[31]
- immune-deficient children should be excluded from early childhood education services or school until three weeks after the last documented case.

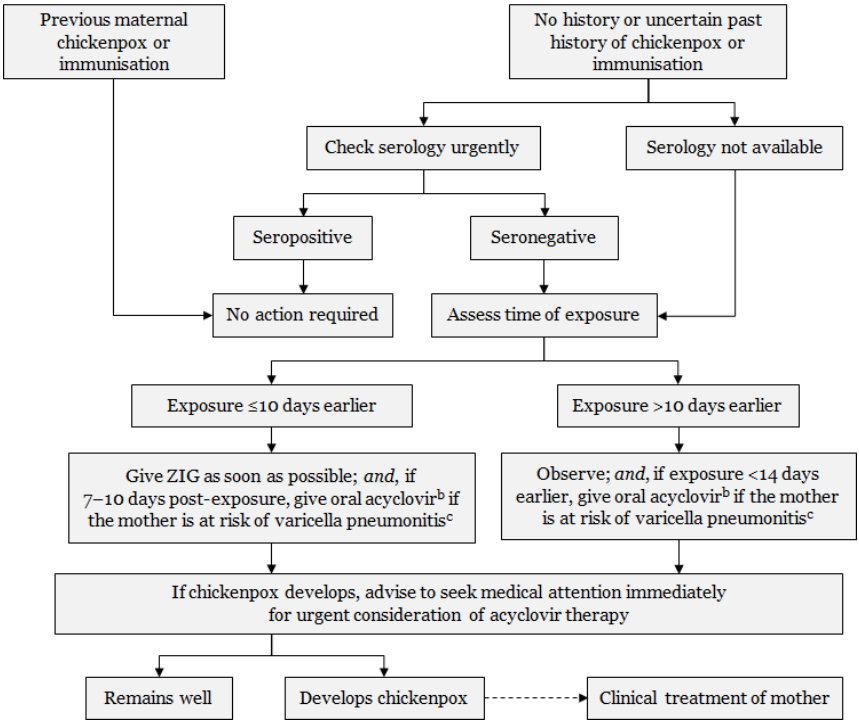
21.8.6 Care of pregnant women after exposure

Pregnant women are at higher risk of severe complications from varicella. If an immune-competent pregnant woman with no history of varicella or vaccination is exposed to varicella, it is recommended, where possible, that her varicella antibodies be assessed (Figure 21.1). If there is no evidence of immunity, two possible courses of action are available: either administer ZIG, or await the onset of symptoms and as soon as possible commence the administration of acyclovir, which is effective in this situation and now regarded as safe in pregnancy. Discuss the clinical circumstances with an infectious diseases physician before deciding on which course of action is best.

Intravenous acyclovir is recommended for the pregnant woman with severe complications of varicella. ZIG given to a pregnant woman within five days of delivery may not protect the fetus/neonate: the neonate should receive ZIG on delivery and may need treatment with acyclovir (Figure 21.2).

Figure 21.1: Management of pregnant women exposed to varicella or zoster

Every effort should be made to confirm the diagnosis in the suspected positive contact and assess significance of exposure.[a] Exposure or symptoms in the final two weeks of pregnancy should always be discussed with a specialist.



a Exposure to varicella or zoster for which ZIG is indicated for susceptible persons includes: living in the same household as a person with active chickenpox or herpes zoster; face-to-face contact with a case of chickenpox for at least 5 minutes; close contact (eg, touching, hugging) with a person with active zoster.

b Efficacy of acyclovir for post-exposure prophylaxis has not been tested in controlled trials. Dose is 800 mg orally, 5 times per day for 7 days.

c The mother is at risk of pneumonitis if: in second half of pregnancy; has underlying lung disease; is immunocompromised; is a smoker.

Adapted from: Australasian Society for Infectious Diseases. 2014. Varicella zoster virus. In: Palasanthiran P, Starr M, Jones C, et al (eds). *Management of Perinatal Infections*. Sydney: Australasian Society for Infectious Diseases (ASID) Inc.

Pregnant women exposed to VZV should be counselled about the risks of congenital varicella syndrome (CVS), a rare but devastating disorder that can occur following varicella zoster infection during pregnancy (see Table 21.4). The risk of CVS is greatest in the first 20 weeks of pregnancy. Large case studies suggest that the rate of CVS is 0.4 percent when maternal infection occurs up to week 12 of pregnancy, and 2 percent from weeks 13 to 20.

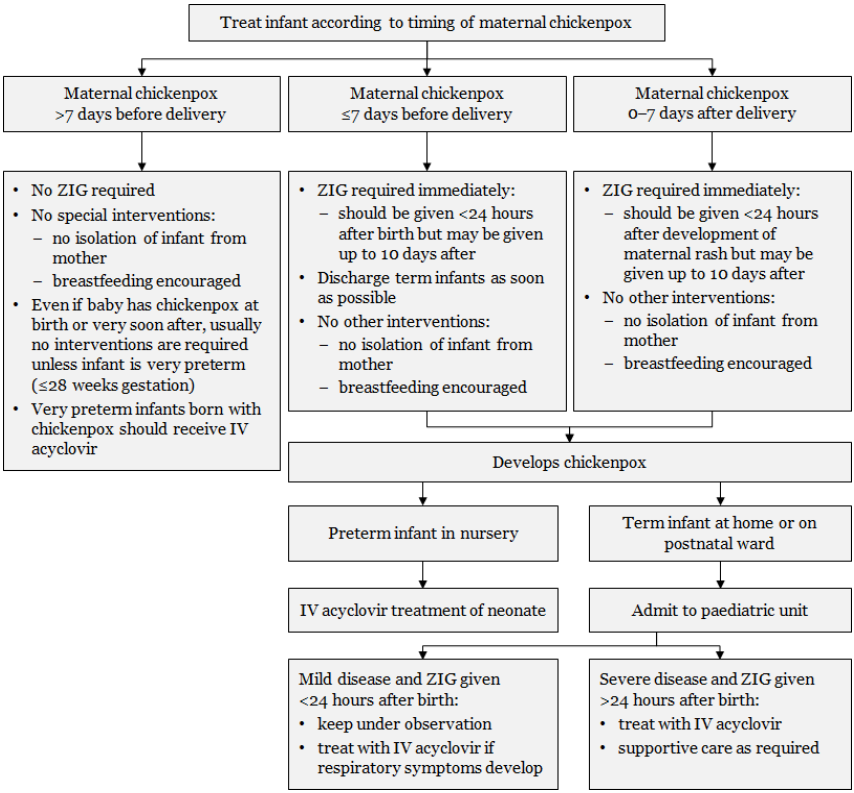
There is no single diagnostic test available for CVS. Regular fetal ultrasound for developing anomalies is recommended. VZV fetal serology is unhelpful but amniocentesis may be considered; negative VZV PCR may be reassuring.

Table 21.4: Sequelae of congenital varicella

Sequelae	Frequency
Skin scars	78%
Eye abnormalities	60%
Limb abnormalities	68%
Prematurity, low birthweight	50%
Cortical atrophy, severe developmental delay	46%
Poor sphincter control	32%
Early death	29%

Adapted from: Australasian Society for Infectious Diseases. 2014. Varicella zoster virus. In: Palasanthiran P, Starr M, Jones C, et al (eds). *Management of Perinatal Infections*. Sydney: Australasian Society for Infectious Diseases (ASID) Inc.

Figure 21.2: Management of infants from mothers with perinatal varicella or zoster



Notes:

- Transplacentally acquired VZV is high-risk and severity is reduced by ZIG.
- ZIG is not always effective in preventing severe disease.

Adapted from: Australasian Society for Infectious Diseases. 2014. Varicella zoster virus. In: Palasanthiran P, Starr M, Jones C, et al (eds). *Management of Perinatal Infections*. Sydney: Australasian Society for Infectious Diseases (ASID) Inc.

21.9 Variations from the vaccine data sheet

The VV (Varilrix) data sheet states that individuals aged 9 months and older should receive two dose of vaccine at least six weeks apart. The Ministry of Health instead recommends a single dose of VV for healthy children at 15 months or 11 years of age (see section 21.5.1) and two doses for individuals with a special groups condition (see section 21.5.2).

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22 Zoster (herpes zoster/ shingles)

Key information

Mode of transmission	Zoster is a reactivation of the varicella zoster virus in someone who has previously had varicella disease. Contact with zoster vesicles can cause varicella in non-immune individuals. Some airborne spread may be possible from immunocompromised patients.
Period of communicability	Until lesions have crusted.
Burden of disease	Increasing incidence with age; lifetime risk about 1 in 3. For those who live to 85 years, the risk is 1 in 2.
Vaccine	Zoster vaccine (Zostavax), a higher titre formulation of the live attenuated varicella vaccine. Zoster vaccine is registered for use from age 50 years. **Do not give to children.**
Dose, presentation, route	0.65 mL per reconstituted dose. Vial of vaccine, plus diluent in a pre-filled syringe. The vaccine must be reconstituted prior to injection. Subcutaneous injection.
Recommended immunisation schedule	From 1 April 2018, 1 dose of HZV is funded for: • individuals at age 65 years, or • catch-up of individuals aged 66–80 years, inclusive (the catch-up programme ceases on 31 March 2020). HZV may be given to individuals with a prior history of zoster. After the zoster episode has resolved the vaccination benefit is unclear – wait at least 1 year before administering the vaccine.
Vaccine efficacy/ effectiveness	Reduces the burden of zoster illness by 61 percent in all adults aged over 60 years, by 66 percent in those aged 60–69 years and by 55 percent in those aged 70 years and older. The role of revaccination is currently unknown.

Continued overleaf

Contraindications	Certain primary and secondary immune deficiencies – consult the individual's specialist for advice. Immunosuppressive therapy, including high-dose steroids. Known systemic hypersensitivity to neomycin. Active untreated TB. Pregnancy.

22.1 Virology

Varicella-zoster virus (VZV) is a DNA virus from the herpesvirus family. Primary infection with VZV causes varicella zoster disease (chickenpox). Herpes zoster (HZ), or 'shingles', is a clinical syndrome caused by reactivation of latent VZV, which resides in the dorsal root or trigeminal nerve ganglia following primary infection.

22.2 Clinical features

HZ (shingles) occurs when the cell-mediated immune response is impaired and unable to prevent latent VZV reactivation (see chapter 21). Zoster occurs only by reactivation of the patient's own virus; it is not acquired from other patients with zoster or varicella.[1]

HZ presents clinically as a unilateral vesicular rash in a dermatomal distribution in the majority of cases. The dermatomal distribution of the rash is the key diagnostic feature. In 70–80 percent of HZ cases in older adults, prodromal pain and/or itching occurs three to four days before the appearance of the rash.[2] In the majority of patients, HZ is an acute and self-limiting disease, with the rash lasting 10 to 15 days. However, complications can occur, especially with increasing age.

The majority of zoster cases occur in adults aged 40 years or older. HZ does occur in infants and children, but it is uncommon. When it occurs in those aged under 2 years it may reflect *in utero* chickenpox, with the greatest risk arising following exposure between 25 and 36 weeks' gestation, with reactivation in early life.

A common complication of zoster is post-herpetic neuralgia, a chronic, often debilitating pain condition that can last months or even years. A systematic review of the incidence and complications of zoster found that the risk of developing post-herpetic neuralgia ranges between 5 and about 30 percent (depending on the type of study design, age distribution of the study populations and definition),[3] although it is uncommon in healthy children and young people and the risk rises with age.

Herpes zoster ophthalmicus (HZO) is another complication of zoster, which occurs when VZV reactivation affects the ophthalmic branch of the trigeminal nerve. HZO can occur with or without eye involvement, and can result in prolonged or permanent pain, facial scarring and loss of vision. About 10 percent of zoster patients develop HZO, and the risk is similar across all age groups.[3]

HZ occurs more commonly in immunosuppressed individuals (eg, cancer treatment or organ transplant patients) and those with HIV. Up to 10 percent of children treated for a malignant neoplasm may develop HZ. In immunocompromised patients,[4] extensive viraemia in the absence of a vigorous immune response can result in a disseminated form of HZ that includes severe multi-organ disease.[2] Other risk factors for developing HZ include rheumatoid arthritis,[5] sleep disorders[6] and type 2 diabetes.[7]

22.3 Epidemiology

22.3.1 Global burden of disease

HZ is a sporadic disease occurring as a reactivation of the VZV in individuals who have previously had chickenpox. Approximately one in three people will develop zoster during their lifetime with the incidence rising as cell-mediated immunity to VZV declines with age.[8] Fifty percent of those who live to 85 years suffer zoster.[9, 10] A systematic review documented an incidence rate between 3 and 5 per 1,000 person-years in North America, Europe and Asia-Pacific.[3] The incidence rate was about 6–8 per 1,000 person-years at age 60 years and 8–12 per 1,000 person-years at age 80 years.

Recurrence is greater in females than males (about 7 percent after eight years compared with 4 percent for males). Third episodes are rare.

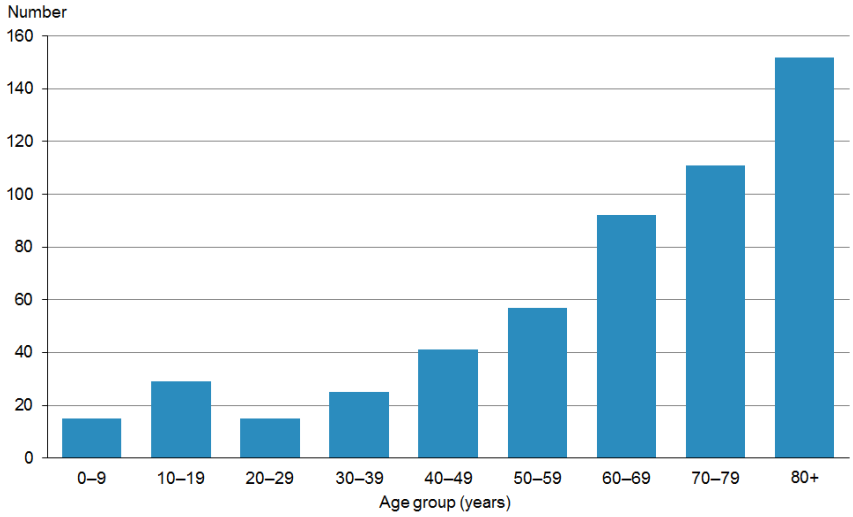
VZV is present in lesions of HZ and is transmissible via contact with the vesicles to other susceptible individuals (causing chickenpox). Airborne transmission can occur from immunocompromised individuals with disseminated HZ. Episodes of HZ in older individuals provide a constant mechanism for reintroducing the virus, causing varicella in non-immune individuals who are in close contact, who then spread the virus to other susceptible individuals.

Following the introduction of VV onto the childhood schedule, exposure to wild-type virus decreases. It has been theorised that a lack of boosting may lead to an increase in HZ in older adults. However, studies that have investigated this issue have been unable to attribute any increase in incidence of HZ to childhood varicella vaccination programmes.[11, 12] Studies from the UK and Canada reported increases in HZ not associated with a vaccination programme, and some US data showed HZ rates were increasing prior to the initiation of their varicella vaccination programme.[13, 14]

22.3.2 New Zealand epidemiology

Zoster hospitalisations by age group during 2015 are shown in Figure 22.1 below, with more than 65 percent occurring in adults aged 60 years and older. Hospitalisations are predicted to account for only a very small proportion of the overall HZ cases as most are managed in primary care. A retrospective review of cases at a large New Zealand general practice suggests an incidence similar to the global incidence estimates described in section 22.3.1 above.[15]

Figure 22.1: Herpes zoster hospitalisations by age group, 2015



Source: Ministry of Health

22.4 Vaccine

22.4.1 Available vaccine

HZV (Zostavax, MSD) is a live attenuated virus vaccine. It is a higher titre formulation of the varicella vaccine and has been tested as a vaccine to protect against HZ.[16] By mimicking the immune response seen following a dose of shingles and boosting cell-mediated immunity in older adults, the incidence and severity of HZ is reduced by the high-titre vaccine.

Funded vaccine

Each 0.65 mL HZV dose of HZV (Zostavax, MSD) contains a minimum of 19,400 PFU of the Oka/Merck strain of VZV. Other components include sucrose, hydrolysed porcine gelatin, urea, sodium chloride, monosodium L-glutamate, sodium phosphate dibasic, potassium phosphate monobasic, potassium chloride, residual components of MRC-5 cells (including DNA and protein), and trace quantities of neomycin and bovine calf serum. The vaccine contains no preservative.

22.4.2 Efficacy and effectiveness

In a large clinical trial (the Shingles Prevention Study) of 38,546 adults aged 60 years and older, with either a history of chickenpox or of having lived in the US for more than 30 years, the participants received the high-dose zoster vaccine or a placebo. The results showed that the zoster vaccine reduced the burden of illness of zoster by 61 percent (95% CI: 51–69) in all age groups, by 66 percent (95% CI: 52–76) in the age group 60–69 years, and by 55 percent (95% CI: 40–67) in those aged 70 years and older. There was also a 67 percent reduction (95% CI: 48–79) in post-herpetic neuralgia in all age groups.[16] A cohort study of individuals in the US aged 65 years and older found zoster vaccine was associated with a 48 percent reduction (95% CI: 39–56) in incident zoster, including a 37 percent reduction (95% CI: 6–58) in those with immunosuppression.[17]

A review of the efficacy of HZV in preventing zoster and post-herpetic neuralgia concluded that zoster vaccine is safe, effective and highly recommended for the immunisation of immune-competent individuals over the age of 60 years.[1]

Duration of protection

The persistence of HZV efficacy was measured for 11 years using a subgroup of individuals from the Shingles Prevention Study discussed above. Vaccine efficacy was statistically significant for the incidence of HZ until eight years post-vaccination.[18] Compared to the original study, estimates for vaccine efficacy decreased from 61.1 percent to 37.3 percent for the HZ burden of illness, from 66.5 percent to 35.4 percent for incidence of postherpetic neuralgia, and from 51.3 percent to 21.1 percent for incidence of HZ. Studies have shown that booster doses in adults are immunogenic, but there are no reports on efficacy of booster doses. The immune response following a booster dose declines with advancing age but is similar to the response seen following first doses of individuals of the same age; ie, a prior dose neither enhances nor impairs the response to a booster dose.[19] At the time of writing, there were no current international guidelines on booster doses.

There do not appear to be any safety concerns with administering a second dose of HZV.[20] Although not currently recommended, individuals who previously received an unfunded HZV dose may choose to receive a funded HZV dose, if eligible.

22.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.[21] Store in the dark at +2°C to +8°C.

The vaccine must be reconstituted with the supplied diluent. Once reconstituted, HZV must be used within 30 minutes.

22.4.4 Dosage and administration

HZV is registered for adults aged 50 years and older. **Do not give to children.**

The dose of reconstituted HZV is 0.65 mL, to be administered subcutaneously in the deltoid area (see section 2.2.3).

Co-administration with other vaccines

HZV can be concurrently administered with influenza vaccine using separate syringes and sites.

Evidence[22] suggests that HZV can be concurrently delivered with 23PPV, despite earlier research to the contrary. The earlier research showed the average antibody titre against VZV was lower in individuals who received HZV and 23PPV at the same visit, compared to those who received these vaccines four weeks apart.

However, there is no evidence to suggest that antibodies against VZV are a measure of protection against HZ.[22] The US Centers for Disease Control and Prevention has not changed its recommendation for either vaccine and continues to recommend that HZV and 23PPV be administered at the same visit if the individual is eligible for both vaccines.[23]

22.5 Recommended immunisation schedule

Table 22.1: Herpes zoster vaccine (HZV) recommendations

Note: Neither history of previous varicella infection nor evidence of prior immunity to VZV is required prior to the routine administration of HZV (with the exception of certain immunocompromised persons, refer below).

Recommended and funded

1 dose of HZV is recommended and funded for:

- individuals at age 65 years, or
- catch-up[a] of individuals aged 66–80 years, inclusive.

For consideration, but not funded

1 dose of HZV may be considered, but is not funded, for individuals aged 50–64 years:

- who are at increased risk of zoster[24, 25, 26, 27] and who may benefit from being vaccinated earlier than the routine schedule:
  - with asymptomatic HIV[b] (if CD4+ lymphocyte count is ≥200 cells/mm^3)
  - with end-stage kidney disease[b] (CKD stages 4–5)
  - at least 4 weeks prior to commencing high-dose immunosuppressive therapy[b,c] and/or solid organ transplantation[b,c]
  - after ceasing high-dose immunosuppressive therapy[b,c]
  - at least 2 years post-HSCT[b,c]
  - with autoimmune disease[b,c] (eg, rheumatoid arthritis, systemic lupus erythematosus, inflammatory bowel disease, Crohn's disease, ulcerative colitis)
  - with a first generation family history of zoster
  - with depression
  - with diabetes
  - with psychiatric disorders
  - with chronic obstructive pulmonary disease.
- who are household contacts of immunocompromised individuals.

a The catch-up programme ceases on 31 March 2020.

b Seek specialist advice. Serological confirmation of previous VZV infection is recommended before administering HZV. If VZV-seronegative, give VV. If VZV-seropositive, give HZV. See also section 4.3.3.

c See Table 22.2: Recommendations for individuals on immunosuppressive therapy.

22.5.1 Recommended and funded

Recommendations for HZV (Zostavax) are in Table 22.1 above. From 1 April 2018, one dose of HZV will be funded for individuals at age 65 years. There will be a catch-up programme from 1 April 2018 until 31 March 2020, with one dose of HZV funded for individuals aged 66 to 80 years, inclusive.

22.5.2 Other considerations

Vaccination of individuals aged 50–64 years (unfunded)

HZV (Zostavax) is registered in New Zealand for individuals aged 50 years or older. It may be considered, but is not funded, for individuals aged 50–64 years who are at increased risk of zoster[24, 25, 26, 27] and who may benefit from being vaccinated earlier than the routine schedule and/or they are a household contact of an immunocompromised individual (see Table 22.1). However, the exact duration of vaccine efficacy is not known, and it is possible that protection following a single vaccine dose wanes with time.[27] The need for revaccination is not yet determined.[27] Dosing with HZV is often strategic and based on clinical consideration (see below).

Individuals with a history of HZ (shingles)

Individuals with a history of a previous episode of HZ can be given HZV. It is possible that a history of previous zoster may be inaccurate or a mistaken diagnosis.[27] In addition, the risk of a repeat episode of zoster has been estimated at approximately 5 percent in immunocompetent individuals.[27]

There are no recognised safety concerns in giving the vaccine to people with prior history of HZ.[28] The length of time following an episode of HZ after which it may be beneficial to vaccinate has not been established.[27] It is suggested that the vaccine could be given at least one year after the episode of HZ has resolved.[27]

Household contacts of immunocompromised individuals

HZV is contraindicated in individuals with current or recent severe immunocompromise due to primary and secondary immune-deficiency states, or due to immunosuppressive therapy (see section 22.6). However, VV or age-appropriate HZV can be given safely to their household contacts. VV is funded for non-immune household contacts of patients who are immunocompromised or undergoing a procedure or treatment leading to immunocompromise. If the household contact is immune to varicella and aged 50 years and older, give HZV (funded at age 65 years with a catch-up, until 31 March 2020, for those aged 66–80 years inclusive; unfunded if aged 50–64 years).

If a vaccinated person develops a varicella- or zoster-like rash, they should cover the rash and avoid contact with persons who are immunocompromised for the duration of the rash.[27]

See also 'Household contacts' in section 4.3.1 for general recommendations for vaccination of household contacts of immunocompromised individuals.

Serological testing

Neither history of previous varicella infection nor evidence of prior immunity to VZV is required prior to the routine administration of the herpes zoster vaccine.[27] Most older people in New Zealand are seropositive to VZV due to previous primary varicella infection.

Serological confirmation of previous VZV infection is recommended before administering HZV to individuals with HIV, and in those who are anticipating significant future immunocompromise or who have ceased immunosuppressive therapy (see section 22.6.2).[27] Individuals in these categories who have negative VZV IgG should generally not be given HZV. Upon specialist advice, VV may be given instead of HZV to seronegative individuals.

Laboratory testing to check for an immune response after HZV is not recommended.[27]

22.6 Contraindications and precautions

See section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

22.6.1 Contraindications

HZV is a live attenuated varicella-zoster vaccine and administration to individuals who are immunosuppressed or immunodeficient may result in disseminated varicella-zoster virus disease, including fatal outcomes. If HZV is inadvertently administered to these individuals, seek specialist advice immediately and notify CARM.

Contraindications to HZV include:

- a history of anaphylactic reaction to neomycin. A history of hypersensitivity to any other component of the vaccine, including gelatin
- primary and secondary immune-deficiency states due to conditions such as acute and chronic leukaemias, lymphoma, other conditions affecting the bone marrow or lymphatic system, immunosuppression due to HIV/AIDS (see section 22.6.2 for asymptomatic HIV infection), cellular immune deficiencies – see sections 4.3.2 and 4.3.3
- immunosuppressive therapy (including high-dose corticosteroids and biologics). Note: HZV is *not* contraindicated for use in individuals who are receiving low-level immunosuppressive therapy, for example: topical/inhaled corticosteroids or low-dose systemic corticosteroids; who are receiving corticosteroids as replacement therapy (eg, for adrenal insufficiency); low-dose weekly methotrexate or azathioprine – see Table 22.2 below and section 4.3.3
- active untreated TB
- pregnancy.

Do not give to children.

22.6.2 Precautions

HIV

Asymptomatic HIV-positive individuals with a CD4+ lymphocyte count ≥200 cells/mm^3 may be vaccinated upon specialist advice. Results of a phase II trial in HIV-infected adults indicated that HZV was generally safe and immunogenic in those with CD4+ lymphocyte count ≥200 cells/mm^3, with no cases of vaccine strain infection.[29, 30]

Serological confirmation of previous VZV infection is recommended prior to vaccination.[27] If seronegative, give VV (funded); if seropositive give HZV (funded at age 65 years with a catch-up, until 31 March 2020, for those aged 66–80 years inclusive; unfunded if aged 50–64 years).

Individuals with symptomatic HIV infection or AIDS should not be vaccinated.

Immunocompromised individuals

HZV is contraindicated in individuals with current or recent severe immunocompromise due to primary and secondary immune-deficiency states, or due to immunosuppressive therapy. However, individuals receiving low-level immunosuppressive therapy may be considered for vaccination upon specialist advice.

Individuals who anticipate significant future immunocompromise because of an existing illness and/or its treatment may be given HZV upon specialist advice.[27] This includes prior to solid organ transplant, chemotherapy or radiation therapy, and individuals with autoimmune disease. Vaccination at least 4 weeks prior to the onset of immunocompromise may be appropriate, upon specialist advice.[27] Individuals whose treatment with high-dose systemic immunosuppressive therapy has ceased may be vaccinated upon specialist advice if an appropriate time interval has passed.[27] Serological confirmation of previous VZV infection is recommended prior to vaccination. If seronegative, give VV (funded if an eligible condition); if seropositive give HZV (funded at age 65 years with a catch-up, until 31 March 2020, for those aged 66–80 years inclusive; unfunded if aged 50–64 years).

Table 22.2 below provides recommendations for the use of HZV in persons on immunosuppressive therapy.

See also section 4.3.3.

Table 22.2: Recommendations for use of herpes zoster vaccine for individuals on immunosuppressive therapy

Immunosuppressive therapy	Treatment regimen	Potential timing of vaccination
High-dose corticosteroid monotherapy (≥20 mg per day of prednisone or equivalent)	<14 days	Immunise 4 weeks before treatment starts OR any time after treatment stops[a]
	≥14 days	Immunise 4 weeks before treatment starts OR at least 4 weeks after treatment stops
DMARDs: • Azathioprine • Methotrexate • All other DMARDs[b,c]	>3.0 mg/kg per day >0.4 mg/kg per week All regimens	Immunise 4 weeks before treatment starts OR at least 3 months after treatment stops
T-cell inhibitors (eg, tacrolimus, cyclosporin)	All regimens	Immunise 4 weeks before treatment starts OR at least 3 months after treatment stops
Other unspecified immunosuppressants (eg, chemotherapy[d])[e]	All regimens	Immunise 4 weeks before treatment starts OR at least 3 months after treatment stops
Targeted biological therapies (eg, monoclonal antibodies)[f]	All regimens	Immunise 4 weeks before treatment starts OR at least 12 months after treatment stops[g]

a Can be given immediately on discontinuation, but delay 2 weeks if possible.

b See Table 4.3 for a list of other DMARDs.

c Does not include sulfasalazine which is considered safe at any dose.

d For patients who have recently received chemotherapy and/or radiotherapy waiting at least 6 months rather than 3 months may be appropriate.

e This does not include individuals who have received HSCT, who should not receive HZV until at least 2 years post-HSCT. (See also the 'Vaccination after haematopoietic stem cell transplant (HSCT)/bone marrow transplant' discussion in section 4.3.3.)

f See Table 4.3 for a list of targeted biological therapies.

Continued overleaf

g In some cases immunosuppression that absolutely contraindicates live attenuated vaccines can persist for a year or more after the last dose of therapy. Live attenuated vaccines should preferably not be given to any patient who has previously received biologic immunotherapies, unless this has been approved by the treating specialist after evaluation of the delay since last treatment and in some cases an assessment of immunological recovery.

Source: Adapted from: Australian Technical Advisory Group on Immunisation (ATAGI). 2017. *The Australian Immunisation Handbook* 10th edition (2017 update), Table 4.24.1. Canberra: Australian Government Department of Health. URL: http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home

22.7 Expected responses and AEFIs

22.7.1 Expected responses

HZV is generally well tolerated. In clinical trials, injection site reactions occurred more commonly in HZV recipients than in placebo recipients. PCR testing of VZV from zoster-like rashes occurring in the 42-day period following vaccination are much more likely to be due to wild VZV than to the vaccine virus.[2]

22.7.2 AEFIs

A large safety review of HZV in 193,083 individuals aged 50 years and older supports the pre-licensure clinical trial data.[31] The HZV was found to be safe and well tolerated with no increased risk for the adverse event groupings of cerebrovascular events, cardiovascular events, meningitis, encephalitis, encephalopathy, Ramsay–Hunt syndrome or Bell's palsy. A small increased risk of allergic reactions one to seven days after vaccination was reported.

A post-marketing observational study of 29,000 individuals aged 60 years and older did not identify any safety concerns within 42 days of receiving HZV vaccine.[32]

22.8 Variations from the vaccine data sheet

The HZV (Zostavax) data sheet states that the HZV vaccine and 23PPV (Pneumovax 23) should not be given concurrently. The Ministry of Health recommends that HZV vaccine and 23PPV may be given concurrently[22, 23] (see section 22.4.4).

The HZV data sheet states that HZV should not be given to individuals with HIV/AIDS. The Ministry of Health recommends that asymptomatic HIV-positive individuals with a CD4+ lymphocyte count ≥200 cells/mm^3 may be vaccinated upon specialist advice (see section 22.6.2).

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Appendix 1: The history of immunisation in New Zealand

This appendix details the history of immunisation in New Zealand. Section A1.1 is a brief summary of when each vaccine was introduced to the National Immunisation Schedule (the Schedule). This summary includes vaccines which were initially introduced as targeted programmes for a defined population and were then added to the Schedule, and those vaccines which were introduced to the Schedule and then changed to targeted programmes. Section A1.2 shows the historical immunisation schedules for New Zealand. Section A1.3 provides detailed information about the history of the Schedule – this information was previously contained within the disease chapters of earlier editions of the *Handbook*.

A1.1 History of the Schedule – summary tables

Table A1.1: Summary of when each vaccine was introduced to New Zealand

Vaccine	Year the vaccine was introduced, plus comments	
Diphtheria	1926	Became available in New Zealand for selected schools and orphanages.
	1941	Offered routinely to children aged under 7 years. See DTwP for more information.
Tetanus	1940–55	Tetanus toxoid became available as a voluntary vaccination. See DTwP for more information.
Pertussis	1945	Introduced by the Department of Health – given on request.
	1953	Combined pertussis-diphtheria vaccine became available, although usage was restricted. See DTwP for more information.

Continued overleaf

Vaccine	Year the vaccine was introduced, plus comments	
BCG	1948	Initially introduced for nurses, then later extended to all adolescents.
	1963	Adolescent BCG programme was discontinued in the South Island. Phased out in the North Island by 1990.
	1976	Neonatal BCG was introduced initially in high-risk districts, and then variably implemented throughout New Zealand.
	1990	Neonatal BCG was given for high-risk groups only. This continues in 2017.
Salk poliomyelitis (IPV)	1956	Became available; initially 8–9-year-olds were targeted, then 5–10-year-olds, then 11–15-year-olds.
	1960	Offered to all those aged 6 months to 21 years.
	2002	IPV replaced OPV on the Schedule, either as IPV or combined with the DTaP vaccine. See Hib for more information.
	2014	IPV became available for (re-)vaccination following immunosuppression (see also DTaP).
DTwP (diphtheria, tetanus, whole-cell pertussis)	1958	DTwP became available and the first Schedule commences.
	1960	DTwP was supplied to medical practitioners free of charge. See Hib for more information.
Sabin poliomyelitis (OPV)	1961	Initially introduced for children aged under 12 months, administered by the Department of Health.
	1962	In April 95% of all school children received 2 doses; in September it was offered to all adults and adolescents (administered by the Department of Health).
	1967	From April GPs were able to administer OPV along with DTwP at ages 3, 4, 5 and 18 months.
	2002	Sabin OPV was replaced by Salk-derived IPV on the Schedule, as DTaP-IPV at ages 6 weeks, 3 and 5 months, and at 4 years, and as IPV at age 11 years. See Hib for more information.

Continued overleaf

Vaccine	Year the vaccine was introduced, plus comments	
Measles	1969	Introduced for children aged 10 months to 5 years and those aged under 10 years at special risk. Due to adverse reactions, the measles programme was suspended in late 1969 until the Edmonston B strain vaccine became available in February 1970.
	1974	The recommended age changed to age 12 months.
	1981	The recommended age changed to age 12–15 months.
	1990	Measles, mumps and rubella (MMR) vaccine was introduced to the Schedule for all infants at age 12–15 months, replacing monovalent measles vaccine. See MMR for more information.
Rubella	1970	Introduced to the Schedule for all children at age 4 years.
	1979	Low uptake at age 4 years, especially by boys, spurred a change to a vaccination for girls at age 11 years (year 7/form 1).
	1990	MMR was introduced to the Schedule for all infants at age 12–15 months. See MMR for more information.
Hepatitis B	1985	Plasma-derived vaccine was introduced for newborn babies born to HBeAg-positive mothers.
	1987	Extended to newborns of HBsAg-positive mothers and newborns in high-risk districts (eg, Northland, South Auckland, Rotorua, Napier, Gisborne).
	1988	In February 1988 it was introduced to the Schedule for all infants (catch-up programmes for preschoolers are implemented during 1988).
	1989	In December 1989 recombinant HepB replaced the plasma-derived vaccine.
	1990	Funded hepatitis B immunisation was extended to all children aged under 16 years (catch-up school programmes were also implemented).
	1996	The third HepB dose was brought forward from 12–15 months to age 5 months. See Hib for more information.
	2014	HepB vaccine became available to individuals at high risk of hepatitis B or its complications (see also DTaP).
	2015	Funding extended to include other high-risk conditions.

Continued overleaf

Vaccine	Year the vaccine was introduced, plus comments	
Measles, mumps and rubella (MMR)	1990	Introduced to the Schedule for all infants at age 12–15 months.
	1992	A second dose was introduced for 11-year-old (school year 7/form 1) boys and girls.
	2001	The second dose of MMR was changed from age 11 years to age 4 years. A school-based catch-up programme was offered for all 5–10-year-olds.
	2014	The 2-dose schedule at ages 15 months and 4 years continues. MMR vaccine became available for (re-)vaccination following immunosuppression.
Haemophilus influenzae type b (Hib)	1994	Hib vaccine was introduced to the Schedule as DTwPH (replacing DTwP) at ages 6 weeks, 3 months and 5 months, and as monovalent Hib at age 18 months. All children aged under 5 years were offered vaccination against Hib.
	1996	Given as DTwPH at ages 6 weeks, 3 months and 5 months, with a booster at age 15 months.
	2000	Given as Hib-HepB at ages 6 weeks and 3 months, and as DTaP/Hib at age 15 months.
	2006	Given as Hib-HepB at ages 6 weeks and 3 months, and as monovalent Hib at age 15 months. Monovalent Hib became available to older children and adults pre- or post-splenectomy.
	2008	Given as DTaP-IPV-HepB/Hib at ages 6 weeks, 3 months and 5 months, and as monovalent Hib at age 15 months. This schedule continues in 2017.
	2014	Monovalent Hib became available for additional high-risk conditions (see also DTaP).
Td (Tetanus-diphtheria)	1994	Introduced to the Schedule, replacing tetanus toxoid. See Tdap for more information.
	2002	Adult Td boosters are introduced at ages 45 and 65 years. These boosters continue in 2017.
	2014	Td became available for (re-)vaccination following immunosuppression.

Continued overleaf

Vaccine	Year the vaccine was introduced, plus comments	
Influenza	1997	Introduced to the Schedule for adults aged 65 years and older.
	1999	Introduced to the Schedule for those aged under 65 years with certain medical conditions.
	2010	Pregnant women became eligible to receive the funded vaccine.
	2013	Children aged under 5 years who have been hospitalised for respiratory illness or have a history of significant respiratory illness became eligible to receive the funded vaccine.
	2015	Funding extended to include other high-risk conditions.
Acellular pertussis (DTaP)	1999	Introduced for infants/children aged under 7 years who have a previous reaction to the whole-cell pertussis in DTwPH.
	2000	In August, DTaP was introduced for all infants to replace whole cell pertussis vaccine at ages 6 weeks, 3 months and 5 months (see also Hib).
	2014	DTaP-IPV-HepB/Hib and DTaP-IPV became available for (re-)vaccination of children with certain high-risk conditions.
Meningo-coccal B (MeNZB)	2004 to 2008	MeNZB was used as an epidemic control vaccine between 2004 and 2008. It was offered in a three-dose schedule to all aged under 20 years. (See the 2011 edition of the *Handbook* for more information.)
Adult-dose acellular pertussis (Tdap)	2006	Introduced to the Schedule at age 11 years, combined with IPV as Tdap-IPV, but changed to Tdap only in 2008. This schedule continues in 2017.
	2013	Pregnant women from 28 to 38 weeks' gestation became eligible for the funded vaccine (under the outbreak policy).
	2014	Tdap became available for (re-)vaccination of children following immunosuppression.
	2015	Tdap became available for (re-)vaccination of patients with certain high-risk conditions. Pregnant women from 28 to 38 weeks' gestation become eligible for the funded vaccine for every pregnancy.

Continued overleaf

Vaccine	Year the vaccine was introduced, plus comments	
Pneumo-coccal conjugate vaccine (PCV)	2006	Introduced as PCV7 for high-risk children.
	2008	Introduced to the Schedule in June as PCV7 at ages 6 weeks, 3 months, 5 months and 15 months.
	2011	PCV10 replaced PCV7 on the Schedule. PCV13 replaced PCV7 for high-risk children.
	2014	PCV13 replaced PCV10 on the Schedule.
	2015	PCV13 became available for patients of any age with certain high-risk conditions.
	2017	PCV10 replaced PCV13 on the Schedule. PCV13 continues for high-risk individuals.
Human papilloma-virus vaccine (HPV)	2008	HPV4 was introduced to the Schedule at age 12 years, for females only. There was a catch-up programme for females born from 1990.
	2013	HPV4 was made available in hospitals for transplant patients, and for boys and men under 26 years with confirmed HIV infection.
	2014	Lower age limit for vaccine eligibility changed to age 9 years. Routine immunisation continued for girls aged 12 years, plus a targeted programme for high-risk individuals. Individuals aged under 26 years with HIV infection became eligible for HPV4.
	2015	Funding extended to include other high-risk conditions.
	2017	Funding extended to include all males and females aged 26 years and under. HPV9 replaced HPV4.
Rotavirus	2014	RV5 vaccine was introduced to the Schedule at ages 6 weeks, 3 months and 5 months.
	2017	RV1 replaced RV5, at ages 6 weeks and 3 months.
Varicella (VV)	2014	Two doses of VV were introduced for high-risk individuals.
	2017	One dose of VV was introduced onto the Schedule for children at age 15 months (born on or after 1 April 2016), with a catch-up for previously unvaccinated children turning 11 years old on or after 1 July 2017 who have not previously had a varicella infection.
Herpes zoster (HZV)	2018	From 1 April, HZV was introduced onto the Schedule as a single dose for adults aged 65 years, with a catch-up programme for adults aged 66–80 years inclusive (the catch-up programme ceases on 31 March 2020).

A1.2 Previous national immunisation schedules

Table A1.2: July 2017 immunisation schedule

	DTaP-IPV-HepB/Hib	PCV10	RV1	Hib	MMR	VV	DTaP-IPV	Tdap	HPV9	Td	Influenza
Pregnancy								●			●
6 weeks	●	●	●								
3 months	●	●	●								
5 months	●	●									
15 months		●		●	●	●					
4 years					●		●				
11 or 12 years								●	●		
45 years										●	
65 years										●	●

Table A1.3: July 2014 immunisation schedule

	DTaP-IPV-HepB/Hib	PCV13	RV5	Hib	MMR	DTaP-IPV	Tdap	HPV4	Td	Influenza
6 weeks	●	●	●							
3 months	●	●	●							
5 months	●	●	●							
15 months		●		●	●					
4 years					●	●				
11 years							●			
12 years (girls only)								● × 3 doses		
45 years									●	
65 years									●	●

Table A1.4: July 2011 immunisation schedule

	DTaP-IPV-HepB/Hib	PCV10	Hib	MMR	DTaP-IPV	Tdap	HPV4	Td	Influenza
6 weeks	●	●							
3 months	●	●							
5 months	●	●							
15 months		●	●	●					
4 years				●	●				
11 years						●			
12 years (girls only)							● × 3 doses		
45 years								●	
65 years								●	●

Table A1.5: June 2008 immunisation schedule

	DTaP-IPV-HepB/Hib	PCV7	Hib	MMR	DTaP-IPV	Tdap	HPV4	Td	Influenza
6 weeks	●	●							
3 months	●	●							
5 months	●	●							
15 months		●	●	●					
4 years				●	●				
11 years						●			
12 years (girls only)							● × 3 doses		
45 years								●	
65 years								●	●

Table A1.6: February 2006 immunisation schedule

	DTaP-IPV	Hib-HepB	Hib	Tdap-IPV	MMR	MeNZB	Td	Influenza
6 weeks	●	●				●		
3 months	●	●				●		
5 months	●	●				●		
10 months						●		
15 months			●		●			
4 years	●				●			
11 years				●				
45 years							●	
65 years							●	●

Table A1.7: February 2002 immunisation schedule

	DTaP-IPV	Hib-HepB	Hep B	DTaP/ Hib	Polio (IPV)	MMR	Td	Influenza
6 weeks	●	●						
3 months	●	●						
5 months	●		●					
15 months				●		●		
4 years	●					●		
11 years					●[a]		●	
45 years							●[b]	
65 years							●[b]	●

a For those children who had not received a fourth dose of polio vaccine.

b With the introduction of Td at ages 45 and 65 years, 10-yearly boosters were no longer recommended.

Table A1.8: January 2001 immunisation schedule

	DTaP	Hib-HepB	HepB	DTaP/Hib	Polio (OPV)	MMR	Td	Influenza
6 weeks	●	●			●			
3 months	●	●			●			
5 months	●		●		●			
15 months				●		●		
4–5 years					●	●[a]		
11 years					●[b]		●	
65 years								●

a MMR was also offered to children aged 5–10 years in a school catch-up programme.

b For those children who had not received a fourth dose of polio vaccine.

Table A1.9: August 2000 immunisation schedule

	DTaP	Hib-HepB	HepB	DTaP/Hib	Polio (OPV)	MMR	Td	Influenza*
6 weeks	●	●			●			
3 months	●	●			●			
5 months	●		●		●			
15 months				●		●		
11 years					●	●	●	
65 years								●

* Influenza vaccine was introduced for adults aged 65 years and older in 1997 and in 1999 for individuals aged 6 months and older at increased risk of influenza complications.

Table A1.10: 1996 immunisation schedule

	DTwPH	HepB	Polio (OPV)	MMR	Td
6 weeks	●	●	●		
3 months	●	●	●		
5 months	●	●	●		
15 months	●			●	
11 years			●	●	●

Table A1.11: 1994 immunisation schedule

	DTwPH	HepB[a]	Polio (OPV)	MMR[b]	DT	Hib	Td
6 weeks	●	●					
3 months	●	●	●				
5 months	●		●				
12–15 months		●		●			
18 months			●		●	●[c]	
5 years			●				
11 years				●			
15 years							●[d]

a Hepatitis B was introduced for all neonates, with catch-up for children aged under 5 years in 1988. In 1990 free immunisation was extended to all children aged under 16 years.

b MMR was introduced at 12–15 months in 1990 and at age 11 years in 1992.

c A single dose of Hib was also offered to all children aged under 5 years.

d Ten-yearly boosters of Td were recommended.

Table A1.12: 1984 immunisation schedule

	DTwP	Polio (OPV)	Measles	DT	Rubella	Tetanus
6 weeks	●					
3 months	●	●				
5 months	●	●				
12–15 months			●*			
18 months		●		●		
5 years		●				
11 years (girls only)					●	
15 years						●

* Measles vaccine administered at age 12 months was changed to age 12–15 months in 1981.

Table A1.13: 1980 immunisation schedule

	DTwP	Polio (OPV)	Measles	DT	Rubella	Tetanus
3 months	●	●				
5 months	●	●				
12 months			●[a]			
18 months		●		●		
5 years		●				
11 years (girls only)					●[b]	
15 years						●

a Measles vaccine administered at age 10 months was changed to age 12 months in 1974.

b Rubella vaccine was introduced in 1979.

Table A1.14: 1971 immunisation schedule

	DTwP	Polio	Measles	DT	Rubella	Tetanus
3 months	●	●				
5 months	●	●				
10 months			●[a]			
18 months		●		●		
4 years					●[b]	
5 years				●		
15 years						●

a Measles vaccine was introduced in 1969 for children aged 10 months to 5 years who had not had measles, and for those aged under 10 years at special risk.

b Rubella vaccine was introduced in 1970 for children at age 4 years, along with a school-based programme for children aged 5–9 years.

Table A1.15: 1967 immunisation schedule

	DTwP	Polio[a]	DT
3 months	●	●	
4 months	●	●	
5 months	●	●	
18 months		●	●[b]
5 years			●

a Between 1961 and 1967 polio vaccine was administered by the Department of Health.

b The DT booster at age 18 months was introduced in 1964.

Table A1.16: 1961 immunisation schedule

	DTwP	DT
3 months	●	
4 months	●	
5 months	●	
5 years		●

A1.3 History of the Schedule: background information

Note that the following information describes the vaccines which have been, or currently are, on the National Immunisation Schedule. Vaccines which are used for targeted programmes only (ie, hepatitis A, meningococcal) are not discussed. Information about the Meningococcal B Immunisation Programme can be found in earlier editions of the *Handbook*.

A1.3.1 Diphtheria-containing vaccines

During the 1920s the Department of Health, at the instigation of individual school medical officers or medical officers of health, began delivering diphtheria immunisations in a few selected schools and orphanages, but there was no national policy. By 1941 diphtheria immunisation was offered routinely to children aged under 7 years through the School Medical Service and the Plunket Society.

From 1960 the Department of Health programme was delivered by GPs using three doses of non-adsorbed triple vaccine (diphtheria, tetanus and whole-cell pertussis vaccine, DTwP) at ages 3, 4 and 5 months, and a dose of double (diphtheria and tetanus, DT) vaccine before school entry at age 5 years. (For the history of the Schedule's diphtheria toxoid-containing vaccine history after 1960, see section A1.3.13 'Tetanus-containing vaccines').

A1.3.2 Hib-containing vaccines

Haemophilus influenzae type b (Hib) vaccine was added to the Schedule in January 1994, which meant that diphtheria, tetanus, whole-cell pertussis and Hib (DTwPH) vaccine replaced the diphtheria, tetanus and whole-cell pertussis (DTwP) vaccine given at ages 6 weeks, 3 months and 5 months. A monovalent Hib vaccine was given at age 18 months, and a catch-up programme of a single dose of monovalent Hib vaccine was recommended for all children aged under 5 years (ie, those born from January 1989).

From February 1996 the fourth dose was changed to age 15 months and given as DTwPH to reduce the two immunisation events in the second year to one at age 15 months.

DTwPH led to a more than 90 percent reduction in the number of invasive Hib cases in those aged under 5 years but resulted in an increase in the percentage of Hib cases occurring in those aged under 6 months, some of whom had received age-appropriate vaccination. When a supply issue resulted in a change of vaccine in 2000, the opportunity was taken to change to PRP-OMP (polyribosylribitol phosphate outer membrane protein, as Comvax, Hib-HepB combination), which offers substantial protection after a single dose.

This vaccine was used until 2008, when a hexavalent vaccine containing PRP-T Hib component was introduced. This vaccine induces a minimal first-dose response, with some protection after the second dose. It was acknowledged that there was a risk that the change would result in an increase in cases aged under 6 months, but this risk was outweighed by the benefit of reducing the number of injections at each of the first three visits and the reduction in IPD with the introduction of pneumococcal conjugate vaccine (PCV7).

The Hib component of Infanrix-hexa, PRP-T, requires a primary course of three doses with a booster dose at age 15 months, though some protection is induced after the second dose.

In 2006, Hib (as PRP-T) was funded for older children and adults pre- or post-splenectomy. In 2014 funding was extended to include other high-risk conditions.

A1.3.3 Hepatitis B-containing vaccines

HepB was added to the Schedule gradually, starting in September 1985, when it was offered to newborn babies of HBeAg-positive mothers. Three 10 μg doses of plasma-derived vaccine were given, as recommended by the manufacturer. In March 1987 the immunisation programme was extended to newborns of all HBsAg-positive mothers and to children born in certain high-risk districts (Northland, Takapuna, Auckland, South Auckland, Rotorua, Napier and Gisborne).

In 1988 a universal infant vaccination programme was introduced using four low doses (2 μg) of the plasma-derived vaccine H-B-Vax. A catch-up campaign for all preschoolers was undertaken in 1989, and household and sexual contacts of HBsAg-positive women identified during antenatal screening were also entitled to free immunisation.

In December 1988 H-B-Vax was replaced by a recombinant vaccine, Engerix-B. This was given at the manufacturer's recommended dose (10 μg) at 6 weeks, 3 months and 15 months of age. Babies of carrier mothers also received a dose of vaccine, plus HBIG at birth. From February 1990 free hepatitis B immunisation was extended to all children aged under 16 years.

In February 1996 the third dose of HepB was brought forward from 15 to 5 months of age to give early protection to infants and to complete the HepB schedule in the first year of life, in the expectation that this would improve vaccine uptake. This schedule continues in 2017, with 10 μg given at ages 6 weeks, 3 months and 5 months as DTaP-IPV-HepB/Hib (Infanrix-hexa). For infants born to HBsAg-positive mothers, an additional dose of HepB (HBvaxPRO, 5 μg) plus HBIG is given at birth.

In 2014, HepB was made available to individuals at high risk of hepatitis B disease or its complications. In 2015, funding was extended to include other high-risk conditions.

A1.3.4 HPV vaccines

Human papillomavirus (HPV) vaccination, using Gardasil, a quadrivalent vaccine containing virus-like particles (VLPs) derived from HPV types 16, 18, 6 and 11, began in New Zealand on 1 September 2008 and was initially offered only to females born in 1990 and 1991. In 2009 the programme was extended to females born from 1992 onwards. In 2009 and 2010 HPV immunisation was offered through most participating schools to females in school years 8 to 13.

From 2011 the HPV immunisation was only offered in participating schools to females in school year 8. HPV immunisation was also available through family doctors, local health centres and most Family Planning clinics for females who did not attend a participating school or who did not want to have it at school. In 2013 HPV vaccine was funded (for delivery in hospitals only) for other groups at risk of HPV-related disease; from 2014, high-risk groups have also been able to access HPV vaccine in primary care. In 2015, funding was extended to include other high-risk conditions.

Males became eligible for HPV vaccine in 2017, with funding extended to include all males and females aged 26 years and under. The nine-valent HPV vaccine (HPV9, Gardasil 9) replaced HPV4, and a two-dose schedule was recommended for children aged 9–14 years.

A1.3.5 Influenza vaccines

Funded influenza immunisation was introduced in 1997 for people aged 65 years and older. From 1999 the vaccine became funded for younger people (aged from 6 months to 64 years) who were at increased risk of influenza complications. In 2010 funded vaccine was extended to pregnant women, and in 2013 to children aged under 5 years who have been hospitalised for respiratory illness or have a history of significant respiratory illness. In 2015, funding was extended to include other high-risk conditions. In 2018, quadrivalent influenza vaccine replaced the previously used trivalent vaccine.

A1.3.6 Measles-containing vaccines

The measles vaccine was introduced in 1969 for children aged 10 months to 5 years who had not had measles, and for those aged under 10 years at special risk. In 1974 the recommended age for measles vaccine was changed from 10 months to 12 months, and in 1981 it was changed to age 12–15 months. These changes attempted to achieve a balance between too early immunisation, where the vaccine is neutralised by maternally acquired antibody, and the requirement to protect the very young during an epidemic.

MMR (measles, mumps and rubella) vaccine was introduced in 1990 to be given at age 12–15 months in place of the measles vaccine. The dose at age 11 years was introduced in 1992. In 1996 the timing of the first dose of MMR was changed to age 15 months, to be given at the same time as the booster dose of diphtheria, tetanus, whole-cell pertussis and *Haemophilus influenzae* type b (DTwPH) vaccine.

At the start of the 1997 epidemic, the measles immunisation campaign, using MMR, targeted all children aged under 10 years. During the campaign the recommended time for the first dose was brought forward to age 12 months, and in Auckland a dose was recommended for children aged 6–11 months, to be repeated at age 15 months.

The national coverage achieved in the campaign is not known, but estimates for the school-aged population range from 55 percent for Auckland to 85 percent for the Wellington region.

In 2001 the Schedule was changed to give the first dose of MMR at age 15 months and the second dose at 4 years. There was a school catch-up programme for the second MMR dose for children aged 5–10 years. This schedule of two doses of MMR at 15 months and 4 years continues.

Vaccine-derived maternal antibody levels, which protect young infants, are lower and wane earlier than the antibody levels derived from natural infection. It is likely that in due course the age of the first dose of measles-containing vaccine will be changed to age 12 months.

In 2014, MMR vaccine became available for (re-)vaccination following immunosuppression (upon specialist advice).

A1.3.7 Mumps-containing vaccines

Mumps vaccine (as MMR) was introduced to the Schedule in 1990 for children aged 12–15 months. (See section A1.3.6.)

A1.3.8 Pertussis-containing vaccines

A monovalent pertussis vaccine was introduced by the Department of Health in 1945, and from 1953 it was also available combined with the diphtheria and tetanus vaccine. Routine childhood immunisation began in 1960 using the plain (ie, no adjuvant, not adsorbed) diphtheria, tetanus and whole-cell pertussis (DTwP) triple vaccine. Three doses were given, at ages 3, 4 and 5 months.

In 1971 the policy was altered to two doses of adsorbed triple vaccine given at ages 3 and 5 months. It was believed efficacy would be unaltered and the risk of serious reactions would be reduced. Following this schedule change, there was a progressive increase in hospitalisation rates in 1974, 1978 and 1982. Review of the increase in hospitalisations led to the addition, in 1984, of a third dose of DTwP, given at age 6 weeks, to provide earlier protection. From 1994 whole-cell pertussis vaccine was administered as a quadrivalent vaccine with diphtheria and tetanus toxoids and conjugate *Haemophilus influenzae* type b (diphtheria, tetanus, whole cell pertussis and *Haemophilus influenzae* type b – DTwPH).

A fourth dose of pertussis vaccine was added in 1996 (as DTwPH vaccine), given at age 15 months, with the goals of increasing protection in young children and reducing risk of transmission to younger siblings.

Acellular pertussis vaccine was introduced in August 2000, and diphtheria, tetanus and acellular pertussis (DTaP) and DTaP/Hib replaced the whole-cell pertussis vaccines. In February 2002 the vaccine given at ages 6 weeks, 3 months and 5 months was changed to DTaP with inactivated polio vaccine (DTaP-IPV), and a booster dose of DTaP-IPV was introduced and given at age 4 years to protect children during the early school years and to decrease transmission of the infection to younger children.

In 2006 the timing of the booster components of the pertussis schedule was changed to extend vaccine-induced protection into adolescence. Following the three doses of a pertussis-containing vaccine in the first

year of life, booster doses are given at ages 4 and 11 years. Since March 2008 the acellular pertussis vaccine has been delivered as DTaP-IPV-HepB/Hib for the primary immunisation series, scheduled at ages 6 weeks, 3 months and 5 months; as DTaP-IPV at age 4 years; and as Tdap at age 11 years. In comparison with DTaP, Tdap contains smaller doses of tetanus and diphtheria toxoids and the pertussis antigens.

Since January 2013 pregnant women have been eligible for a booster dose of Tdap vaccine. Initially, this was under the outbreak policy and became part of high-risk funded vaccine criteria in July 2015. In 2014, pertussis-containing vaccines (as DTaP-IPV-HepB/Hib, DTaP-IPV and Tdap) became available for (re-)vaccination of children with certain high-risk conditions. This was extended to high-risk adults (as Tdap) in 2015.

A1.3.9 Pneumococcal vaccines

The 7-valent pneumococcal conjugate vaccine (PCV7, Prevenar 7) and the 23-valent pneumococcal polysaccharide vaccine (23PPV, Pneumovax 23) were introduced in 2006 for high-risk individuals. PCV7 became part of the Schedule in June 2008, with four doses recommended at ages 6 weeks, 3 months, 5 months and 15 months.

In July 2011 the 10-valent pneumococcal conjugate vaccine (PCV10, Synflorix) replaced PCV7 and the 13-valent pneumococcal conjugate vaccine (PCV13, Prevenar 13) was introduced for some high-risk children. PCV13 replaced PCV10 on the Schedule in July 2014. In 2015, PCV13 became available for adults with certain high-risk conditions.

In July 2017, PCV10 replaced PCV13 on the usual childhood schedule, with PCV13 and 23PPV continuing for high-risk individuals.

A1.3.10 Poliomyelitis-containing vaccines

Limited supplies of the Salk vaccine (inactivated polio vaccine, IPV) became available in 1956, and immunisation initially targeted 8- and 9-year-old children. As supplies improved, immunisation was extended to include all 5–10-year-olds, then children aged 11–15 years, with approximately 80 percent coverage. By 1960 immunisation was offered to everyone between 6 months and 21 years of age (with three doses of vaccine).

The Sabin vaccine (oral polio vaccine, OPV) was introduced in August 1961, initially for children up to age 12 months; eight months later it was made available to all school children. On completion of this programme in September 1962 the vaccine was offered to adolescents and adults.

In 1967 OPV was given with diphtheria, tetanus and whole-cell pertussis (DTwP) vaccine at ages 3, 4, 5 and 18 months. The deletion of the DTwP dose at age 4 months in 1971 meant the OPV dose at age 4 months was also removed. An extra dose of polio vaccine was added at age 5 years in 1980, based on serological data, which showed decreased immunity to poliovirus types 1 and 3 in school entrants.

In 1996, as part of the Schedule changes, the third dose of the primary series was moved back to the first year of life, with OPV given at ages 6 weeks, 3 months and 5 months. The booster dose was moved to age 11 years, to be given at the same time as the MMR and adult tetanus and diphtheria (Td) vaccines. In 2001 the Schedule was changed to give the fourth dose of OPV at age 4 years, at the same time as the second dose of MMR. Students aged 5–10 years in 2001 who did not receive the fourth dose of polio vaccine at age 4 years were offered a dose at age 11 years.

IPV replaced OPV in 2002 and was included in three doses of DTaP-IPV in the first year of life, with a booster at age 4 years. Those children who had not received four doses of polio vaccine were offered IPV with Tdap, as Tdap-IPV (Boostrix-IPV) at age 11 years in 2006 and 2007. From 2008 Tdap has been offered at age 11 years, as all children should now have received four doses of polio vaccine by age 4 years.

Combined diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated polio vaccine and *Haemophilus influenzae* type b vaccine (DTaP-IPV-HepB/Hib, Infanrix-hexa) replaced DTaP-IPV (Infanrix-IPV) and Hib-HepB (Comvax) on the Schedule in March 2008.

In 2014, IPV vaccine became available for (re-)vaccination following immunosuppression.

A1.3.11 Rotavirus vaccines

The three-dose pentavalent rotavirus vaccine (RV5, RotaTeq) was introduced to the Schedule in 2014, for infants at ages 6 weeks, 3 months and 5 months. In 2017, the two-dose monovalent vaccine (RV1, Rotarix) replaced RV5 on the Schedule, for infants at ages 6 weeks and 3 months.

A1.3.12 Rubella-containing vaccines

Immunisation with an attenuated rubella vaccine (Cendehill strain) was first offered to all 4-year-old New Zealand children in 1970, the rationale being to prevent transmission of the wild virus in 5–9-year-old children, who were the main sufferers from clinical disease. At the same time, the Department of Health delivered a school-based programme, which succeeded in immunising 95 percent of children aged 5–9 years. The acceptance rate of the preschool entry dose of rubella was only about 40 percent, and many practitioners did not feel it was appropriate to immunise males.

In 1979 the immunisation policy for rubella was altered to offer the vaccine to girls aged 11 years, in school year 7 (form 1). The aim was to immunise females before they attained childbearing age. In 1990 MMR was introduced at age 12–15 months for all children, and rubella vaccine continued to be offered to girls in school year 7. Since 1992 two doses of rubella vaccine – as measles, mumps and rubella (MMR) vaccine – have been offered to all children, the first dose in the second year of life and the second dose at age 11 years. This was changed in 2001, maintaining the first dose of MMR at age 15 months and changing the second to age 4 years. The aim of this strategy was to prevent rubella epidemics, reduce the background incidence of rubella and continue to protect women before childbearing, therefore eventually eliminating CRS.

In 2001 there was an MMR school catch-up programme throughout the country for all children aged 5–10 years who would no longer receive an MMR dose in school year 7.

The rubella schedule continues as two doses of MMR vaccine offered at ages 15 months and 4 years.

In 2014, MMR vaccine became available for (re-)vaccination following immunosuppression (upon specialist advice).

A1.3.13 Tetanus-containing vaccines

The history of tetanus vaccine use prior to the 1960 introduction of diphtheria, tetanus and whole-cell pertussis (DTwP) vaccine is not well recorded, but tetanus vaccine was widely used in World War II and subsequently by the armed forces. In New Zealand, universal infant immunisation with tetanus toxoid began in 1960 with the use of three doses of triple vaccine. Anyone born before 1960 is less likely to have received a primary series, unless they were in the armed forces. Older women appear to be at particular risk.

The first scheduled vaccine used for infants (from 1960) was the DTwP vaccine, with three doses at monthly intervals at ages 3, 4 and 5 months, and a diphtheria and tetanus (DT) booster before school entry (at age 5 years). A DT booster at age 18 months was added in 1964, primarily to enhance protection against tetanus. There was a change to a more immunogenic adsorbed vaccine in 1971, and the dose given at age 4 months was dropped.

In 1980 the dose of DT given at age 5 years was replaced by the monovalent tetanus toxoid given at age 15 years, as part of a move from 10-yearly to 20-yearly boosters for tetanus. It was considered that more frequent boosters were unnecessary and the cause of significant local reactions. There was a return to a three-dose primary series of DTwP (by the addition of a 6-weeks-of-age vaccination) in 1984 because two doses had been inadequate to control pertussis. In 1996 the booster of Td, which had been changed from tetanus toxoid in 1994 (see below), and previously given at age 15 years, was changed to age 11 years.

In 2002 the primary schedule for tetanus, given in combination vaccines at ages 6 weeks, 3 months and 5 months, followed by a dose at 15 months, was changed when a further dose was introduced at age 4 years. The Td given at age 11 years continued.

Since 2006 the childhood schedule for tetanus has been given in combination vaccines at ages 6 weeks, 3 months, 5 months (DTaP-IPV-HepB/Hib), 4 years (DTaP-IPV) and 11 years (Tdap).

Td replaced the tetanus toxoid vaccine in 1994, and 10-yearly boosters were recommended. The change was recommended to maintain the adult population's immunity to diphtheria, in response to outbreaks overseas affecting adults and the absence of natural boosting because the disease had become rare. From 2002 adult boosters have been recommended at ages 45 and 65 years (instead of 10-yearly) as a pragmatic attempt to increase coverage in the adult population.

In 2014, Td became available for (re-)vaccination following immunosuppression.

A1.3.14 BCG vaccines

BCG immunisation was first introduced to New Zealand in 1948 and later extended to all adolescents. BCG immunisation of neonates was introduced in 1976, initially in districts with high rates of active TB.

Universal screening and vaccination of 13-year-olds was discontinued in the South Island in 1963, was phased out in regions of the North Island in the 1980s, and had ceased by 1990. It was stopped because TB had declined to a point at which the advantages of vaccination were outweighed by the disadvantages (cost, side-effects and reduced diagnostic value of the Mantoux test). BCG vaccine is now only available to neonates and children aged under 5 years at high risk of TB.

A1.3.15 Varicella vaccines

In 2014 two doses of varicella vaccine (VV, Varilrix) were introduced for individuals at high risk of varicella infection. In 2017 one dose of VV was introduced to the Schedule at age 15 months (for children who were born on or after 1 April 2016). One catch-up VV dose was introduced for previously unvaccinated children turning 11 years old on or after 1 July 2017 who had not previously had a varicella infection.

A1.3.16 Herpes zoster vaccines

HZV was introduced onto the Schedule on 1 April 2018, as a single dose for adults aged 65 years, with a catch-up programme for adults aged 66–80 years inclusive (the catch-up programme ceases on 31 March 2020).

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Appendix 2: Planning immunisation catch-ups

It is essential that vaccinators have a sound understanding of the number of antigens and the most effective spacing of doses required for a primary course and subsequent boosters in order to assess an individual's immunisation requirements. The principles described below will help vaccinators in this process.

Section A2.2 discusses catch-up requirements for children aged under 18 years, and section A2.3 discusses the requirements for adults.

Plan and document your complete catch-up schedule in the patient notes and recall system to ensure continuity of care.

For assistance with planning catch-up schedules, contact your immunisation coordinator, the IMAC freephone line on 0800 466 863, or discuss with an experienced colleague.

A2.1 Eligibility for publicly funded vaccines

The *Health and Disability Services Eligibility Direction 2011* (the Eligibility Direction) issued by the Minister of Health sets out the eligibility criteria for publicly funded health and disability services in New Zealand. Only people who meet the eligibility criteria defined in the Eligibility Direction can receive publicly funded (ie, free or subsidised) health and disability services.

Note that regardless of their immigration and citizenship status, all children aged under 18 years are eligible to receive Schedule vaccines, and providers can claim the immunisation benefit for administering the vaccines.

A2.2 For infants, children and adolescents aged under 18 years who start their vaccinations late or who are more than one month behind a due vaccination date

When planning a catch-up schedule, start by focusing on the antigens already received and the additional antigens required, not the vaccine combinations available or trade names. There is no need to think in terms of events missed (eg, the 6-week, 3-month, 5-month, 15-month vaccination event). It is important to note the age of the child when the antigens were received.

Although catch-up tables are provided in this appendix, children may not fit these unless they are completely unvaccinated, or there is no documented history and they are assumed to be unvaccinated. Trying to fit a child's vaccine requirements to a table can result in too many or not enough antigens being administered.

Use the following principles to establish what antigens the infant, child or adolescent requires.

A2.2.1 Principles of catch-up for infants and children aged under 10 years

1. The best approach is to ascertain the antigens required for their current age, subtract any already given and then develop the individual's catch-up schedule.

2. There is considerable flexibility when planning catch-up schedules. To offer the best protection in the shortest time possible, most vaccines can be given simultaneously and the catch-up schedule shortened to four-weekly intervals to ensure the required number of doses are administered.

3. If the Schedule has been interrupted, do not repeat prior doses regardless of how long ago the previous doses were given. Exceptions to this principle are the following vaccines given to children aged under 12 months: MMR or measles-containing

vaccine (see point 8 below), Hib vaccine (see point 9) and PCV vaccine (see point 10).

4. If the immunisation status of a child is uncertain or unknown, plan the catch-up schedule assuming the vaccines have not been given.

5. If a child infrequently attends general practice and failure to return for future immunisation is a concern, it is prudent to administer as many antigens as possible at every visit.

6. For infants and children aged under 10 years, use DTaP-IPV-HepB/Hib or DTaP-IPV for primary immunisation. Tdap may be used as an alternative for primary immunisation of children aged 7 to under 18 years (note that Tdap [Boostrix] is not registered for primary immunisation, but there is no evidence of safety concerns).

7. The first dose of rotavirus vaccine (RV1, Rotarix) should be given before age 15 weeks (ie, the latest is 14 weeks and 6 days) and the second dose administered a minimum of four weeks later. An infant who has not had the first dose before age 15 weeks will not be eligible to commence the rotavirus course. Where the first dose is inadvertently given at age 15 weeks or older, the remaining dose should be given, but both doses should be given before age 25 weeks (ie, 24 weeks and 6 days). While it is preferable for infants to complete the rotavirus course with the same vaccine, both RV5 (RotaTeq) and RV1 (Rotarix) vaccines may be used interchangeably, providing the upper age limits are met. See Table A2.4 for infants who are transitioning from RV5 to RV1.

8. The first dose of MMR is scheduled at age 15 months but may be given to children from age 12 months at the parents'/guardians' request. If there are concerns about the child returning for follow-up visits, give MMR at the first visit from age 12 months. MMR or any single-antigen measles vaccine given before age 12 months is not counted as part of the two-dose MMR schedule.

9. A single dose of Hib is required for all children aged 12 months to under 5 years regardless of the number of doses given in their first year. Healthy children aged 5 years and older do not need Hib.

10. Ideally, the primary course of PCV should be completed with the same manufacturer's vaccine. Where this is not possible, it is acceptable to use the available PCV vaccine. For healthy infants

commencing PCV vaccination at ages 7–11 months, a primary course is two doses with a minimum of four weeks between doses. A booster dose is given after age 12 months – at age 15 months or at least eight weeks after the completion of the primary course. Unimmunised healthy children aged 12 months to under 5 years require two PCV doses at least eight weeks apart. If a child did not complete their primary course when under 12 months of age, do not count the given doses when determining the number of PCV catch-up doses required. Healthy children aged 5 years and older do not need PCV. See chapter 15 'Pneumococcal disease' for PCV13 schedules for high-risk children.

11. One dose of varicella vaccine is funded for children who were born on or after 1 April 2016.

12. Remember to check whether the infant/child has any specific health conditions that may make them eligible for additional vaccines or additional doses of vaccine (see chapter 4 'Immunisation of special groups').

13. Once the child has received the appropriate vaccines for their age, they should continue on the Schedule as usual.

Table A2.1: Minimum number of antigens required, by age at time of presentation, for infants and children aged <10 years

<12 months	12 months to <5 years	5 years to <10 years
3 DTaP[a]	3 or 4 DTaP[a]	4 DTaP[a]
3 IPV[a]	3 or 4 IPV[a,e]	3 or 4 IPV[e]
3 HepB[b]	3 HepB[b]	3 HepB[b]
3 Hib	1 Hib[f]	2 MMR
2 or 3 PCV[c]	2 PCV[c]	
2 RV[d]	1 or 2 MMR[g]	
	1 VV[h]	

a Use DTaP-IPV-HepB/Hib or DTaP-IPV for the 3-dose primary series (at a minimum of 4-weekly intervals), then continue on the usual childhood schedule with a booster dose of DTaP-IPV given at age 4 years. If the child commences immunisation at age 4 years or older, give the booster dose at least 6 months after the 3rd dose of the primary series.

b If the child received HepB at birth, they will require a total of 4 HepB doses. Children born to HBsAg-positive mothers require serological testing – see section 8.5.2.

c For healthy infants commencing PCV vaccination at ages 7–11 months, a primary course is 2 doses with a minimum of 4 weeks between doses. A booster dose is given after 12 months of age – at age 15 months or at least 8 weeks after the completion of the primary course. For healthy children aged 12 months to under 5 years who are commencing immunisation or with an incomplete course, 2 doses of PCV at least 8 weeks apart are required. (See chapter 15 'Pneumococcal disease' for PCV13 schedules for high-risk children.)

d The 1st dose of rotavirus vaccine should be given before age 15 weeks (ie, the latest is 14 weeks and 6 days) and the 2nd dose administered a minimum of 4 weeks later. Both doses must be given before age 25 weeks (ie, the latest is 24 weeks and 6 days). Where the 1st dose is inadvertently given at age 15 weeks or older, the 2nd dose should be given, but both doses must be given before age 25 weeks (24 weeks and 6 days). See Table A2.4 for infants who are transitioning from RV5 to RV1.

e A minimum of 3 polio doses are required for the primary series (at a minimum of 4-weekly intervals) for children aged under 10 years, but 4 doses may be given when combination vaccines are used (eg, DTaP-IPV-HepB/Hib or DTaP-IPV).

f A single dose of Hib is required for all children from age 12 months to under 5 years, regardless of the number of doses given before age 12 months.

g Children commencing immunisation at age 12 months to under 4 years require 1 dose of MMR, then continue on the usual childhood schedule with a 2nd dose of MMR given at age 4 years, or at least 4 weeks after the 1st MMR dose at the parents'/guardians' request. Children commencing immunisation at age 4 years require 2 doses of MMR 4 weeks apart.

h One dose of varicella vaccine is funded for children born on or after 1 April 2016.

A2.2.2 Principles of catch-up for children and adolescents aged 10 to under 18 years

1. The best approach is to ascertain the antigens required for current age, subtract any already given and then develop the individual's catch-up schedule.

2. There is considerable flexibility when planning catch-up schedules. To offer the best protection in the shortest time possible, most vaccines can be given simultaneously and the catch-up schedule shortened to four-weekly intervals to ensure the required number of doses are administered.

3. If the Schedule has been interrupted, do not repeat prior doses regardless of how long ago the previous doses were given.

4. If the immunisation status of an individual is uncertain or unknown, plan the catch-up schedule assuming the vaccine has not been given.

5. If an individual infrequently attends general practice and failure to return for future immunisation is a concern, it is prudent to administer as many antigens as possible at every visit. If aged 12 months or older administer MMR at the first visit.

6. For individuals aged 10 years to under 18 years, Tdap is recommended and funded for primary and booster immunisation. While Tdap is not approved for use (registered) as a primary course, no safety concerns are expected when using Tdap for primary immunisation in individuals aged 10 to under 18 years. Therefore, using Tdap should be considered for all catch-up schedules for primary and booster immunisations.

7. For individuals aged 11–15 years, an alternative two-dose hepatitis B catch-up schedule may be considered using the monovalent HepB (HBvaxPRO 10 μg; use Engerix B 20 μg if HBvaxPRO 10 μg is not available), with the second dose given four to six months after the first. (Note: While not approved for a two-dose schedule, there is no reason to expect that two doses of Engerix-B 20 μg, given four to six months apart, would not provide the same level of protection as two doses of HBvaxPRO 10 μg.)

8. Individuals aged 14 years and under receive two doses of HPV at 0 and 6–12 months. Individuals aged 15 years and older receive three doses of HPV at 0, 2 and 6 months. If a shortened schedule is required for those aged 15 years and older, give the 2nd dose at least 1 month after the 1st dose and the 3rd dose at least 3 months after the 2nd dose. Those who started with HPV4 may complete their remaining doses with HPV9. Non-residents who were under age 18 years when they commenced HPV vaccination are currently funded to complete the course, even if they are aged 18 years or older when they complete it. See Table A2.10 for HPV catch-up schedules.

9. One dose of varicella vaccine is funded for previously unvaccinated children turning 11 years old on or after 1 July 2017 who have not previously had a varicella infection.

10. Remember to also check whether the individual has any specific health conditions that may make them eligible for additional vaccines or additional doses of vaccine (see chapter 4 'Immunisation of special groups').

11. Once the individual has received the appropriate vaccines for their age they should continue on the Schedule as usual.

Table A2.2: Minimum number of antigens required by individuals aged 10 to under 18 years at the time of presentation

10 years to <18 years
4 Tdap[a]
3 IPV[b]
3 HepB (5 µg) for children aged 10 to <18 years; or 2 HepB doses (10 µg) for children aged 11–15 years[c]
2 MMR
2 HPV[d,e,f] for those aged 11–14 years, or 3 HPV[d,g] for those aged 15 years and older
1 VV[h]

a If aged 10 years to under 18 years, use Tdap for the primary series and the booster dose, with a minimum interval of 6 months between doses 3 and 4 (the primary series and the booster dose).

b A minimum of 3 polio doses are required for the primary series (at a minimum of 4-weekly intervals).

c If aged 10 years to under 18 years, 3 doses of HepB (HBvaxPRO 5 µg) are required. An alternative 2-dose schedule of HepB (HBvaxPRO 10 µg) may be used for children aged 11–15 years with the 2nd dose given 4–6 months after the 1st. If HBvaxPRO 5 µg or 10 µg are not available, use Engerix B 20 µg instead (2 or 3 doses, depending on age at 1st dose).

d Individuals who started with HPV4 may complete their remaining doses with HPV9.

e For those aged 11–14 years, the 2nd HPV dose is preferably given at least 6 months after the 1st. If the 2nd dose is given earlier than 5 months after the 1st, a 3rd HPV dose is recommended and funded. Give the 3rd dose at least 6 months after the 1st dose.

f Regardless of the age at the 1st dose, if the 2nd HPV dose is given at age 15 years or older a 3rd HPV dose is recommended and funded. Give the 3rd dose at least 4 months after the 2nd dose.

g For those aged 15 years and older, give a 3-dose HPV course at 0, 2 and 6 months. If a shortened schedule is required for these older individuals, give the 2nd dose at least 1 month after the 1st dose and the 3rd dose at least 3 months after the 2nd dose.

h One dose of varicella vaccine is funded for previously unvaccinated children turning 11 years old on or after 1 July 2017 who have not previously had a varicella infection.

A2.2.3 National Immunisation Schedule catch-up guides for infants, children and adolescents aged under 18 years

Note, these are a guide only and the principles described in sections A2.2.1 and A2.2.2 should be followed. The vaccinator must subtract any previous doses given. It is important to note the age at which the antigens have been given.

Table A2.3: Age at presentation: 3–6 months

Note: Subtract previous doses given.

Dose	Vaccines		
First dose*	DTaP-IPV-HepB/Hib	PCV	RV*
4 weeks later	DTaP-IPV-HepB/Hib	PCV	RV*
4 weeks later	DTaP-IPV-HepB/Hib	PCV	
Once the child has received the appropriate vaccines for their age, continue on the Schedule as usual.			

* Only eligible for RV if the 1st dose is given before age 15 weeks (ie, 14 weeks and 6 days). The 2nd dose must be given before age 25 weeks (ie, 24 weeks and 6 days). See Table A2.4 for infants who are transitioning from RV5 (RotaTeq) to RV1 (Rotarix).

Table A2.4: Recommendations for infants aged under 25 weeks who are transitioning from RV5 (RotaTeq) to RV1 (Rotarix)

Number of RV5 doses previously received	Number of RV1 doses required
3 RV5	Fully immunised – no RV1 required
2 RV5	1 RV1* at least 4 weeks after the 2nd RV5
1 RV5	2 RV1* at least 4 weeks between each of the doses

* All doses of RV1 must be given before age 25 weeks (ie, the latest is 24 weeks and 6 days).

Table A2.5: Age at presentation: 7–11 months

Note: Subtract previous doses given.

Dose	Vaccines	
First dose	DTaP-IPV-HepB/Hib	PCV*
4 weeks later	DTaP-IPV-HepB/Hib	PCV
4 weeks later	DTaP-IPV-HepB/Hib	
Once the infant has received the appropriate vaccines for their age, continue on the Schedule as usual.		

* Healthy infants commencing PCV vaccination at age 7–11 months require a primary course of 2 PCV doses. Those who received 1 PCV dose before age 7 months should receive 2 further doses of PCV whilst aged under 12 months to complete the primary course. (See chapter 15 'Pneumococcal disease' for PCV13 schedules for high-risk children.)

Table A2.6: Age at presentation: 12–23 months

Note: Subtract previous doses given.

Dose	Vaccines			
First dose	DTaP-IPV-HepB/Hib[a]	PCV[b]	MMR[c]	VV[d]
4 weeks later	DTaP-IPV-HepB/Hib[e]			
4 weeks later or at age 15 months, whichever is applicable	DTaP-IPV-HepB/Hib[e]	PCV[b]		
Once the child has received the appropriate vaccines for their age, continue on the Schedule as usual.				

a One dose of Hib is required from age 12 months to under 5 years regardless of previous doses.

b Healthy children commencing immunisation at age 12–23 months require 2 PCV doses, with a minimum interval of 8 weeks between doses. If the child did not complete a primary course of PCV when under 12 months of age, do not count the previously given doses when determining the number of PCV catch-up doses required. If the child completed a primary course of PCV before age 12 months, give a booster dose at age 15 months or at least 8 weeks after the completion of the primary course. (See chapter 15 'Pneumococcal disease' for PCV13 schedules for high-risk children.)

c The 1st dose of MMR is scheduled at age 15 months but may be given to children from age 12 months at the parents'/guardians' request. If there are concerns about the child returning for follow-up visits, give MMR at the 1st visit from age 12 months.

d One dose of varicella vaccine is funded for children born on or after 1 April 2016.

e Parents/guardians should be informed that their child will receive extra doses of Hib but there are no safety concerns with these extra doses. If the parents/guardians prefer, vaccinators may administer the DTaP-IPV and HepB vaccines as 2 separate injections instead of the combination DTaP-IPV-HepB/Hib vaccine.

Table A2.7: Age at presentation: 2 years to under 5 years

Note: Subtract previous doses given.

Dose	Vaccines			
First dose	DTaP-IPV-HepB/Hib[a]	PCV[b]	MMR	VV[c]
4 weeks later	DTaP-IPV-HepB/Hib[d]		MMR[e]	
4 weeks later	DTaP-IPV-HepB/Hib[d]	PCV[b]		
6 months later	DTaP-IPV[f]			
Once the child has received the appropriate vaccines for their age, continue on the Schedule as usual.				

a One dose of Hib is required from age 12 months to under 5 years regardless of previous doses.

b For a healthy child who presents at age 2 years to under 5 years: if previously unvaccinated, give 2 PCV doses at least 8 weeks apart; if they completed a primary PCV course before age 12 months, give 1 PCV dose; if they started but did not complete a primary PCV course before age 12 months, give 2 PCV doses at least 8 weeks apart (this is the exception to the principle of counting previous doses given). (See chapter 15 'Pneumococcal disease' for PCV13 schedules for high-risk children.)

c One dose of varicella vaccine is funded for children who were born on or after 1 April 2016.

d Parents/guardians should be informed that their child will receive extra doses of Hib, but there are no safety concerns with these extra doses. If the parents/guardians prefer, vaccinators may administer the DTaP-IPV and HepB vaccines as 2 separate injections instead of the combination DTaP-IPV-HepB/Hib vaccine.

e Administer the 2nd MMR dose at age 4 years or a minimum of 4 weeks after the 1st dose at the parents'/guardians' request. If the child is older than age 4 years at presentation, administer the 2nd MMR dose a minimum of 4 weeks after the 1st dose.

f Administer DTaP-IPV at age 4 years, a minimum of 6 months after the 3rd DTaP-IPV-HepB/Hib dose. If the child is aged 4 years or older at presentation, administer DTaP-IPV a minimum of 6 months after the 3rd DTaP-IPV-HepB/Hib dose.

Table A2.8: Age at presentation: 5 years to under 10 years

Note: Subtract previous doses given.

Dose	Vaccines	
First dose	DTaP-IPV-HepB/Hib[a,b]	MMR
4 weeks later	DTaP-IPV-HepB/Hib[a,b,c]	MMR
4 weeks later	DTaP-IPV-HepB/Hib[a,b,c]	
6 months later	DTaP-IPV[c]	
Once the child has received the appropriate vaccines for their age, continue on the Schedule as usual.		

a Healthy children aged 5 years and older do not need Hib. However, DTaP-IPV-HepB/Hib should be offered to reduce the number of injections at each visit. Parents/guardians should be informed that their child will receive extra doses of Hib but there are no safety concerns with these extra doses.

b If the parents/guardians prefer, vaccinators may administer DTaP-IPV and HepB vaccines as 2 separate injections instead of the combination DTaP-IPV-HepB/Hib vaccine.

c If a child turns 10 years old before completing their catch-up programme, they should continue on the 10 years to under 18 years catch-up schedule (refer to Table A2.9).

Table A2.9: Age at presentation: 10 years to under 18 years – excluding HPV

Note: Subtract previous doses given.

Dose	Vaccines				
First dose	Tdap[a]	IPV[b]	HepB[c]	MMR	
4 weeks later	Tdap[a]	IPV[b]	HepB	MMR	
4 weeks later	Tdap[a]	IPV[b]	HepB		
6 months later, or at age 11 years	Tdap				
At age ≥11 years					VV[d]

a Use Tdap for the primary series and the booster dose, with a 6-month interval between the primary series and the booster (doses 3 and 4).

b A minimum of 3 IPV doses are required for the primary series (at a minimum of 4-weekly intervals).

c If aged 10 years to under 18 years, 3 doses of HepB (HBvaxPRO 5 µg) are required. An alternative 2-dose schedule of HepB (HBvaxPRO 10 µg) may be used for children aged 11–15 years with the 2nd dose given 4–6 months after the 1st. If HBvaxPRO 5 µg or 10 µg are not available, use Engerix B 20 µg instead (2 or 3 doses, depending on age at 1st dose).

d One dose of varicella vaccine is funded for previously unvaccinated children turning 11 years old on or after 1 July 2017 who have not previously had a varicella infection.

Table A2.10: Age at presentation: 11 years to under 18 years – HPV only

Note: Subtract previous doses given.

Dose	Vaccine
Age 11–14 years[a,b] at presentation	
First dose	HPV
6–12 months later[c,d]	HPV
Age 15 years and older[b,e] at presentation	
First dose	HPV
2 months later	HPV
4 months later	HPV

a Although the usual schedule is at age 11 or 12 years (school year 7 or 8), HPV vaccine may be given from age 9 years.

b Individuals who started with HPV4 may complete their remaining doses with HPV9.

c For those aged 11–14 years, the 2nd dose is preferably given at least 6 months after the 1st. However, if the 2nd dose is given less than 5 months after the 1st, a 3rd HPV dose is recommended and funded. Give the 3rd dose at least 6 months after the 1st.

d Regardless of the age at the 1st dose, if the 2nd HPV dose is given at age 15 years or older, a 3rd HPV dose is recommended and funded. Give the 3rd HPV dose at least 4 months after the 2nd.

e If a shortened schedule is required for those aged 15 years and older, give the 2nd dose at least 1 month after the 1st dose and the 3rd dose at least 3 months after the 2nd dose.

A2.3 Immunisation catch-up for eligible adults aged 18 years and older

When seen at general practice or by vaccination providers, adults should be checked to see that they have received protection against the following diseases and have received a primary immunisation course as in Table A2.11 below.

1. If the requisite number of doses has not been received, catch-up vaccination is recommended. There is flexibility when planning catch-up schedules. To offer the best protection in the shortest time possible, most vaccines may be given simultaneously and the catch-up schedule shortened to four-weekly intervals to ensure the required number of doses are administered.

2. Do not repeat prior doses regardless of how long ago the previous doses were given.

3. All adults should be reminded of the necessity for age-appropriate boosters for tetanus and diphtheria at 45 and 65 years of age.

4. Pertussis (Tdap; given between 28 and 38 weeks' gestation) and influenza vaccines are recommended and funded in every pregnancy. A single dose of unfunded Tdap and influenza vaccines may be considered for adults requesting pertussis and influenza protection, especially for those in close contact with young babies.

5. Women of childbearing age should know whether they are immune to rubella. If the patient does not have two documented doses of MMR, two doses of funded MMR should be offered four weeks apart (MMR cannot be given in pregnancy and pregnancy should be avoided for four weeks following vaccination). If they have received one documented dose of MMR, a second dose should be administered.

6. Previously unvaccinated males and females aged 15 years to 26 years inclusive may receive three doses of HPV vaccine. Those who started with HPV4 may complete their remaining doses with HPV9. Those who were aged under 27 years when they commenced but did not complete HPV vaccination are currently funded to complete the three-dose course even if they are aged 27 years or older when they complete it. Non-residents who were under age 18 years when they commenced HPV vaccination are currently funded to complete the course, even if they are aged 18 years or older when they complete it.

7. From 1 April 2018, one dose of HZV will be funded for individuals at age 65 years. There will be a catch-up programme from 1 April 2018 until 31 March 2020, with one dose of HZV funded for individuals aged 66 to 80 years, inclusive.

8. Check whether the individual has any additional immunisation requirements, such as specific health conditions or occupational risk (see chapter 4 'Immunisation of special groups').

Table A2.11: Primary immunisation requirements for adults

Antigens and number of doses required
3 Td[a]
3 polio (IPV)[b]
2 MMR[c]
3 HPV[d,e] (aged 26 years and under)

a A primary course of 3 doses of Td vaccines (at a minimum of 4-weekly intervals) is recommended and funded for unimmunised or partially immunised adults. Unfunded Tdap may be offered as an alternative to Td for pertussis protection. At ages 45 and 65 years, the Td booster immunisation administration (the immunisation benefit) is not funded, although the vaccine is free.

b A primary course of 3 polio (IPV) doses (at a minimum of 4-weekly intervals) is recommended and funded for unimmunised or partially immunised adults.

c Two doses of MMR (given a minimum of 4 weeks apart) are recommended and funded for unimmunised adults who are susceptible to any one of the three diseases. Those born in New Zealand before 1969 are considered to be immune to measles.

d HPV vaccine is recommended and funded for all individuals aged 26 years and under. Give the 3-dose course at 0, 2 and 6-months. If a shortened schedule is required, give the 2nd dose at least 1 month after the 1st dose and the 3rd dose at least 3 months after the 2nd dose.

e Those who were under age 27 years when they commenced HPV vaccination are currently funded to complete the 3-dose course, even if they are aged 27 years or older when they complete it. Non-residents who were under age 18 years when they commenced HPV vaccination are currently funded to complete the course, even if they are aged 18 years or older when they complete it.

Appendix 3: Immunisation standards for vaccinators and guidelines for organisations offering immunisation services

A3.1 Purpose

The 'Immunisation standards for vaccinators' (see section A3.3) are quality levels all vaccinators should achieve to ensure they can competently deliver safe and effective immunisation services.

The 'Immunisation standards for vaccinators' and the 'Guidelines for organisations storing vaccines and/or offering immunisation services' (see section A3.4) apply to all vaccinators, including those delivering National Immunisation Schedule vaccines, vaccines on an authorised programme or privately purchased vaccines.

The Schedule aims to protect children and adults against 15 serious vaccine-preventable diseases and offers publicly funded immunisation to individuals at risk of hepatitis A, influenza, varicella, TB, meningococcal and/or pneumococcal disease.

Note: The term 'vaccinator' used throughout these standards applies to *any* health professional offering a vaccinator service, including registered nurse vaccinators, authorised vaccinators, pharmacist vaccinators, GPs and midwives.

A3.2 Health and Disability Commissioner (Code of Health and Disability Services Consumers' Rights) Regulations 1996

It is expected that all organisations and providers offering immunisation services practise in accordance with the Health and Disability Commissioner (Code of Health and Disability Services Consumers' Rights) Regulations 1996. The Regulations establish the rights of consumers and the obligations and duties of providers to comply with the Code of Rights made pursuant to the Health and Disability Commissioner Act 1994.

The obligation under the Regulations is to take 'reasonable actions in the circumstances to give effect to the rights, and comply with the duties' in the Code of Rights. The Code of Rights is as follows.

Right 1: Right to be treated with respect

Right 2: Right to freedom from discrimination, coercion, harassment and exploitation

Right 3: Right to dignity and independence

Right 4: Right to services of an appropriate standard

Right 5: Right to effective communication

Right 6: Right to be fully informed

Right 7: Right to make an informed choice and give informed consent

Right 8: Right to support

Right 9: Rights in respect of teaching or research

Right 10: Right to complain

For more detailed information on the Code of Health and Disability Services Consumers' Rights, refer to the Health and Disability Commissioner's website (www.hdc.org.nz).

A3.3 Immunisation standards for vaccinators

Standard 1: The vaccinator is competent in all aspects of the immunisation technique and has the appropriate knowledge and skills for the task

Required characteristics of the vaccinator

1.1 The vaccinator completes an appropriate training programme approved by the Ministry of Health. If a vaccinator is working as an authorised vaccinator or as a pharmacist vaccinator, they will also have undertaken a clinical assessment and vaccinate in accordance with their Scope of Practice.[1]

1.2 All vaccinators are required to have a summary[2] of their immunisation practice over the past 12 months.

1.3 The vaccinator remains current with developments in immunisation theory, practice and policy. At least every two years the vaccinator is required to have completed a vaccinator update course that meets the current *Vaccinator Update Course Standards*[3] and have evidence of completion.

1.4 The vaccinator maintains linkages with other providers associated with immunisation delivery; for example, immunisation coordinators, outreach immunisation providers and their local DHB NIR team.

1.5 Vaccinators are recommended to carry indemnity insurance for their personal/professional protection.

1 Refer to Appendix 4.

2 The summary should include type of immunisation practice as a vaccinator (eg, general practice, occupational health, pharmacy, etc); types of vaccinations given (eg, intramuscular, subcutaneous, intradermal); and other responsibilities related to immunisation (eg, cold chain-designated person, etc).

3 Published by IMAC.

Standard 2: The vaccinator obtains informed consent to immunise

Required characteristics of the vaccinator

2.1 The vaccinator is able to assess the knowledge of the individual/parent/guardian regarding vaccine-preventable diseases and the process of immunity, and is able to provide evidence-based information to enable individuals/parent/guardian to make an informed choice and give informed consent.

2.2 The vaccinator communicates in a form, language and manner that enables the individual/parent/guardian to understand the information provided. Communication should be supported by evidence-based health information material.[4]

2.3 The vaccinator allows time to answer questions and obtains feedback indicating that the individual/parent/guardian understands which vaccine is being recommended and why.

2.4 The vaccinator informs the individual/parent/guardian about the NIR, including information on the use and disclosure of the information held on the NIR, how the information is stored, and that all vaccinations given will be recorded on the NIR (if applicable) unless the individual/parent/guardian chooses to opt off the NIR. If an individual/parent/guardian chooses to opt off the NIR, this process must be explained to them.

2.5 Consent does not need to be given in writing (except for school-based immunisation programmes and BCG vaccination), but the vaccinator must document in the clinical notes a summary of the discussion and note that verbal consent was obtained.

2.6 The vaccinator obtains consent for each immunisation episode and documents that the individual/parent/guardian has been made aware of the benefits and risks of the disease and the vaccine in order to make an informed choice about immunisation and the immunisation programme, including the NIR.[5]

4 Refer to chapter 2, section 2.1.2.

5 Refer to chapter 2, section 2.3.5.

2.7 If the individual/parent/guardian declines to be immunised/to immunise their child, the vaccinator provides information about keeping themselves and others healthy. The individual/parent/guardian should be advised that they can reconsider their decision at any time, and the declined immunisation will be offered again by their health provider.

Standard 3: The vaccinator provides safe immunisation

Required characteristics of the vaccinator and immunisation setting

3.1 The venue provides for privacy and is appropriate for the individual/parent/guardian. Facilities are available for assessment and management of adverse events, including anaphylaxis.[6]

3.2 If the venue is a non-clinical setting (eg, in a home, workplace or school) then a minimum of two immunisation team members must be present for vaccination; one of whom must be an authorised vaccinator or pharmacist vaccinator, the other must be a competent adult who is able to call for emergency support and has a current basic life support certificate.

3.4 The vaccinator can manage AEFIs, including anaphylaxis, and has a contingency plan for seeking emergency assistance.

3.5 Because of the potential for anaphylactic reactions, vaccinees (with their parents/guardians if applicable) are required to remain under observation for a minimum of 20 minutes after immunisation.

3.6 The vaccinator ensures continuity of the cold chain and adheres to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*[7] and the practice/clinic cold chain management policy. The vaccinator ensures the practice/clinic achieves Cold Chain Accreditation.[8]

6 Refer chapter 2, section 2.3.3.

7 Available at www.health.govt.nz/coldchain

8 See the Cold Chain pages on the Ministry of Health website (www.health.govt.nz/coldchain).

3.7 Before vaccinating, the vaccinator undertakes an appropriate clinical assessment (pre-vaccination screen).[9]

3.8 The vaccinator uses clean techniques in the preparation and administration of all vaccines,[10] visually checks the vaccine, checks expiry date, prepares vaccine as appropriate and uses vaccines within the recommended period after preparation.

3.9 The vaccinator provides verbal and written information that is evidence based and follows best practice principles about care after immunisation.[11]

Standard 4: The vaccinator documents information on the vaccine(s) administered, and maintains patient confidentiality

Required characteristics of the vaccinator

4.1 The vaccinator has had training in the correct use of their PMS, the SBVS or the NIR manual forms to enable them to correctly enter an individual's information on the NIR (if applicable) and to claim an immunisation benefit (if applicable).

4.2 The vaccinator documents the individual's personal details, including NHI number, name, date of birth, ethnicity, address, contact telephone number, next of kin details and primary health care provider (if the vaccinator is not the usual primary health care provider).

4.3 Having chosen the appropriate immunisation schedule, the vaccinator documents the following details:

- consent obtained
- date vaccine administered
- vaccine type and number in the series
- batch number and expiry date

9 Refer to chapter 2, section 2.1.3.

10 Refer to chapter 2, section 2.1, and Appendix 7.

11 Refer to chapter 2, sections 2.1.2 and 2.3.1.

- injection site (eg, 'right deltoid' not 'upper arm')
- needle length
- that the patient was observed for 20 minutes post-vaccination
- if the vaccine was given by a non-standard route (the reasons must be documented)
- the immunisation event in the child's *Well Child Tamariki Ora My Health Book* (if applicable)
- the date for the next immunisation in the child's *Well Child Tamariki Ora My Health Book* (if applicable)
- advice and resources given.

4.4 The vaccinator ensures the immunisation information is sent to the NIR (ie, electronically or manually) where applicable, unless the individual/parent/guardian has opted off the collection of their/their child's immunisation information on the NIR.

4.5 The vaccinator ensures the immunisation certificate[12] is accurately completed following the 15-month and 4-year immunisation events.

4.6 If the practice/clinic is not the usual primary health care provider, then the individual's primary health care provider is informed by the vaccinator within five working days of giving the vaccine, unless the individual declines for this to occur.

4.7 All clinical documentation is appropriately managed and stored to maintain confidentiality, and is made available to the individual/parent/guardian on request.

[12] Refer to Appendix 5.

Standard 5: The vaccinator administers all vaccine doses for which the vaccinee is due at each visit and only follows true contraindications

Required characteristics of the vaccinator

5.1 The vaccinator adheres to the National Immunisation Schedule and delivers all the immunisations recommended for that visit, unless the individual/parent/guardian does not consent to this.

5.2 When catch-up immunisation is required, this is planned with the minimum number of visits/injections and in conjunction with the individual/parent/guardian.

5.3 A dose of vaccine is deferred or avoided only when contraindicated or the individual/parent/guardian has chosen to defer/avoid it. The reason for deferral or avoidance must be documented.[13]

Standard 6: The vaccinator reports AEFIs promptly, accurately and completely

Required characteristics of the vaccinator

6.1 All serious or unexpected AEFIs are reported by the vaccinator to the Medical Assessor, CARM,[14] and to the individual's primary health care provider (if the vaccinator is another person). If the individual/parent/guardian does not consent to being identified, the report should be made without personal identification.

6.2 The vaccinator informs the individual/parent/guardian that if an adverse event occurs, they can also report it to CARM.

6.3 When a CARM report is received, and further doses of the vaccine have been contraindicated, the vaccinator advises the local DHB NIR Administrator so that an appropriate AEFI code is recorded in the individual's NIR record.

[13] Refer to chapter 2, section 2.1.4, and the specific disease chapters.

[14] Refer to chapter 1, section 1.6.3, for the adverse event reporting process.

6.4 The vaccinator seeks specialist (eg, GP, paediatrician, infectious diseases physician or medical officer of health) opinion if uncertain about the safety of further doses, and referral is made to secondary care if required.

6.5 The vaccinator ensures the adverse event, and any subsequent decisions relating to the event, are effectively communicated to the individual/parent/guardian and clearly documented in the child's *Well Child Tamariki Ora My Health Book* (if applicable) and in the patient records, and appropriate follow-up is carried out.

A3.4 Guidelines for organisations storing vaccines and/or offering immunisation services

These guidelines apply to all organisations who store vaccines and/or offer immunisation services, including (but not limited to) general practices, public health units, community pharmacies, travel clinics, occupational health clinics, emergency medical services, research units and hospital wards/clinics/departments/pharmacies.

The organisation that employs vaccinators to offer immunisation services has links to primary health care and to Well Child Tamariki Ora providers

Required characteristics

- Immunisation is delivered, not in isolation, but as an integrated part of primary health care services, including Well Child Tamariki Ora for children.
- If possible, at the time of immunisation, the organisation undertakes other health promotion and/or disease prevention activities as applicable, such as the Well Child National Schedule or Care Plus.
- Immunisation events, childhood and adult, are well communicated to other health services linked to the individual (eg, primary health care, outreach immunisation services, pharmacies, occupational health).

The organisation achieves high immunisation coverage of its population

Required characteristics

- The organisation has an effective, secure, NHI-based system for recording and reporting immunisations and identifying individuals requiring immunisation.
- Respecting the individual's/parent's/guardian's rights to make an informed choice, the organisation takes all steps to ensure that an individual's immunisation schedule commences on time and that subsequent events are administered on the due date.
- The organisation has electronic linkage to the NIR for registration and immunisation event notification, and uses the NIR to assist with follow-up. If electronic linking is not available, manual processes must be used.
- The organisation has a robust reminder (pre-call) system which encourages the delivery of on-time immunisation and timely follow-up for overdue immunisation.
- The organisation has an effective communication strategy to target high-needs population groups.
- Attendance at the practice/organisation is used as an opportunity to remind individuals/parents/guardians of the importance of immunisation and, if appropriate, to check and offer to bring up to date the individual's immunisation status.
- Those who do not respond to recall and who have not declined to take part are referred to the outreach immunisation service, as per local protocol.

The organisation supports vaccinators and NIR administrators

Required characteristics

- The organisation has comprehensive immunisation-related policies based on best practice, informed consent, the vaccination process and management of adverse events.

- The organisation uses a pharmaceutical refrigerator to store vaccines, has a vaccine cold chain policy in place and achieves Cold Chain Accreditation[15] for all areas within the organisation storing vaccines.
- The organisation provides training and support workers (eg, kaiāwhina, community health workers) for vaccinators working in the community.
- The organisation supports the need for vaccinators to have access to ongoing education and training on all aspects of immunisation at least every two years and when there are changes to the Schedule.
- The organisation provides initial and ongoing training and support specific to the NIR, PMS, and/or the SBVS (if applicable).

The service is readily available, with no barriers to access

Required characteristics

- No fee is charged to the individual/guardian for the immunisations that are on the Schedule or high-risk programmes (or for completing the child's immunisation certificate), except for an administration fee for the tetanus-diphtheria boosters at ages 45 and 65 years.
- Regardless of their immigration and citizenship status, all children aged under 18 years are eligible to receive funded Schedule vaccines, and providers may claim the immunisation benefit for these children. Non-residents who were under age 18 years when they commenced HPV vaccination are currently funded to complete the course, even if they are aged 18 years or older when they complete it. Further information on eligibility can be found on the Ministry of Health website.[16]
- Immunisations are provided to both enrolled and casual patients at all times when the organisation or service is open.
- A person's immunisation status is checked at each visit to the service.

15 See the Cold Chain pages on the Ministry of Health website (www.health.govt.nz/coldchain).

16 See www.health.govt.nz/eligibility

- The organisation is culturally appropriate (ie, all health workers are assessed as culturally competent, reflect the populations they serve and offer a range of health information resources[17] in different languages).

A3.5 Recommended resources

Ministry of Health (available at www.health.govt.nz/our-work/preventative-health-wellness/immunisation)

- The current *Immunisation Handbook*
- National Immunisation Register Privacy Policy
- The current *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*
- Cold Chain Management Policy Template
- Cold Chain Accreditation Provider Self-Assessment Form
- Cold Chain Accreditation Provider Reviewer Form
- *Kōrero Mārama: Health Literacy and Māori – Results from the 2006 Adult Literacy and Life Skills Survey*, February 2010 (www.health.govt.nz/system/files/documents/publications/korero-marama.pdf)

Immunisation Advisory Centre (www.immune.org.nz)

- *Vaccinator Training Course Standards*
- *Vaccinator Update Course Standards*

Other

- Medical Council of New Zealand. 2010. *Best Health Outcomes for Pacific Peoples: Practice implications*. URL: www.mcnz.org.nz
- Royal New Zealand College of General Practitioners. *Aiming for Excellence: CORNERSTONE accreditation programme*. URL: www.rnzcgp.org.nz/RNZCGP/I_m_a_Practice/Quality_standards/A

[17] Ministry of Health immunisation resources are available in English and a variety of languages from the HealthEd website (www.healthed.govt.nz) or from the local health education authorised provider.

iming_for_Excellence/RNZCGP/Im_a_practice/Aiming_for_Excellence/Aiming_for_Excellence.aspx

- Pharmacy Council of New Zealand. 2016. *Pharmacist Vaccinator Statement*. URL: www.pharmacycouncil.org.nz/New-Zealand-Registered-Pharmacists/Standards-and-Guidelines/Standards-and-guidelines

A3.6 Relevant legislation and regulations[18]

- Health (Immunisation) Regulations 1995
- Medicines Act 1981
- Medicines Regulations 1984
- Health (Infectious and Notifiable Diseases) Regulations 1966, Amendment No. 2, regulation 44A
- Health Act 1956, section 22F
- Health Information Privacy Code 1994
- Health and Disability Commissioner Act 1994: Code of Health and Disability Services Consumers' Rights 1996[19]
- Health Practitioners Competence Assurance Act 2003
- Privacy Act 1993
- Care of Children Act 2004
- Accident Compensation Act 2001
- Health and Safety at Work Act 2015
- Resource Management Act 1991
- Primary Maternity Services Notice 2007,[20] pursuant to section 88 of the New Zealand Public Health and Disability Act 2000

18 See www.legislation.govt.nz

19 See www.hdc.org.nz

20 See www.health.govt.nz

Appendix 4: Authorisation of vaccinators and criteria for pharmacist vaccinators

A4.1 Protocol for authorisation of vaccinators and pharmacist vaccinators

A4.1.1 Authority

Authorised vaccinators[21]

The authorisation of vaccinators in New Zealand is in accordance with the Medicines Regulations 1984, clause 44A(2). The Director-General of Health or a medical officer of health may authorise any person to administer a vaccine (which is a prescription medicine) for the purposes of an approved immunisation programme.[22]

Clause 44A(2) stipulates that the person seeking approval must apply in writing to the Director-General or a medical officer of health and provide documentary evidence that they:

a. can carry out basic emergency techniques, resuscitation and the treatment of anaphylaxis; and

b. have knowledge of the safe and effective handling of immunisation products and equipment; and

c. can demonstrate clinical interpersonal skills; and

[21] Authorised vaccinators were previously called 'authorised independent vaccinators'.

[22] See the Ministry of Health document *Definition of an Approved Immunisation Programme* (available for download from www.health.govt.nz/our-work/preventative-health-wellness/immunisation).

d. have knowledge of the relevant diseases and vaccines in order to be able to explain the vaccination to the individual, parent or guardian of the individual who is to consent to the vaccination on behalf of the individual, to ensure that the individual or parent or guardian of the individual can give informed consent to the vaccination.

The current protocol requires authorised vaccinator applications to be submitted to a medical officer of health in the applicant's local region. Any authorisation given under subclause (2) of the Regulation is valid for a period of two years from the date of initial vaccinator training course (VTC), and is subject to such conditions as the Director-General or the medical officer of health thinks fit.

Successful applicants will be authorised to administer either all or specific vaccines on the National Immunisation Schedule[23] and any other vaccine as authorised by a medical officer of health.

Pharmacist vaccinators

Since 2011, a number of vaccines have been reclassified by the Medicines Classification Committee, from prescription medicines to restricted medicines when administered by a registered pharmacist who has successfully completed a VTC approved by the Ministry of Health and is complying with the immunisation standards of the Ministry of Health.

The reclassification means that pharmacists are able to administer specific vaccines as pharmacist vaccinators if they have successfully completed a Ministry of Health-approved VTC (including the open-book assessment) and clinical assessment, and are complying with the immunisation standards and guidelines as described in Appendix 3 of this *Handbook*.

Under the vaccine reclassification, pharmacist vaccinators are not required to apply to a medical officer of health for authorised vaccinator status as the vaccine is not a prescription medicine when administered by a pharmacist vaccinator (who meets the conditions of the vaccine classification).

[23] See the 'Introduction' chapter in this *Handbook* or www.health.govt.nz/our-work/preventative-health-wellness/immunisation for more information about the National Immunisation Schedule.

The Pharmaceutical Society of New Zealand (PSNZ), maintains a register of pharmacist vaccinators. Pharmacist vaccinators should notify PSNZ when they have completed the requirements specified above, including the course completion date.

Pharmacist vaccinator status is valid for two years from the date of the initial VTC.

A4.1.2 Process for all vaccinators

In order to achieve authorised vaccinator or pharmacist vaccinator status, all applicants must first meet the following requirements.

1. Demonstrate that within the preceding 12 months they have attended, completed and passed a VTC and have received a vaccinator training certificate. The VTC must meet the current *Vaccinator Training Course Standards*[24] and the course should consist of:
   - a minimum of 16 hours' educational input
   - a written open-book assessment (minimum one-hour duration), which may be oral at the facilitator's discretion.
2. Undergo an independent clinical assessment by an immunisation coordinator or an approved assessor (as agreed by the medical officer of health). Information about the practice environment will be collected at the time of the clinical assessment including cold chain and emergency management processes.
3. Have evidence that they hold a current practising certificate from their registration authority (eg, Nursing Council of New Zealand, Pharmacy Council of New Zealand).
4. Have a current cardiopulmonary resuscitation (CPR) certificate (see section A4.2 for details).

[24] Published by IMAC.

Authorised vaccinators

Authorised vaccinator applicants[25] (eg, registered nurses) who have successfully completed their clinical assessment will then need to apply for authorisation by submitting an application, including the documentation described above, to their local medical officer of health.

Pharmacist vaccinators

Pharmacist vaccinators[26] should notify PSNZ when they have completed the requirements specified above, including the course completion date.

A4.1.3 Additional endorsement process for BCG vaccinators

As of 4 January 2017, the requirement for gazetting of BCG vaccinators no longer applies.

All new BCG vaccinators will need to become authorised vaccinators with BCG endorsement, authorised by the local medical officer of health as described below.

BCG vaccinators who were gazetted prior to 4 January 2017 will be granted one-off national BCG endorsement by the Ministry of Health for a two-year period up until 4 January 2019, after which they will be required to seek regional BCG endorsement from their local medical officer of health.

New BCG vaccinators and gazetted BCG vaccinators seeking regional BCG endorsement.

To be endorsed as a BCG vaccinator, the applicant needs to:

1. be an authorised vaccinator
2. be nominated by their employer to become a BCG vaccinator
3. successfully complete a Ministry of Health-approved online BCG vaccination course

[25] Authorised vaccinators will not be able to vaccinate without a prescription or standing order until they have completed all of the required processes.

[26] Pharmacist vaccinators will not be able to vaccinate without a prescription or standing order until they have completed all of the required processes.

4. complete under clinical supervision a minimum of 5 BCG vaccinations
5. successfully complete a BCG clinical assessment by an approved BCG assessor
6. apply to the medical officer of health for BCG endorsement approval, providing documented evidence of these requirements.

For more information, see the Ministry of Health policy *Bacillus Calmette-Guérin (BCG) Vaccinator Endorsement* (www.health.govt.nz/our-work/preventative-health-wellness/immunisation/immunisation-programme-decisions/bacillus-calmette-guerin-bcg-vaccinator-endorsement).

A4.1.4 Process for two-yearly renewal of vaccinator status for all vaccinators

Authorised vaccinator or pharmacist vaccinator status is valid for two years from the date of the initial VTC, but it can be renewed two-yearly if the vaccinator meets the requirements specified below.

To renew their vaccinator status, all vaccinators are required to:

1. during the past two years, have attended a vaccinator update course that meets the current *Vaccinator Update Course Standards*[27] and have evidence of attendance
2. have a summary[28] of their immunisation practice over the past 12 months
3. have evidence of a current practising certificate
4. have evidence of a current CPR certificate (see section A4.2 for details).

[27] Published by IMAC.

[28] The summary should include type of immunisation practice as a vaccinator (eg, general practice, occupational health, pharmacy etc); types of vaccinations given (eg, intramuscular, subcutaneous, intradermal); and other responsibilities related to immunisation (eg, cold chain-designated person, etc).

Authorised vaccinators

Prior to the expiry of their authorised vaccinator status, authorised vaccinators are required to apply for renewal of their authorisation to their local medical officer of health and submit all relevant documentation (ie, immunisation update, CPR certificates and immunisation summary).

Pharmacist vaccinators

Prior to the expiry of their pharmacist vaccinator status, pharmacist vaccinators should notify PSNZ when they have completed the requirements specified above.

A4.1.5 Process when vaccinator status has not been renewed or has not been achieved

If it is less than five years since the vaccinator status expired and the vaccinator has been attending vaccinator update training every two years

When a vaccinator has failed to renew their vaccinator status, they must:

1. have a further clinical assessment by an immunisation coordinator or approved assessor (as approved by the medical officer of health) within the past three months
2. for each two-year period since they were last renewed, have attended a vaccinator update course that meets the current *Vaccinator Update Course Standards*[29] and have evidence of attendance
3. have a summary of their immunisation practice over the past 12 months
4. have evidence of a current practising certificate
5. have evidence of a current CPR certificate (see section A4.2 for details).

[29] Published by IMAC.

Authorised vaccinators

Authorised vaccinator applicants must submit the documentation described above to the medical officer of health. Applicants will be assessed on a case-by-case basis.

Pharmacist vaccinators

Pharmacist vaccinators should notify PSNZ when they have completed the requirements specified above.

If it is less than five years since the applicant completed vaccinator training but they have not achieved vaccinator status

To achieve authorised vaccinator or pharmacist vaccinator status, the applicant must:

1. within the past three months, have had a clinical assessment by an immunisation coordinator or approved assessor (as approved by the medical officer of health)
2. within the past five years, have successfully attended, completed and passed a VTC that meets the current *Vaccinator Training Course Standards*[30] and have received a vaccinator training certificate
3. during each two-year period since they completed the VTC, have attended a vaccinator update course that meets the current *Vaccinator Update Course Standards*[31] and have evidence of attendance
4. have a summary of their immunisation practice over the past 12 months
5. have evidence of a current practising certificate
6. have evidence of a current CPR certificate (see section A4.2 for details).

Note: If the applicant has not attended the two-yearly vaccinator update courses, they may be required to attend, complete and pass another VTC.

30 Published by IMAC.

31 Published by IMAC.

Authorised vaccinators

Authorised vaccinator applicants must submit the documentation described above to their local medical officer of health. Applicants will be assessed on a case-by-case basis.

Pharmacist vaccinators

Pharmacist vaccinators are advised to notify PSNZ when they have completed the requirements specified above.

If it is more than five years since the applicant completed vaccinator training and they have not achieved or renewed vaccinator status

If it is more than five years since the applicant completed their initial VTC, they will be required to attend, complete and pass another VTC. This is because there will have been significant developments in vaccination delivery in the intervening interval.

All applicants are required to:

1. undergo a clinical assessment by an immunisation coordinator or approved assessor (as agreed by the medical officer of health) – information about the practice environment will be collected at the time of this assessment
2. have attended, completed and passed a VTC that meets the current *Vaccinator Training Course Standards*[32] and have received a vaccinator training certificate
3. have a summary of their immunisation practice over the past 12 months
4. have evidence that they hold a current practising certificate
5. have evidence of a current CPR certificate (see section A4.2 for details).

[32] Published by IMAC.

Authorised vaccinators

Applicants must submit the documentation described above to their local medical officer of health. Applicants will be assessed on a case-by-case basis.

Pharmacist vaccinators

Pharmacist vaccinators are advised to notify PSNZ when they have completed the requirements specified above.

A4.1.6 Process when an authorised vaccinator is new to the health district in which they intend to practise

If an authorised vaccinator wishes to practise in another health district, they must get authorisation from the local medical officer of health before practising as an authorised vaccinator. The applicant will be required to provide:

1. evidence of current authorisation in another health district
2. evidence of a current practising certificate
3. evidence of a current CPR certificate (see section A4.2 for details)
4. details of their proposed work in the district.

A4.2 Resuscitation requirements for all authorised vaccinators and pharmacist vaccinators

All vaccinators, by virtue of their occupation, need to be able to resuscitate patients and therefore need to achieve and maintain the following resuscitation skills:

1. infant, child and adult CPR, including mouth-to-mouth, mouth-to-mask and the management of choking
2. use of airway adjuncts, including the sizing and insertion of oropharyngeal airways
3. use of an automated external defibrillator

4. one- and two-person bag valve mask ventilation and mouth-to-mask technique
5. use of supplemental oxygen
6. use of laryngeal mask airways (only if included in the emergency equipment).

Resuscitation training for all vaccinators should be at a standard equivalent to that set for New Zealand Resuscitation Council: 'Health Professional Responder, CORE Immediate – Adult and Child' (www.nzrc.org.nz/training/rescuers). The first five specific skills outlined above must be included in any vaccinator resuscitation course. The insertion of intravenous lines and the preparation of emergency medications (except for intramuscular adrenaline) are not skills specifically required of a vaccinator.

All vaccinators must demonstrate/validate their resuscitation certification every two years. (Note: Employer protocols may require this more frequently.)

All vaccinators need to be able to administer intramuscular adrenaline in the event of an anaphylactic reaction to an immunisation event (refer to section 2.3.3).

All vaccinators must meet the emergency equipment and management requirements, regardless of the immunisation setting (eg, in general practice and in non-clinical settings, such as homes, schools, rest homes, workplaces and pharmacies), as listed in section 2.3.3.

A4.3 Authorised vaccinators delivering a local immunisation programme

A local immunisation programme may be approved by the Director-General or a medical officer of health. For example, a medical officer of health may approve the use of unfunded vaccines to meet a specific need within their region, such as:

- influenza vaccination to healthy adults aged 64 years and under, in general practice and workplace settings; or
- hepatitis B vaccination in occupational health settings.

Authorisation for vaccinating non-funded populations will require application to the medical officer of health for approval.

Authorised vaccinators need to supply the following details of their practice, which will be considered if they decide to seek medical officer of health approval for a local immunisation programme. Application forms are available from the local regional public health office.

		Office use only
1.	**Location/s** (specify)	Yes / No
2.	**Staff** There should be two people present for outreach or non-clinical setting immunisations, one of whom must be an authorised vaccinator; the other must be a competent adult who is able to call for emergency support and has a basic life support certificate.	Yes / No
3.	**Linkages with the immunisation coordinator** Do you have processes for regular contact with your immunisation coordinator?	Yes / No
4.	**Person specification**. Attach copies of the following documentation:	Yes / No
	• current approval as an authorised vaccinator issued by the local medical officer of health for all vaccinators covered by the local programme is required (provide list of names on the last page of this document and attach copies of the authorised vaccinator approvals)*	
	• indemnity insurance.*	
5.	**Legal** You should have knowledge of the provisions contained in the following legislation: • Health and Disability Commissioner (Code of Health and Disability Services Consumers' Rights) Regulations 1996 • Privacy Act 1993 (in relation to the storage and transfer of information) • Health and Safety in Employment Act 1992 (in relation to having a suitable area for post-vaccination observation, correct disposal of vaccines, etc) • Medicines Act 1981.	Yes / No

Note: Please ensure that you have included the documentation marked with an asterisk (*).

Continued overleaf

		Office use only
6.	**Venue** The venue must allow for the safe management of delivering of immunisations, including: • privacy • a resting space • a waiting space • ensuring privacy of records.	Yes / No
7.	**Documentation** You should have documented processes for the following. • Pre-vaccination – What information is provided to individuals (including consent and, if applicable, information about the NIR)?* – How do you identify persons eligible for free vaccination?* • Post-vaccination – How will an individual's details be recorded?* – What are the means of recording administration of a vaccine(s) and any post-vaccination adverse events?* – How will notice of administration be provided to the primary health care provider?* – What information will be provided to the vaccinee post-vaccination (including provision of emergency care)?* – How will information on adverse reactions be reported?* Note: For influenza vaccinations delivered by occupational health without NIR access, it will be necessary to provide the following information to the medical officer of health: • number of recipients who were ≥65 years (free vaccines) • number of people <65 years eligible for free influenza vaccine • number of non-eligible influenza vaccines given.	Yes / No

Note: Please ensure that you have included the documentation marked with an asterisk (*).

Continued overleaf

		Office use only
8.	**Equipment** The following should be available: • cellphone or phone access • an oxygen cylinder, flow meter, tubing and paediatric/adult masks • airways – infant through to adult • bag valve mask resuscitator (eg, Ambu bag) suitable for the population being vaccinated • adrenaline • syringes (1 mL, 2.5 mL, 5 mL), needles (1.58 cm to 3.8 cm) • sharps box • alcohol swabs, cotton wool balls, gauze • thermometer and blood pressure monitoring equipment • vaccines • appropriately monitored insulated vaccine containers and equipment for transporting vaccine off-site • data logger with a probe, external display and alarm# • gloves • 0.5% hypochlorite • approved biohazard bag.	Yes / No
9.	**Optional additional emergency equipment** Intravenous cannula and administration sets: • intravenous fluids • hydrocortisone for injection • sodium bicarbonate solution • saline flush.	Yes / No

Consider using a secondary back-up device, in case the data logger gets damaged. See the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017* (available at www.health.govt.nz/coldchain).

List of vaccinators taking part in the programme (all vaccinators must be fully authorised, with copies of approval document attached):

Note: Please ensure that you have included the documentation marked with an asterisk (*).

Applicant's name:

Applicant's signature: Date:

Appendix 5: Immunisation certificate

A5.1 Introduction

The Health (Immunisation) Regulations 1995 require parents/guardians of children born from 1 January 1995 to show their child's immunisation certificate when these children start at an early childhood service and on entry to primary school (school year 1). The immunisation certificate shows whether a child is fully immunised or not. Information must be recorded at age 15 months when the early childhood vaccinations are complete, and after the immunisations at age 4 years. For those parents/guardians who decline to have their child vaccinated, the immunisation certificate may be completed at any time, but the completed immunisation certificate must still be shown when the child starts at an early childhood service or primary school.

A5.2 Parent/guardian responsibilities

Parents or guardians can choose whether or not to vaccinate their child, but they must show the immunisation certificate when their child starts at an early childhood service and on school entry, regardless of the child's immunisation status.

A5.3 Vaccinator responsibilities

When completing and signing the immunisation certificate, vaccinators should be confident that a child is fully vaccinated. The primary concern is the child's protection. If the previous vaccination history is uncertain and parents/guardians do not wish their child to be vaccinated, the child should be certified as 'not fully immunised'. Children who have not received the necessary doses of a vaccine or have no evidence of laboratory-proven disease should be recorded as 'not fully immunised'.

The immunisation certificate is included in the *Well Child Tamariki Ora My Health Book*. This book also contains the record of the child's vaccinations. Vaccinators should ensure they record vaccination and other relevant health information in this book. This becomes particularly important if the child sees different health professionals. If the child's book is lost, it should be replaced. Copies of the *Well Child Tamariki Ora My Health Book* and immunisation certificate pads can be obtained from the authorised provider of health education materials, usually the local public health service, or ordered from the HealthEd website (www.healthed.govt.nz).

A5.4 Early childhood services and school responsibilities

All early childhood services and primary schools, including kōhanga reo, independent schools and kura kaupapa Māori, must keep an immunisation register for children born from 1 January 1995. The register is a tool to help reduce the spread of vaccine-preventable diseases in early childhood services and schools, as well as in the wider community. Registers are available from the authorised provider of health education materials, or from the HealthEd website (www.healthed.govt.nz).

The early childhood service or school has the responsibility to:

- advise the child's parent/guardian that an immunisation certificate is required
- ensure the parent or guardian is asked to provide the immunisation certificate
- record the information from the immunisation certificate (or the fact that it was not shown) on the register
- advise the parent/guardian that a GP, practice nurse or public health nurse can help them to get an immunisation certificate if they do not have one.

Appendix 6: Passive immunisation

A6.1 Introduction

Passive immunisation involves administering pre-formed antibody as human immunoglobulin to a recipient who is thought to have either no natural immunity to one or more infections, or who has impaired antibody production. CSL Behring Australia is the primary manufacturer of immunoglobulin products for the New Zealand Blood Service (NZBS). These products are prepared by fractionating large pools of plasma collected from blood donors to NZBS.

In New Zealand, blood donations are only collected from voluntary, unpaid donors who are in good health and who do not have any conditions identifiable by the standard questionnaire that all blood donors complete or by the mandatory testing for HIV/AIDS, hepatitis B, hepatitis C and syphilis on each donation. Blood donations are only used if the tests show no evidence that these infections are present. Similar standards apply to the manufacture of rabies immunoglobulin (RIG), which is obtained from an overseas commercial source but is not registered as a medicine in New Zealand.

A6.2 Preparations available in New Zealand

Immunoglobulin products available in New Zealand include human normal immunoglobulin for intramuscular (IM) use, specific immunoglobulins for intramuscular use, human normal immunoglobulin for intravenous use (IVIG) and human normal immunoglobulin for subcutaneous use (SCIG). All of these products have an excellent safety record in both Australia and New Zealand.

A6.2.1 Human normal immunoglobulin for intramuscular use

Human normal immunoglobulin for intramuscular use (available as Normal Immunoglobulin-VF) is a sterile, preservative-free, pasteurised solution containing 160 mg/mL human plasma proteins and 22.5 mg/mL glycine. The solution has a pH of 6.6. At least 98 percent of the protein comprises immunoglobulins, mainly immunoglobulin G (IgG). Normal Immunoglobulin-VF is intended for IM injection and is available in 5 mL preservative-free vials. It is prepared by Cohn cold ethanol fractionation of human plasma. The manufacturing process involves specific viral removal steps to reduce the possibility of virus transmission, and includes pasteurisation for viral inactivation and nanofiltration for virus removal.

A6.2.2 Specific immunoglobulin for intramuscular use

Specific human immunoglobulin preparations for IM use are available, including those for tetanus, hepatitis B, varicella zoster and anti-D. These are manufactured from plasma pools containing donations from individuals known to have high levels of the appropriate antibody. These preparations are available in single vials containing the specific antibody. The volume of the product will be determined by the potency for the appropriate antibody. In unusual circumstances, when supplies of specific immunoglobulin products manufactured from New Zealand plasma are not available, commercial products from alternative donor sources may be supplied by NZBS.

RIG is imported from a commercial source and is held at NZBS sites in Auckland, Christchurch and Wellington. The product is not registered as a medicine in New Zealand. It may be accessed and supplied under section 29 of the Medicines Act 1981 after discussion with an NZBS medical officer.

A6.2.3 Human normal immunoglobulin for intravenous use

The current human normal immunoglobulins for intravenous use in New Zealand are Intragam P and Privigen. Intragam P is produced by CSL Behring Australia and Privigen is produced by CSL Behring in the US. The latter commercial product has been introduced as stocks of IVIG from New Zealand plasma have not been sufficient to meet overall clinical requests for IVIG.

Intragam P is a sterile, preservative-free solution containing 6 g of human protein and 10 g of maltose in each 100 mL. The solution has a pH of 4.25. Isotonicity is achieved by the addition of maltose. At least 98 percent of the protein has the electrophoretic mobility of IgG. At least 90 percent of the protein is IgG monomer and dimer. Intragam P contains only trace amounts of immunoglobulin A (IgA) (nominally <0.025 mg/mL).

Intragam P and Privigen are produced by chromatographic fractionation of large pools of human plasma obtained from voluntary blood donors. The protein has not been chemically or enzymatically modified. The manufacturing process contains special steps to reduce the possibility of virus transmission, including pasteurisation (heating at 60°C for 10 hours) and incubation at low pH.

Note: In New Zealand, Intragam P is used to provide intravenous (high dose) tetanus immunoglobulin. Because the level of immunoglobulin in each batch varies and this indication is not included in the product registration, consultation with an NZBS medical officer is required prior to issuing a prescription.[1]

Privigen is a sterile, preservative-free 10 percent solution containing 10 g/100 mL of normal immunoglobulin; it is available in 50 mL, 100 mL and 200 mL vials. The solution has a pH of approximately 4.8, has a low sodium content, contains 250 mmol/L of proline, a non-essential amino acid, as a stabiliser and is approximately isotonic. It contains no carbohydrate stabiliser.

Privigen is made by cold ethanol fractionation, octanoic acid fractionation and anion exchange chromatography of large pools of human plasma obtained from blood donors in Europe and the US. The distribution of IgG subclasses in Privigen is similar to that in plasma;

only trace amount of IgA are present, typically <0.025 mg/mL. The protein has not been enzymatically modified. The manufacturing process involves special steps to reduce the possibility of virus transmission including pasteurisation (heating to 60°C for 10 hours) and nanofiltration.

A6.2.4 Human normal immunoglobulin for subcutaneous use

Human normal immunoglobulin for subcutaneous use (Evogam) is produced by CSL Behring, Australia, from NZBS New Zealand-sourced plasma. It is a sterile solution containing 16 g per 100 mL of human immunoglobulin with a purity of at least 98 percent immunoglobulin G (IgG). At least 85 percent consists of monomers and dimers (typically >90 percent), and less than 10 percent of the IgG is aggregates. The distribution of the IgG subclasses closely resembles that found in normal human plasma.

The pH value of the solution is 6.6. It contains 2.25 g/100 mL of glycine as a stabiliser. It does not contain a carbohydrate stabiliser (eg, sucrose, maltose) and contains no preservative. Evogam contains only trace amounts of IgA, typically <0.025 mg/mL.

Evogam is produced by chromatographic fractionation of large pools of human plasma obtained from New Zealand's voluntary blood donors. The manufacturing process involves special steps to reduce the possibility of virus transmission, including pasteurisation (heating at 60°C for 10 hours) and nanofiltration.

A6.2.5 Accessing immunoglobulin or contacting NZBS for advice

NZBS operates a 24-hour on-call service for medical advice and access to these products. Details of the medical officer on call can be obtained from any DHB hospital blood bank in New Zealand.

Product can be requested using the NZBS request form. This can be accessed online (www.nzblood.co.nz/Clinical-information/Transfusion-medicine/Information-for-Health-Professionals/Request-forms), or by contacting your local blood bank, or writing to:

New Zealand Blood Service
Private Bag 92071
Victoria Street West
Auckland 1142

or by telephone (during normal office hours): (09) 523 5744.

A6.3 Indications for use

A6.3.1 Passive immunisation

For advice on the use of immunoglobulin products and specific dosages of these products, please contact a medical officer at NZBS. Copies of the product data sheet are available on the NZBS website (www.nzblood.co.nz/Clinical-information/Transfusion-medicine/Health-professionals-medicine-datasheets/Immunoglobulins).

Normal Immunoglobulin-VF is available for passive immunisation (pre- or post-exposure prophylaxis) against measles (see section 11.8.2) and hepatitis A (see section 7.8) where active vaccination is not appropriate or is contraindicated. It is not recommended for the prevention of rubella or mumps. Guidance on the use of specific preparations is provided in other sections of this *Handbook*: for pre- or post-exposure prophylaxis against hepatitis B (sections 8.5.2 and section 8.8.1), tetanus (section 19.5.5) and varicella zoster (section 21.8.2).

A6.3.2 Management of primary and acquired immune deficiency

Recurrent infections can occur in individuals who have low or absent levels of circulating immunoglobulins – so-called humoral immune deficiency. This can arise as a congenital disorder, or it can be acquired as a consequence of a number of diseases. Humoral immune deficiency can exist alone or as part of a wider immune deficiency syndrome. Immunoglobulin products can be used to prevent recurrent infections in these patients.

Until recently, IVIG was the product of choice for managing these patients. A subcutaneous IgG product (Evogam) is also now available, which can be infused by patients at home. This avoids the need for outpatient or day-case admission for infusion of IVIG and is preferred by some patients. The subcutaneous preparation is not suitable for use in prophylaxis against hepatitis A or measles infection.

For replacement therapy in antibody deficiency disorders, monthly administration of IVIG is given, usually at a dosage of 0.2 to 0.6 g/kg of body weight.[2] Subcutaneous product is administered one to two times per week, with the overall monthly dosage similar to that of IVIG. For both types of product, the dosage and frequency of infusion should be based on the effectiveness in the individual patient. In general, however, the aim of treatment should be to maintain the serum IgG at or above a level of 5 g/L.

A6.4 Storage and administration

Immunoglobulin products must be stored at +2°C to +8°C and must not be frozen. They should also be protected from light. If the product appears turbid or contains sediment, it must not be used. Always check and observe the manufacturer's expiry date before injecting the product. The product does not contain an antimicrobial preservative and must be used immediately after opening the vial; any unused portions should be discarded. Information on the batch number and dose injected must be kept in the recipient's records.

The intramuscular and subcutaneous forms of normal immunoglobulin should be brought to room temperature before use. They *must not* be given intravenously because of the possible reactions discussed in section A6.7.[2]

The intramuscular product, Normal Immunoglobulin-VF, should be given slowly by deep IM injection, using a needle of appropriate gauge and length. If a large volume (more than 5 mL) is required, administration in divided doses at different sites is recommended.

The subcutaneous product, Evogam, is normally given using an infusion pump. Information on infusion rates is provided in the medicine's data sheet.

A6.4.1 Interactions with other drugs

Immunoglobulin should not be mixed with other pharmaceutical products, except as indicated by the manufacturer.

Passively acquired antibody can interfere with the response to live attenuated virus vaccines. Live virus vaccines should be given at least three weeks before, or deferred for up to 11 months after, doses of human normal immunoglobulin or other blood products. The interval will be determined by the blood product and dose received (Table A6.1).

Table A6.1: Suggested intervals between immunoglobulin product administration or blood transfusion and MMR or varicella vaccination (does not apply to rotavirus vaccine)

Product or indication	Route	Dose	Interval (months)[a]
Tetanus immunoglobulin (250 IU/vial)	IM	250 IU if <24h 500 IU if >24h or gross contamination or burns	3
Hepatitis A prophylaxis (with human normal immunoglobulin)			
• Contact and short-term travel (<3 months prophylaxis)	IM	0.03 mL/kg	3
• International travel (>3 months)[b], other requirement for long-term prophylaxis – repeated 6-monthly	IM	0.06 mL/kg	3
Hepatitis B immunoglobulin (A different low-volume product is provided for neonatal use)	IM	Adults 400 IU Neonates 100 IU	3
Rabies immunoglobulin	IM	20 IU/kg	4
Varicella prophylaxis (with zoster immunoglobulin, 200 IU/vial)	IM	125 IU/10 kg (max 625 IU) 0–10 kg: 1 vial 10.1–30 kg: 2 vials >30 kg: 3 vials	5
Measles prophylaxis (with human normal immunoglobulin)			
• standard contact	IM	0.2 mL/kg	5
• immunocompromised contact	IM	0.6 mL/kg	6
Blood transfusion:			
• washed RBCs	IV	10 mL/kg	0
• RBCs, resuspended	IV	10 mL/kg	3
• whole blood, allogeneic	IV	10 mL/kg	6
• platelets in PAS	IV	1 unit	5
• plasma	IV	10 mL/kg	7
• platelets suspended in plasma	IV	1 unit	6

Continued overleaf

Product or indication	Route	Dose	Interval (months)[a]
Cytomegalovirus immunoglobulin[c]	IV	Contact NZBS MO to discuss product and dose	6
Replacement (or therapy) of immune deficiencies (with IVIG)	IV	0.3–0.4 g/kg occasionally higher	8
IVIG therapy for autoimmune or inflammatory disorders	IV	0.4 g/kg	8
		1–1.5 g/kg	10
		1.6–2 g/kg	11
Monoclonal antibody (as palivizumab[d]) to respiratory syncytial virus	IM	15 mg/kg	None

Key: IM = intramuscular; IU = international units; IV = intravenous; IVIG = intravenous immunoglobulin; NZBS MO = New Zealand Blood Service medical officer; PAS = platelet additive solution; RBCs = red blood cells.

Notes

a Unvaccinated persons might not be protected fully against measles during the entire recommended interval, and additional doses of immunoglobulin or measles vaccine might be indicated after measles exposure.

b Immunoglobulin is not normally available or recommended in New Zealand for pre-travel use.

c Cytomegalovirus immunoglobulin is not available in New Zealand. Contact NZBS MO to discuss access to an alternative product.

d Palivizumab contains antibody only to respiratory syncytial virus and does not interfere with the immune response to live or inactivated vaccines.

Adapted from: Centers for Disease Control and Prevention. 2011. General recommendations on immunization. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *Morbidity and Mortality Weekly Report* 60(RR2): 1–61. Table 5. Deferral interval for vaccination after blood components and products calculated from NZBS data.

Note: The above does not apply to rotavirus vaccines.

Inactivated vaccines may be administered concurrently with passive antibody (although in separate syringes) to induce active immunity, as is done for some tetanus-prone wounds and for babies born to HBsAg-positive mothers.

A6.4.2 Passive transfer of antibodies and interference with serological testing

Serological testing after the administration of immunoglobulin may detect transfused antibodies for several months after administration. Serological testing for any infection after immunoglobulin should therefore be discussed with an expert.

A6.5 Duration of effect

The estimated half-life of *intramuscular* human normal immunoglobulin is 27 ± 7 days (mean ± standard deviation [SD]).[2] The duration of effect is linked to the initial dosage.

The estimated half-life of *intravenous* human normal immunoglobulin is 40 ± 8 days (mean ± SD).[2]

The estimated half-life of *subcutaneous* human normal immunoglobulin is 55 days (range 14–165 days).[2]

A6.6 Contraindications and precautions

A6.6.1 Contraindications

Immunoglobulin products intended for subcutaneous and intramuscular injection must not be administered intravenously because of the potential for anaphylactic reactions.

Health professionals should check the package insert for the immunoglobulin product to be administered.

Skin tests should not be conducted with immunoglobulin preparations. Intradermal injection of any concentrated immunoglobulin product may cause a local inflammatory reaction, which can be misinterpreted as a positive allergic reaction. Allergic responses to normal immunoglobulin given in the prescribed IM route are extremely rare, but may occur in those with complete immunoglobulin A (IgA) deficiency in whom anti-IgA is present.

Intramuscular injection of immunoglobulin products should be avoided in patients with a low platelet count or with any coagulation disorder that would contraindicate IM injections. In these circumstances, the injection may be given subcutaneously, with a lightly applied pressure pad if prone to bruising; for example, if thrombocytopenia or von Willebrand disease is present.[1]

A6.6.2 Precautions

Injections of Normal Immunoglobulin-VF must be IM, and care should be taken to draw back on the plunger of the syringe before injection in order to be certain that the needle is not in a blood vessel (see section 2.2.3).

As with any injection, there is a risk of anaphylaxis. Adrenaline and other means of treating acute reactions should therefore be immediately available (see section 2.3.3).

A6.7 Expected responses and adverse events following passive immunisation

Clinicians in New Zealand are requested to notify all adverse reactions arising from, or in association with, the use of blood products. Reactions to any immunoglobulin product should be reported on a form obtainable from NZBS or any local DHB hospital blood bank.

Local tenderness, erythema and muscle stiffness occasionally occur at the site of injection and may persist for several hours after intramuscular injection. An occasional recipient may react more strongly, with a low-grade fever. Systemic reactions, including nausea, urticaria and generalised hypersensitivity reactions, may occur.[1, 2]

Reactions to IVIG tend to be related to the infusion rate and are most likely to occur during the first hour of the infusion. However, delayed reactions can occur, and include nausea, vomiting, chest pains, rigors, dizziness or aching legs. Systemic and local reactions are more common in those being treated for hypogammaglobulinaemia than in those with normal gammaglobulin levels who are being treated with immunoglobulin preparations for autoimmune conditions.

Occasional reports exist of renal failure following infusion of IVIG. These largely relate to sucrose-containing products. Intragam P and Privigen, the IVIG products available in New Zealand, do not contain sucrose, but patients should be adequately hydrated prior to their administration. Renal function should be monitored in patients considered to be at increased risk.

Aseptic meningitis has been reported following treatment with IVIG. This may present up to two days following treatment. Anaphylactic reactions, although rare, have been reported following injection of immunoglobulin products, although anaphylaxis is more likely to occur following intravenous infusion. Other significant adverse events that have been observed in New Zealand and are mostly associated with large or ongoing treatment with high dose IVIG or SCIG include: haemolysis, rashes, febrile events, pain or hypotension.

Immunoglobulin products may interfere with the immune response to live virus vaccines. In general, live vaccines should be given at least 3 weeks before or up to 11 months after the immunoglobulin preparation (see Table A6.1). This does not apply to the yellow fever vaccine, because New Zealand blood donors are very unlikely to have antibodies to this virus. For travellers abroad, the necessary interval may not be possible. No evidence of adverse interaction with rotavirus vaccine has been reported.

See section 1.6.3 for further information about adverse events and reporting.

References

1. New Zealand Blood Service. 2016. Transfusion Medicine Handbook Third Edition, 2016: A guide to the clinical use of blood components, blood products and blood transfusion procedures in New Zealand. URL: www.nzblood.co.nz/clinical-information/transfusion-medicine/transfusion-medicine-handbook

2. CSL Behring. 2013. CSL Immunoglobulin Product Data Sheets. URL: www.nzblood.co.nz/Clinical-information/Transfusion-medicine/Health-professionals-medicine-datasheets/Immunoglobulins

Appendix 7: Vaccine presentation, preparation, disposal, and needle-stick recommendations

A7.1 Presentation of vaccines

Most of the vaccines in current use are supplied in prefilled syringes or vials. The exceptions to this are the rotavirus vaccine, which is supplied as a syringe-style oral applicator, and the BCG vaccine, which is supplied as a multi-dose vial.

A vial is a glass container with a rubber[33] seal on the top, protected by a metal or plastic cap until it is ready for use. Vials contain either liquid or powder (freeze-dried or pellet/cake) preparations.

Vaccines should not be mixed in the same syringe, unless the manufacturer's data sheet specifically states it is permitted (eg, the DTaP-IPV-HepB vaccine is mixed with the Hib pellet for the Infanrix-hexa vaccine).

A7.2 Preparation and administration of vaccines

In order to minimise the risk of spread of infection and needle-stick injury, vaccinators should observe standard occupational health and safety guidelines.

- Ensure proper hygiene is maintained (ie, regularly wash hands for at least 20 seconds and dry them for 20 seconds, or regularly use an alcohol-based hand rub if hands are not visibly soiled).
- Prepare the appropriate injection equipment for the vaccines to be administered (see section 2.2).

33 Assume the rubber seal is latex unless stated 'latex-free'.

- Ensure the refrigerator temperature is within the required range of +2°C to +8°C before removing the vaccines (refer to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*[34]).
- Ensure the correct vaccine is taken from the refrigerator and that it is within the expiry date.
- Vaccines should only be drawn up after informed consent has been obtained and the vaccine requirements determined. This should include an NIR status query (if applicable) if there is uncertainty about previous doses. Any vaccines drawn up and not used should be discarded unless otherwise stated.

Vaccines in vials require one needle to draw the vaccine into the syringe, and then a new needle to administer the vaccine. The passage of needles through rubber seals causes blunting, resulting in increased tissue trauma if that needle is used to administer the injection. Also, a new needle prevents tracking the vaccine through the skin and subcutaneous tissue, thereby reducing the risk of local reactions. Do not expel the air contained in the new needle – it is sterile and minute in quantity (see chapter 2, Table 2.7).

A7.2.1 Preparing vaccines supplied as a liquid preparation

- Where applicable, remove the detachable portion of the label from the vial or syringe and place it on (or with) the appropriate documentation. If there is no detachable label, note the batch number and expiry date.
- Inspect the vaccine for any foreign particulate matter and/or variation in the physical appearance described by the manufacturer – if either is observed, do not use.
- Shake the vial: Most inactivated vaccines contain an adjuvant, and to obtain a uniform suspension they must be shaken vigorously prior to being drawn up.
- Flip the plastic cap off the vial, taking care not to touch the rubber seal.

34 Available at www.health.govt.nz/coldchain

- With the vial upright, insert the tip of the needle through the centre of the rubber seal, where it is thinner and easier to penetrate.
- Invert the vial and draw up the entire volume into the syringe.
- Withdraw the needle from the vial.
- Change the needle, choosing the appropriate gauge and length for administration.
- Administer the vaccine.
- Dispose of the empty vials, used syringes and needles into the sharps container.
- Complete the required documentation (eg, in the PMS).

A7.2.2 Preparing vaccines supplied as powder/ pellet vaccines

Some vaccines are presented as a prefilled syringe and freeze-dried (lyophilised) combination vaccines where:

- the pellet or powder preparation is reconstituted with the diluent (vial or prefilled syringe) supplied by the manufacturer (eg, MMR or Hib), or
- the pellet or powder preparation is reconstituted with a prefilled syringe containing vaccine (eg, DTaP-IPV-HepB/Hib).

The method for reconstituting the vaccine varies depending upon whether vials or prefilled syringes are used, as follows.

Reconstituting vaccines where the diluent is in a vial

- Where applicable, remove the detachable portion of the label from the diluent and/or vaccine (powder/pellet) vials and place these on (or with) the appropriate documentation. If there are no detachable labels, note the batch number and expiry date for both vaccine and diluent.
- Inspect the vaccine (powder/pellet) and diluent vials for any foreign particulate matter and/or variation in the physical appearance described by the manufacturer – if either is observed, do not use.
- Flip the plastic cap off the diluent vial, taking care not to touch the rubber seal.

- With the diluent vial upright, insert the needle tip through the centre of the rubber seal, where it is thinner and easier to penetrate.
- Invert the vial and draw up the entire volume of diluent into the syringe.
- Flip the plastic cap off the powder/pellet vial, and slowly, to avoid frothing, empty the contents of the syringe (diluent) into the powder/pellet vial, using the vial entry technique mentioned above.
- Swirl the vial gently to dissolve the powder/pellet. The needle and syringe may be removed or left in place.
- After reconstitution the vaccine should be checked to see that the colour compares with the information supplied by the manufacturer on the data sheet and that there is no particulate matter present. If the colour does not match the manufacturer's information, do not use.
- Withdraw the entire volume of the reconstituted vaccine into the syringe.
- Withdraw the needle from the vial.
- Change the needle, choosing the appropriate gauge and length for administration.
- Once reconstituted, the vaccine must be used within the manufacturer's recommended period. See the respective vaccine data sheets for more information.
- Administer the vaccine.
- Dispose of the empty vials, used syringes and needles into the sharps container.
- Complete the required documentation (eg, in the PMS).

Reconstituting vaccines where the vaccine or diluent is in a prefilled syringe

- Where applicable, remove the detachable portion of the label from the prefilled syringe and/or vaccine (powder/pellet) vial and place these on (or with) the appropriate documentation. If there are no detachable labels, note the batch number and expiry date for both the prefilled syringe and the vaccine (powder/pellet) vial.

- Inspect the prefilled syringe and vaccine (powder/pellet) vial for any foreign particulate matter and/or variation in the physical appearance described by the manufacturer – if either is observed, do not use.
- Flip the plastic cap off the powder/pellet vial, and with the vial upright, insert the prefilled syringe needle tip through the centre of the rubber seal, where it is thinner and easier to penetrate.
- Slowly, to avoid frothing, empty the contents of the prefilled syringe into the vial.
- Swirl the vial gently to dissolve the powder/pellet. The needle and syringe may be removed or left in place.
- After reconstitution the vaccine should be checked to see that the colour compares with the information supplied by the manufacturer on the data sheet and that there is no particulate matter present. If the colour or presentation does not match the manufacturer's information, do not use.
- Withdraw the entire volume of the reconstituted vaccine into the syringe.
- Withdraw the needle from the vial.
- Change the needle, choosing the appropriate gauge and length for administration.
- Once reconstituted, the vaccine must be used within the manufacturer's recommended period. See the respective vaccine data sheets for more information.
- Administer the vaccine.
- Dispose of the empty vials, used syringes and needles into the sharps container.
- Complete the required documentation (eg, in the PMS).

A7.2.3 Preparing vaccines supplied as prefilled syringes

- Where applicable, remove the detachable portion of the label from the prefilled syringe and place it on (or with) the appropriate documentation. If there is no detachable label, note the batch number and expiry date.

- Inspect the vaccine for any foreign particulate matter and/or variation in the physical appearance described by the manufacturer – if either is observed, do not use.
- Shake the syringe: Most inactivated vaccines contain an adjuvant, and to obtain a uniform suspension they must be shaken vigorously prior to being drawn up.
- Do not expel air if the needle is fixed (eg, with an influenza vaccine). This prevents tracking the vaccine through the skin and subcutaneous tissue, thereby reducing the risk of local reactions.
- When the needle is not fixed, expel the air to the hub of the syringe and then attach an appropriate length needle.
- Administer the vaccine.
- Dispose of the used syringe and needle into the sharps container.
- Complete the required documentation (eg, in the PMS).

A7.2.4 Preparing the rotavirus vaccine

The rotavirus vaccine is administered orally. It is available as a syringe-type applicator with a plunger stopper.

- Remove the detachable portion of the label (which includes the batch number but not the expiry date) and place it on (or with) the appropriate documentation. Note the expiry date.
- Inspect the vaccine for any foreign particulate matter and/or variation in the physical appearance described by the manufacturer – if either is observed, do not use.
- Remove the protective tip cap from the oral applicator.
- Administer the entire contents of the oral applicator into the infant's mouth, towards the inner cheek.
- Discard the empty applicator and cap into the sharps container.

For more information, refer to the manufacturer's data sheet (available on the Medsafe website, www.medsafe.govt.nz).

A7.2.5 Preparing vaccines supplied as multi-dose vials[35]

- The vial should be marked with the date and time of opening and the vaccinator's initials.
- Shake the vial before use and before drawing up subsequent vaccine doses.
- Inspect the vaccine for any foreign particulate matter and/or variation in the physical appearance described by the manufacturer – if either is observed, do not use.
- To ensure optimal vial dosage and minimal vaccine wastage, use a 1 mL syringe.
- Flip the plastic cap off the vial, taking care not to touch the rubber seal.
- Inspect the rubber seal. If there is any doubt about the integrity of the seal (eg, the vial leaks when turned upside down), *do not use*.
- Ideally, draw up all doses of the vaccine at the same time; this allows the drawing-up needle to remain in the vial and avoids the need for alcohol swabbing (of the rubber seal).
- Alcohol swabs should be used with caution. There is an increased risk of alcohol contamination when the swabbed rubber seal is repeatedly pierced. If an alcohol swab is used, allow 30 seconds for the alcohol to completely dry before inserting the needle into the rubber seal.
- Use each vial in one session of vaccinating and discard the vial four hours after first opening (or, follow the manufacturer's instructions), even if the vaccine has not been used.

35 Sources: World Health Organization. 2014. *WHO Policy Statement: Multi-dose Vial Policy (MDVP) – Handling of multi-dose vaccine vials after opening*. URL: http://apps.who.int/iris/bitstream/10665/135972/1/WHO_IVB_14.07_eng.pdf; the Australian Technical Advisory Group on Immunisation and the National Centre for Immunisation Research and Surveillance.

A7.3 Disposal of needles, syringes and vaccine vials

Note: For information about returning vaccines for destruction (such as in the event of a cold chain excursion or failure), see the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.[36]

- Do not separate needles from syringes or recap needles, unless a recapping device is used.
- All needles plus empty or partly used vials, syringes, dosing tubes and caps should be discarded into the sharps container for crush incineration.

A7.3.1 Sharps containers

- Sharps containers should be made of rigid, leak- and puncture-proof material. They must be fitted with a carrying handle and have an opening that is wide enough to allow disposable materials to be dropped into the container with one hand while still preventing removal of the contents.
- Sharps containers should be situated out of children's reach and available in every area where vaccinations take place.
- Sharps containers should be filled only to the indicated line, then sealed and given to an approved hazardous waste disposal person for incineration (as per the Resource Management Act 1991).

A7.3.2 Spillages

- In the event of blood or vaccine splashes on the skin, thoroughly wash the area under cold running water, then wash with soap and water or the hand wash that vaccinators have available.
- In the event of spills on work surfaces, put on gloves and treat the spill by wiping the area with a disposable pad soaked in 0.5 percent hypochlorite (household bleach diluted 1 to 9 parts water). Repeat with the hypochlorite solution and a fresh pad, then clean up with water or a commercial detergent. Alternatively, granular

[36] Available at www.health.govt.nz/coldchain

hypochlorite can be used for liquid spills, by applying sufficient granules to absorb the spilt fluid and then cleaning up after 10 minutes' contact time. Carefully seal all contaminated material in an approved biohazard bag for incineration by an approved hazardous waste disposal person.

- Contaminated linen is adequately treated by a routine hot wash cycle (60–70°C) using an ordinary bleach concentration.

A7.3.3 Recommendations following a needle-stick injury

In the event of a needle-stick injury, follow the guidelines below.

- The vaccinator should stop what they are doing and attend to the injury.
- Wounds and skin sites should be washed with soap and water. There is no evidence that encouraging bleeding or applying antiseptic reduces the risk of infection, but these actions are not contraindicated.
- The injury should be immediately reported to the medical advisor or employer, who should consider what immediate action is advisable.
- When the needle-stick injury involves exposure to an individual's blood, serological testing of that source individual should be sought and undertaken as soon as possible.
- Blood should be withdrawn from the affected vaccinator within a few days after the injury and counselling arranged. Testing for hepatitis B, hepatitis C and HIV serology should be undertaken.
- Depending on the infection status of the individual and the immune status of the injured vaccinator, it may be appropriate to start anti-HIV medications within the next few hours or to administer HBIG within the next few days.
- The blood-borne viruses of main concern in needle-stick injuries are hepatitis B, hepatitis C and HIV. All vaccinators should be immunised against hepatitis B and their antibody status known. Currently in New Zealand most HIV-infected individuals (or their parents/guardians) are likely to know their status at the time of immunisation, so HIV testing in case of needle-stick injuries is not routinely advocated. If there is a possibility that the individual could

be HIV infected, the informed consent of the individual/parent/guardian is required before blood is drawn for testing.

- Blood-borne virus exposures after vaccination are rarely of high risk: because of the small needle size there is seldom visible blood, and there is a low risk of blood-borne viruses in the community.

For more information, see also section 8.5.7 for serological testing guidelines for hepatitis B, the *Starship Clinical Guidelines for Needle-stick Injuries*[37] (for needle-stick injuries from needles discarded in the community) or your local DHB guidelines (if available).

[37] Available at https://www.starship.org.nz/for-health-professionals/starship-clinical-guidelines/n/needlestick-injuries/

Appendix 8: High-incidence TB countries

Neonatal BCG is recommended and funded for infants at increased risk of TB, defined as those who:

- will be living in a house or family/whānau with a person with either current TB or a history of TB
- have one or both parents or household members or carers who within the last five years lived for a period of six months or longer in countries with a TB rate ≥40 per 100,000
- during their first five years will be living for three months or longer in a country with a TB rate ≥40 per 100,000.

See Table A8.1 below for a list of high-incidence TB countries (TB rate ≥40 per 100,000).

Table A8.1: Countries with tuberculosis rate of ≥40 per 100,000 population (2015 WHO estimates)

Country	WHO region	Rate[a]	Cases[b]
Afghanistan	EMR	189	61,000
Algeria	AFR	75	30,000
Angola	AFR	370	93,000
Armenia	EUR	41	1,200
Azerbaijan	EUR	69	6,800
Bangladesh	SEA	225	362,000
Belarus	EUR	55	5,200
Benin	AFR	60	6,600
Bhutan	SEA	155	1,200
Bolivia (Plurinational State of)	AMR	117	13,000
Botswana	AFR	356	8,000
Brazil	AMR	41	84,000
Brunei Darussalam	WPR	58	240
Burkina Faso	AFR	52	9,400
Burundi	AFR	122	14,000
Cabo Verde	AFR	139	720
Cambodia	WPR	380	59,000
Cameroon	AFR	212	49,000
Central African Republic	AFR	391	19,000
Chad	AFR	152	21,000
China	WPR	67	918,000
China, Hong Kong SAR	WPR	71	5,200
China, Macao SAR	WPR	72	430
Côte d'Ivoire	AFR	159	36,000
Congo	AFR	379	18,000
Democratic People's Republic of Korea	SEA	561	141,000
Democratic Republic of the Congo	AFR	324	250,000
Djibouti	EMR	378	3,400
Dominican Republic	AMR	60	6,300

Continued overleaf

Country	WHO region	Rate[a]	Cases[b]
Ecuador	AMR	52	8,400
El Salvador	AMR	43	2,700
Equatorial Guinea	AFR	172	1,500
Eritrea	AFR	65	3,400
Ethiopia	AFR	192	191,000
Fiji	WPR	51	450
Gabon	AFR	465	8,000
Gambia	AFR	174	3,500
Georgia	EUR	99	4,000
Ghana	AFR	160	44,000
Greenland	EUR	164	92
Guam	WPR	51	87
Guinea	AFR	177	22,000
Guinea-Bissau	AFR	373	6,900
Guyana	AMR	93	710
Haiti	AMR	194	21,000
Honduras	AMR	43	3,500
India	SEA	217	2,840,000
Indonesia	SEA	395	1,020,000
Iraq	EMR	43	16,000
Kazakhstan	EUR	89	16,000
Kenya	AFR	233	107,000
Kiribati	WPR	551	620
Kyrgyzstan	EUR	144	8,500
Lao People's Democratic Republic	WPR	182	12,000
Latvia	EUR	41	800
Lesotho	AFR	788	17,000
Liberia	AFR	308	14,000
Libya	EMR	40	2,500
Lithuania	EUR	56	1,600
Madagascar	AFR	236	57,000

Continued overleaf

Country	WHO region	Rate[a]	Cases[b]
Malawi	AFR	193	33,000
Malaysia	WPR	89	27,000
Maldives	SEA	53	190
Mali	AFR	57	10,000
Marshall Islands	WPR	344	180
Mauritania	AFR	107	4,300
Micronesia (Federated States of)	WPR	124	130
Mongolia	WPR	428	13,000
Morocco	EMR	107	37,000
Mozambique	AFR	551	154,000
Myanmar	SEA	365	197,000
Namibia	AFR	489	12,000
Nauru	WPR	113	12
Nepal	SEA	156	44,000
Nicaragua	AMR	51	3,100
Niger	AFR	95	19,000
Nigeria	AFR	322	586,000
Northern Mariana Islands	WPR	58	32
Pakistan	EMR	270	510,000
Palau	WPR	76	16
Panama	AMR	50	2,000
Papua New Guinea	WPR	432	33,000
Paraguay	AMR	41	2,700
Peru	AMR	119	37,000
Philippines	WPR	322	324,000
Republic of Korea	WPR	80	40,000
Republic of Moldova	EUR	152	6,200
Romania	EUR	84	16,000
Russian Federation	EUR	80	115,000
Rwanda	AFR	56	6,600
Sao Tome and Principe	AFR	97	180

Continued overleaf

Country	WHO region	Rate[a]	Cases[b]
Senegal	AFR	139	21,000
Sierra Leone	AFR	307	20,000
Singapore	WPR	44	2,500
Solomon Islands	WPR	89	520
Somalia	EMR	274	30,000
South Africa	AFR	834	454,000
South Sudan	AFR	146	18,000
Sri Lanka	SEA	65	13,000
Sudan	EMR	88	35,000
Swaziland	AFR	565	7,300
Taiwan[c]	n/a	45.6	n/a
Tajikistan	EUR	87	7,400
Thailand	SEA	172	117,000
Timor-Leste	SEA	498	5,900
Togo	AFR	52	3,800
Turkmenistan	EUR	70	3,800
Tuvalu	WPR	232	23
Uganda	AFR	202	79,000
Ukraine	EUR	91	41,000
United Republic of Tanzania	AFR	306	164,000
Uzbekistan	EUR	79	24,000
Vanuatu	WPR	63	170
Viet Nam	WPR	137	128,000
Yemen	EMR	48	13,000
Zambia	AFR	391	63,000
Zimbabwe	AFR	242	38,000

Key: AFR = Africa; AMR = The Americas; EMR = Eastern Mediterranean; EUR = Europe; SEA = South East Asia; WPR = Western Pacific.

a Rate is the estimated incidence (all forms) per 100,000 population.

b Cases are the estimated number of incident cases (all forms).

c Taiwan source: http://www.cdc.gov.tw/english/info.aspx?treeid=bc2d4e89b154059b&nowtreeid=ee0a2987cfba3222&tid=5EC2D55596791C61 (accessed 8 November 2016).

Source: World Health Organization. 2016. *Tuberculosis (TB).* URL: http://www.who.int/tb/country/data/download/en/ (accessed 7 November 2016).

Appendix 9: Websites

A9.1 New Zealand-based websites

Ministry of Health

www.health.govt.nz

The official website for the Ministry of Health.

Immunisation

www.health.govt.nz/immunisation *and*
www.health.govt.nz/our-work/preventative-health-wellness/immunisation

Ministry of Health information about immunisation in New Zealand, including vaccination laws and practices, information for parents/guardians, young people and health professionals about the vaccines and the disease they protect against, immunisation coverage, and links to other reputable national and international websites. Electronic versions of the *Handbook* (pdf, html and ebook) are also available.

Pregnancy and kids

www.health.govt.nz/your-health/pregnancy-and-kids

Ministry of Health information for parents, guardians and whānau about pregnancy, labour and birth, and caring for children during their first 5 years.

Pharmaceutical Management Agency (PHARMAC)

www.pharmac.govt.nz

Information about the medicines (including vaccines) and related products which are funded on the Pharmaceutical Schedule for use in the community and public hospitals. Electronic versions of the

Pharmaceutical Schedule and updates (pdf and html) are published on the website (www.pharmac.govt.nz/tools-resources/pharmaceutical-schedule).

Medsafe – New Zealand Medicines and Medical Devices Safety Authority

www.medsafe.govt.nz

Information on the regulation of medicines and medical devices in New Zealand and the safe use of medicines, including medicine data sheets for health professionals and consumer medicine information for consumers.

Institute of Environmental Science and Research Ltd (ESR)

www.esr.cri.nz

A source of New Zealand infectious disease epidemiology, including regular surveillance reports for a number of diseases (www.surv.esr.cri.nz).

HealthEd

www.healthed.govt.nz

A source of public health education resources, including immunisation and communicable diseases, for health professionals and the public. Resources can be viewed, downloaded and/or ordered from this site.

Immunisation Advisory Centre (IMAC)

www.immune.org.nz

Information for parents and clinicians, including newsletters for providers of immunisation services in New Zealand.

KidsHealth

www.kidshealth.org.nz

A joint initiative between the Paediatric Society of New Zealand Inc and the Starship Foundation. The KidsHealth website provides accurate and reliable information about children's health for New Zealand parents and caregivers, the wider family and whānau, and health professionals working with parents.

Health Promotion Agency (HPA)

www.hpa.org.nz

The HPA works closely with the Ministry of Health to deliver immunisation messages to the general public.

A9.2 International websites

World Health Organization (WHO)

www.who.int/immunization/en/

A source of statistics, graphs and maps for immunisation profiles, by country. Useful for the practitioner planning vaccination of an immigrant child based on the current Schedule.

Centers for Disease Control and Prevention (CDC)

www.cdc.gov/vaccines

This site includes sections on the vaccines recommended (in the US) by age and for specific groups of people, and also includes safety factsheets for individual vaccines.

Immunization Action Coalition

www.immunize.org

Educational information for both clinicians and parents. This site includes an 'Unprotected people reports' section and has its own search facility.

Healthychildren.org – American Academy of Pediatrics

www.healthychildren.org

Information for parents and clinicians, which includes colourful (and graphic) pictures (www.healthychildren.org/immunizations). Useful articles include 'Why immunize your child?' and 'Vaccine safety: examine the evidence'.

Institute for Vaccine Safety

www.vaccinesafety.edu

Information on the safety of recommended vaccines and current vaccine issues in the media. Based at Johns Hopkins University, Baltimore, USA.

The Vaccine Page

www.vaccines.org

The latest information and news about vaccines for adults, parents, practitioners and researchers. This site also has links to journals and other vaccine-related sites.

National Centre for Immunisation Research & Surveillance (NCIRS)

www.ncirs.edu.au

An Australian-based research organisation that provides independent expert advice on all aspects of vaccine-preventable diseases and social and other issues related to immunisation.

A9.3 Influenza-related websites

National Influenza Specialist Group

www.influenza.org.nz

Influenza immunisation programme for health professionals. Information for consumers is available on the Fight Flu website (www.fightflu.co.nz).

Ministry of Health – Pandemic planning and response

www.health.govt.nz/our-work/emergency-management/pandemic-planning-and-response

Pandemic planning and response information, including the current pandemic influenza alert status and pandemic influenza plans, policies and other guidance for the health sector.

Institute of Environmental Science and Research Ltd

Virological surveillance

www.surv.esr.cri.nz/virology/virology.php

Weekly, monthly and annual influenza surveillance reports.

WHO Collaborating Centre for Reference and Research on Influenza, Melbourne, Australia

www.influenzacentre.org

Part of the WHO's Global Influenza Surveillance and Response System. The Centre analyses influenza viruses currently circulating in the human population in different countries around the world.

WHO – Global Influenza Programme

www.who.int/influenza/en

Information on national influenza centres and vaccine manufacturers around the world, as well as global surveillance data and links to reports of the *Weekly Epidemiological Record*.

WHO – FluNet

www.who.int/influenza/gisrs_laboratory/flunet/en

The WHO's geographical information system for monitoring global influenza activity. Recent activity is featured in a series of animated maps and news reports, and listings of participating centres, influenza vaccine manufacturers and related websites are provided.

CDC – Influenza (Flu)

www.cdc.gov/flu/index.htm

Information for the general public and health professionals on influenza viruses, vaccines, and antiviral agents, and on the clinical features and natural history of human influenza.

A9.4 Travel-related websites

Ministry of Health – Travelling

www.health.govt.nz/your-health/healthy-living/travelling

Information to help travellers manage risk and stay well. Includes links to other New Zealand-based travel websites.

Ministry of Foreign Affairs and Trade – Safe Travel

www.safetravel.govt.nz

Official advice for New Zealanders living and travelling overseas.

WHO – International travel and health

www.who.int/ith/en/

Immunisation and disease information for travellers.

CDC – Travelers' health

wwwnc.cdc.gov/travel

US-based information for travellers and health professionals, including updates on national and international disease outbreaks.

Fitfortravel

www.fitfortravel.nhs.uk

Travel health information for people travelling abroad from the UK, including updates on national and international disease outbreaks.

Funded vaccines for special groups

These vaccines may be given in addition to or instead of the routine Schedule vaccines. See the Pharmaceutical Schedule (www.pharmac.govt.nz) for the number of funded doses and any changes to the funding decisions.

Vaccine	Individuals eligible for funded vaccine
Hib	Post-HSCT or chemotherapy; pre- or post-splenectomy or with functional asplenia; pre- or post-solid organ transplant (SOT), pre- or post-cochlear implants, renal dialysis and other severely immunosuppressive regimens. Testing for primary immune deficiency.
Hep A	Transplant patients. Children with chronic liver disease. Close contacts of hepatitis A cases.
HepB and HBIG	HepB and HBIG at birth for babies of mothers with chronic HBV infection. HepB for: household or sexual contacts of HBsAg-positive patients; children <18 years who have not achieved positive serology and who require additional vaccination; HIV- or hepatitis C-positive patients; following non-consensual sexual intercourse; following immunosuppression; SOT; post-HSCT; following needle-stick injury; dialysis and liver or kidney transplant.
HPV	Individuals aged 9–26 years: with confirmed HIV infection; transplant (including stem cell) patients; post-chemotherapy.
Influenza	Pregnant women. Individuals aged 6 months to <65 years with certain medical conditions.
MMR	For (re-)vaccination following immunosuppression.
MenCCV and MCV4-D	Pre- or post-splenectomy or with functional asplenia; with HIV, complement deficiency (acquired or inherited) or pre- or post-SOT; close contacts of meningococcal cases; HSCT patients; following immunosuppression.
Pertussis-containing vaccine	Tdap for pregnant women, from 28 to 38 weeks' gestation. Tdap, DTaP-IPV-HepB/Hib or DTaP-IPV for (re-)vaccination: post-HSCT or chemotherapy; pre- or post-splenectomy; pre- or post-SOT, renal dialysis and other severely immunosuppressive regimens.
PCV13 and 23PPV	Children and adults with eligible conditions. PCV13 and 23PPV for testing for primary immune deficiency.
IPV	For (re-)vaccination following immunosuppression.
Td	For (re-)vaccination following immunosuppression; boosting of patients with tetanus-prone wounds; testing for primary immune deficiency.
BCG	Infants and children <5 years at increased risk of TB.
Varicella	Non-immune patients: with chronic liver disease who may need a transplant in the future; with deteriorating renal function before transplant; prior to SOT; prior to elective immunosuppression; for post-exposure prophylaxis of immune-competent in-patients. Patients at least 2 years after bone marrow transplant or at least 6 months after completion of chemotherapy, on advice of their specialist. HIV-positive patients with mild or moderate immunosuppression who are non-immune to varicella, on advice of their specialist. Patients with inborn errors of metabolism at risk of major metabolic decompensation, with no clinical history of varicella. Household contacts of paediatric patients who are immunocompromised, or undergoing a procedure leading to immunocompromise, where the household contact has no clinical history of varicella. Household contacts of adult patients who have no clinical history of varicella and who are severely immunocompromised or undergoing a procedure leading to immunocompromise, where the household contact has no clinical history of varicella.

Anaphylaxis

Call for help – send for professional assistance (ambulance, doctor). Never leave the individual alone.

Assess – Assess responsiveness, and check Airway, Breathing, Circulation.

- If they are conscious, lie the individual down in the recovery position.
- If they are unconscious and breathing normally, lie the individual down in the recovery position, ensuring that the airway is open.
- If they are unconscious and not breathing normally, institute standard procedures for basic life support. If cardiorespiratory arrest occurs, administer age-appropriate CPR and life-support measures.

Administer 1:1,000 adrenaline by deep intramuscular injection – see below for dosage. If necessary, adrenaline can be repeated at 5–15-minute intervals, to a maximum of three doses.

Administer oxygen at high flow rates where there is respiratory distress, stridor or wheeze.

If hypotensive, elevate legs**. If stridor is present,** elevate head and chest**.**

Record vital signs every 5–10 minutes and document fully all symptoms and treatment given.

Admit to hospital – all cases of anaphylaxis should be admitted to hospital for observation.

Adrenaline dosage for 1:1,000 formulation is 0.01 mL/kg, up to a maximum of 0.5 mL.

If weight unknown:

Recipient	Age	Adrenaline (1:1,000 mL)
Infant	Under 1 year	0.05–0.1 mL
Child	Under 2 years	0.1 mL
Child	2–4 years	0.2 mL
Child	5–10 years	0.3 mL
Adolescent	≥11 years	0.3–0.5 mL
Adult		0.5 mL

National Immunisation Schedule

Antigen(s)	DTaP-IPV-HepB/Hib	PCV10	RV1	MMR	Hib	VV	DTaP-IPV	Tdap	HPV9	Td	Influenza	HZV
Brand name	**Infanrix-hexa**	**Synflorix**	**Rotarix**	**Priorix**	**Hiberix**	**Varilrix**	**Infanrix-IPV**	**Boostrix**	**Gardasil 9**	**ADT Booster**	**Influvac Tetra**	**Zostavax**
Pregnancy								Tdap			Influenza	
6 weeks	DTaP-IPV-HepB/Hib	PCV10	RV1									
3 months	DTaP-IPV-HepB/Hib	PCV10	RV1									
5 months	DTaP-IPV-HepB/Hib	PCV10										
15 months		PCV10		MMR	Hib	VV						
4 years				MMR			DTaP-IPV					
11 or 12 years								Tdap	HPV9 (2 doses)			
45 years										Td		
65 years										Td	Influenza (annually)	HZV

Key:

D = diphtheria; T = tetanus; aP = acellular pertussis; IPV = inactivated polio vaccine; HepB = hepatitis B; Hib = *Haemophilus influenzae* type b; PCV10 = 10-valent pneumococcal conjugate vaccine; RV1 = rotavirus vaccine (monovalent); MMR = measles, mumps and rubella; VV = varicella vaccine; d = adult diphtheria; ap = adult acellular pertussis; HPV9 = human papillomavirus (9 serotypes); HZV = herpes zoster vaccine.