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Amirthalingam G, Andrews N, Campbell H et al. Effectiveness of maternal pertussis vaccination in England: an observational study. Lancet. 2014; 384: 1521-8.

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Update on immunization and pregnancy: tetanus, diphtheria, and pertussis vaccination: The American College of Obstetricians and Gynecologists, Committee on Obstetric Practice2013.

To see Linda Hill's thesis go to: https://ourarchive.otago.ac.nz/handle/10523/5833

Summary for Pertussis vaccine between 1 Jan 2000 and 31 Dec 2016
Number of reports for Pertussis vaccine: 10530

Number reports where death was reported: 0

Number of reactions: 17997

System Organ Class	MedDRA Reaction Term	Number of Reports
Blood and lymphatic system disorders	Anaemia	4
	Immune thrombocytopenic purpura	2
	Leukocytosis	2
	Lymphadenitis	11
	Lymphadenopathy	78
	Lymphopenia	1
	Neutropenia	2
	Thrombocytopenia	2
Cardiac disorders	Bradycardia	22
	Cardiac arrest	1
	Cyanosis	31
	Extrasystoles	1
	Palpitations	4
	Tachycardia	41
Ear and labyrinth disorders	Ear disorder	1
	Ear pain	5
	Hypoacusis	2
	Tinnitus	1
Eye disorders	Blindness	1
	Conjunctival haemorrhage	1
	Diplopia	1
	Eye movement disorder	7
	Eye pain	5
	Eyelid ptosis	1
	Keratitis	1
	Lacrimation disorder	1
	Lacrimation increased	2
	Mydriasis	1
	Oculogyric crisis	1
	Periorbital oedema	34
	Photophobia	6
	Pupils unequal	1

	Strabismus	1
	Vision blurred	2
	Visual acuity reduced	2
Gastrointestinal disorders	Abdominal distension	3
	Abdominal pain	94
	Change of bowel habit	1
	Constipation	8
	Diarrhoea	136
	Diarrhoea haemorrhagic	1
	Dry mouth	2
	Dyspepsia	1
	Dysphagia	2
	Eructation	1
	Faeces discoloured	1
	Flatulence	2
	Frequent bowel movements	2
	Gastrointestinal disorder	4
	Gastrooesophageal reflux disease	6
	Haematemesis	1
	Haematochezia	1
	Hypoaesthesia oral	2
	Lip swelling	11
	Mouth ulceration	2
	Nausea	100
	Oedema mouth	1
	Oral pain	1
	Paraesthesia oral	1
	Proctalgia	1
	Retching	2
	Salivary hypersecretion	1
	Swollen tongue	2
	Tongue oedema	1
	Toothache	1
	Vomiting	483
General disorders and administration site conditions	Asthenia	1
	Axillary pain	1
	Chest discomfort	3
	Chest pain	3

	Chills	21
	Crying	687
	Developmental delay	2
	Face oedema	14
	Fatigue	68
	Feeling cold	4
	Feeling hot	14
	Feeling of body temperature change	7
	Gait disturbance	1
	Gravitational oedema	1
	Hangover	1
	Hypothermia	4
	Influenza like illness	15
	Infusion site bruising	1
	Injection site abscess sterile	8
	Injection site bruising	149
	Injection site dermatitis	2
	Injection site erythema	870
	Injection site fibrosis	1
	Injection site granuloma	1
	Injection site haematoma	5
	Injection site haemorrhage	4
	Injection site induration	75
	Injection site inflammation	6455
	Injection site mass	91
	Injection site pain	1056
	Injection site pruritus	720
	Injection site rash	80
	Injection site reaction	23
	Injection site scar	3
	Injection site swelling	62
	Injection site ulcer	1
	Injection site urticaria	89
	Injection site vesicles	46
	Instillation site inflammation	1
	Localised oedema	1
	Malaise	20
	Oedema	4

	Oedema peripheral	17
	Pain	2
	Pyrexia	1455
Hepatobiliary disorders	Jaundice	1
Immune system disorders	Anaphylactic reaction	7
	Anaphylactoid reaction	1
	Autoimmune disorder	1
	Serum sickness-like reaction	1
Infections and infestations	Abscess	1
	Bronchiolitis	3
	Candida infection	2
	Cellulitis	25
	Conjunctivitis	13
	Infection	8
	Injection site abscess	30
	Injection site cellulitis	141
	Injection site infection	9
	Lymphangitis	2
	Measles	1
	Meningitis	2
	Otitis media	10
	Pertussis	1
	Pharyngitis	13
	Pneumonia	3
	Rash pustular	1
	Rhinitis	12
	Tonsillitis	6
	Upper respiratory tract infection	23
	Urinary tract infection	3
	Varicella	2
	Viral infection	3
Injury, poisoning and procedural complications	Bite	1
	Exposure during pregnancy	1
	Fall	2
	Laceration	2
	Maternal drugs affecting foetus	1
Investigations	Cold agglutinins positive	1
	C-reactive protein increased	2

	Electrocardiogram abnormal	1
	Hepatic enzyme increased	1
	Oxygen saturation decreased	4
	Tri-iodothyronine decreased	1
Metabolism and nutrition disorders	Decreased appetite	126
	Dehydration	5
	Diabetes mellitus	1
	Hyperglycaemia	1
	Hypoglycaemia	1
Musculoskeletal and connective tissue disorders	Ankylosing spondylitis	1
	Arthralgia	19
	Back pain	6
	Bursitis	1
	Joint effusion	1
	Joint stiffness	1
	Joint swelling	1
	Limb discomfort	1
	Mobility decreased	2
	Muscle spasms	1
	Muscle twitching	3
	Muscular weakness	10
	Musculoskeletal pain	12
	Musculoskeletal stiffness	5
	Myalgia	44
	Pain in extremity	380
	Rotator cuff syndrome	1
	Sjogren's syndrome	1
	Synovitis	3
	Tendon disorder	1
	Torticollis	1
	Trismus	1
Nervous system disorders	Ataxia	6
	Brain oedema	1
	Coma	2
	Depressed level of consciousness	6
	Disturbance in attention	3
	Dizziness	63
	Dysaesthesia	2

	Encephalopathy	1
	Febrile convulsion	46
	Fontanelle bulging	4
	Generalised tonic-clonic seizure	8
	Headache	161
	Hyperaesthesia	1
	Hyperkinesia	1
	Hypertonia	14
	Hypoaesthesia	9
	Hypokinesia	28
	Hyporeflexia	1
	Hypotonia	104
	Hypotonic-hyporesponsive episode	227
	Intracranial pressure increased	1
	Lethargy	161
	Loss of consciousness	3
	Migraine	1
	Monoplegia	1
	Muscle contractions involuntary	11
	Myoclonus	1
	Neuritis	1
	Neuropathy peripheral	1
	Nystagmus	2
	Opisthotonus	2
	Paraesthesia	14
	Paralysis	1
	Petit mal epilepsy	9
	Presyncope	100
	Psychomotor hyperactivity	1
	Radiculitis brachial	3
	Sedation	1
	Seizure	57
	Sensory disturbance	1
	Somnolence	181
	Speech disorder	1
	Syncope	26
	Tremor	30
	Foetal disorder	1

Pregnancy, puerperium and perinatal conditions	Foetal hypokinesia	1
Psychiatric disorders	Abnormal behaviour	5
	Abnormal dreams	1
	Affect lability	1
	Agitation	6
	Anxiety	2
	Apathy	1
	Breath holding	13
	Confusional state	3
	Delirium	8
	Delusion	1
	Depersonalisation/derealisation disorder	4
	Hallucination	9
	Hallucination, visual	1
	Insomnia	16
	Irritability	527
	Nightmare	2
	Personality change	2
	Personality disorder	1
	Selective eating disorder	2
	Sleep disorder	30
Renal and urinary disorders	Acute kidney injury	1
	Nephrotic syndrome	2
	Pollakiuria	3
	Urinary incontinence	1
	Urine flow decreased	2
Reproductive system and breast disorders	Balanoposthitis	1
	Penis disorder	1
Respiratory, thoracic and mediastinal disorders	Apnoea	67
	Aspiration	1
	Bradypnoea	6
	Bronchospasm	19
	Choking	5
	Cough	44
	Dry throat	1
	Dyspnoea	30
	Epistaxis	3

	Hyperventilation	2
	Hypoxia	4
	Laryngeal oedema	1
	Nasal congestion	1
	Oropharyngeal pain	14
	Respiratory depression	1
	Respiratory disorder	4
	Respiratory distress	3
	Respiratory failure	1
	Rhinorrhoea	25
	Stridor	3
	Tachypnoea	14
	Throat irritation	8
	Throat tightness	8
Skin and subcutaneous tissue disorders	Angioedema	16
	Blister	6
	Cold sweat	9
	Dermatitis	1
	Dermatitis bullous	12
	Dermatitis exfoliative	1
	Dry skin	6
	Ecchymosis	1
	Eczema	12
	Erythema	22
	Erythema multiforme	14
	Henoch-Schonlein purpura	2
	Hyperhidrosis	9
	Hypersensitivity vasculitis	1
	Hypertrichosis	1
	Lipoatrophy	1
	Mechanical urticaria	3
	Miliaria	1
	Night sweats	2
	Palmar-plantar erythrodysaesthesia syndrome	1
	Pemphigoid	1
	Petechiae	28
	Photosensitivity reaction	1

	Pigmentation disorder	2
	Pruritus	78
	Purpura	8
	Rash	344
	Rash erythematous	119
	Rash macular	130
	Rash maculo-papular	82
	Rash morbilliform	59
	Rash papular	11
	Rash pruritic	48
	Rash vesicular	15
	Rosacea	1
	Seborrhoeic dermatitis	1
	Skin discolouration	9
	Skin exfoliation	1
	Skin reaction	1
	Urticaria	257
Vascular disorders	Flushing	55
	Haematoma	1
	Hot flush	2
	Hypertension	3
	Hypotension	6
	Pallor	182
	Peripheral coldness	4
	Shock symptom	1

About the release of this information

This information is released in keeping with the purpose of the Official Information Act 1982 to progressively increase the availability of official information to the people of New Zealand. The data contained in SMARS does not include any personal information within the meaning of the Privacy Act 1993.

Advice for industry

To avoid creating duplicate reports, cases viewed in SMARS should not be submitted as new reports back to CARM. The SMARS database contains anonymised information from reports that have previously been received by CARM. If follow-up information is required to be submitted for a case, please quote the original report number when submitting so this can be linked to the original report.

Use of SMARS data

If you wish to copy or circulate information from SMARS please ensure that a copy of this guideline is provided. Prior to any publication of this data you must contact CARMand Medsafe and include in the publication:

- the source of this information

- the limitations of this information
- that the information does not represent the opinion of CARM or Medsafe

Further information

If you require further information please contact Medsafe by emailing medsafeadrquery@moh.govt.nz or by telephoning 04 819 6800.

If you have any concerns talk to a trained registered nurse - 0800 611 116
Or concerns about poisoning - Poisons Information Centre 0800 764 766 (0800 POISON)

Appendix 5

Examples of country, state or region and minimum age for vaccination where pharmacists can vaccinate children

Region	Minimum age	Comments
British Columbia, Canada[1]	Over 5 years	State rule
Alberta[1]	Over 9 years	State rule
New Brunswick, Canada[1]	5 years and over	State rule
Ontario[1]	5 years and over	State rule
Nova Scotia[1]	5 years and over	State rule
Manitoba, Canada[2]	7 years and over	State rule
London, UK[3]	13 and over	Example of an influenza patient group direction, not a specific requirement
Pharmacy PGD across England[4]	5 years and over	Example of a patient group direction for meningitis B vaccination (by injection) for pharmacists

A graph from the American Pharmacists' Association from 2015 is also attached

References

[1]. Influenza immunization guide for pharmacists. Canadian Pharmacists Association; 2013. Available at: http://www.pharmacists.ca/cpha-ca/assets/File/education-practice-resources/Flu2013-InfluenzaGuideEN.pdf (accessed July 2015).

[2]. Caetano P, Baydack R. Pharmacist Administration of Vacines in Manitoba (letter). Winnipeg, Manitoba, Canada: Manitoba Health; 2014. Available at: http://mpha.in1touch.org/uploaded/web/New%20Pharmaceutical%20Act/Immunization%20Info%20for%20Pharmacists%20Feb%202014%20FINAL%20(2).pdf (accessed July 2015).

[3]. Patient group direction for the administration of trivalent seasonal inactivated influenza vaccine by pharmacists during the 2013/14 season. London: NHS England (London Region); 2013. Available at: http://psnc.org.uk/city-and-hackney-lpc/wp-content/uploads/sites/69/2013/08/PGD-Community-Pharmacy-Seasonal-Flu.20130919.pdf (accessed July 2015).

[4]. Meningitis B Vaccine Patient Group Direction. England: Pharmacy PGD. Available at: https://www.pharmacypgd.co.uk/about-pgds/available-pgds/meningitis-b-vaccine-pgd (accessed July 2015).

NEW ZEALAND DATA SHEET

1 PRODUCT NAME (strength, pharmaceutical form)

ADACEL® 0.5 mL suspension for injection vial.

Pertussis Vaccine-Acellular Combined with Diphtheria and Tetanus Toxoids (Adsorbed).

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 0.5 mL dose of ADACEL contains:

2.5 mcg	pertussis toxoid
5 mcg	pertussis filamentous haemagglutinin
5 mcg	pertussis fimbriae types 2 and 3
3 mcg	pertussis pertactin
≥ 2 IU (2 LfU)	diphtheria toxoid
≥ 20 IU (5 LfU)*	tetanus toxoid
1.5 mg	aluminium phosphate (equivalent to 0.33mg aluminium)
0.6% v/v	phenoxyethanol
≤ 0.005mg	formaldehyde
≤ 0.02mg	glutaraldehyde
water for injections to	0.5mL

*The formulated content of 5LfU per 0.5mL dose of tetanus toxoid is the same as the related product Tripacel®.

The vaccine is prepared from: adsorbed purified and formaldehyde detoxified diphtheria and tetanus toxins; adsorbed purified and glutaraldehyde detoxified pertussis toxin (pertussis toxoid or PT); adsorbed purified and formaldehyde treated filamentous haemagglutinin (FHA); adsorbed purified pertactin (PRN) and fimbriae types 2 and 3 (FIM).

ADACEL is an adult/adolescent formulation diphtheria-tetanus-acellular pertussis (dTpa) combination vaccine with reduced content of pertussis toxoid, filamentous haemagglutinin and diphtheria toxoid compared to paediatric diphtheria-tetanus-acellular pertussis (DTaP) formulations.

The manufacture of this product includes exposure to bovine materials. No evidence exists that any case of vCJD (considered to be the human form of bovine spongiform encephalopathy) has resulted from the administration of any vaccine product.

3 PHARMACEUTICAL FORM

ADACEL is a sterile, uniform, cloudy, white suspension for injection.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

ADACEL is indicated for active immunisation against tetanus, diphtheria and pertussis in persons aged 10 years and over as a booster following primary immunisation.

4.2 Dose and method of administration

The same dosage, a single 0.5 mL dose, applies to all age groups.

Booster doses of ADACEL should be given according to the current New Zealand immunisation guidelines.

Individuals with an incomplete, or no, history of a primary series of diphtheria and tetanus toxoids should not be vaccinated with ADACEL. A booster response will only be elicited in individuals who have been previously primed by vaccination.

The vaccine's normal appearance is a uniform, cloudy, white suspension which may sediment during storage. Shake the vial well to uniformly distribute the suspension before withdrawing the dose.

Parenteral biological products should be inspected visually for extraneous particulate matter and/or discolouration prior to administration. If these conditions exist, the product should not be administered.

When administering a dose from a stoppered vial, do not remove either the stopper or the metal seal holding it in place. Once the vial has been opened, any of its contents not used immediately should be discarded. Aseptic technique must be used for withdrawal of the dose. Before injection, the skin over the site should be cleansed with a suitable germicide.

ADACEL should be administered intramuscularly. The preferred site is into the deltoid muscle.

The intravascular or subcutaneous routes should not be used (for exception, see under 4.4 Special warnings and precautions for use).

After insertion of the needle, ensure that the needle has not entered a blood vessel.

ADACEL must not be mixed in the same syringe with other vaccines or other parenterally administered drugs or co-administered in the same syringe.

Product is for single use in one patient on one occasion only. Discard any residue.

4.3 Contraindications

ADACEL should not be administered to individuals who have previously had a hypersensitivity reaction to any vaccine containing diphtheria or tetanus toxoids, or pertussis (acellular or whole cell).

ADACEL should not be administered to individuals known to be hypersensitive to any component of the vaccine (see components listed in 2. QUALITATIVE AND QUANTITATIVE COMPOSITION) or residues carried over from manufacture (such as formaldehyde and glutaraldehyde).

ADACEL should not be administered to subjects who experienced an encephalopathy of unknown origin within 7 days of previous immunisation with a pertussis-containing vaccine, or to subjects who have experienced other neurological complications following previous immunisation with any of the antigens in ADACEL.

4.4 Special warnings and precautions for use

The use of ADACEL as a primary series, or to complete the primary series, has not been studied. A booster response will only be elicited in individuals who have been previously primed by vaccination. Individuals with an incomplete, or no, history of a primary series of diphtheria and tetanus toxoids should not be vaccinated with ADACEL.

Diphtheria and tetanus toxoid containing vaccines should be avoided in persons who have received a booster with a vaccine containing these toxoids within the previous five years because of the potential increased frequency of local adverse reactions.

There are currently no data upon which to base a recommendation for the optimal interval for administering subsequent booster doses with ADACEL to maintain antibody levels against pertussis. There are no data on the duration of protection against pertussis following vaccination with ADACEL.

As with all injectable vaccines, appropriate medical treatment and supervision should be readily available for immediate use in case of a rare anaphylactic reaction following the administration of vaccine. As a precautionary measure, adrenaline injection (1:1,000) must be immediately available in case of unexpected anaphylactic or serious allergic reactions.

The vaccine must be given intramuscularly, as subcutaneous administration increases the chances of a local reaction. Do not administer by intravascular injection. A persistent nodule at the site of injection may occur with all adsorbed vaccines particularly if administered into the superficial layers of the subcutaneous tissue.

Intramuscular injections should be given with care in patients suffering from coagulation disorders because of the risk of haemorrhage. In these situations administration of ADACEL by deep subcutaneous injection may be considered, although there is a risk of increased local reactions.

ADACEL should not be administered into the buttocks due to the varying amounts of fatty tissue in this region, nor by the intradermal route, since these methods of administration may induce a weaker immune response.

Formaldehyde and glutaraldehyde have been used in the manufacturing process of this product and trace residual amounts may be present in the final product. Therefore, a hypersensitivity reaction may occur.

If Guillain-Barré syndrome or brachial neuritis has occurred following receipt of prior vaccine containing tetanus toxoid, the decision to give any vaccine containing tetanus toxoid should be based on careful consideration of the potential benefits and possible risks.

ADACEL should not be administered to individuals with progressive or unstable neurological disorders, uncontrolled epilepsy or progressive encephalopathy until a treatment regimen has been established, the condition has stabilised and the benefit clearly outweighs the risk.

The immunogenicity of the vaccine could be reduced by immunosuppressive treatment or immunodeficiency. It is recommended to postpone the vaccination until the end of such disease or treatment if practical.

Nevertheless, vaccination of HIV infected subjects or subjects with chronic immunodeficiency, such as AIDS, is recommended even if the antibody response might be limited.

As with any vaccine, immunisation with ADACEL may not protect 100% of susceptible individuals.

Vaccination should be deferred in the presence of any acute illness, including febrile illness. A minor afebrile illness such as mild upper respiratory infection is not usually a reason to defer immunisation.

Carcinogenicity, mutagenicity

ADACEL has not been evaluated for carcinogenicity or mutagenicity.

Paediatric population

ADACEL should not be used for primary immunisation.

ADACEL is indicated for use in children aged 10 years and over.

4.5 Interaction with other medicines and other forms of interaction

ADACEL can be administered concomitantly with Hepatitis B vaccine, using a separate limb for the site of injection. Concomitant administration of other vaccines with ADACEL has not been studied.

In the case of immunosuppressive therapy, refer to 4.4 Special warnings and precautions for use.

4.6 Fertility, pregnancy and lactation

Use in pregnancy (Category B2)

The effect of ADACEL on the development of the embryo and foetus has not been assessed. Vaccination in pregnancy is not recommended unless there is a definite risk of acquiring pertussis. As the vaccine is detoxified, risk to the embryo or the foetus is highly improbable. The benefits versus the risks of administering ADACEL in pregnancy should carefully be evaluated when there

is a high probable risk of exposure to a household contact or during an outbreak in the community.

Breastfeeding

The effect of administration of ADACEL during lactation has not been assessed. As ADACEL is detoxified; any risk to the mother or the infant is highly improbable. The benefits versus the risks of administering ADACEL during lactation should carefully be evaluated by the health-care provider, particularly when there is a high probable risk of disease transmission through exposure to a household contact, or during an outbreak in the community. The risks of disease transmission from the infected mother to the infant who may not have been fully immunised should also be evaluated.

Fertility

ADACEL has not been evaluated for impairment of fertility.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

The reactions are listed within body systems and categorised by frequency according to the following definitions:

Very common	(≥ 1/10)			
Common	(<1/10	and	≥	1/100)
Uncommon	(<1/100	and	≥	1/1,000)

Clinical Trial Experience

In clinical studies with 324 adolescents and 638 adults given ADACEL, the most frequently reported adverse reactions occurring during the first 24 hours included the following:

Very common	Pain, swelling, redness at the injection site Headache, decreased energy, generalised body-ache
Common	Fever, chills, nausea, diarrhoea, sore or swollen joints
Uncommon	Vomiting

A causal relationship to vaccination was not established in all cases. All adverse reactions were generally mild and transient in duration. Fever was reported in less than 3% of vaccinees. There were no reports of fever over 39.9ºC. This adverse reaction profile was shown to be comparable to that seen in vaccinees who received a booster with Td adsorbed vaccine (tetanus (5 LfU) and diphtheria (2 LfU) toxoids adsorbed). Late-onset local adverse reactions (i.e. a local adverse

reaction which had an onset or increase in severity 3 to 8 days post-immunisation) such as redness, swelling and pain, occurred in less than 2%.

The following table summarises Adverse Events (%) in ADACEL (dTpa) recipients 0 - 24 hours post vaccination:

	ADOLESCENTS**			ADULTS	
Event	**TC9704**	**TD9805**		**TC9704**	
	dTpa N = 59	**dTpa N = 135**	**dTpa +Hep B N = 134**	**dTpa*** N = 390**	**Td N = 151§**
Local Reactions					
Redness	8.5	9.6	12.7	7.2	6.6
Swelling	18.6	15.6	20.1	11.3	13.9
Pain	94.9	69.6	75.4	84.6	86.1
Systemic Reactions					
Fever*	5.1	0.7	1.5	1.3	1.3
Headache	37.3	28.1	23.9	14.4	13.9
Chills	15.3	12.6	13.4	3.6	2.0
Body ache	15.3	18.5	19.4	11.8	8.6
Tiredness	23.7	37.0	31.3	11.5	14.6
Sore Joints	3.4	19.3	12.7	5.4	4.0
Nausea	6.8	12.6	12.7	6.9	5.3
Vomiting	1.7	0.0	1.5	0.5	0.0
Diarrhoea	1.7	4.4	3.0	2.3	1.3

* Includes fever ≥ 37.5ºC and ≥ 39.1ºC
** 12 - 18 years of age in TC9704 and 11-12 years of age in TD9805
*** >19 years of age
§ Includes (N=20) adolescents

Post-marketing Experience

In addition to the data from clinical studies, the following adverse events have been reported during the commercial use of ADACEL. All the adverse events have been very rarely reported (<0.01%); however, the exact incidence rates cannot precisely be calculated. This computation is based on the number of adverse events reported per estimated number of vaccinated patients.

Immune system disorders:

Hypersensitivity (anaphylactic) reaction (angioedema, oedema, rash, hypotension)

Nervous system disorders:

Paraesthesia, hypoesthesia, Guillain-Barré syndrome, brachial neuritis, facial palsy, convulsion, syncope, myelitis

Metabolism and Nutrition Disorders:

Anorexia

Cardiac Disorders:

Myocarditis

Skin and subcutaneous tissue disorders:

Pruritus, urticaria

Musculoskeletal and Connective Tissue Disorders:

Myositis, myalgia

General disorders and administration site conditions:

Large injection site reactions (> 50 mm) and extensive limb swelling from the injection site beyond one or both joints occur after administration of ADACEL in adolescents and adults. These reactions usually start within 24 - 72 hours after vaccination, may be associated with erythema, warmth, tenderness or pain at the injection site and resolve spontaneously within 3 - 5 days.

Injection site bruising, sterile abscess

Underarm lymph node swelling

Potential Adverse Events

Other adverse events not listed above have been reported with other similar vaccines and should be considered potential adverse reactions to ADACEL. Although rarely, severe local reactions such as whole arm swelling following adsorbed tetanus vaccine has occurred and may be associated with high levels of antitoxin resulting from over-immunisation.

In addition, neurological conditions including peripheral neuropathies and demyelinating diseases of the central nervous system have been reported in temporal association with some tetanus or tetanus and diphtheria toxoid-containing vaccines.

Clinical data for use of ADACEL in individuals who have only received DTaP vaccines for priming in infancy and early childhood are currently not available.

Very rarely, large local reactions, consisting of redness and/or swelling > 50mm, some with circumferential swelling of the injected limb, have been reported following the fourth and fifth paediatric doses of some acellular pertussis-containing vaccine.

4.9 Overdose

Not applicable.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Pertussis, purified antigen, combinations with toxoids, ATC code: J07AJ52

Clinical efficacy and safety

A total of 962 individuals (324 adolescents and 638 adults), who had not been immunised against tetanus, diphtheria, or pertussis within the previous five years, received a single 0.5 mL dose of ADACEL in three clinical trials (TC9704, TD9805 and TC9707).

In TC9704, 449 (55 adolescents 12 to 17 years of age and 394 adults 18 to 54 years of age) received three lots of ADACEL (dTpa), while 300 (37 adolescents and 263 adults) were given a single 0.5 mL dose with an adult formulation diphtheria-tetanus vaccine (Td) and a monovalent acellular Pertussis (aP) vaccine, given separately, one month apart. In TD9805, 269 adolescents 11 to 12 years of age were vaccinated: 135 received ADACEL given alone followed by the first dose of a 3-dose primary series with Hepatitis B vaccine (HB), one month later, and 134 were given ADACEL concurrently with the first dose of HB.

In TC9704, the safety and immunogenicity profile of ADACEL was shown to be comparable to that observed with a single booster dose of Td and aP containing the same amount of tetanus and diphtheria toxoids and pertussis antigens, administered separately. In TD9805, the safety and immunogenicity of concomitant administration of Hepatitis B vaccine with ADACEL (dTpa+HB) was comparable to that observed with ADACEL alone. Antibody responses observed in adolescents and adults from TD9805 and TC9704 are presented in the tables below:

	TD9805 11 to 12 years				**TC9704 12 to 54 years**			
Antitoxin	**Vaccine**	**N**	**GMC**	**% ≥ 0.10 IU/mL***	**Vaccine**	**N**	**GMC**	**% ≥ 0.10 IU/mL***
Tetanus	dTpa	118	28.6	100.0	dTpa	446	15.7	100.0
	dTpa+HB	129	26.1	100.0	Td	151	16.0	99.3
Diphtheria	dTpa	118	8.4	100.0	dTpa	446	0.8	85.0
	dTpa+HB	129	6.8	100.0	Td	151	1.2	89.4

* Tetanus and diphtheria antitoxin levels were measured in EU and IU/mL, respectively

	TD9805 11 to 12 years			**TC9704 12 to 54 years**		
Pertussis Antibody	**Vaccine**	**N**	**GMC****	**Vaccine**	**N**	**GMC**
Anti-PT	dTpa	118	169	dTpa	445	144
	dTpa+HB	129	144	aP	149	191
Anti-FHA	dTpa	118	445	dTpa	446	328

	dTpa+HB	129	375	aP	149	349
Anti-PRN	dTpa	118	280	dTpa	446	279
	dTpa+HB	129	303	aP	149	191
Anti-FIM	dTpa	118	1033	dTpa	446	995
	dTpa+HB	129	1130	aP	149	1825

** All GMCs (Geometric Mean Concentrations) are in EU/mL

In TD9707, 244 adults (19 to 60 years of age) received ADACEL, while 126 received Td and aP, given separately, one month apart. The safety and immunogenicity profile of ADACEL was also shown to be comparable to that observed with a single booster dose of Td and aP in study TD9707.

The mechanism of protection from *B pertussis* disease is not well understood. In a pertussis efficacy trial conducted in Sweden between 1992 and 1995, primary immunisation with Sanofi Pasteur Limited's acellular pertussis infant DTaP formulation conferred a protective efficacy of 85% against typical pertussis disease (WHO definition). Although ADACEL contains only one quarter of the amount of pertussis toxoid present in this acellular pertussis infant DTaP formulation, the antibody responses to ADACEL were superior to those observed in the pertussis efficacy trial.

5.2 Pharmacokinetic properties

Not relevant.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

ADACEL contains aluminium phosphate, phenoxyethanol, formaldehyde, glutaraldehyde and water for injections as excipients.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months from date of manufacture.

6.4 Special precautions for storage

Store at 2º to 8ºC. REFRIGERATE. DO NOT FREEZE. Do not use after expiry date.

6.5 Nature and contents of container

ADACEL is supplied as a single dose (0.5 mL) in a 2 mL glass vial in packs containing 1 vial and in packs containing 5 vials (5's not currently marketed).

6.6 Special precautions for disposal

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7 MEDICINE SCHEDULE

Prescription Medicine

8 SPONSOR

Australia

sanofi-aventis australia pty ltd

Building D, 12-24 Talavera Road

Macquarie Park NSW 2113

Australia

Tel: 1800 829 468

New Zealand

sanofi-aventis new zealand pty ltd

Level 8

56 Cawley St

Ellerslie

Auckland

New Zealand

Tel: 0800 727 838

9 DATE OF FIRST APPROVAL

31 May 2007

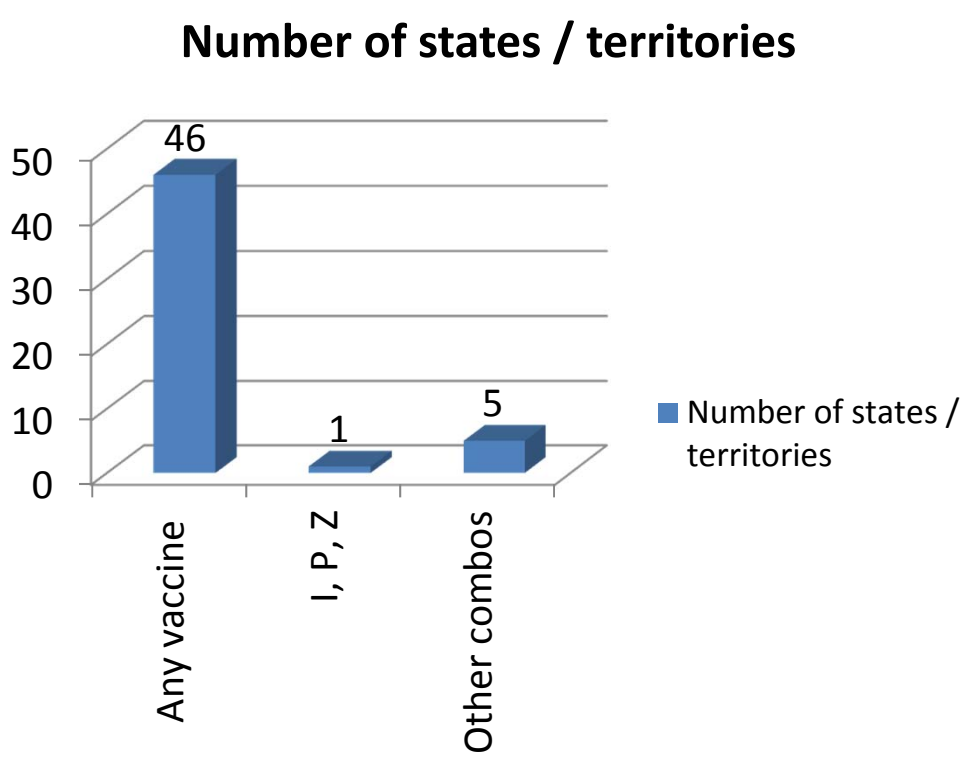
10 DATE OF REVISION OF THE TEXT

4 January 2017

Pharmacist Administered Vaccines

Types of Vaccines Authorized to Administer

Based upon APhA / NASPA Survey of State IZ Laws/ Rules



Any vaccine	**AL, AK*, AZ*, AR*, CA, CO, CT, DC*, DE*, GA*, HI*, ID,IL, IN*, IA, KS, KY*, LA*, MA, ME, MD, MO*, MI*, MN, MS, MT, NE, NV ,NJ*, NM, NC, ND, OK, OR, PA, PR*, RI, SC*, SD* TN, TX, UT*, VT, VA*, WA, WI**
Influenza, Pneumo and Zoster (I, P, Z)	NH
Other combos	FL, NY, OH**[will change to any 3/15/15], WV**, WY**

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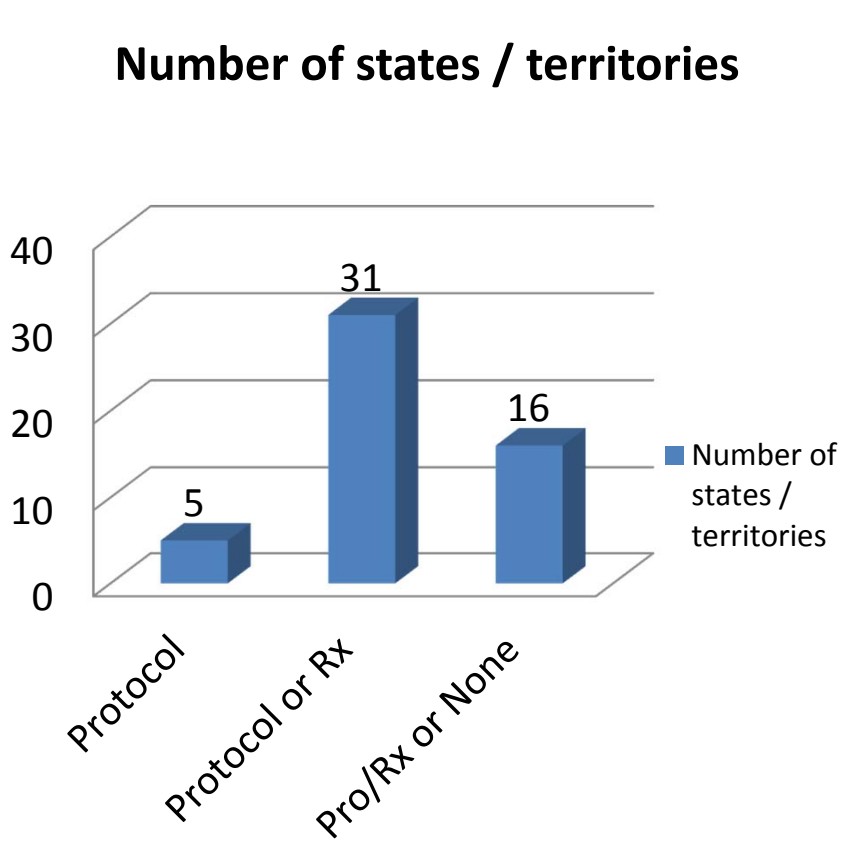
Updated January 31, 2015

* Via Rx for some; ** broad list of vaccines

Pharmacist Administered Vaccines
Prescriber issued protocols vs Rx

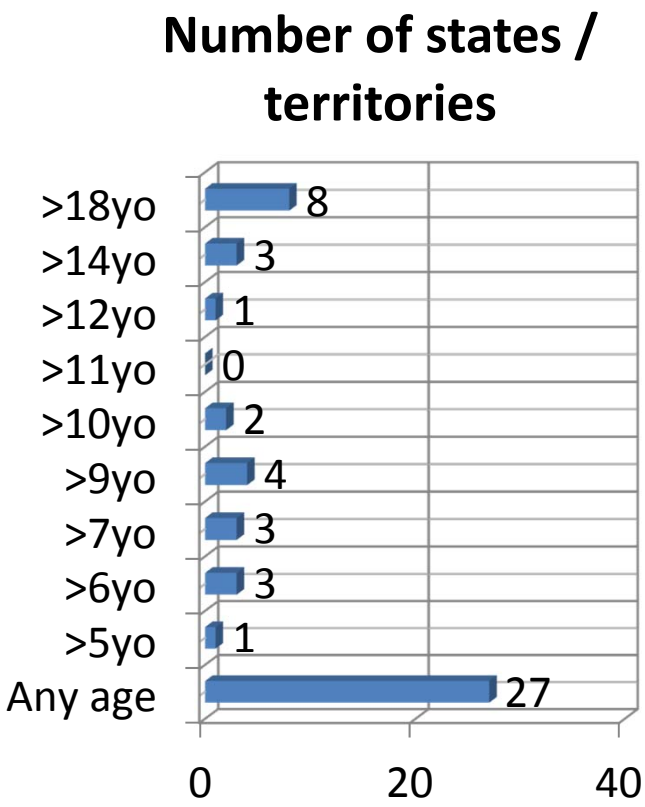
Based upon APhA / NASPA Survey of State IZ Laws/ Rules



Protocol	FL, KS, MN, NV, WI
Protocol **or** Rx (depending on age and/or vaccine)	AL, AK, AR, CO, CT, DC, DE, GA,HI, IL, IN, IA, KY, MA, MI, MS, MO, NE, NY, NC, ND OH, OK, PA, PR, RI, TN, TX, UT, VT, WA
Protocol/Rx **or** No Prescriber/Rx Needed (depending on age and/or vaccine)	AZ, CA, ID, LA, ME, MD, MT NH, NJ, NM, OR, SC, SD, VA, WV, WY

Pharmacist Administered Vaccines
Patient-Age Limitations

Based upon APhA / NASPA Survey of State IZ Laws/ Rules



≥18yo	**CT, FL,, MA, NY, PA, PR*, VT, WV**
≥14yo	**HI*, NC[L], OH*[will change 3/15/ 2015]**
≥12 yo	**MT***
≥10yo	**IL *,[L], MN[L],**
≥9yo	**DE, ME[L], MD*,[L], RI[L]**
≥7yo	**AR*,[L], NJ*,[L], WY[L]**
≥6yo	**AZ[L], KS[L], WI***
≥5yo	**ND[L]**
Any age	**AL, AK, CA,CO, DC*, GA*, ID*, IN*, IA*, KY*, LA*, MI, MS, MO, NE, NV, NH[L], NM, OK, OR*, SC*, SD*, TN, TX*, UT, VA*, WA**

* Scope varies

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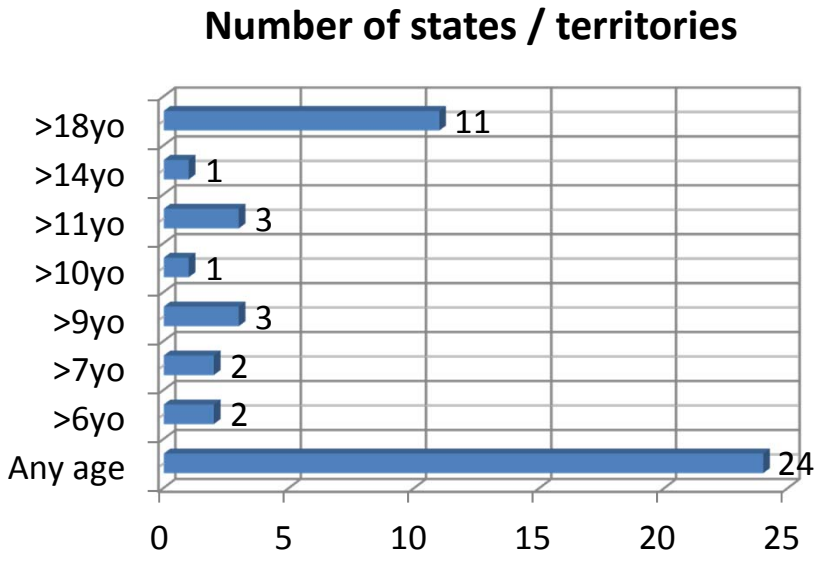
* Via Rx
[L] Limited to certain vaccines

Pharmacist Administered Vaccines
Patient-Age Limitations via RX

Based upon APhA / NASPA Survey of State IZ Laws/ Rules



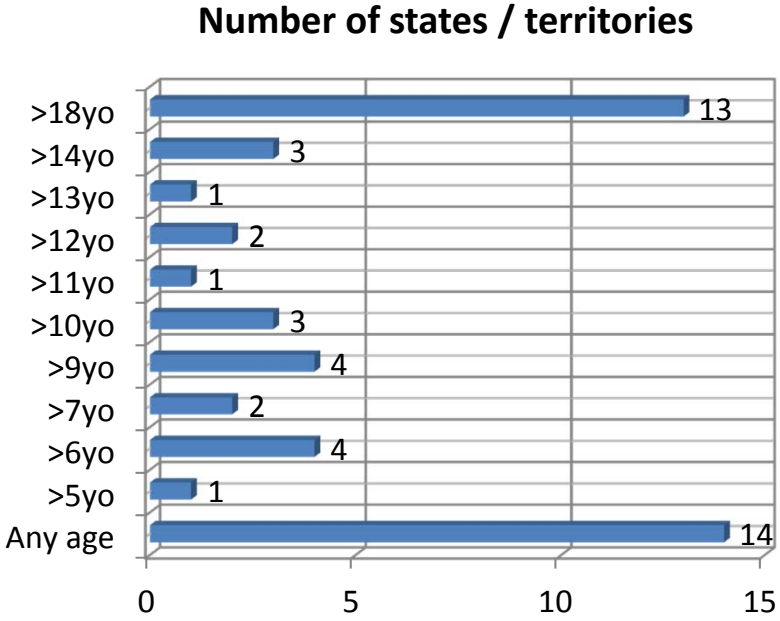
≥18yo	**CT, ME, MA, NY*, NC, PA, PR, SC, VT, WV, WY**
≥14yo	**HI*,**
≥11yo	**IN, MD*, ND**
≥10yo	**IL***
≥9yo	**DE, MD*, RI***
≥7yo	**AR, NJ***
≥6yo	**AZ, WI***
Any age	**AL, AK, CA, CO, DC, GA, ID, IN, IA, KY, LA, MI, MS MO, NE, OK, OR, SC, SD, TN, TX, UT, VA, WA,**

- Scope varies
- OH will be added age 7 on 3/15/2015

Pharmacist Administered Vaccines

Patient-Age Limitations via prescriber protocol

Based upon APhA / NASPA Survey of State IZ Laws/ Rules



≥18yo	CT, FL*, HI, ME, MA, MT*,NJ, NY*, PA,PR*, SC*, VT, VA
≥14yo	HI*, NC*, OH*[will change 3/15/15]
≥13yo	GA*
≥12yo	DC, MO*
≥11yo	IN
≥10yo	IL*, IN*, MN*
≥9yo	DE, KY*, ME*, RI*
≥7yo	AR, TX*
≥6yo	IA* , KS*, WI, VA*
≥5yo	ND*
Any age	AL, AK, CA, CO, MI, MS, MT, NE, NM, NV, OK, SD, TN, UT, WA

Pharmacist Administered Vaccines

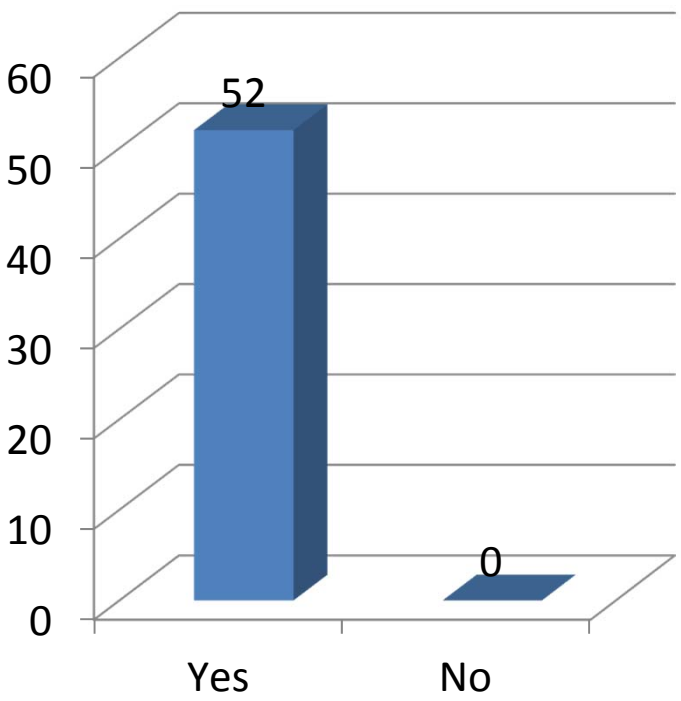
May student interns administer vaccines?

Based upon APhA / NASPA Survey of State IZ Laws/ Rules (effective January1, 2014)

Number of states / territories allowing	**44**
States / territories not authorized	8 (FL, MA, NH, NJ, NY, PA, PR, SC)
Criteria common among states	•Student must be trained (complete Certificate Training Program) • Operating under supervision of trained pharmacist

Pharmacist Administered Vaccines
Authority to Administer Pneumococcal Vaccine

Based upon APhA / NASPA Survey of State IZ Laws/ Rules



States	
Part B Vaccine	AL, AK*, AZ*, AR, CA, CO, CT, DC*, DE, FL, GA*, HI, IA, ID, IL, IN, KS, KY*, LA*, MA*, MD*, ME, MI, MN, MO, MS, MT**, NE, NH, NV , NJ, NM, NC, ND, NY, OH, OK, OR, PA, PR, RI, SC*, SD* TN, TX, UT, VT, VA, WA, WV, WI, WY***

*Via Rx / pt specific protocol for some
**Pneumococcal polysaccharide without an Rx; all other forms under protocol ***Pneumococcal polysaccharide only

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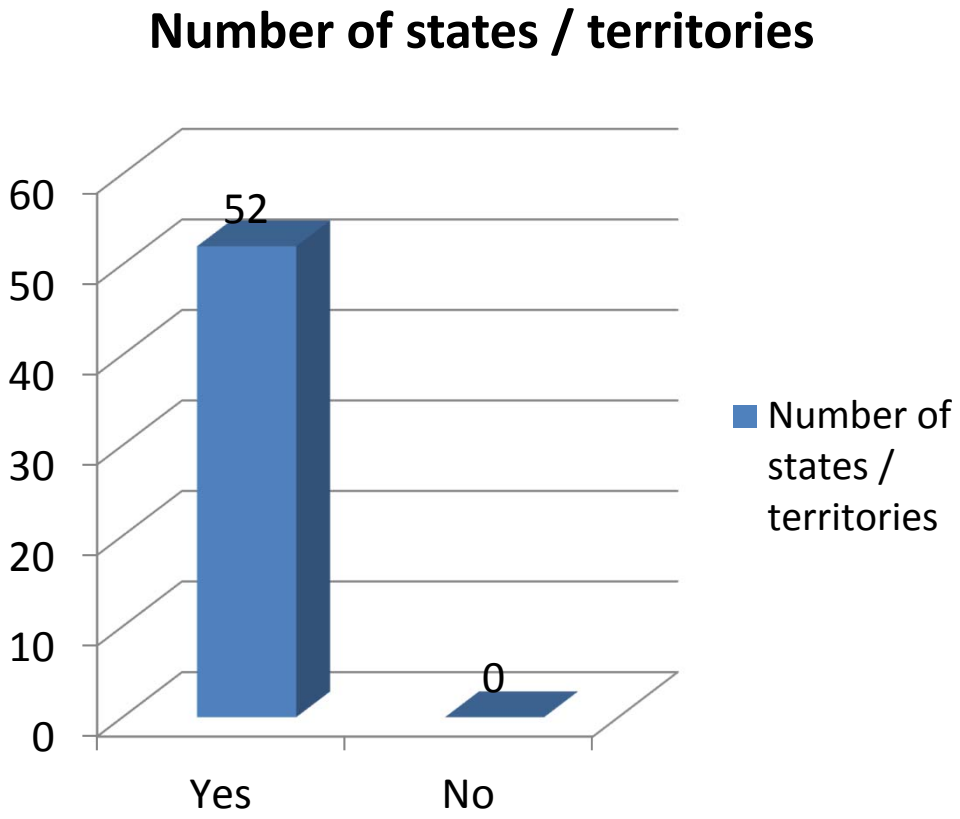
Pharmacist Administered Vaccines

Authority to Administer Zoster Vaccine

Based upon APhA / NASPA Survey of State IZ Laws/ Rules



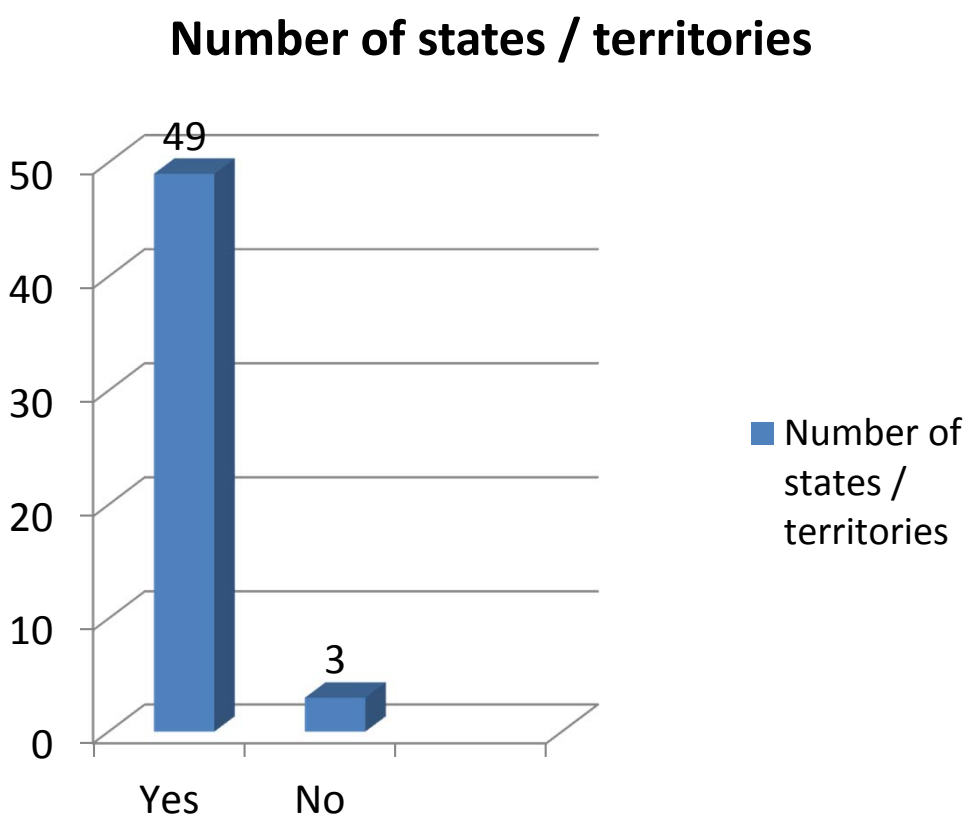
Yes	AL, AK, AZ, AR, CA, CO, CT, DC, DE, FL,GA*, HI, ID, IL, IN, IA , KS, KY, LA, MA, MD, ME, MI, MN, MO, MS, MT, NE, NH, NY* , NV ,NJ, NM, NC, ND, OH, OK, OR, PA, PR*, RI, SC*, SD, TN, ,TX, UT, VT, VA, WA, WI, WV, WY

*Via Rx only

Pharmacist Administered Vaccines

Authority to Administer Td / Tdap

Based upon APhA / NASPA Survey of State IZ Laws/ Rules



Yes	**AL, AK, AZ, AR, CA, CO, CT, DC, DE, GA*, HI, IA, ID, IL, IN, KS, KY, LA, MA, MD, ME, MI, MN, MO, MS, MT, NE, NV , NJ, NM, NC, ND, OH, OK, OR, PA, PR*, RI, SC*, SD, TN, TX, UT, VA,VT, WA, WI, WV, WY**
No	FL, NH, NY

*Via Rx only
Many have age restrictions

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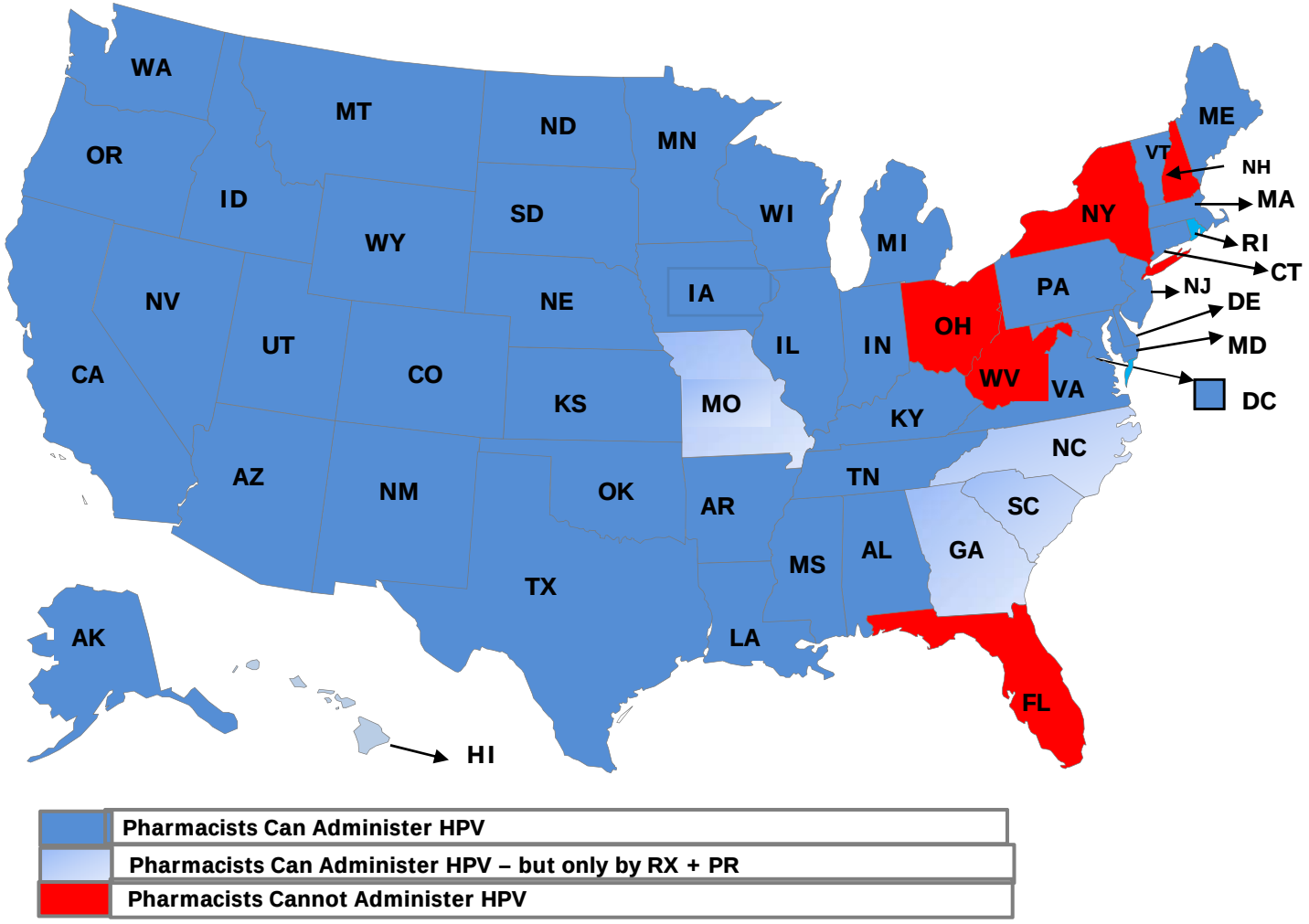
Pharmacist Administered Vaccines
Authority to Administer HPV Vaccine



Based upon APhA/NASPA Survey of State IZ Laws/ Rules Updated January 31,2015

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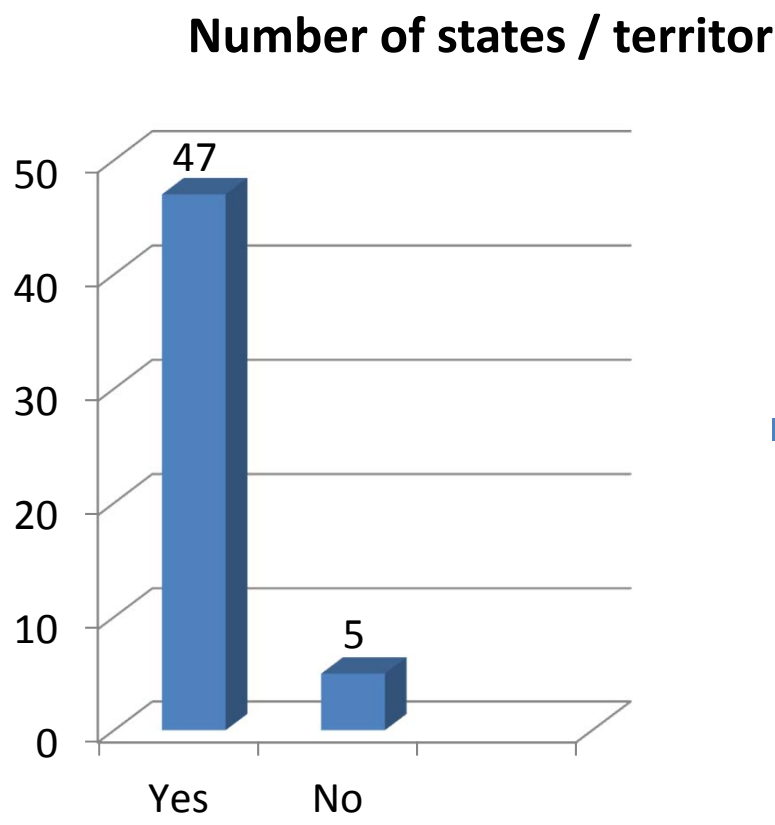
Pharmacist Administered Vaccines

Authority to Administer HPV

Based upon APhA / NASPA Survey of State IZ Laws/ Rules



Yes	AL , AK, AZ , AR, CA , CO , CT [A], DE, GA [R] , HI [A], ID, IL [A], ,IN , IA , KS [A] , KY, LA, ME [A], MD*, MA [A], MI, MN [A], MO, MS, MT, NE,NJ [A] , NH, NM, NC [A], ND , NV, OK, OR, PA [A], RI [A], PR [A, R], SC [R], SD ,TN, TX, UT, VT [A], VA, WA, WI, WY, DC
No	FL, NH, NY, OH*, WV

[R] Via Rx only
[A] Age limitation IF greater than 12 y.o, may require Rx
* OH will be a yes effective 3/15/15

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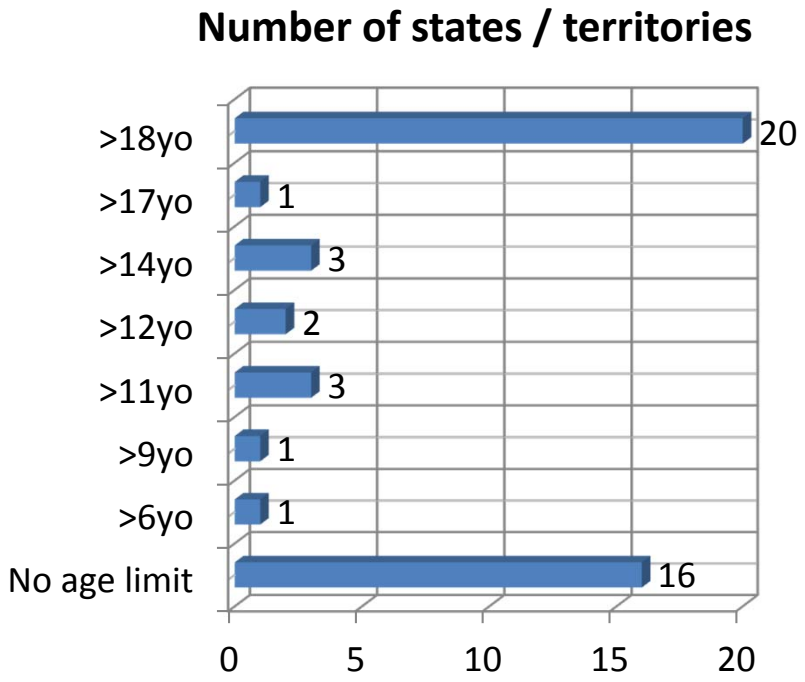
Pharmacist Administered Vaccines

Patient-Age Limitations – for HPV Vaccination

Based upon APhA / NASPA Survey of State IZ Laws/ Rules



>18yo	**AZ*, AR*,CT, HI, IA*, KS, ME, MD*, MA, MN, MT, NC[R], NJ,PA, PR[R], RI, SC[R], VA*, VT, WY**
>17yo	**LA***
>14yo	**IL, KY*, TX***
>12yo	**ID*, DC***
>11yo	**IN*, ND, OR***
>9yo	**DE**
>6yo	**WI**
No Age Limit	**AL, AK, CA, CO, GA[R] MI, MS, MO[R], NE, NV, NM ,OK, SD, TN, UT, WA**

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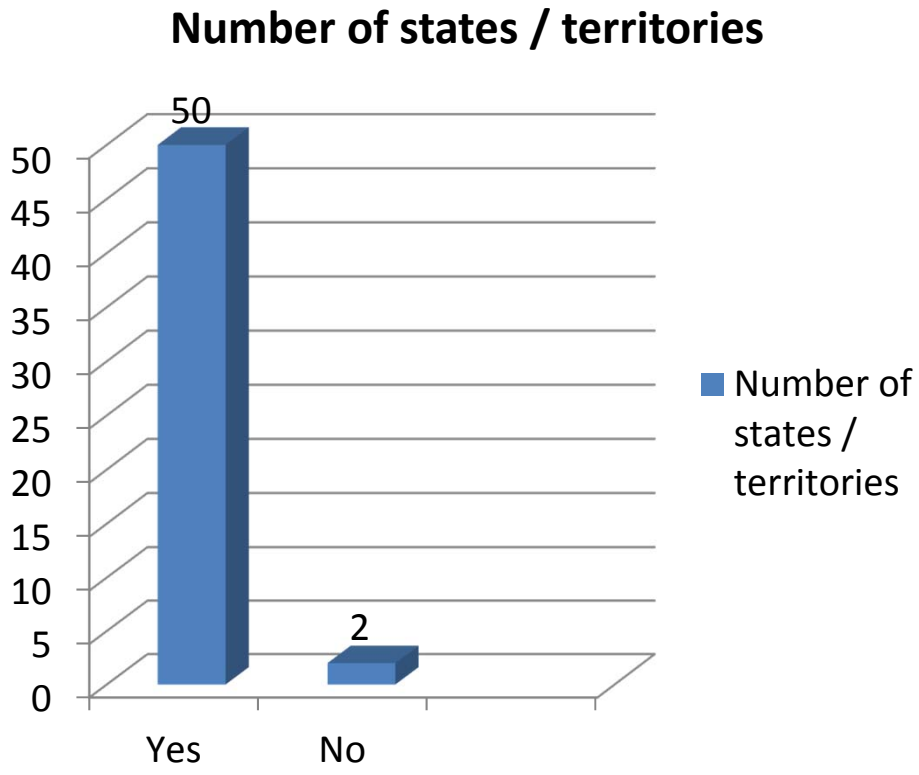
*Younger ages under prescription/protocol
[R] Requires a prescription

Pharmacist Administered Vaccines

Authority to Administer Meningococcal

Based upon APhA / NASPA Survey of State IZ Laws/ Rules



Yes	**AL, AK, AZ, AR, CA, CO, CT[A,*], DC, DE, FL[A] GA[R], HI[A] ID, IL[A], IA, IN, KS[A], KY, LA, ME[A], MA[A], MD, MI MN[A], MO, MS, MT, NC[A], ND, NE, NJ[A], NM, NY[A], NV, OH[A], OK, OR, PA[A], PR[R, A], RI[A], SC[R], SD, TN, TX, UT*, VT[A], VA, WA, WI, WY[A]**
No	NH, WV

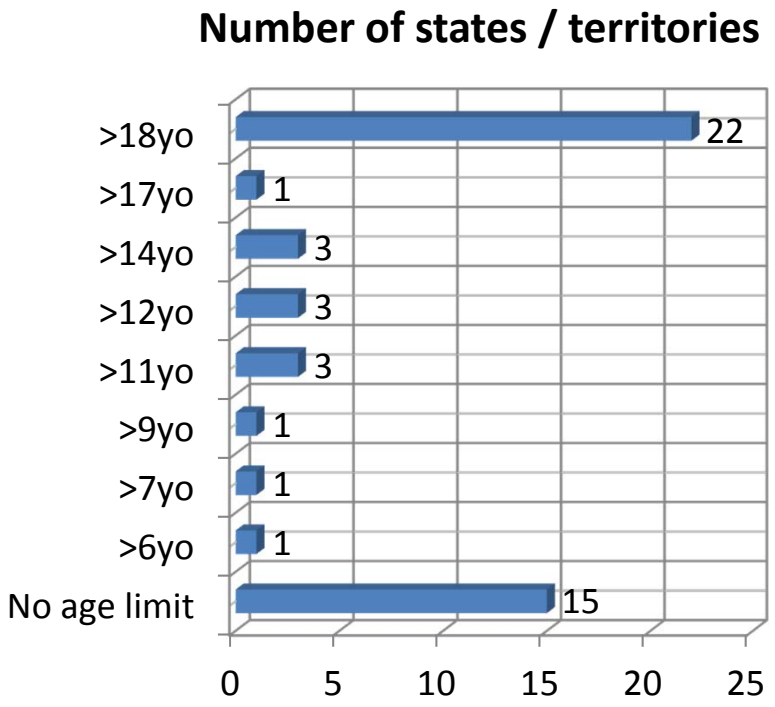
[R] Via Rx only

[A] Age limitation IF greater than 12 y.o,may require Rx

Pharmacist Administered Vaccines

Patient-Age Limitations – for Meningococcal

Based upon APhA / NASPA Survey of State IZ Laws/ Rules



>18yo	AZ*, CT, FL, HI, IA*, KS, ME, MD*, MA, MN, MT, NC, NJ, NY, OH, PA,RI, PR[R] ,SC[R] , VT, VA*, WY
>17yo	LA*
>14yo	IL, KY*, TX*
>12yo	DC, ID, MO*
>11yo	IN*, ND,OR*
>9yo	DE
>7yo	AR
>6yo	WI
No Age Limit	AL, AK, CA, CO, GA[R] , MI, MS, NE, NV NM, OK, SD, TN, UT, WA

*May allow for younger ages under prescription

[R] Via Rx only

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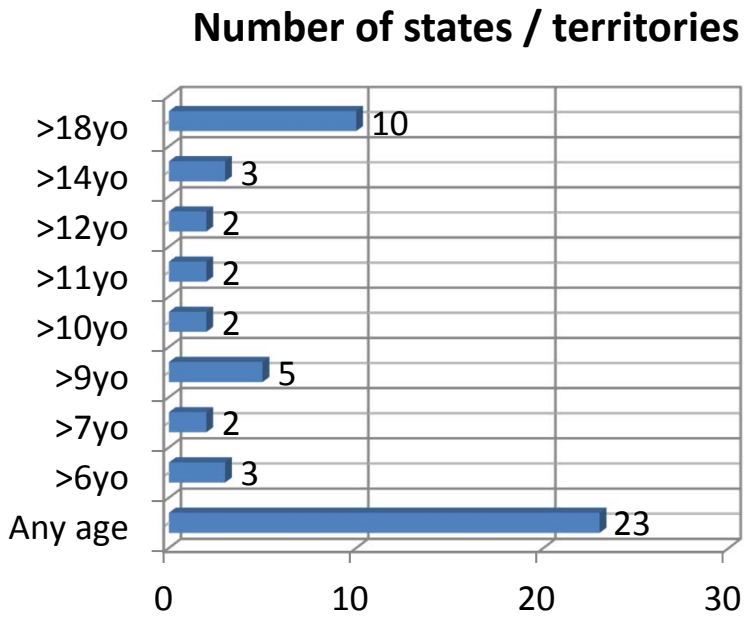
Pharmacist Administered Vaccines

Influenza - Age of Administration Authorized

by Any Provision

Based upon APhA / NASPA Survey of State IZ Laws/ Rules

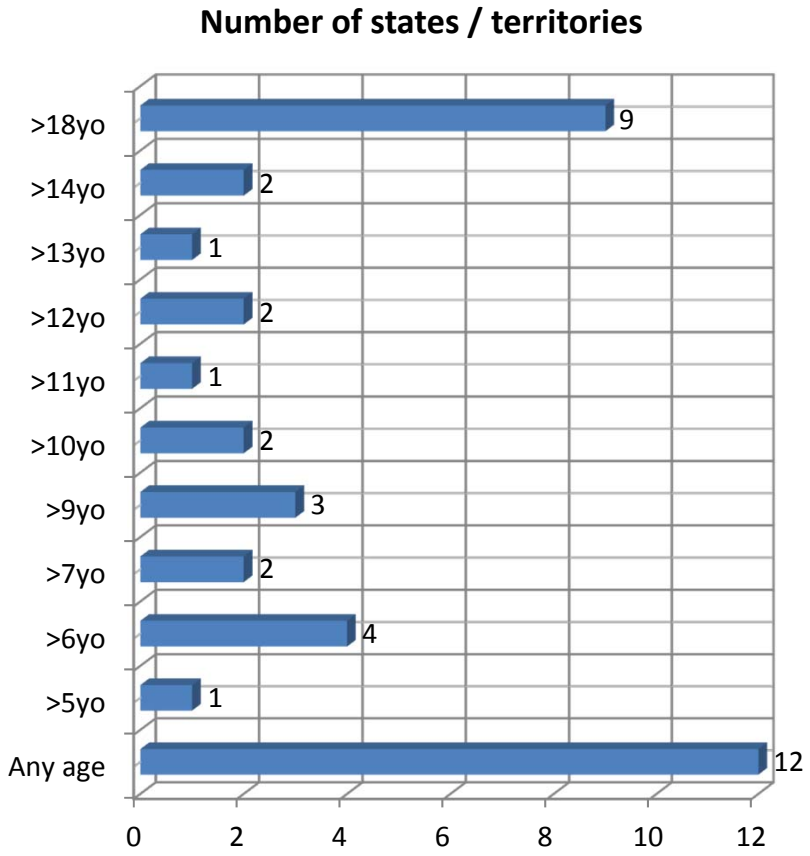


≥18yo	CT, FL, MA, NY, PA, PR, VT, WV
≥14yo	HI*,NC, OH
≥12yo	ID, MT
≥10yo	IL, MN
≥9yo	DE, ME, MD, RI
≥7yo	AR, WY
≥6yo	AZ, KS, NJ*, WI
≥5yo	ND
Any age	AL, AK, CA , CO, DC*, GA*,IN*, IA*, KY*, LA*, MI, MS, MO*, NE, NH, NM, NV, OK, OR*, SD, SC*, TN, TX*, UT, VA*, WA

Pharmacist Administered Vaccines

Influenza - Age of Adm Authorized by Protocol

Based upon APhA / NASPA Survey of State IZ Laws/ Rules

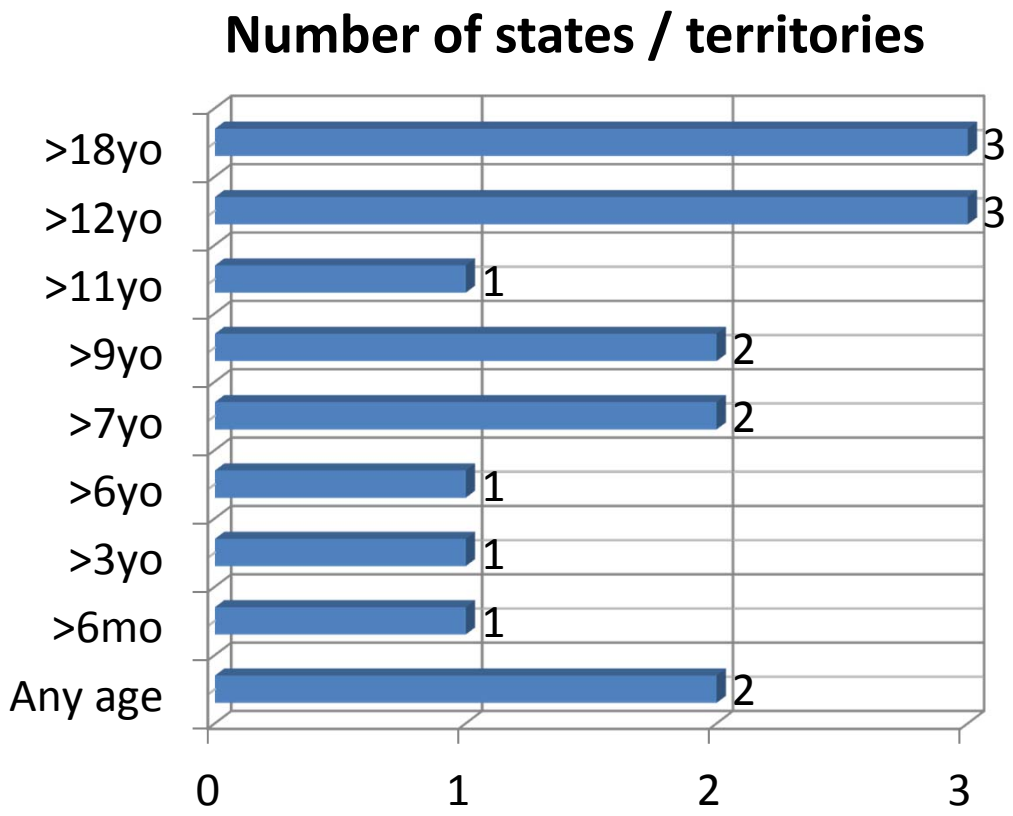


≥18yo	CT, FL, HI, MA, NJ, NY, PA, PR, VT
≥14yo	NC, OH
≥13yo	GA
≥12 yo	DC, MO
≥11yo	IN
≥10yo	IL, MN
≥9yo	DE, KY, RI
≥7yo	AR, TX
≥6yo	AZ, IA , KS, WI
≥5yo	ND
Any age	AL, AK,CA, CO,MI, MS, NE, NV, OK, SD,TN, UT, WA

Pharmacist Administered Vaccines

Influenza No MD protocol or Rx Needed

Based upon APhA / NASPA Survey of State IZ Laws/ Rules



≥18yo	SC, SD WV
≥12yo	ID, MT, NJ
≥11yo	OR
≥9yo	ME, MD
≥7yo	LA, WY
≥6yo	AZ
≥3yo	CA
≥6mo	VA
Any age	NH, NM,

Note: authority comes from statute and/or regulation from BOP or Public Health

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New Zealand Data Sheet

BOOSTRIX®

Combined diphtheria-tetanus-acellular pertussis (dTpa) vaccine

DESCRIPTION

BOOSTRIX dTpa vaccine is a sterile suspension which contains diphtheria toxoid, tetanus toxoid and three purified antigens of *Bordetella pertussis* [pertussis toxoid (PT), pertussis filamentous haemagglutinin (FHA) and pertussis 69 kilodalton (kDa) outer membrane protein (OMP)] adsorbed onto aluminium salts.

Qualitative and Quantitative Composition

Suspension for injection.

1 dose (0.5 ml) contains:

Diphtheria toxoid[1]	not less than 2 International Units (IU) (2.5 Lf)
Tetanus toxoid[1]	not less than 20 International Units (IU) (5 Lf)
Bordetella pertussis antigens	
Pertussis toxoid[1]	8 micrograms
Filamentous Haemagglutinin[1]	8 micrograms
Pertactin[1]	2.5 micrograms
[1] adsorbed on aluminium hydroxide, hydrated ($Al(OH)_3$)	0.3 milligrams Al^{3+}
and aluminium phosphate ($AlPO_4$)	0.2 milligrams Al^{3+}

The diphtheria toxoid, tetanus toxoid and acellular pertussis vaccine (dTpa) components are adsorbed on 0.5mg aluminium and suspended in isotonic sodium chloride.

Presentation

BOOSTRIX is a turbid white suspension for injection

CLINICAL PHARMACOLOGY

BOOSTRIX (dTpa vaccine), induces antibodies against all vaccine components.

Clinical Trials

Immune response results to the diphtheria, tetanus and acellular pertussis components in clinical studies are presented in the table below. Approximately one month following booster vaccination with BOOSTRIX, the following seroprotection / seropositivity rates were observed:

Antigen	Seroprotection / Seropositivity	Adults and adolescents from the age of 10 years onwards, at least 1690 subjects (% vaccinees)	Children from 4 to 9 years of age, at least 415 subjects (% vaccinees)
Diphtheria	≥ 0.1 IU/ml*	97.2%	99.8%
Tetanus	≥ 0.1 IU/ml*	99.0%	100.0%
Pertussis: - Pertussis toxoid - Filamentous haemagglutinin - Pertactin	 ≥ 5 EL.U/ml ≥ 5 EL.U/ml ≥ 5 EL.U/ml	 97.8% 99.9% 99.4%	 99.0% 100.0% 99.8%

*cut-off accepted as indicative of protection

Results of the comparative studies with commercial dT vaccines indicates that the degree and duration of protection would not be different from those obtained with these vaccines.

Protective efficacy of pertussis

There is currently no correlate of protection defined for pertussis; however, the protective efficacy of GlaxoSmithKline Biologicals' DTPa (INFANRIX) vaccine against WHO-defined typical pertussis (≥ 21 days of paroxysmal cough with laboratory confirmation) was demonstrated in the following 3-dose primary studies:

- a prospective blinded household contact study performed in Germany (3, 4, 5 months schedule) based on data collected from secondary contacts in households where there was an index case with typical pertussis, the protective efficacy of the vaccine was 88.7%. Protection against laboratory confirmed mild disease, defined as 14 days or more of cough of any type was 73% and 67% when defined as 7 days or more of cough of any type; and

- an NIH sponsored efficacy study performed in Italy (2, 4, 6 months schedule).The vaccine efficacy was found to be 84%. When the definition of pertussis was expanded to include clinically milder cases with respect to type and duration of cough, the efficacy of INFANRIX™ was calculated to be 71% against >7 days of any cough and 73% against >14 days of any cough.
  In a follow-up of the same cohort, the efficacy was confirmed up to 5 years after completion of primary vaccination without administration of a booster dose of pertussis.
  The study assessed duration of protection of Infanrix given in a 3 dose schedule to infants. A similar duration of protection cannot be assumed to apply to older children or adults given a single dose of BOOSTRIX, regardless of previous vaccination against pertussis.

Although the protective efficacy of BOOSTRIX has not been demonstrated in adolescents and adult age groups, vaccinees in these age groups who received BOOSTRIX achieved anti-pertussis antibody titres greater than those in the German household contact study where the protective efficacy of INFANRIX was 88.7%.

There are currently no data which demonstrate a reduction of transmission of pertussis after immunisation with BOOSTRIX. However, it could be expected that immunisation of immediate close contacts of newborn infants, such as parents, grandparents healthcare workers and childcare workers would reduce exposure of pertussis to infants not yet adequately protected through immunisation.

Persistence of immunity to diphtheria, tetanus and pertussis after vaccination with BOOSTRIX in children, adolescents and adults

The following seroprotection / seropositivity rates were observed 3 to 3.5 years, 5 to 6 years and 10 years following vaccination with BOOSTRIX:

Antigen	Seroprotection/ seropositivity	Adults and adolescents from the age of 10 years onwards (% vaccinees)						Children from the age of 4 years onwards (% vaccinees)	
		3-3.5 years persistence		5 years persistence		10 years persistence		3-3.5 years persistence	5 to 6 years persistence
		Adult	Adole-scent	Adult	Adole-scent	Adult	Adole-scent		
Diphtheria	≥ 0.1 IU/ml*	71.2%	91.6%	84.1%	86.8%	64.6%	82.4%	97.5 %	94.2 %
	≥ 0.016 IU/ml*	97.4%	100%	94.4%	99.2%	89.9%	98.6%	100 %	Not determined
Tetanus	≥ 0.1 IU/ml	94.8%	100%	96.2%	100%	95.0%	97.3%	98.4 %	98.5 %
Pertussis									
Pertussis toxoid	≥ 5 EL.U/ml	90.6%	81.6%	89.5%	76.8%	85.6%	61.3%	58.7 %	51.5 %
Filamentous haemagglutinin		100%	100%	100%	100%	99.4%	100%	100 %	100 %
Pertactin		94.8%	99.2%	95.0%	98.1%	95.0%	96.0%	99.2 %	100 %

* Percentage of subjects with antibody concentrations associated with protection against disease (≥ 0.1 IU/ml by ELISA assay or ≥ 0.016 IU/ml by an in-vitro Vero-cell neutralisation assay).

BOOSTRIX administered in subjects ≥40 years of age with an incomplete, unknown or no history of a primary series of diphtheria and tetanus toxoid vaccination history induced an antibody response against pertussis in more than 98.5% of adults and provided seroprotection against diphtheria and tetanus in 81.5% and 93.4% of adults respectively.

Two subsequent doses maximised the vaccine response against diphtheria and tetanus when administered at one and six months (99.3% and 100% respectively).

Vaccination with second dose of BOOSTRIX

The immunogenicity of BOOSTRIX, administered 10 years after a previous booster dose with BOOSTRIX or reduced-antigen content diphtheria, tetanus and acellular pertussis vaccines has been evaluated in adults. One month after the decennial BOOSTRIX dose, ≥99 % of subjects were seroprotected against diphtheria and tetanus and all were seropositive for antibodies against pertussis antigens PT, FHA and PRN.

INDICATIONS

BOOSTRIX is indicated for booster vaccination against diphtheria, tetanus and pertussis of individuals aged four years and older.

CONTRAINDICATIONS

BOOSTRIX should not be administered to subjects with known hypersensitivity to any component of the vaccine, or to subjects having shown signs of hypersensitivity after previous administration of diphtheria, tetanus or pertussis vaccines.

As with other vaccines, the administration of BOOSTRIX should be postponed in subjects suffering from acute severe febrile illness. The presence of a minor infection, however, is not a contraindication.

BOOSTRIX is contra-indicated if the subject has experienced an encephalopathy of unknown aetiology, occurring within 7 days following previous vaccination with pertussis-containing vaccine. In these circumstances, pertussis vaccination should be discontinued and the vaccination course should be continued with diphtheria and tetanus vaccines.

BOOSTRIX should not be administered to subjects who have experienced transient thrombocytopenia or neurological complications following an earlier immunisation against diphtheria and/or tetanus (for convulsions or hypotonic-hyporesponsive episodes, see PRECAUTIONS).

WARNINGS AND PRECAUTIONS

BOOSTRIX should under no circumstances be administered intravenously.

It is good clinical practice that immunisation should be preceded by a review of the medical history (especially with regard to previous immunisation and possible occurrence of undesirable events) and a clinical examination.

If any of the following events have occurred in temporal relation to receipt of pertussis containing vaccines, the decision to give doses of pertussis containing vaccines, should be carefully considered. There may be circumstances, such as a high incidence of pertussis, when the potential benefits outweigh possible risks, particularly since these events are not associated with permanent sequelae.

- Temperature of ≥40.0°C within 48 hours of vaccination, not due to another identifiable cause.
- Collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours of vaccination.

- Persistent, inconsolable crying lasting ≥3 hours, occurring within 48 hours of vaccination.
- Convulsions with or without fever, occurring within 3 days of vaccination.

In children with progressive neurological disorders, including infantile spasms, uncontrolled epilepsy or progressive encephalopathy, it is better to defer pertussis (Pa or Pw) immunisation until the condition is corrected or stable. However, the decision to give pertussis vaccine must be made on an individual basis after careful consideration of the risks and benefits.

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of rare anaphylactic reactions following the administration of the vaccine.

BOOSTRIX should be administered with caution to subjects with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these subjects. Firm pressure should be applied to the injection site (without rubbing) for at least two minutes.

A history or a family history of convulsions and a family history of an adverse event following DTP vaccination do not constitute contra-indications.

Human Immunodeficiency Virus (HIV) infection is not considered a contraindication for diphtheria, tetanus and pertussis (whole-cell or acellular) immunisation. However in patients with immunodeficiency or in patients receiving immunosuppressive therapy, an adequate immunologic response may not be achieved. In these patients, when tetanus vaccine is needed for tetanus prone wound, plain tetanus vaccine should be used.

Extremely rare cases of collapse or shock-like state (hypotonic-hyporesponsiveness episode) and convulsions within 2 to 3 days of vaccination have been reported in DTPa and DTPa combination vaccines.

Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. It is important that procedures are in place to avoid injury from faints.

As with any vaccine, a protective immune response may not be elicited in all vaccinees.

Interactions

Concomitant use with other inactivated vaccines and with immunoglobulin is unlikely to result in interference with the immune responses.

When considered necessary, BOOSTRIX can be administered simultaneously with other vaccines or immunoglobulins.
If BOOSTRIX is to be given at the same time as another injectable vaccine or immunoglobulin, the products should always be administered at different sites.

BOOSTRIX must not be mixed with other vaccines.

Effects on fertility
No human data available. Non-clinical data obtained with BOOSTRIX reveal no specific hazard for humans based on conventional studies of female fertility in rats and rabbits.

Use In Pregnancy (Category B1)
Safety data from a prospective observational study where BOOSTRIX was administered to pregnant women during the third trimester (793 pregnancy outcomes) as well as data from post-marketing surveillance where pregnant women were exposed to BOOSTRIX or to BOOSTRIX-IPV (dTpa-inactivated poliovirus vaccine) indicate no vaccine related adverse effect on pregnancy or on the health of the foetus/newborn child.

The use of BOOSTRIX may be considered during the third trimester of pregnancy.

Human data from prospective clinical studies on the use of BOOSTRIX during the first and second trimester of pregnancy are not available.

Limited data indicate that maternal antibodies may reduce the magnitude of the immune response to some vaccines in infants born from mothers vaccinated with BOOSTRIX during pregnancy. The clinical relevance of this observation is unknown.

Non-clinical data obtained with BOOSTRIX reveal no specific hazard for humans based on conventional studies of embryo-foetal development in rats and rabbits, and also of parturition and postnatal toxicity in rats (up to the end of the lactation period).

BOOSTRIX may be used during pregnancy when the possible advantages outweigh the possible risks for the foetus. When protection against tetanus is sought, consideration should be given to tetanus or combined diphtheria-tetanus vaccines.

Use In Lactation

The safety of BOOSTRIX when administered to breast-feeding women has not been evaluated.

It is unknown whether BOOSTRIX is excreted in human breast milk.

BOOSTRIX should only be used during breast-feeding when the possible advantages outweigh the potential risks.

Effects on the ability to drive and use machines
The vaccine is unlikely to produce an effect on the ability to drive and use machines.

ADVERSE EFFECTS

Clinical Trials

The safety profile below is based on data from clinical trials where BOOSTRIX was administered to 839 children (from 4 to 9 years of age) and 1931 adults, adolescents and children (above 10 years of age).

Adverse reactions reported are listed according to the following frequency:

Very common: ≥1/10
Common: ≥1/100 and <1/10
Uncommon: ≥1/1000 and <1/100
Rare: ≥1/10,000 and <1/1000
Very rare: <1/10,000

Children from 4 to 9 years of age

Infections and infestations

Uncommon: upper respiratory tract infection

Metabolism and nutrition disorders

Common: anorexia

Psychiatric disorders

Very common: irritability

Nervous system disorders

Very common: somnolence
Common: headache
Uncommon: disturbances in attention

Eye disorders

Uncommon: conjunctivitis

Gastrointestinal disorders

Common: diarrhoea, vomiting, gastrointestinal disorders

Skin and subcutaneous tissue disorders

Uncommon: rash

General disorders and administration site conditions

Very common: injection site reactions (including pain, redness and swelling), fatigue
Common: fever ≥ 37.5 °C (including fever > 39 °C),
Uncommon: other injection site reactions (such as induration), pain

Adults, adolescents and children from the age of 10 years onwards

Infections and infestations

Uncommon: upper respiratory tract infection, pharyngitis

Blood and lymphatic system disorders

Uncommon: lymphadenopathy

Nervous system disorders

Very common: headache
Common: dizziness
Uncommon: syncope

Respiratory, thoracic and mediastinal disorders

Uncommon: cough

Gastrointestinal disorders

Common: nausea, gastrointestinal disorders
Uncommon: diarrhoea, vomiting

Skin and subcutaneous tissue disorders

Uncommon: hyperhidrosis, pruritus, rash

Musculoskeletal and connective tissue disorders

Uncommon: arthralgia, myalgia, joint stiffness, musculoskeletal stiffness

General disorders and administration site conditions

Very common: injection site reactions (including pain, redness and swelling), fatigue, malaise
Common: fever ≥ 37.5 °C, injection site reactions (such as injection site mass and injection site abscess sterile)
Uncommon: fever > 39 °C, influenza like illness, pain

Post-marketing experience

Blood and lymphatic system disorders

Rare: angioedema

Immune system disorders

Very rare: allergic reactions, including anaphylactic and anaphylactoid reactions

Nervous system disorders

Rare: convulsions (with or without fever)

Skin and subcutaneous tissue disorders

Rare: urticaria

General disorders and administration site conditions

Rare: extensive swelling of the vaccinated limb, asthenia

Data on 146 subjects suggest a small increase in local reactogenicity (pain, redness, swelling) with repeated vaccination according to a 0, 1, 6 months schedule in adults (> 40 years of age).

Subjects fully primed with 4 doses of DTPw followed by a BOOSTRIX dose around 10 years of age show an increase of local reactogenicity after an additional BOOSTRIX dose administered 10 years later.

DOSAGE AND ADMINISTRATION

All parenteral drug and vaccine products should be inspected visually for any particulate matter or discolouration prior to administration. Before use of BOOSTRIX, the vaccine should be well shaken to obtain a homogenous turbid suspension. Discard the vaccine if it appears otherwise.

Dosage

Each dose consists of a 0.5mL ready to use sterile suspension.

Administration

BOOSTRIX is administered by deep intramuscular injection, preferably in the deltoid region. THE VACCINE SHOULD NEVER BE ADMINISTERED INTRAVENOUSLY.

This product is for use by one patient on a single occasion. Any unused product or waste material should be disposed of in accordance with local requirements.

Immunisation Schedule

BOOSTRIX can be given in accordance with the current local medical practices for booster vaccination with adult-type combined diphtheria-tetanus vaccine, when a booster against pertussis is desired.

Repeat vaccination against diphtheria, tetanus and pertussis should be performed at intervals as per official recommendations (generally 10 years).

BOOSTRIX can be used in the management of tetanus prone injuries in persons who have previously received a primary vaccination series of tetanus toxoid vaccine. Tetanus immunoglobulin should be administered concomitantly in accordance with official recommendations.

OVERDOSAGE

Cases of overdose have been reported during post-marketing surveillance. Adverse events following overdosage, when reported, were similar to those reported with normal vaccine administration.

FURTHER INFORMATION

Excipients

Aluminium hydroxide, aluminium phosphate, sodium chloride and water for injections.

Residues

Formaldehyde, polysorbate 80 and glycine.

SPECIAL PRECAUTIONS FOR STORAGE

BOOSTRIX should be stored at +2°C and +8°C. DO NOT FREEZE. Discard if vaccine has been frozen. The expiry date of the vaccine is indicated on the label and packaging.

PRESENTATIONS

BOOSTRIX is presented as a turbid white suspension in a glass prefilled syringe. Upon storage a white deposit and clear supernatant can be observed.
This is a normal finding .

The prefilled syringes are made of neutral glass type I, which conforms to European Pharmacopoeia Requirements.

BOOSTRIX is presented in single dose packs of 1 or 10.

MEDICINE SCHEDULE

Prescription Only Medicine

SPONSOR DETAILS

GlaxoSmithKline NZ Ltd

Private Bag 106600
Downtown
Auckland
NEW ZEALAND

ph (09) 367 2900
fax (09) 367 2910

DATE OF PREPARATION: 3 May 2016

Version 7.0

Private Bag 3200
Hamilton 3240

1 November 2016

To: PHOs, GPs, Practice Nurses, Midwives, Lead Maternity Carers and other health professionals who work in the wider maternity sector

ANNOUNCEMENT: Free Pertussis vaccinations for pregnant women at selected pharmacies in the Waikato.

Waikato DHB is pleased to announce that selected community pharmacies in the Waikato region will start to offer free pertussis (whooping cough) vaccination to pregnant women from 1 November 2016. It is a New Zealand first and allows another avenue for pregnant women to have the vaccination, which is also available to them free at GPs and Health Centres.

Currently only around 20 per cent of pregnant women receive pertussis vaccination in the latter stages of pregnancy which exposes our newborn infants to significant risk should they come into contact with this serious illness. Recent information confirms that numbers of pertussis cases in the Waikato region amongst adults are again on the rise.

This initiative significantly improves access and choice for pregnant women around pertussis vaccination and we will be monitoring whether vaccination rates increase.

All pertussis vaccinations given by pharmacies to pregnant women will be entered into the national immunisations register ensuring general practices are kept informed when their patients receive a vaccination.

Increasing rates of pertussis vaccination for pregnant women is a key area for Waikato's Maternity Quality and Safety Programme.

A recent report from the Child and Youth Mortality Committee has highlighted the impact of pertussis on infants too young to have gained protection from their own vaccinations[1]. Both mortality and morbidity rates are highest for those aged less than 3 months with seven of the eight deaths reported occurring in this age range.

This reinforces the importance of maternal booster doses of Boostrix vaccine (Tdap) in the third trimester of pregnancy to protect both mother and child. Pertussis vaccine is both safe and effective, and now funded, for women at 28-38 weeks gestation[2].

It is important that all health professionals are aware of this and support and enable pregnant women to receive this free vaccine. This is particularly important for Maori and Pacific women as the mortality and morbidity rates are highest among Maori and Pacific infants.

1. Mortality and morbidity of pertussis in children and young people in New Zealand. Child and Youth Mortality Review Committee, 2015
2. Immunisation Handbook 2014, Ministry of Health, 2014

Free pertussis vaccinations are available at the following pharmacies:

https://www.midcpg.co.nz/

We encourage health professionals who work in the maternity sector to pass on this information.

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Clinical Director Primary and Integrated Care
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Immunisation for Pregnant Women

Audience research with pregnant women

Prepared for the Ministry of Health

28 July 2015

Contents

Preface

This report was prepared for the Ministry of Health by Sally Duckworth, Litmus.

Litmus acknowledges Lisa Davies and Neralee Mahuika (Kaipuke) and Catherine Poutasi, Odette Frost-Kruse and Analosa Veukiso-Ulugia (Integrity Professionals) for contributing to fieldwork and analysis, and peer reviewing this report.

Litmus also acknowledges the guidance and support received from Bonnie Jones and Diana Murfitt (Immunisation Team, Ministry of Health), Dr Nikki Turner (Immunisation Advisory Centre), Joan Carll (Registered Midwife), and the New Zealand College of Midwives.

Finally, Litmus acknowledges the women and providers who contributed their perspectives, insights and time to the research.

If you have any questions about this report, please contact Sally Duckworth, Sally@litmus.co.nz.

1. Executive Summary

This report summarises 59 pregnant women and women who have given birth in the last 12 months' beliefs about immunisation in pregnancy, their motivations and enabling factors to immunise and the barriers to immunise in pregnancy. The research was conducted between February and April 2015. The overall goal of the research was to target segments and tailor communications and interventions to raise the uptake of vaccines during pregnancy.

Key findings

Pregnant women's beliefs about immunisation in pregnancy

Most women are confident immunising their infants and themselves when they are not pregnant (e.g. tetanus and travel vaccinations). However, they feel less comfortable immunising themselves when they are pregnant. Women's confidence to immunise stems from a range of beliefs about their vulnerability to infection, the severity of infection and the benefits of immunisation. Women are concerned about the safety of immunisation for their unborn baby.

Pregnant women's motivations to immunise in pregnancy

Pregnant women's motivations to immunise against influenza and whooping cough would be to protect their unborn babies from the consequences of severe infection and give them the best possible start in life. Pregnant women are less motivated to protect themselves from infection, unless they are asthmatic and see immunisation as being important for their health and wellbeing.

Pregnant women's awareness of immunisation entitlement

Most women's key point of contact for pregnancy-related information and advice is from their Lead Maternity Carer (LMC). The quality of the information and advice given by LMCs to pregnant women on the availability of free immunisations against influenza and whooping cough is variable.

Approximately one half of women say they had a conversation with their LMC about immunisation against influenza and/or whooping cough. Women more likely to recall having had a conversation about immunisation in pregnancy with their LMC are Pākehā.

Women are more likely to be motivated to immunise against influenza and/or whooping cough if their LMC recommends it as being important for protecting their unborn babies. Had they known they could be immunised in pregnancy and it was recommended and safe for their unborn child, most women were likely to have opted to be immunised.

Most pregnant women say they went infrequently to their general practice during pregnancy for their own health needs and therefore had few opportunities to receive information about immunisation from their general practice.

Pregnant women's access to immunisation

The pathway for pregnant women receiving immunisation is not convenient and women face many barriers accessing immunisation through their general practice. Māori and Pacific pregnant women face more barriers to accessing immunisation through their general practice than Pākehā pregnant women. These barriers include transportation, arranging childcare and time off work. Some women are also reluctant to visit their general practice, if they owe money for consultations and prescriptions.

There is a strong preference amongst pregnant women for LMCs to deliver immunisations within routine antenatal appointments. Women who went to their general practice to be immunised said they would have found the process more convenient if their LMC could have administered the vaccination.

Free immunisation for pregnant women is a significant enabler, particularly for Māori and Pacific women.

Immunisation messages

Messages that talk about immunisation protecting unborn babies from the consequences of infection are more persuasive than messages that talk about immunisation being effective at protecting the woman. Messages that say immunisation is safe in pregnancy provide reassurance. However, generic vaccine safety messages are not compelling, and cause concern. Messages that say influenza is serious for unborn babies make pregnant women take notice. Messages that say immunisation is free for pregnant women resonate strongly with Māori and Pacific women.

Communicating immunisation content

Most pregnancy-related information provided by LMCs, general practices, and antenatal educators to pregnant women is in print format (pamphlets, fact sheets and posters), and pregnant women feel overwhelmed by the amount of print material they receive. There is a general feeling amongst pregnant women that reaching them with pregnancy and health information almost exclusively through print is an outmoded form of communication.

Most women are accessing information online to support and complement the verbal information they receive from their LMC or in place of pamphlets. They are also using social media for pregnancy and child-related health information. For Māori and Pacific women in particular, social media is a less intimidating channel for receiving information and asking questions, and provides an opportunity for receiving and sharing information in more interactive ways (e.g. photos, videos, and stories).

Provider perspectives

A small number of providers (community midwives, hospital midwives, general practice nurses, and antenatal educators) were interviewed as part of the main study to understand provider perspectives on pregnant women's attitudes to immunisation, and the enablers and barriers to immunisation. These discussions suggest that with the exception of general practice nurses, providers often do not feel informed, confident, or comfortable informing and discussing immunisation against influenza and whooping cough with women, and therefore many women are missing out on important information. Providers also support pregnant women's views that immunisation delivered outside of antenatal appointments is not convenient for women.

Conclusions

The findings from this research conclude that the most significant barrier to immunisation uptake in pregnancy is a lack of accessible information and advice on immunisation from LMCs and structural barriers for accessing services through general practices.

The research found that Māori and Pacific pregnant women face more barriers to immunisation in pregnancy than Pākehā pregnant women. They are less likely to receive effective immunisation information from their LMCs, and face more barriers accessing immunisation through general practices. The challenges the researchers had finding Māori and Pacific pregnant women who had immunised for this research also indicates that actual immunisation uptake is low for Māori and Pacific pregnant women. Therefore the research concludes that segments that need to be targeted are Māori and Pacific pregnant women and LMCs who work with these women.

The findings from the research conclude that persuasive messages that talk about immunisation protecting unborn babies from the consequences of infection are persuasive. Messages that say immunisation is safe in pregnancy provide reassurance to pregnant women who are concerned about the safety of vaccines for their unborn babies. Messages that say influenza is serious for unborn babies make pregnant women who do not consider influenza serious to take notice. Messages that say immunisation is free for pregnant women resonate particularly strongly with Māori and Pacific pregnant women.

The findings from this research also conclude that traditional print media is not cutting through to all pregnant women and social media tools need to be considered for sharing relevant immunisation content.

2. Background

Influenza and whooping cough

Influenza circulates in New Zealand seasonally each year. Pregnant women and their babies are at increased risk of severe disease and complications from influenza. Pregnant women are up to 18 times more likely to go to hospital because of problems from getting sick with influenza than non-pregnant women[1]. Women who catch influenza when they are pregnant have higher rates of pregnancy complications, such as premature birth, still birth and poor baby growth during pregnancy[2].

Whooping cough epidemics occur in New Zealand every three to five years[3]. If a baby gets whooping cough it can cause severe, prolonged attacks and lead to serious problems, including pneumonia and brain damage. Babies can catch whooping cough from their parents or older siblings. Babies are not fully protected against whooping cough until they have had the first three immunisations. Pregnant women who are immunised against whooping cough can help protect their babies through passing on some of their immunity to their babies[4].

Pregnant women have been able to access fully funded influenza and whooping cough vaccines during pregnancy since 2010 and 2012 respectively. It is not possible to quantify the number of pregnant women currently being immunised against influenza and/or whooping cough, because pregnancy is not defined as a category on the National Immunisation Register. Furthermore, no research has been published in New Zealand on pregnant women's knowledge, attitudes and behaviour to immunisation in pregnancy.

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Irving, W.L., et al., Influenza virus infection in the second and third trimesters of pregnancy: a clinical and seroepidemiological study. BJOG: An International Journal of Obstetrics & Gynaecology, 2000. 107(10): p. 1282-1289.

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4 Amirthalingam, G et al., Effectiveness of maternal pertussis vaccination in England: an observational study. The Lancet, 2014. 384 (9953) : p. 1521–1528.

Audience research

The Ministry of Health commissioned Litmus Ltd to undertake audience research on pregnant women to understand their knowledge, attitudes and behaviour with respect to immunisation in pregnancy. The overall goal of the research was to target segments and tailor communications and interventions effectively to raise the uptake of vaccines during pregnancy.

The research explored pregnant women's beliefs and attitudes about immunisation and their skills and confidence to immunise during pregnancy. It also investigated the role of family/whānau, maternity and health providers in immunisation, and environmental factors that enable or act as barriers to women immunising in pregnancy. The research also tested potential messages aimed at encouraging pregnant women to immunise. Focus groups and interviews were conducted with 59 pregnant women and women who had given birth in the last 12 months. Fifteen supporting interviews were also undertaken with maternity and health providers. The research was conducted February to April 2015.

Research questions

The key research questions were as follows:

1. What are pregnant women's knowledge, feelings and opinions about the influenza and whooping cough vaccines?
2. What are the key factors that motivate pregnant women to immunise against influenza and whooping cough?
3. What are the key factors that enable pregnant women to immunise against influenza and whooping cough?
4. What are the key factors that act as barriers to pregnant women immunising against influenza and whooping cough?

Method and sample

Focus groups and interviews with pregnant women and women who had given birth in the last 12 months

Seven focus groups and 16 in-depth interviews were conducted with Pākehā, Māori and Pacific women living in urban and provincial areas with both higher and lower rates of whooping cough. Focus groups were structured by ethnicity and immunisation status. Fieldwork was conducted in Counties Manukau, Waikato (Hamilton and Tokoroa), MidCentral (Palmerston North, Bulls and Linton), Capital and Coast

(Wellington, Paraparaumu and Raumati), Nelson Marlborough (Nelson, Richmond and Motueka), and Canterbury District Health Board (Christchurch city and suburbs) catchment areas. Women were recruited for the research from qualitative research panels, health, education and social services NGOs, Student Job Search and by asking recruited participants to nominate other eligible women.

The sample was designed to include pregnant women who had been immunised against influenza and/or whooping cough, and women who had not received either of these vaccines in pregnancy. Women who rejected immunisation for religious or moral grounds either for themselves or their children were excluded from the research.

Finding Māori and Pacific women who had been immunised in pregnancy was challenging, with many Māori and Pacific women contacted to take part in the research saying they did not know about the vaccines, and had not been given information on the vaccines by their LMC or general practice. In some cases, Māori and Pacific women were unsure whether they had been immunised for influenza and/or whooping cough. Conversely, finding Pākehā women who had not been immunised against influenza and/or whooping cough during pregnancy was also challenging. The final sample interviewed was 44 women who had not been immunised during pregnancy against influenza and/or whooping cough and 15 women who had received at least one of these vaccines in pregnancy.

Table 1: Women who participated in the research

District Health Board	Ethnicity	Whooping cough only	Influenza only	Whooping cough and influenza	Non-immunised	Total
Capital and Coast	Pākehā	3	2	2	8	15
Nelson Marlborough	Pākehā	1		1	6	8
MidCentral	Māori			1	9	10
Christchurch	7 Māori and 1 Pacific			3	5	8
Counties Manukau	Pacific		1		7	8
Waikato	Pacific		1		9	10
TOTAL		**4**	**4**	**7**	**44**	**59**

Focus groups and in-depth interviews were conducted face-to-face in community meeting rooms, qualitative meeting rooms, and women's homes. Focus groups lasted two hours and in-depth interviews lasted 60 minutes. Women received a koha to acknowledge their time and contribution to the research.

Interviews with maternity and health providers

Fifteen interviews were conducted with maternity and health providers (community and hospital midwifes, general practice nurses and antenatal educators) across the same six District Health Boards to understand providers' views on women's attitudes to immunisation in pregnancy and the enablers and barriers pregnant women face to immunisation. Providers were recruited for the research from public online directories and from providers nominating other eligible providers. Interviews were conducted by telephone and lasted 20-30 minutes.

Table 2: Maternity and health providers who participated in the research

District Health Board	Community and hospital midwives	General Practice Nurses	Antenatal Educators	Total
Counties Manukau	1	1	1	3
Waikato	1	1	1	3
MidCentral	1	1	1	3
Capital and Coast	1	1		2
Nelson Marlborough	1	1		2
Christchurch	1	1		2
TOTAL	**6**	**6**	**3**	**15**

Analysis

All focus group and interview data was analysed to find patterns and themes to answer the research questions. This involved reviewing transcripts and field notes to identify common patterns in knowledge, feelings, opinions and behaviour with respect to immunisation in pregnancy, building an argument for selecting the themes and their relative weighting, and selecting supporting evidence (quotes and examples) to include in the report. The fieldwork team also participated in analysis workshops to interpret the data and draw conclusions.

Caveats

The information contained in this report represents the views of 59 women and 15 maternity and health providers in Counties Manukau, Waikato, MidCentral, Capital and Coast, Nelson Marlborough and Canterbury District Health Board catchment areas. Given the research was qualitative, the research findings cannot be generalised to the wider population of pregnant women and providers. However, key research themes described in this report were consistent across the focus groups and interviews, increasing the dependability and rigour of the findings.

3. Pregnant women's beliefs about immunisation in pregnancy

Most women are confident immunising their infants and themselves when they are not pregnant (e.g. tetanus and travel vaccinations). However, they feel less comfortable immunising themselves when they are pregnant. Women's confidence to immunise when they are pregnant stems from a range of beliefs about their vulnerability to infection, the severity of infection and the benefits of immunisation. Women's concerns about the safety of immunisation to their unborn babies also contribute to their views of immunising in pregnancy.

Beliefs over their vulnerability to infection

Most pregnant women living in areas that have outbreaks of whooping cough believe their babies are susceptible to whooping cough. Pregnant women do not understand that immunity to whooping cough gets weaker over time, and most Pākehā and some Pacific pregnant women assume that if they were immunised against whooping cough as a child they are immunised against the infection for life. Most women do not understand that babies are not protected from whooping cough until they have had their first three immunisations.

Pregnant women also feel vulnerable if they have had a personal experience of whooping cough. For example, two women immunised against whooping cough as they had a family member with whooping cough, and another one immunised because she remembers having whooping cough as a child. Some women are also motivated to immunise after reading or hearing local tragedies involving parents and children who were not immunised against whooping cough.

> 'Not long before I immunised I read something in the paper. A father had whooping cough and he passed it onto the baby and the **baby may have passed away**. This was a huge motivator to me.' (Pacific, Canterbury)

Most pregnant women believe they are healthy and do not understand that their immune system is compromised in pregnancy, and therefore susceptible to influenza. They believe influenza mainly affects older people and chronically ill people. However, the case in Nelson Marlborough of a pregnant women dying from influenza was poignant and resulted in local women feeling vulnerable.

> 'There was a young pregnant woman here in Nelson who died of flu. It was two or three years ago now, and it was around the time I had the flu jab. She had been encouraged to get the immunisation but she didn't and **she died in bed at home at 32 weeks pregnant**. They (doctors) aren't saying that the immunisation would have saved her life, but they might have had. Reading this makes you think more about the vaccines.' (Pākehā, Nelson Marlborough)

Some Māori women also doubt the necessity of immunisation against whooping cough and/or influenza, as they didn't immunise in their previous pregnancies and their babies were healthy. Another view that was raised was that previous generations (including their mothers) had not immunised and their babies were fine.

> 'Back in the day my ancestors didn't have immunisations.' (Māori, Canterbury)

Beliefs there are consequences to infections

Most pregnant women consider whooping cough is a serious infection, particularly for infants. Videos of infants with whooping cough struggling to breathe are particularly effective at reminding pregnant women of the seriousness of the infection, and the importance of immunising their infants. Women with asthma believe there are maternal consequences to infection.

With the exception of Pākehā pregnant women living in Nelson Marlborough, most do not consider there are serious consequences to influenza. Most pregnant women (particularly Māori) believe if they are unfortunate to contract influenza, they just need to suffer and get over it.

Beliefs over the benefit to immunisation

Pregnant women tend to have high trust in the efficacy of the whooping cough vaccine and women have either immunised or intend to immunise their infants against whooping cough to protect them from infection. On the other hand most pregnant women have low trust in the efficacy of the influenza vaccine. Some women believe it is not as effective as other immunisations, meaning it does not reliably prevent influenza, and other women believe the vaccine can give people influenza.

> 'I wouldn't do it. **It makes you sick before you get better**. Both midwife and my doctor suggested it. Nah you get over the flu.' (Māori, MidCentral)

> 'I know if you get the flu vaccine **you can get the flu as a result of the injection**.' (Pākehā, Nelson Marlborough)

Safety concerns

Women commonly believe that they cannot be immunised in pregnancy, as it may be unsafe for their unborn baby.

Some Pākehā pregnant women are concerned that if they were immunised, they would not be able to tell if their unborn babies experienced side effects from the immunisations, and seek help or provide a remedy. A few Pākehā pregnant women would be fearful of getting sick from the influenza vaccine, which could harm their unborn babies and mean they would be less able to care for their older children.

> 'It wasn't mentioned to me until about two weeks from my due date. I had heard of people getting sick from it. **I thought what if it happens to me and I just drop**. Being that pregnant all you want to do is sit on the couch, and you don't want to have to deal with a cold and feeling miserable as well.'(Pākehā, Nelson Marlborough)

Some Māori and Pākehā women are skeptical of the 'newness' of immunisation in pregnancy, and believe they are being treated as guinea pigs, or that the long term effects of immunisation on pregnant women and their unborn babies are not known.

Desire for a healthy pregnancy

All pregnant women desire a healthy pregnancy, and women often take a number of steps to achieve this, including watching what they eat, keeping fit, avoiding alcohol, reducing caffeine, taking care of their emotional health, and being careful about using medicines and supplements. Some women feel that injecting vaccines in pregnancy goes against their views of wanting to do the right thing for their unborn baby.

> 'I mostly controlled my diet. I cut everything out, coke, takeaways. At restaurants I made sure everything was well cooked. **I didn't want to put something in my body that I couldn't control**.' I didn't know exactly what the vaccine was. I know that they say it is completely safe, but **I'm a bit funny when I am pregnant**. (Pākehā, Capital and Coast)

4. Pregnant women's motivation to immunise in pregnancy

Pregnant women's motivation to get immunised against influenza and whooping cough would be to protect themselves so their unborn babies could be protected from the consequences of severe infection and to give them the best possible start in life.

Most pregnant women would not be motivated to immunise if it was for personal protection and did not result in protecting their unborn babies. However, a few pregnant women who are asthmatic immunised against influenza as they saw it as important for their health and wellbeing. However, before immunising these women sought assurance from their LMC or general practice that immunisation was safe for their unborn baby.

> 'For me the protection of my baby was more important than me getting influenza. **My motivation was to protect her.'** (Pākehā, Capital and Coast)

> 'I wasn't told about it for any of my 5 kids and I have a 2 and a 3 year old. If I had information I would have forced myself to do it. **I don't get into that sort of stuff for myself but I would have done it for my tamariki.** I would have pushed myself to do it for my babies. (Māori, Canterbury)

5. Pregnant women's awareness of immunisation entitlement

Information provided by LMCs[5]

Pregnant women trust their LMC to impart information that is of relevance to their pregnancy, and to steer them with decisions that are in the best interest of their and their unborn baby's health and wellbeing. The role of LMCs in imparting immunisation information is critical and can either facilitate or prevent uptake.

Women who had a conversation with their LMC about immunisation

Approximately one half of women say they had a conversation with their LMC about immunisation against influenza and/or whooping cough for pregnant women with their LMC. Women more likely to have had a conversation about immunisation in pregnancy with their LMC are mainly Pākehā and Pacific.

Very few women who had a conversation with their LMC about immunisation in pregnancy were aware they could get immunised against both infections. While seasonality may be a factor in knowledge of immunisation against influenza, it is not known why women knew about the availability of the influenza vaccine but not the whooping cough vaccine.

In most cases the conversation was initiated by the LMC and in a few cases the conversation was initiated by the woman, as she had seen a poster, pamphlet or seen or heard an advertisement promoting immunisation for pregnant women.

Some of these women experienced informed conversations with their LMC about their susceptibility to infection, the severity of the infection and its impact on their unborn babies and the benefits of immunisation. In these cases, LMCs recommended immunisations. As a result, these women thought immunisation was important for the health of their unborn baby, and were motivated to take the next steps to make an appointment with a general practice for immunisation.

> 'My midwife was great. She has experience with lots of different people and cultures and a good worldview on things. **I felt I could definitely trust her advice on the vaccines.** She gave me the information I needed. The thing I liked was that she explained the importance of it, but

[5] All 59 women had an LMC. In all but three cases, women's LMCs were community midwives.

she didn't make me feel pressured. She didn't push her own opinions. She just gave me the information so I could ask questions if I needed to.' (Pacific, Canterbury)

In other cases, women reported that LMCs gave them information on immunisation without explaining their susceptibility and severity of infection and the benefits of immunisation. They presented immunisation as an option they might like to consider, without recommending it.

'The context that the midwife gave the information was that that you needed them if you were **high risk** – poor diet, poor housing or pre-existing condition.' (Pākehā, Nelson Marlborough)

Some Pacific women who have large families said their LMCs didn't fully explain things to them when they were pregnant, as their LMCs may have assumed they knew everything. These women felt their midwives did not fully explain how immunisation protects their unborn babies, and therefore thought it was to protect the woman. As a result, in spite of being told of the availability of the free vaccines, these women were not motivated to take the next steps to make an appointment with a general practice for immunisation.

'Sometimes I feel like because it is **my seventh baby** it's like 'oh you are alright you know everything'. You have had so many babies so we don't need to go over everything again. It would have been helpful if I was told that this was important, as it would help me make better informed decisions.' (Pacific, Waikato)

'My midwife gave me heaps of pamphlets and said 'you need this and this and this'. However, when we talked about the injections **it didn't seem like I needed them**. They didn't seem important because she didn't enforce it. I basically got a pamphlet for me to read myself. If she had spoken to me for a little longer about how important they are for my baby, because I don't care about myself, I would have considered it. (Pacific, Waikato)

Women who <u>did not</u> have a conversation with their LMC about immunisation

Most Māori women say they were not provided with information about immunisation from their LMC, and are disappointed that their LMC did not disclose this information to them. By far the majority of these women indicate that had they been provided with information about the benefits of immunisation during pregnancy they would have wanted to be immunised. Effective targeting of this group with accessible information would likely lead to an increased uptake of immunisation.

'**I feel like I didn't get told anything**. If I had of, I would have done it. It would have been good to have an option.' (Māori, Canterbury)

Information provided by general practices

Most pregnant women say they went infrequently to their general practice during pregnancy for their own health needs and therefore had few opportunities to receive information about immunisation from their general practice. Māori were the least likely group of pregnant women to visit a general practice for their own health needs. Most women said they engaged with their general practice to confirm their first pregnancy, but were less likely to engage with their general practice to confirm later pregnancies. Occasionally, pregnant women engaged with their general practices when they were sick or injured.

A few first-time pregnant women who visited their general practice in early pregnancy recall their doctors being proactive in recommending immunisation against influenza and/or whooping cough later in pregnancy. However, they couldn't recall their general practices reminding them about immunisation.

Pregnant women often visited their practice because their older children were sick or needed immunising. None of these women who visited their practice because of their children recall being informed about the vaccines.

Information provided by others

A few pregnant women were recommended by an older member of their family/ whānau to be immunised against influenza. One woman spoke of receiving information from family/ whānau about eligibility to the whooping cough vaccine for pregnant women. However no family/ whānau mentioned the immunisations were to protect the woman to protect her baby.

6. Pregnant women's access to immunisation

Receiving immunisation from a general practice

In most instances, pregnant women are required to get their immunisations from their general practice. This pathway for immunisation is not convenient and women (particularly Māori and Pacific) face many barriers to accessing immunisation. These include transportation to their general practice, arranging childcare and time off work. Furthermore, some women do not have a general practice, live in different towns from their general practice, or would be reluctant to visit their practice, if they owe money for consultations and prescriptions. A number of women (particularly Māori) also identified that having to take a number of children to their general practice and the waiting prior to and after the immunisation is a disincentive. Due to the above challenges, women have a strong preference for their LMC to be able to deliver immunisations, during routine antenatal appointments.

> **'It would be great if the midwife could do the vaccine right then and there at the antenatal appointment.** I have five children so I am pretty busy and have to try and squeeze the vaccines in.' (Pākehā, Nelson Marlborough)

Pregnant women who overcame these logistical barriers and immunised were mainly Pākehā. They were more confident to take their LMC's advice, had stable relationships with general practice, and experienced fewer practical difficulties accessing services than women who were not immunised in pregnancy. Most women received appointments within a few days of request, and the immunisations were performed professionally.

Opportunistic immunisation

Two Pākehā pregnant women were immunised opportunistically at their general practice. The first woman received the whooping cough vaccine when her practice nurse recommended the vaccine during a dressing change and the second woman received both vaccines shortly after visiting her doctor because she was sick. A third Pākehā woman who had a high risk pregnancy received both vaccines at a hospital appointment. All three women found the process of immunisation more convenient, than women who made a specific appointment for immunisation at their general practice.

Employer initiated immunisation

A few Pākehā, one Māori and one Pacific pregnant woman received immunisation against influenza through a work based programme. Women were immunised because their employers were promoting it, because their colleagues were being immunised, because the vaccinators came to their workplace and because it was free. Women did not get immunised because they felt vulnerable to the seriousness of influenza infection in pregnancy. Some women questioned with the vaccinator whether it was safe to immunise in pregnancy, and were reassured it was safe. Women found the process of immunisation convenient and say they would be unlikely to proactively seek immunisation against influenza from their general practice.

> **'There were no barriers to getting the immunisations.** I did it one day at work. It was very convenient.' (Māori, MidCentral)

Home visits

A number of Māori women, especially in Canterbury, noted that an "in-home" service had vaccinated their children, which was far more convenient than taking a number of young children to their general practice. These women would find a similar service for immunisations in pregnancy more convenient.

> 'What made it easier for me was the **convenience**, you are already there and you just do it.' (Māori, Canterbury)

Free immunisation

Māori and Pacific women express that being told by the LMC or general practice nurse that immunisations were free played an important part in their decision to get immunised, and those who did not immunise say that free immunisations would enable them to get immunised. These women are not working or on low incomes, and spending money on their own health needs is neither feasible or a priority. Immunisation for pregnant women being free signals to <u>all</u> women that immunisation is recommended, and is an entitlement that all pregnant women are eligible for.

> 'Having it **free** made it an easier decision.' (Māori, MidCentral)

Women who got their partners and other family members immunised were generally those who could afford to, and in a few cases Pacific women stretched their family's finances so partners could be

immunised. Māori women in particular feel that immunisation for whānau members (in particular Dads) should also be free and that women should be able to get immunised after they have given birth for a specified time (such as while they are breast feeding).

> 'I've always got the kids immunised as it does protect them. My midwife bought it up at about 25 weeks and encouraged me to get it done around 30 weeks at local doctors. There was no charge. My midwife encouraged us to get husband immunised as well because he's a teacher. **He had to pay $40.'** (Māori, Canterbury)

While immunisation is fully funded, some women experienced costs getting to their general practice for immunisation (petrol, parking, and bus fares), and in at least one case a woman paid a surcharge on top of her vaccine.

In spite of most immunised women having to make a specific appointment for immunisations at their general practice, all but one woman (who believes the influenza vaccine gave her the flu) says they would get immunised in future pregnancies.

7. Immunisation messages

Messages to encourage women to immunise in pregnancy were tested with women to see which ones are most effective[6]. Messages tested included protecting pregnant women and unborn/newborn babies from infection, vaccine safety and efficacy and immunisation access.

Protection messages

1. **'If you're pregnant, influenza can be particularly risky. Immunisation is a great way to protect you and your baby. It will also give some protection to your new-born baby.'**

   This influenza-specific message has universal appeal and comes across as positive and friendly. While influenza is not an everyday term, most women know what it is, and it sounds more serious than "flu". This message introduces the idea that the influenza infection can be particularly severe for pregnant women. The second sentence resonates strongly, as it taps into women's desire to protect their unborn/newborn babies from infection. Pacific women think the message should be shortened, as they feel the second and third sentences are saying the same thing.

   'This message stands out to me the most. It's just the way it is worded and letting me know that **she is protected** before and after her first immunisation is due to roll around.' (Māori, MidCentral)

   'This message gives you just the right amount of information and it doesn't use too many words like vaccine and vaccinated. It gives you the information that you need to know. It tells you that vaccinations are a good way to **protect your baby**. And it also tells you that it gives them protection after they are born.' (Pacific, Counties Manukau)

2. **'Using whooping cough and influenza vaccines in pregnancy are an effective way of reducing the risks to mother and baby of these diseases.'**

   Most women like this message, as it is authentic. It talks about reducing the risk of infection, rather than overselling immunisation. This message also highlights that immunisation in

[6] The Ministry of Health developed the messages for the purpose of message testing. The Immunisation Advisory Centre (IMAC) also contributed to the wording of the messages tested.

pregnancy benefits both mother and child. However, this message is more distant and does not speak directly to pregnant women.

'I like the way it says **"an effective way of reducing risks".** It makes it sound like there is a definite risk whether you vaccinate or not, but vaccinating reduces the risk.' (Pākehā, Capital and Coast)

3. **'Immunisation helps to protect your baby, before and after they are born, your family and our community.'**

Most women had to read this message several times to understand it. It doesn't say immunisation is given to pregnant women, so women are unsure how immunisation is going to protect their baby before he/she is born. Furthermore, the link between immunisation and protecting the community is not well understood.

'The whole thing doesn't make sense to me, especially the part that says **'our community.'** Why would the community be interested in whether I am immunised?'(Pacific, Waikato)

'I had to read it a few times to think…how is it going to make **my community safer**?' (Māori, MidCentral)

4. **'Pertussis and influenza can be serious when you're pregnant. For best protection, talk to your midwife or family doctor about immunisations.'**

This message is weak. Most women do not know what pertussis is, and coupled with the unfamiliar term influenza, this message sounds medical/technical. Pacific women say they would 'skip over' pertussis if they saw it on a poster or in a pamphlet. This message doesn't resonate, as it implies protection is for the pregnant woman, not for her unborn/newborn baby. While the second sentence of this message gives women 'permission' to bring up immunisations with their midwife or doctor, due to the medical terminology, most Pacific women would not feel confident bringing it up with their midwife or doctor.

5. **'Pregnant women and new-born babies are at particularly high risk of severe outcomes from influenza.'**

Women consider this message is serious. It introduces the fact that influenza is severe for pregnant women and unborn babies. While this message catches women's attention, it is seen negatively, in that some women (particularly Pacific) find it scary and others find it scaremongering.

6. **'You need two MMR vaccinations to be protected against Measles, Mumps and Rubella. Talk to your family doctor about immunisation BEFORE you get pregnant.'**

   Women consider this message important, as Measles, Mumps and Rubella are considered serious. This message is also considered to impart good advice, as most women would prefer to immunise before they are pregnant or after they give birth, rather than when they are pregnant due to safety concerns. However, the reality is that while some women plan their pregnancies and can take advantage of this advice, many do not plan their pregnancies.

Vaccine safety and efficacy messages

7. **'The influenza vaccine has an excellent safety record and has been proven to provide effective protection both for most vaccinated people, including pregnant women and their unborn or new-born babies'.**

   Some women like the positive and reassuring statement "excellent safety record". However, this message misses the mark, as it doesn't alleviate most women's concerns about vaccine safety in pregnancy. Some Māori and Pacific women found this message too long and wordy, and that it wasn't talking to them personally. Some Pākehā women who made a conscious decision not to immunise in pregnancy say this message oversells the safety of immunisation and therefore doubt this message's authenticity. In spite of this message's weakness in regard to safety, most women like the positive efficacy sentiment of this message.

   '**This message is too wordy**. Providing effective protection for pregnant women is confusing. It's also not talking to you. It's talking to others.' (Māori, MidCentral)

   'Excellent safety record' sounds more definitive and scaremongering. **It makes me shut my mind off**.' (Pākehā, Capital and Coast)

8. **'Vaccines against influenza and whooping cough are used internationally safely in pregnancy.'**

   While this message aims to tackle women's concerns over vaccine safety in pregnancy, its international framing, and its lack of mention of the safety of the unborn baby makes this message weak. Women are more interested in knowing whether immunisation in pregnancy is proven to be safe for the unborn baby in New Zealand and Australia, and are less interested in knowing what happens internationally. For some women, this message infers that immunisation in pregnant women is used in other countries, which is welcomed.

   'It doesn't give me the information I need in that it doesn't say it protects my baby and is going to be safe. **I don't care that overseas people getting it**. I care more about what is happening here with our people.' (Pacific, Waikato)

Access message

9. **'The immunisations you need when you're pregnant are free. Talk to your midwife, family doctor or nurse about getting immunised.'**

   This message resonates strongly with women on low incomes and/or with big families. It therefore has high resonance amongst Māori and Pacific women. Being free also signals that immunisation is recommended in pregnancy, and is an entitlement that all pregnant women are eligible for. The second sentence gives women more confidence to ask for their free immunisation from their midwife or doctor. While being free is a powerful message, women also want to know that immunisation is important for protecting their unborn babies/newborns against infection and safe in pregnancy. This message is not popular with all women, however. The words "the immunisations you need when you're pregnant" is not liked by women who made a conscious decision not to immunise in pregnancy. The term family doctor is not familiar.

   'This message would probably **make me pick up the phone** and talk to my midwife and say "can I organise a free immunisation"?' (Pacific, Counties Manukau)

   '**I really don't like the word "need"**. Who says we need it? Do we need it, or is it for the baby? Where is the evidence that we really need it?' (Pākehā, Capital and Coast)

8. Communication channels

Print information

Most pregnancy-related information provided by LMCs, general practices and antenatal educators to pregnant women is in print format (pamphlets, fact sheets and posters), and pregnant women feel overwhelmed by the amount of print material they receive. There is a general feeling amongst pregnant women that reaching them with pregnancy and health information almost exclusively through print is an outmoded form of communication.

While some women (particularly Pākehā women pregnant with their first child) read most of what they receive, other women are more selective over what they read, and women who have low English literacy read little of the information they receive. Most Māori and Pacific pregnant women feel particularly overloaded with the amount of written information they receive.

Online information and social media

Most women are accessing information online to support and complement the verbal information they receive from their LMC or in place of pamphlets. They are also using social media for pregnancy and child-related health information.

For Māori and Pacific women in particular, social media is a less intimidating channel for receiving information and asking questions, and provides an opportunity for receiving and sharing information in more interactive ways (e.g. photos, videos, and stories). Some of these women lack trust in public health information, or immunisation advice given to them by LMCs and general practices, and have a history of poor experience of maternity and health services. Women who use this channel note that the 'anti-immunisation' perspective is strong while the 'pro-immunisation' perspective is silent.

> 'I wouldn't read it [a pamphlet]. I don't want to read it now. If I was handed this – It would go in the car and I wouldn't read it. Why don't they make a YouTube video? **Everyone watches YouTube.'** (Māori, Canterbury)

> 'If you **make your own channel about immunisations**, you can see it. Instant. Quick fix. Facebook and YouTube and Snapchat. On demand. I would tag all my pregnant friends.' (Māori, Canterbury)

> 'On Facebook I've seen a lot of stuff on certain sites; a lot of controversy that **immunising your kids and adults is not good.'** (Pākehā, Mid Central)

9. Brochure test

‘Immunisation for Pregnant Women’ draft pamphlet

Pregnant women were asked to read and provide feedback on a draft pamphlet developed by the Ministry of Health titled ‘Immunisation for Pregnant Women’. The pamphlet is an early draft, and contains information on immunisation before women become pregnant and when they are pregnant. The draft pamphlet also mentions immunisation in children. The draft is not formatted and has no pictures.

Most women comment that information about immunisation before pregnancy and immunisation in pregnancy should not be combined in the one pamphlet. Pregnant women who are not immunised against Rubella and Chickenpox became distressed on finding out that it is too late for them to be immunised against these infections. Often pregnancy is not planned, and therefore women cannot take advantage of this advice. However, brief information about Rubella and Chickenpox immunisations could be put at the end of the pamphlet for women to consider after they have given birth.

The draft pamphlet lacks a prominent and compelling ‘call to action’ (instruction) for women to act e.g. “Protect your unborn baby from whooping cough, *call your doctor today and ask for your free immunisation.*”

The draft pamphlet contains important messages that encourage women to immunise. Women particularly like the influenza content that informs them of the seriousness of influenza in pregnancy (increased likelihood of hospitalisation, premature birth and stillbirth) and that the vaccine will not harm their unborn baby. However, key messages such as immunisation being free are not prominent.

Most women (particularly Māori and Pacific) consider the pamphlet is too long for what they need to know to immunise in pregnancy, and do not find it engaging. While women understand it is a draft pamphlet without pictures, women have a strong preference for the final pamphlet to contain pictures, shorter paragraphs and key facts/statistics rather than lengthy text.

> **‘This is too long**. You would probably give it to your kids to play and make an airplane with.’ (Pacific, Counties Manukau)

‘Avoiding Flu during Pregnancy’ pamphlet

Women were also given a copy of the National Influenza Specialist Group’s ‘Avoid Flu during Pregnancy’ pamphlet for their information at the end of the interview. None of the women had seen this pamphlet before.

While this pamphlet was not formally tested, feedback is positive. Women like the engaging pictures of the pregnant woman and child. They also like the bold headings, the short paragraphs and the bulleted text. Contributing to this positive feedback is the fact that the pamphlet effectively ‘nails’ many of the key messages for encouraging women to immunise in pregnancy e.g. ‘pregnant women are more susceptible to influenza’, ‘influenza is severe for pregnant women and their unborn babies’, ‘immunisation against influenza is effective protection against infection’, ‘immunisation in pregnancy is safe’ and ‘immunisation is free’. The pamphlet also has a good ‘call to action’ on the front page ‘Avoid Flu during pregnancy, *make sure you get your free influenza vaccine.’*

> ‘The whole thing is great**. It answers heaps of questions**, and there is stuff in here that I didn’t know**. It’s direct and has key points**. I like the bullet point page. **It’s really simple**.’ (Pākehā, Capital and Coast)

> ‘**The attractive thing about the pamphlet was the picture**. It was nice and colourful and bold. I especially like the one on the inside which had a likable picture. It was nicer. The information was good too.’(Pacific, Canterbury)

10. Provider perspectives

A small number of interviews were undertaken with community midwives, hospital midwives, general practice nurses, and antenatal educators across the same six District Health Boards to confirm or expand on the experiences of pregnant women in regards to immunisation in pregnancy.

Informing women on immunisation

Amongst the four community midwives spoken to, two actively encourage their clients to be immunised against influenza (in season) and whooping cough, while the other two are more reactive and refer clients to do their own research, if their clients bring it up with them. Midwives mention that their clients' main concern is whether immunisation in pregnancy is safe. They also worry about whether the influenza vaccine will make them sick, and some clients don't like needles. In general, midwives say they don't follow up whether their clients have received the immunisations, so they are not sure who has and has not had them.

> '**I tell them that the vaccine is recommended** and that it will protect the baby before the immunisation programme starts, and that Wellington is endemic with whooping cough.' (Community midwife, Capital and Coast)

> '**It's a controversial subject. I would prefer not to be involved**. I would want further training on immunisation and vaccines to be able to say yes vaccination is OK.' (Community midwife, Waikato)

> 'We have 'pro immunisation' posters up and get enquiries from women asking what they should do, but I say **'it's your choice, it's your baby, check the information and make the decision based on what is right for you.'** (Community midwife, MidCentral)

Hospital midwives working with women who don't have a LMC or have a high risk pregnancy say there is information on immunisation in waiting rooms. However, due to the high needs of many of these women, and the relatively limited time midwives have to engage with them they focus conversations around matters they consider most important, such as breastfeeding, nutrition, quitting smoking, family violence, and immunisation in pregnancy is rarely mentioned.

> 'The key messages I give to pregnant women when I speak to them are about smoking, screening for domestic violence, dietary advice because many of them have poor nutrition, promoting breastfeeding, safe sleeping**. Information about immunisation may be in the DHB leaflet we give to them, or in pamphlets and posters in waiting rooms.'** (Hospital midwife, Counties Manukau)

Amongst the six general practice nurses spoken to, all are confident having discussions with patients in early pregnancy that immunisation against influenza and whooping cough is available and recommended, and most say they remind women when their immunisations are due. However, general practice nurses confirm they mainly have contact with first time pregnant women and have less contact with women who have been pregnant before who go directly to LMCs.

The few antenatal educators spoken to confirm that they don't include information on immunisation for pregnant women in their classes. There are many reasons for not including this information, including not feeling informed enough to discuss immunisation, not wanting to talk about it in a group setting (as they feel it is controversial), not wanting to be asked their opinion on immunisation in pregnancy (if they are opposed), or because their programme is full.

> 'I don't make a big thing of immunisation because it's very controversial. What I am trying to avoid is the situation where you get heated debate with parents on opposing views. I think it's a private decision that people should draw on their own experience, values and philosophies. **Immunisation for pregnant women is relatively new and I'm not required to talk about it.**' (Antenatal educator, MidCentral)

Accessing immunisation

Midwives confirm that pregnant women receiving immunisations through their general practice is not convenient. Midwives acknowledge that there are obstacles that would need to be overcome if immunisations were provided outside of general practice (e.g. transporting vaccines and conducting immunisations in a safe environment). However, they consider other ways to deliver immunisations need to be considered to make it more convenient for women e.g. LMCs providing vaccination, or placing services where women go for blood tests or scans.

General practice nurses believe that making a specific appointment with a general practice for immunisation in pregnancy is a structural barrier, as women often need to arrange transport, childcare and time off work. They also believe some women will be put off attending a practice for immunisations if they have debts with the practice.

> 'Another barrier is that women owe money to the practice and receptionists sometimes target these women for unpaid bills. **They may need to pay $10 despite immunisation being free**. I can imagine women not coming because of that.' (General practice nurse, Waikato)

General practice nurses give priority to pregnant women who want to be immunised, do not make women wait long for an appointment, and immunise women without an appointment. General practice nurses also opportunistically immunise women, if they visit the practice for another matter.

> '**This practice is staunch on immunisation**. At our practice everything gets dropped for an immunisation, even when patients do not have an appointment.' (General practice nurse, Waikato)

Providers endorse that free immunisations, particularly for low income women, is a significant enabler for pregnant women receiving immunisations.

Messages and communication

Midwives, general practice nurses and antennal educators confirm that pregnant women are overwhelmed by the quantity of print information provided and most women do not read everything they are given, particularly women with low literacy. Providers confirm that messages to encourage pregnant women to immunise against influenza and whooping cough need to be short, positive and friendly. They believe messages that tap into women's desires to protect their unborn babies will be most compelling. They confirm that pregnant women generally put their baby's wellbeing above their own, and providers working in low socio-economic areas confirm that women often don't place value on their own protection from infection, and therefore messages about maternal health and wellbeing are likely to be less compelling.

11. Conclusions

The findings from this research conclude that the most significant barrier to immunisation uptake in pregnancy is a lack of accessible information and advice on immunisation from LMCs and structural barriers for accessing services through general practices.

Most pregnant women say that had their LMCs informed them about the benefits of immunisation, their susceptibility to infection, the severity of the infection and its impact on their unborn babies, and that immunisation in pregnancy was safe they would have opted to be immunised. Furthermore, if women's LMCs could have administered the vaccination this would have made the process of immunisation more convenient.

Māori and Pacific pregnant women face more barriers to immunisation in pregnancy than Pākehā pregnant women. They are more likely to say they did not receive effective information on immunisation from their LMCs, and face more barriers accessing immunisation through general practices. The challenges the researchers had finding Māori and Pacific pregnant women who had immunised for this research indicates that actual immunisation uptake is low for Māori and Pacific pregnant women.

The overall goal of the research was to target segments and tailor communications and interventions effectively and raise the uptake of vaccines during pregnancy. The research concludes that segments that need to be targeted are Māori and Pacific pregnant women and LMCs who work with these women.

The findings from the research conclude that persuasive messages that talk about immunisation protecting unborn babies from the consequences of infection are persuasive. Messages that say immunisation is safe in pregnancy provide reassurance to pregnant women who are concerned about the safety of vaccines for their unborn babies. Messages that say influenza is serious for unborn babies cause pregnant women who do not consider influenza serious to take notice. Messages that say immunisation is free for pregnant women resonate particularly strongly with Māori and Pacific pregnant women.

The findings from this research also conclude that traditional print media is not cutting through to all pregnant women and social media tools need to be considered for sharing relevant immunisation content.

Health Quality & Safety Commission New Zealand
Kupu Taurangi Hauora o Aotearoa

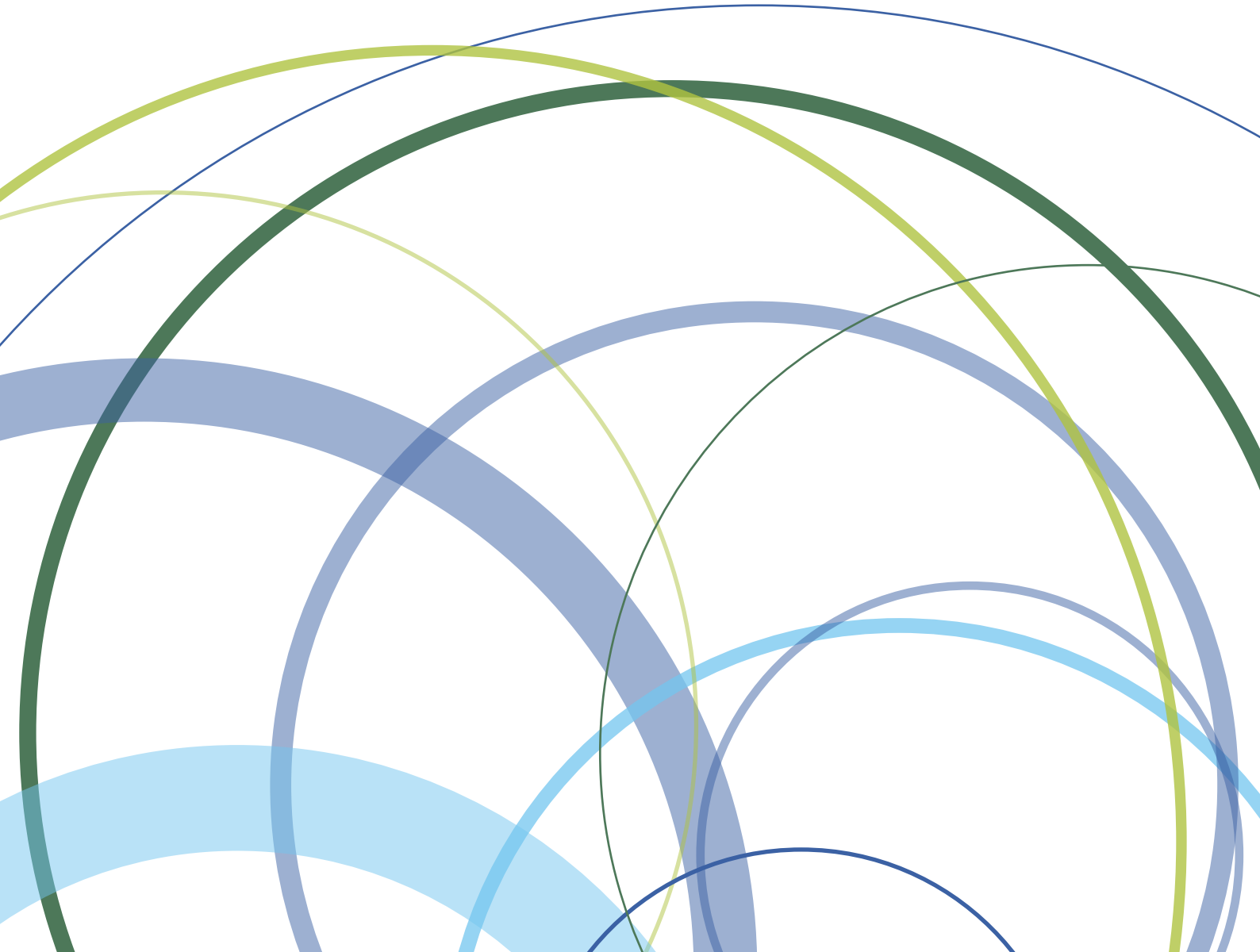
"... Unuhia i te rito o te harakeke ..." "... taken away too early ..."

Child and Youth Mortality Review Committee

Mortality and morbidity of pertussis in children and young people in New Zealand

Special report

2002–14



This report was written for the Child and Youth Mortality Review Committee by Joanna Minster,
Dr Gabrielle McDonald, Dr Stuart Dalziel and Dr Felicity Dumble.

Citation: Child and Youth Mortality Review Committee, Te Rōpū Arotake Auau Mate o te Hunga Tamariki, Taiohi. 2015. *Mortality and morbidity of pertussis in children and young people in New Zealand: Special report 2002–14.* Wellington: Child and Youth Mortality Review Committee.

Published in December 2015 by the Health Quality & Safety Commission,
PO Box 25496, Wellington 6146, New Zealand.

ISBN 978-0-908345-12-0 (Print)
ISBN 978-0-908345-13-7 (Online)

This document is available on the Health Quality & Safety Commission website: www.hqsc.govt.nz.

For information on this report please contact info@hqsc.govt.nz

Acknowledgements

The Child and Youth Mortality Review Committee (CYMRC) would like to thank the following groups and individuals for their involvement in the development of this report.

- The New Zealand Mortality Review Data Group at the University of Otago for extracting, collating and analysing the data. In particular, Dr Gabrielle McDonald for leading the analyses, Joseph Hii for his contribution to the analyses and Dr John Holmes for his preliminary work, case definition and ascertainment, and supply and advice on the EpiSurv data set.
- The Ministry of Health and the Institute for Environmental and Scientific Research for supplying data used for the report analyses.
- The organisations, academics, policy makers and medical professionals who provided feedback on the report recommendations, including:
  - Dr Nikki Turner, director, Immunisation Advisory Centre
  - Diana Murfitt, senior advisor, Immunisation team (Ministry of Health)
  - Bonnie Jones, senior advisor stakeholder engagement, Immunisation team (Ministry of Health)
  - Laura Ross, principal advisor, Child and Family Programmes (Ministry of Health)
  - Maternal Child Health Service Integration team (Ministry of Health)
  - Dr Pat Tuohy, chief advisor, Child and Youth Health (Ministry of Health)
  - Lucy Curtis, senior policy advisor, National Health IT Board (Ministry of Health)
  - Perinatal and Maternal Mortality Review Committee
  - Lesley Dixon, midwifery advisor and research development (New Zealand College of Midwives)
  - Jeanette McKeogh, Michael Thorn and Frances Townsend (Royal New Zealand College of General Practitioners)
  - Kanchan Sharma, national programme manager, Integrated Performance and Incentive Framework (IPIF) (Ministry of Health)
  - the Māori Caucus convened by the Health Quality & Safety Commission: Assoc Prof Denise Wilson (chair), Ngaroma Grant (deputy chair), Maria Baker, Dr Terryann Clark, Dr Sue Crengle, Dr Paula King and Dr Jonathan Koea
  - district health board chief medical officers and department directors: Dr Susan Fleming, director, National Women's Health (Auckland DHB), Dr Rob Weir, clinical director/medical officer of health, Public Health Services (MidCentral DHB), Dr Kenneth Clark, chief medical officer (MidCentral DHB) and Hugh Lees, chief medical officer (Bay of Plenty DHB)
  - Marilyn Head, senior policy analyst (New Zealand Nurses Organisation).
- The Local Child and Youth Mortality Review Groups (LCYMRGs) that reviewed the details of some of the pertussis deaths included in this report.
- Ngaroma (Mala) Grant, who was co-opted to the CYMRC while Dr Terryann Clark was on maternity leave.
- The CYMRC Secretariat based at the Health Quality & Safety Commission, particularly:
  - Joanna Minster (contractor, senior policy analyst, writer)
  - Shelley Hanifan (manager)
  - Clifton King (programme manager)
  - Sue Willoughby (lead coordinator)
  - Dez McCormack (committees coordinator)
  - Dr Brandy Griffin (senior policy analyst).

Child and Youth Mortality Review Committee

The New Zealand Child and Youth Mortality Review Committee (CYMRC) is a mortality review committee appointed by the Health Quality & Safety Commission under section 59E of the New Zealand Public Health and Disability Act 2000. The CYMRC reviews and reports to the Health Quality & Safety Commission on deaths that fall within its scope, with a view to preventing these deaths and supporting continuous quality improvement throughout the health sector.

One of the ways this is achieved is through Local Child and Youth Mortality Review Groups (LCYMRGs). LCYMRGs collect data and review deaths of children and young persons aged between 28 days and 24 years. The local review process provides a mechanism for identifying causal pathways associated with deaths in this age group. By monitoring patterns over time, or specific clusters of events, the review process can provide evidence-based information on systems and services. This information is used to guide the formation of sector-wide recommendations and assist the development of strategies and initiatives that have the potential to reduce preventable deaths.

CYMRC members

- Dr Felicity Dumble (Chair)
- Dr Stuart Dalziel (Deputy Chair)
- Dr Terryann Clark
- Dr Paula King
- Dr Ed Mitchell
- Dr Janine Ryland (ex-officio member, Ministry of Health)
- Paul Nixon (ex-officio member, Ministry of Social Development) and Gillian Buchanan (Child, Youth and Family), who attends CYMRC meetings on behalf of Paul.
- Jacqui Moynihan (co-opted member, Horowhenua/Otaki Children's Team director)

Contents

Foreword

The Health Quality & Safety Commission is pleased to release *Mortality and morbidity of pertussis in children and young people in New Zealand: Special report 2002–14* by the Child and Youth Mortality Review Committee (CYMRC).

Pertussis (whooping cough) occurs in cycles of epidemics every 3–5 years in New Zealand. This report shows infants under 3 months of age are most at risk of being affected by severe pertussis. The higher hospitalisation rate and disproportionate number of deaths in these infants reflect their incomplete protection from the three pertussis vaccinations in their primary course, scheduled for 5 weeks, 3 months and 5 months.

These findings emphasise the need for extending existing immunisation strategies to ensure very young infants are protected from birth until they receive the third vaccination from their primary course. Immunising pregnant women in their third trimester with a pertussis-containing booster vaccination is a cost-effective strategy, recommended by the World Health Organization, that is increasingly being adopted in countries comparable with New Zealand. Maternal immunisation provides protection against pertussis for young infants for the first few months of life because the mother's antibodies cross the placenta to the unborn baby. It is therefore very pleasing that in New Zealand the pertussis-containing Tdap vaccination has recently become free for pregnant women, regardless of epidemic status.

The CYMRC's recommendations acknowledge that there needs to be a number of actions to support increasing maternal immunisation. These include raising awareness among pregnant women and health care workers, particularly lead maternity carers, who are a key source of information during pregnancy. Having national systems to record uptake of antenatal vaccinations and transferring this to the infant's immunisation record are important for monitoring the effectiveness of the strategy. We also need systems for recalling pregnant women for the vaccination in their third trimester to encourage uptake.

This report also highlights significant equity issues for Māori and Pacific infants, who experience significantly more hospitalisations for pertussis. The health sector has seen impressive improvements in immunisation coverage for Māori and Pacific children at 8 months and 2 years. Timeliness is still problematic during the first 6 months of life, particularly for those living in high deprivation areas. Data from the most recent pertussis epidemic, between August 2011 and December 2013, show complete coverage of the three pertussis doses at age 6 months is lowest among Māori and Pacific infants, and those living in the most deprived households (Kiedrzynski et al 2015). These populations face a number of barriers that impact their ability to access immunisations.

There is clearly still work to be done to ensure our vaccination strategy suits the broad range of settings we need to cover. Integrated primary care models should be supported to ensure the timely immunisation of all New Zealanders.

This report draws attention to some very precious lives that could have been saved relatively easily – we need to save similar lives in the future.

Prof Alan Merry, ONZM FRSNZ
Chair, Health Quality & Safety Commission

Chair's introduction

Outbreaks of pertussis have been occurring regularly in our communities and are expected to continue to do so for some time.

Pertussis (also known as whooping cough) can be very serious, even fatal. This report demonstrates that the impact of the illness is not distributed equitably among New Zealand children and young people. There is significant variation by age and ethnicity, with very young babies being most at risk.

Vaccination against pertussis reduces the incidence and severity of disease. The Child and Youth Mortality Review Committee strongly supports timely vaccination as outlined in the National Immunisation Schedule.

Maternal immunisation with a pertussis-containing vaccine is a key strategy for protecting mothers and children. It results in protective antibodies passing directly from mother to baby (via the placenta) before birth, and also reduces the risk of a mother passing pertussis on to her baby. This provides protection for young babies in the early months of life, before they can gain lasting protection from their own vaccinations. It is now funded for pregnant women in their third trimester.

During pregnancy, mothers must be very careful about what is taken into their bodies. There needs to be increased awareness that, while some vaccines are not to be given during pregnancy, vaccination against pertussis is safe and effective. The recommendations of this report include measures to better inform the public about the benefits of pertussis vaccination and improve access to the vaccine during pregnancy for all ages and ethnicities.

Midwives and general practitioners are essential in this process. Working together with them, we can significantly improve pertussis vaccination coverage and save lives.

Dr Felicity Dumble

Chair, Child and Youth Mortality Review Committee

Key findings

Over the last 13 years (during 2002–14) for which data are available in New Zealand for children and young people aged under 25 years:

- there were eight deaths attributable to pertussis. Seven of these deaths were in infants under 3 months of age, who had either no or inadequate protection against pertussis[1]
- there were just under 13,000 notified cases of confirmed, probable or suspected pertussis – an average of 992 cases per year
- there were 1515 hospital admissions attributable to pertussis. Over three-quarters of these admissions were in infants under 6 months of age who had either no or inadequate protection against pertussis
- infants aged under 3 months had the highest notification rate (407.9 per 100,000) and the highest hospitalisation rate (468.2 per 100,000) for pertussis
- when examined by ethnicity, Māori and Pacific infants, children and young people were significantly more likely to be hospitalised with pertussis than non-Māori/non-Pacific infants. Ethnic inequities were particularly marked for both Māori and Pacific infants aged under 3 months of age, who were an estimated 2.7 and 3.6 times more likely to be hospitalised for pertussis compared with non-Māori/non-Pacific infants respectively.

The Child and Youth Mortality Review Committee (CYMRC) notes:

- maternal immunisation with pertussis booster vaccinations is protective for infants under 3 months of age
- maternal immunisation with pertussis booster vaccinations is safe for pregnant women and their infants
- increasing uptake of antenatal pertussis booster vaccinations among pregnant women in the third trimester requires increasing awareness of the vaccine among health care providers and pregnant women. A wide range of educational resources targeting pregnant women, lead maternity carers and primary health care providers are needed to achieve this
- having local- and national-level systems in place can help both improve coverage and record the uptake of pertussis booster vaccinations among pregnant women. Systems in primary care settings that recall pregnant women for the vaccination in their third trimester can help increase uptake. Uptake of the vaccination by pregnant women should also be recorded at a national level and transferred onto the infant's immunisation record at birth
- barriers to immunisation service access should be addressed through national policies that aim to achieve equitable and on-time immunisation coverage by providing pertussis booster vaccinations in a broad range of settings.

Maternal immunisation for pertussis involves giving pregnant women a pertussis-containing booster vaccination in their third trimester (between 28 and 38 weeks gestation). This vaccination protects the baby from pertussis during the first few months of life because antibodies from the mother cross the placenta to the baby during pregnancy, providing passive immunity against the disease. Maternal immunisation also protects the mother against disease, limiting transmission from mother to baby.

1 Infants receive three doses of a pertussis-containing vaccination at 6 weeks, 3 months and 5 months of age under the current National Immunisation Schedule. Protection from pertussis increases with each successive dose and infants are not fully protected until the third dose (Ministry of Health 2014).

Introduction

Pertussis (or 'whooping cough') is a contagious respiratory disease caused by the bacterium *Bordetella pertussis*. It is one of the most infectious vaccine-preventable diseases and is transmitted by droplets in the air from infected individuals. Pertussis illness is characterised by prolonged coughing episodes, often accompanied by an inspiratory 'whoop' sound (Faulkner et al 2015; World Health Organization (WHO) 2015).

Box 1: What is pertussis?

Pertussis is characterised by progression through a series of clinical stages: (1) the catarrhal stage, during which the disease is most infectious and those infected develop a runny nose and cough; (2) the paroxysmal stage, in which those infected develop short coughing episodes or 'paroxysms' characterised by a gasping 'whoop' sound when breathing in; and (3) the convalescent stage (WHO 2015). In very young infants or immunocompromised children, severe bouts of coughing may be accompanied by apnoea, cyanosis and vomiting. This severe disease presentation commonly requires hospitalisation. In very severe cases, the disease may progress to seizures and encephalopathy, due to cerebral oxygen deprivation (Ministry of Health 2014a; WHO 2015).

Pertussis affects people of all ages and is most common among children aged under 5 years (WHO 2015). Disease presentation differs among age groups. Healthy adults and adolescents with acquired immunity from vaccination or previous infection may experience few or mild symptoms, and can unknowingly transmit disease to young infants (Faulkner et al 2015; WHO 2015). Infants aged under 12 months and those too young to be immunised are most at risk from infection (Ministry of Health 2014a). Around 5 in 10 infants who catch pertussis before age 6 months will require hospitalisation (Immunisation Advisory Centre 2015).

Globally, pertussis was a common cause of child and infant mortality in the pre-vaccine era. With the introduction of routine child vaccination programmes in developed countries in the 1940s, the incidence of pertussis began to decline. However, recently there has been an increase in pertussis incidence in some developed countries, despite high immunisation coverage among children (Faulkner et al 2015; WHO 2014). Multiple factors likely to have contributed to this resurgence include improved diagnostic testing, switching from whole-cell to acellular vaccines,[2] and possible molecular changes in the bacterium over time (Faulkner et al 2015; WHO 2015).

Pertussis is a notifiable disease in New Zealand and data on case notifications have been collected under the national surveillance system since 1996. Pertussis occurs in cycles of outbreaks, with epidemics recurring every 3–5 years (Immunisation Advisory Centre 2015). Since the disease became notifiable, three epidemics have occurred, with case notifications peaking in 2000, 2004 and 2012. The most recent New Zealand pertussis epidemic occurred between 2011 and 2014 (bpac^{NZ} 2014; Grant 2015; Ministry of Health 2014a).

Pertussis notification data analysed for the peak time of the most recent epidemic, from August 2011 to December 2013, showed an average annual total population rate of 102 per 100,000, with the highest rate (801 per 100,000) observed in infants aged under 6 months. There were three deaths from pertussis during this period – all among children and two among infants aged under 1 year (Kiedrzynski et al 2015). Overall, there are marked inequities in hospitalisations for pertussis, with Māori and Pacific infants and infants living in households in the most deprived quintiles being more likely to be hospitalised with the disease than European/Other infants and those living in households in the least deprived quintiles (Ministry of Health 2014a).

2 Whole-cell vaccines were the first type of pertussis vaccination introduced. These were gradually replaced with acellular vaccines in the 1990s, due to a need to reduce adverse reactions among those vaccinated. However, recent evidence suggests acellular pertussis vaccines may provide a shorter duration of protection against infection compared with whole-cell vaccines (eg, see Burns et al 2014; Meade et al 2014; WHO 2015; Witt et al 2013).

The pertussis vaccine was introduced into New Zealand in 1945 (Grant 2015; Ministry of Health 2014a). A whole-cell vaccine was used for routine immunisation from 1960 and replaced with an acellular pertussis vaccine in 2000. Under the current National Immunisation Schedule, a primary course of three pertussis vaccines are given in the first year of life, with doses at 6 weeks, 3 months and 5 months of age (Ministry of Health 2014a). The entire primary course of pertussis immunisations is required to achieve the most effective protection, resulting in young infants having incomplete protection until they have completed the full series of three vaccine doses.

Protection with the primary course is effective against severe disease through to the booster vaccination given at 4 years of age (Radke et al 2015, manuscript in preparation). However, immunity following booster doses wanes after several years as the acellular vaccines currently used do not give long-lasting protection and cannot eliminate pertussis from the community. Therefore pertussis immunisation strategies focus on preventing severe disease in infants who are most at risk.

Pertussis immunisations are delivered as pertussis-containing vaccines that protect against a number of other vaccine-preventable diseases. The Tdap vaccination available for pregnant women, for example, protects against tetanus, diptheria and pertussis. For the purposes of this report, the CYMRC refers to pertussis-containing vaccinations simply as 'pertussis vaccinations', although the former is technically correct.

Structure of this report

In this report, the CYMRC has examined pertussis as an example vaccine-preventable disease. Both morbidity data and mortality data have been included, as this gives a wider picture of the burden of disease caused by pertussis.

Section A provides an overview of mortality and morbidity associated with pertussis. Mortality data are provided from the Mortality Review Database from 2002 to 2014. Morbidity data from the same period are provided via pertussis notification data from the EpiSurv database and hospitalisation data from the Ministry of Health.

Section B discusses the current strategies used for pertussis prevention in New Zealand and other prevention strategies discussed in the literature. This section also discusses the issues and themes identified from local reviews and the national committee.

Section C presents the national policy recommendations, local recommendations and community messages for pertussis prevention.

Method

Definition

The analyses in this report include children and young people between birth and 24 years of age with mortality and morbidity from pertussis in New Zealand between 1 January 2002 and 31 December 2014.

In all analyses, the year of death relates to the calendar year in which the individual died, rather than the year the death was registered. This is different to some official collections, where the year the death is registered is used.

Data sources

The data used in this report were taken from three sources: the Mortality Review Database, EpiSurv and the Ministry of Health.

1. Mortality Review Database: This database is housed by the New Zealand Mortality Review Data Group on behalf of the CYMRC. It contains information from a number of sources, including the Ministry of Health; Births, Deaths and Marriages; Coronial Services Unit and individual coroners; Child, Youth and Family; Ministry of Transport; Water Safety New Zealand; and data entered by the LCYMRG coordinator on completion of an LCYMRG death review. These data were extracted on 7 July 2015 and also viewed on the live database (October and November 2015).

2. EpiSurv is the national notifiable disease surveillance database. Information about notifiable diseases is collected from public health services and collated on a real-time basis. Information includes demographic details on cases, clinical features and risk factors. It is operated by the Institute for Environmental and Scientific Research (ESR), on behalf of the Ministry of Health (EpiSurv 2015). Data on notifications and deaths were taken from an extract from EpiSurv taken on 7 October 2015 and the details of the deaths were checked with the Mortality Review Database. Only cases of pertussis with a status of 'suspect', 'probable' or 'confirmed' were used for the tabulations. These definitions are:

- suspect (in children under 5 years of age): any paroxysmal cough with whoop, vomit or apnoea for which there is no other known cause
- probable: a clinically compatible illness with a high *B. pertussis* IgA test or a significant increase in antibody levels between paired sera at the same laboratory, or a cough lasting longer than two weeks and with one or more of the following, for which there is no other known cause:
  - paroxysmal cough
  - cough ending in vomiting or apnoea
  - inspiratory whoop
- confirmed: a clinically compatible illness that is laboratory confirmed, or is epidemiologically linked to a confirmed case (Ministry of Health 2012).

The 'report date' was used to indicate 'year' for tables with notifications. This is because the information regarding the onset date of disease was too incomplete.

Immunisation status on EpiSurv is based on documentary evidence from the patient record or parental recall. 'Immunised' means the individual had received at least one dose of a pertussis-containing vaccination at any time before becoming ill. This includes infants who have completed the primary course of all three pertussis-containing vaccination doses and those infants who have received at least one dose of the vaccine but not yet completed the full primary course. 'Not immunised' means the individual had not received any doses of a pertussis-containing vaccination at any time before becoming ill.

3. Ministry of Health: The Ministry of Health provided data on the number of publicly funded hospital discharges with an ICD-10 code of A37 (Whooping cough). Day cases were excluded from the analyses. Ethnicity was provided in three groups: Māori, Pacific and Other. These data were extracted on 10 August 2015.

Denominators

The denominators used in the analyses are from two sources. The denominator for those aged 1–24 years is based on the estimated resident population from census years 2001, 2006 and 2013, as supplied by Statistics New Zealand. Data for the years in between censuses and for 2014 were calculated by applying fitting quadratic polynomial functions to the estimated resident population by prioritised ethnic and age groups.

The denominator used for those aged under 1 year was the live births data set, as supplied by the Ministry of Health. The number of births each year was divided by four to obtain the population estimates for those aged under 3 months and those aged 3–5 months. The number of live births each year was divided by two to obtain the population estimate for those aged 6–11 months.

Ethnicity

Prioritised ethnic group data for the cases where pertussis caused death were determined using the information in the Mortality Review Database. The sources of ethnicity data in the Mortality Review Database are Births, Deaths and Marriages; the Ministry of Health; and Coronial Services records. These data sources are prioritised based on evidence as to their accuracy generally in New Zealand.

Ethnic group data for publicly funded hospital discharges were supplied by the Ministry of Health.

Statistical method

The data presented in this report were computed from the above sources by the New Zealand Mortality Review Data Group. Percentages, rates and confidence intervals are expressed to one decimal point.

Rates in this report are presented as per 100,000 age-specific population for all age groups.

Where presented, 95 percent confidence intervals for rates have been calculated using the method described by Fay and Feuer (1997) according to the Centers for Disease Control and Prevention's National Vital Statistics Report (Murphy et al 2013).

Discrepancies with other collections

When interpreting CYMRC data it must be remembered they are derived from a database that is constantly being updated. As well as details of new cases, there can also be new information for existing cases, and at times changing information for existing cases. The result of this is that details can change from year to year, even for cases where death occurred some years previously.

The data presented in this report may differ from other official collections. This is due, in part, to the multiple data sources, which may provide more comprehensive data than other collections. In addition, the way that data are coded may result in variations from official collections. For example, as mentioned above, the CYMRC uses the date of death to assign year of death, whereas some other collections use date of registration of death.

Limitations

It should be noted that disease notifications do not reflect the true incidence of disease. While it is a legal requirement for health professionals to notify the relevant medical officer of health where pertussis is suspected or diagnosed, this does not always occur. It is estimated that only about 6–25 percent of cases are notified and these will represent the severe end of the disease spectrum (Ministry of Health 2014a). For example, in this report the notification rate for infants under 3 months of age is smaller than the hospitalisation rate.

A. Analysis of pertussis notifications, hospitalisations and data from the Mortality Review Database

Pertussis case notifications

There were nearly 13,000 notifications of pertussis infection during the 13-year study period from 2002 to 2014, with an average of 992 cases per year. However, the total annual notifications over this time period varied widely, ranging from 133 cases in 2007 to 3173 cases in 2012. There was a marked variation in notification rate by age group. Infants aged under 3 months had the highest notification rate of 407.9 per 100,000 for the study period, compared with young people aged 20–24 years who had a rate of notification of 26.2 per 100,000 population. This infant notification rate was statistically significantly higher than the rate in any other age group. Pertussis notification rates decreased with increasing age, with each age group being statistically significantly less likely than the age group younger than them to have notified disease (Table 1).

Table 1: Annual notifications of pertussis by age group and year of notification, New Zealand 2002–14

AGE GROUP	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	Total	Rate (CI)
<3 months	58	44	81	49	13	19	29	66	42	71	176	110	47	805	407.9 (379.7–436.1)
3–5 months	32	14	45	38	9	7	6	28	24	23	120	71	16	433	219.4 (198.7–240.1)
6–11 months	36	30	46	30	12	1	5	23	20	34	123	83	25	468	118.6 (107.8–129.3)
1–4 years	233	110	349	194	52	30	21	142	119	272	897	556	129	3104	99.6 (96.1–103.1)
5–9 years	287	121	646	305	74	19	26	146	90	302	759	367	70	3212	83.8 (80.9–86.7)
10–14 years	134	75	592	335	89	21	41	103	47	229	539	221	55	2481	62.7 (60.2–65.1)
15–19 years	36	33	258	197	89	23	27	120	54	95	280	136	38	1386	34.3 (32.5–36.2)
20–24 years	24	7	101	95	62	13	13	62	48	75	279	178	58	1015	26.2 (24.5–27.8)
Total	**840**	**434**	**2118**	**1243**	**400**	**133**	**168**	**690**	**444**	**1101**	**3173**	**1722**	**438**	**12,904**	**65.8 (64.7–66.9)**

Note: Rates are per 100,000 population; 'CI' indicates 95% confidence interval.

Sources:
Numerator: EpiSurv.
Denominator: Ministry of Health live births, Mortality Review Population Estimates 2002–14.

Pertussis hospitalisations

As with case notifications, there was a marked decrease in hospitalisations for pertussis with increasing age during the period 2002–14. The hospitalisation rate in infants aged under 3 months was over 2000 times higher than the hospitalisation rate in young people aged 20–24 years. The rate of hospitalisation was highest in infants aged under 3 months at 468.2 per 100,000 followed by infants aged 3–5 months (145.9 per 100,000) (Table 2).

The yearly fluctuation in notifications was also evident in the hospitalisation data, with these following the same trends year by year (Figure 1).

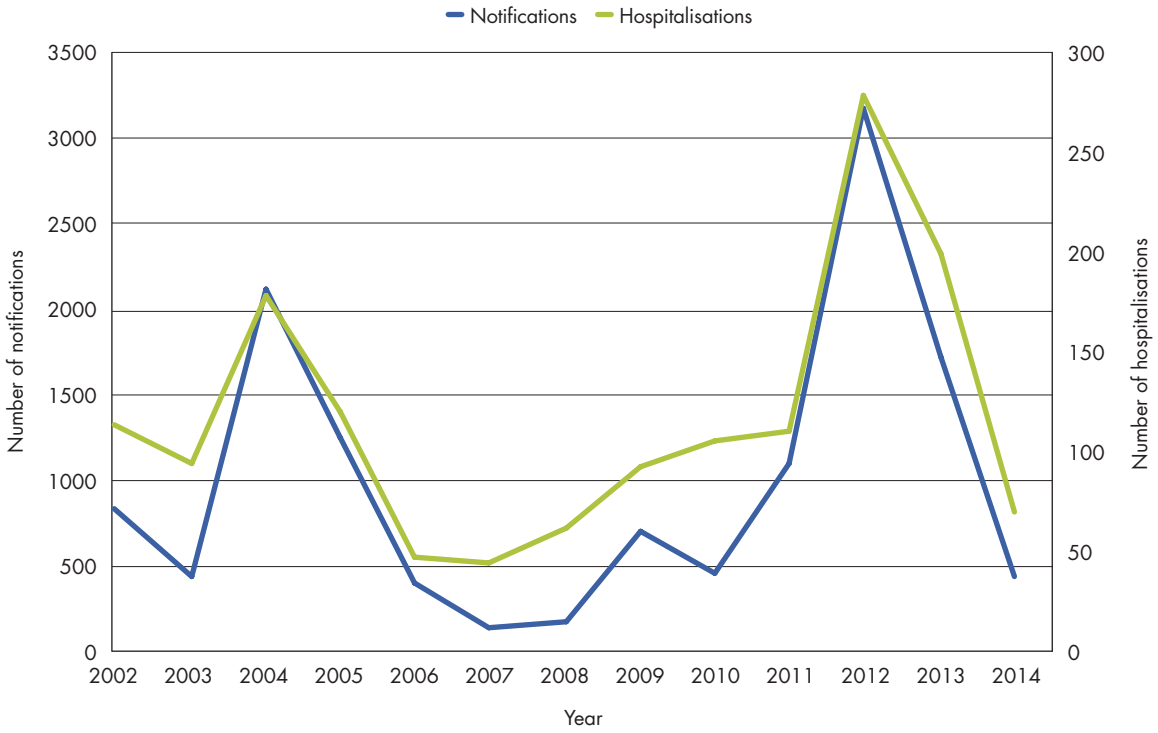
Table 2: Annual hospitalisations due to pertussis by age group and year of discharge, New Zealand 2002–14

AGE GROUP	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	Total	Rate (CI)
<3 months	64	59	113	63	20	26	37	62	61	81	168	125	45	924	468.2 (438–498.4)
3–5 months	23	12	20	31	8	12	18	14	19	17	60	42	12	288	145.9 (129.1–162.8)
6–11 months	7	8	16	4	9	1	2	4	14	1	19	16	4	105	26.6 (21.5–31.7)
1–4 years	14	7	16	13	6	1	4	8	8	10	12	9	5	113	3.6 (3–4.3)
5–9 years	4	6	8	1	4	2		2			7	3	2	39	1 (0.7–1.4)
10–14 years	2	2	2	6		1	1	1	2		7	4		28	0.7 (0.5–1)
15–19 years			1	1		1		1	1		5			10	0.2 (0.1–0.5)
20–24 years			2	1					1	1	2		1	8	0.2 (0.1–0.4)
Total	**114**	**94**	**178**	**120**	**47**	**44**	**62**	**92**	**106**	**110**	**280**	**199**	**69**	**1515**	**7.7 (7.3–8.1)**

Note: Rates are per 100,000 population; 'CI' indicates 95% confidence interval.

Sources:
Numerator: Ministry of Health.
Denominator: Ministry of Health live births, Mortality Review Population Estimates 2002–14.

Figure 1: Annual notifications and hospitalisations due to pertussis by year, children and young people aged 0–24 years, New Zealand 2002–14



Sources:
Notifications: EpiSurv.
Hospitalisations: Ministry of Health.

When hospitalisation rates are examined by ethnicity, Māori and Pacific children and young people were statistically significantly more likely to be hospitalised with pertussis than non-Māori/non-Pacific children and young people. For Māori the rate was 14.0 per 100,000 and for Pacific 16.1 per 100,000, compared with a rate of 4.6 per 100,000 for non-Māori/non-Pacific (Table 3).

Statistically significant ethnic inequities were observed for Māori and Pacific infants compared with non-Māori/non-Pacific infants. For example, Māori infants aged under 3 months were 2.7 times more likely (rate ratio 2.7, 95 percent CI 2.4–3.2) to be admitted to hospital and Pacific infants aged less than 3 months were 3.6 times more likely (rate ratio 3.6, 95 percent CI 3.0–4.3) to be admitted to hospital for pertussis than non-Māori/non-Pacific infants in the same age group (data not shown in table).

Table 3: Annual hospitalisations due to pertussis by age group and ethnicity, New Zealand 2002–14

AGE GROUP	Māori		Pacific peoples		Non-Māori/Non-Pacific		Total	
	number	rate (CI)	number	rate (CI)	number	rate (CI)	number	rate (CI)
<3 months	409	718.1 (648.5–787.7)	203	939.2 (810–1068.4)	312	262.6 (233.5–291.8)	924	468.2 (438–498.4)
3–5 months	129	226.5 (187.4–265.6)	53	245.2 (183.7–320.7)	106	89.2 (72.2–106.2)	288	145.9 (129.1–162.8)
6–11 months	34	29.8 (20.7–41.7)	12	27.8 (14.3–48.5)	59	24.8 (18.9–32)	105	26.6 (21.5–31.7)
1–4 years	32	4.1 (2.8–5.7)	6	2 (0.7–4.4)	75	3.7 (2.9–4.6)	113	3.6 (3–4.3)
5–9 years	11	1.2 (0.6–2.1)	2	s	26	1 (0.7–1.5)	39	1 (0.7–1.4)
10–14 years	3	0.3 (0.1–0.9)	3	0.8 (0.2–2.5)	22	0.8 (0.5–1.2)	28	0.7 (0.5–1)
15–19 years	1	s			9	0.3 (0.1–0.6)	10	0.2 (0.1–0.5)
20–24 years	3	0.4 (0.1–1.3)	1	s	4	0.1 (0–0.4)	8	0.2 (0.1–0.4)
Total	**622**	**14 (12.9–15.1)**	**280**	**16.1 (14.2–17.9)**	**613**	**4.6 (4.2–4.9)**	**1515**	**7.7 (7.3–8.1)**

s – no rate calculated due to small numbers.

Note: Rates are per 100,000 population; 'CI' indicates 95% confidence interval.

Sources:
Numerator: Ministry of Health.
Denominator: Ministry of Health live births, Mortality Review Population Estimates 2002–14.

Pertussis mortality

There were eight deaths due to pertussis during the study period. All but one of these deaths occurred in an infant aged under 3 months (Table 4). When mortality rates are examined by ethnicity, there was a disproportionately high number of deaths for Māori and Pacific infants compared with non-Māori/non-Pacific infants, although the numbers were too small to calculate meaningful rates (Table 5).

Table 4: Pertussis deaths by age group and year of death, New Zealand 2002–14

AGE GROUP	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	Total
<3 months	1	1	1	1					1		1	1		7
3–5 months														
6–11 months														
1–24 years											1			1
Total	**1**	**1**	**1**	**1**					**1**		**2**	**1**		**8**

Sources: EpiSurv and Mortality Review Database.

Table 5: Pertussis deaths by age group and ethnicity, New Zealand 2002–14 combined

AGE GROUP	Māori	Pacific peoples	Non-Māori/ Non-Pacific	Total
<3 months	3	3	1	7
3–5 months				
6–11 months				
1–24 years			1	1
Total	**3**	**3**	**2**	**8**

Source: Mortality Review Database.

Pertussis notifications and mortality by immunisation status

Notifications on EpiSurv indicate immunisation status of affected individuals. However, as only children born in New Zealand from 2005 onwards are included in the National Immunisation Register, the vast majority of this information is based on parental recall or review of the Well Child immunisation record. The immunisation status was confirmed from documentary evidence in 51.2 percent of cases and parental recall in 14.7 percent. The source of information was recorded as 'unknown' in 33.8 percent of those recorded as 'immunised' (data not shown). Children aged under 3 months who were notified as having pertussis were the least likely to have been immunised (Table 6).

Table 6: Immunisation status of cases notified with pertussis by age group, New Zealand 2002–14 combined

AGE GROUP	Immunised	Not immunised	Unknown*	% immunised**	Total
<3 months	285	443	77	35.4	805
3–5 months	295	104	34	68.1	433
6–11 months	298	126	44	63.7	468
1–4 years	2080	805	219	67.0	3104
5–9 years	2106	719	387	65.6	3212
10–14 years	1697	379	405	68.4	2481
15–19 years	775	118	493	55.9	1386
20–24 years	356	97	562	35.1	1015
Total	**7892**	**2791**	**2221**	**61.2**	**12,904**

* 'Unknown' indicates the immunisation status was either recorded as 'unknown', or this field was blank.

** Where percent immunised is equal to the percentage of total cases within each age group recorded as being immunised on the EpiSurv database.

Source: EpiSurv.

Immunisation records of the eight deceased cases were further checked against the data supplied by the Ministry of Health and contained in the Mortality Review Database. One case had received pertussis immunisation according to the current National Immunisation Schedule, but due to their young age had only received the first dose of the vaccine. The remaining seven cases either were not vaccinated, or they died or were admitted with pertussis infection prior to the age of 6 weeks, when the first vaccination is scheduled to occur (Table 7).

Table 7: Immunisation status of notified cases of pertussis who died from the disease by age group, New Zealand 2002–14 combined

AGE GROUP	Immunised	Not immunised	Unknown	Total
<3 months	1	6		7
3–5 months				
6–11 months				
1–24 years		1		1
Total	**1**	**7**		**8**

Sources: EpiSurv and Mortality Review Database.

B. Strategies for pertussis prevention and issues, and themes identified from mortality review

Strategies for pertussis prevention

Child immunisation in New Zealand

In New Zealand, pertussis immunisation for infants and children is included in the National Immunisation Schedule and offered free of charge. A primary course of the pertussis-containing vaccine DTaP-IPV-HepB/Hib (which protects against diphtheria, tetanus, pertussis, poliomyelitis, hepatitis B and *Haemophilus influenzae* type b diseases) is offered to infants in three doses at 6 weeks, 3 months and 5 months of age. The primary course is followed by pertussis-containing boosters, with a dose of DTaP-IPV offered at 4 years and a Tdap booster vaccination given at age 11 years (Ministry of Health 2014a).

The timeliness of the three primary doses among young infants is an important factor that contributes to the level of protection against pertussis. Studies have consistently shown that protection from pertussis infection increases incrementally after each dose, demonstrating the importance of completing all three doses to obtain full protection (WHO 2015). Current New Zealand data suggest pertussis immunisation in infants is effective at 41 percent (95 percent CI 23–55) after the first dose of the primary series, 78 percent (95 percent CI 68–95) after the second dose, and 89 percent (95 percent CI 85–92) following the third dose (Immunisation Advisory Centre 2015).

To help prevent a number of vaccine-preventable diseases in New Zealand, improving immunisation coverage in children has been a national health target since 2009–10. Initially the target was set so that 85 percent of 2-year-olds would be fully immunised by July 2010; this increased to 90 percent by July 2011 and 95 percent by July 2012 (Ministry of Health 2015a).

The introduction of the immunisation targets helped increase coverage among 2-year-olds to 93 percent in 2012; however, outbreaks of vaccine-preventable diseases such as pertussis and measles continued to occur due to low immunisation rates in preceding years (Ministry of Health 2015a). In 2012, the focus of the target was shifted to infants aged 8 months, so that 85 percent of 8-month-olds would have received their primary course of immunisation (at 6 weeks, 3 months and 5 months) on time, increasing to 90 percent by July 2014 and 95 percent by December 2015. National coverage in 8-month-olds has increased from 86 percent in June 2012 to 93 percent in September 2015 (Ministry of Health 2015b).

There is still room to improve pertussis immunisation coverage at age 6 months for Māori and Pacific peoples, as well as those from deprived households. Data from the peak of the most recent 2011–14 pertussis epidemic show coverage of infants with the three vaccine doses at age 6 months is lowest among those living in the most deprived household areas and among Māori and Pacific infants (Kiedrzynski et al 2015).

Coverage of all three pertussis vaccine doses at 6 months was lowest for Māori (62 percent) and Pacific peoples (73 percent) compared with NZ Europeans (81 percent) and for those living in most deprived households (67 percent coverage compared with 81 percent coverage for those in the least deprived households). For these populations, lower immunisation coverage in infants aged under 6 months, but improved coverage seen by 12 months, suggests underlying issues associated with receiving their scheduled immunisations on time in the early stages of life (Kiedrzynski et al 2015). Ensuring the three pertussis vaccine doses are received on time is important for maximising protection against the disease and reducing inequities.

Maternal immunisation in New Zealand

Because very young infants are not fully protected from pertussis until they complete their third dose of the primary vaccine schedule, developed countries are increasingly complementing routine childhood pertussis immunisation strategies with vaccinating pregnant women (WHO 2015). Maternal pertussis vaccinations provide passive immunity in the unborn child, as an immunised mother's antibodies are passed through the placenta to the baby before birth, providing increased protection against pertussis for young infants during the first few months of life (Amirthalingham et al 2014). This protection occurs during the time of greatest risk of pertussis as demonstrated by the New Zealand data. The timing of the vaccination given during pregnancy is important as the concentration of antibodies produced by the mother decreases relatively quickly after pertussis immunisation (bpac^{NZ} 2013; 2014).

Pertussis booster vaccinations are recommended for pregnant women in the third trimester between 28 and 38 weeks gestation (Ministry of Health 2014a). In New Zealand, PHARMAC has funded pertussis boosters to all pregnant women in the third trimester of pregnancy since January 2013. This funded pertussis immunisation was initially introduced as an epidemic control strategy for disease outbreak situations. Since 1 August 2015, PHARMAC agreed to fund a pertussis booster for all pregnant women in the third trimester of pregnancy via the community pharmaceutical section of the New Zealand Pharmaceutical Schedule, irrespective of the current level of disease in the community.

Box 2: Effectiveness and safety of maternal pertussis immunisation

A maternal pertussis vaccination programme was trialled across the UK in October 2012, in response to a pertussis outbreak in England. The UK Department of Health offered all pregnant women a five-component DTaP-IPV booster vaccination between 28 and 38 weeks of pregnancy (Amirthalingham et al 2014). Analyses of national surveillance data and hospital admissions between 2008 and 2013 showed confirmed pertussis cases and hospitalisations decreased more among those infants whose mothers received the maternal vaccination compared with infants with unvaccinated mothers. The greatest decline in confirmed cases and hospital admissions was observed among infants aged under 3 months (Amirthalingham et al 2014).

The UK maternal pertussis vaccination programme quickly achieved vaccine coverage of 64 percent over the study period. Vaccine effectiveness was assessed based on comparing maternal immunisation status of mothers of infants with confirmed pertussis, with immunisation coverage among pregnant women. Findings showed that a pertussis booster given to women during the third trimester of pregnancy is 91 percent (95 percent CI 84–95) effective in reducing pertussis infection in infants up to 3 months of age – the period of greatest risk of severe disease (Amirthalingham et al 2014).

A national strategy for protecting pregnant women (and their babies) against pertussis with the Tdap vaccine has also been implemented in Argentina since 2012, with recent analyses showing an 87 percent reduction in absolute pertussis mortality. No adverse events involving the vaccine were reported (Vizzotti et al 2015).

A recent study compared adverse events related to pregnancy (eg, stillbirth, accelerated time to delivery) in a large cohort of the pregnant women who received pertussis vaccination under the UK maternal vaccination programme, with a matched cohort of unvaccinated women. Findings showed there was no increased risk of stillbirth immediately after the vaccination or throughout the remainder of the pregnancy among vaccinated pregnant women. There was also no increased risk of maternal or neonatal death, (pre-)eclampsia, haemorrhage, fetal distress, uterine rupture, caesarean delivery or low birthweight (Donegan et al 2014). The safety of maternal pertussis vaccination has also been corroborated by other retrospective cohort studies in the USA (eg, Kharbanda et al 2014; Sukamaran et al 2015).

Cocooning

Cocooning is a strategy involving immunising those in close contact with infants who are too young (under 6 months) to have completed their full pertussis vaccination course (WHO 2015; Wiley et al 2013). The aim of the strategy is to limit the risk of pertussis exposure through household and other contacts by providing a protective 'cocoon' around infants in the early months of life (Swamy and Wheeler 2014).

Cocooning was initially recommended by a number of health institutions in developed countries (eg, Centers for Disease Control and Prevention, European Centre for Disease Prevention and Control) as a prevention response to continuing high-incidence pertussis, despite existing routine child immunisation strategies (Rivero-Santana et al 2014). A number of countries trialled various cocooning strategies, most of which targeted household members, as they were identified as the most common source of pertussis infection among young infants (Amirthalingham 2013; Wiley et al 2013).

Current evidence for the effectiveness of cocooning strategies is inconclusive as there are very few cohort studies demonstrating direct evidence of the strategy's efficacy (Rivero-Santana et al 2014). Among the existing body

of evidence, recent reviews show there are mixed findings, with some studies reporting reduced risk of pertussis among infants and others reporting no effect (Berti et al 2014; Bechini et al 2012; Rivero-Santana et al 2014; Wiley et al 2013).

Cocooning approaches require delivering multiple vaccinations to protect one infant and, therefore, are not as cost-effective or as easy to implement as maternal immunisation strategies (Amirthalingham 2013). Although there is some evidence of the acceptability of opportunistic cocooning (eg, vaccinations offered to both parents in maternity wards after birth before discharge; see Rossmann Beel et al 2014; Frère et al 2013), so far only small-scale cohort studies have been conducted.

Because of the logistical and practical difficulties associated with implementation, some researchers recommend a cocooning strategy sits alongside other strategies, such as maternal immunisation (eg, Cantey et al 2014; Chiappini et al 2013; Lugnér et al 2013). Others recommend a more selective form of cocooning, targeting those infants most at risk from infection (eg, Guzman-Cottrill et al 2012).

Overall, more evidence is required to evaluate both the efficacy and cost-effectiveness of cocooning strategies, though it is generally agreed the impact and cost-effectiveness of cocooning is likely lower than that of maternal immunisation strategies (WHO 2015).

Immunising health care workers

Health care workers are a source of pertussis transmission, particularly those who work with newborns and neonates in community and hospital maternity settings, or those who work with immunocompromised infants and children (WHO 2015). Establishing immunisation programmes for health care workers is an important strategy for preventing disease transmission to patients. Vaccinating health care workers for pertussis is a recommended strategy in some countries and a mandatory strategy in others (WHO 2015). The Advisory Committee on Immunization Practices provides advice to the Centers for Disease Control and Prevention, and recommends all adults (including health care workers) aged over 65 years receive a single dose of Tdap if they have not received one previously. Priority should be given to those in direct contact with infants aged under 12 months (CDC 2011).

There is no published evidence assessing the effectiveness of immunising health care workers for preventing pertussis transmission in health care settings (WHO 2015). Although health care personnel immunisation programmes have been established, very few of these incorporate evaluation processes into the programme to assess their effectiveness (Carrico et al 2014). The extent to which disease transmission from health care workers is prevented is, therefore, unclear, and immunising health care workers is only considered a partially effective prevention strategy (WHO 2015).

In New Zealand, the Tdap booster vaccination for pertussis is recommended by the Ministry of Health, but not funded in the community for lead maternity carers (LMCs) and other health care personnel working in neonatal units and other clinical settings where they are exposed to infants, especially those with pre-existing conditions (Ministry of Health 2014a). There have been known outbreaks of pertussis in New Zealand in maternity and neonatal units and childcare facilities. Some district health boards (DHBs) have responded to these outbreaks by providing pertussis immunisation programmes for staff in close contact with infants (Grant and Reid 2010; Grant 2015).

Issues and themes identified by the CYMRC and LCYMRGs

The following key issues and themes were identified by the CYMRC from the data analysed in Section A and mortality reviews from the LCYMRGs. These issues and themes, together with current trends identifed in the international literature on strategies for pertussis prevention, led to the development of the recommendations in Section C of this report.

1. Maternal immunisation for pertussis – uptake and awareness in pregnant women

Young infants aged under 6 months who have not fully completed the course of their three pertussis-containing vaccinations are most at risk from infection as they are not fully protected. Maternal immunisation strategies are a more cost-effective way to prevent pertussis among very young infants compared with cocooning strategies (WHO 2015). There is strong evidence demonstrating the effectiveness of maternal immunisation strategies in reducing infant pertussis cases, hospitalisations and deaths, in both the UK and the USA (Amirthalingham et al 2014; Terranella et al 2013).

Current data in New Zealand suggest uptake of the Tdap booster vaccination is low among pregnant women – estimated at around 13 percent (bpac^{NZ} 2014). There is evidence suggesting maternal vaccination is viewed as acceptable by pregnant mothers if the motivation is to protect their unborn child and give them the best start in life (see Box 3).

The CYMRC recognises a need to raise awareness of the safety and efficacy of the booster vaccination to increase uptake. LMCs, general practitioners (GPs) and antenatal educators are crucial for providing immunisation information to pregnant women. The most common source of immunisation information that parents reported encouraged immunisation uptake in the Growing Up in New Zealand study was a midwife, followed by GPs (Growing Up in New Zealand 2015). The Ministry of Health is central to ensuring a wide range of information resources are available for both health care workers and pregnant women, and has been developing such resources during the completion of this report. The first of these 'Let's talk about immunisation' resources is a guide for health professionals to use when talking about immunisation to expectant and new parents; this is due for release in December 2015.

Box 3: Evidence for acceptability of immunisations during pregnancy in New Zealand

A recent qualitative study in New Zealand used interviews with 59 pregnant women and women who had given birth in the previous 12 months to examine their beliefs about immunisation during pregnancy (Litmus Ltd 2015). Key findings showed:

- most women's key contact for the provision of pregnancy-related information and advice is their LMC. Approximately half of women interviewed reported having a conversation with their LMC about immunisation for influenza and/or pertussis
- pregnant women find immunisation during pregnancy acceptable if the primary reason for the immunisation is to protect their unborn child
- women are concerned about the safety of immunisation for their unborn baby; messages that emphasise the safety of immunisation during pregnancy are reassuring (Litmus Ltd 2015).

A recent survey study of 596 post-partum women in the Canterbury DHB region showed the two main motivations among women who received the Tdap vaccination in pregnancy were the desire to protect their unborn baby (96 percent) and because it was recommended by a health professional (84 percent). Among those who did not have the Tdap vaccine, the main reasons were that they did not know it was available (73 percent), they feared vaccine side effects (68 percent) and they were doubtful of the vaccine's effectiveness (56 percent) (Hill 2015).

2. Having systems to facilitate maternal immunisation

Increasing awareness and uptake of the pertussis booster vaccination among pregnant women requires having systems in place to facilitate the processes involved. At a general practice level, those who confirm pregnancies (eg, nurses and GPs) should be able to initiate the recall of their patients in the third trimester for their booster vaccination. A system should also be in place to notify LMCs when their clients have received their vaccination. At a national level, a system should be in place that records maternal immunisations on the National Immunisation Register and also transfers this information to the infant's immunisation record after birth.

The National Health IT Board is currently developing a national maternity clinical information system. The system will link information from hospital- and community-based maternity care settings about women and their babies, from pregnancy until the baby is 4–6 weeks old (Ministry of Health 2014b).

A shared maternity record view is also being developed alongside the maternity clinical information system. This shared record will enable all health professionals caring for a woman and her baby to record details of care, including midwifery notes, medications prescribed, and screening and test results, as well as access the information via a secure online portal. Over time, women will also be able to access their summary maternity care information via an online portal (Ministry of Health 2014b).

Having a shared source of maternity information will allow health practitioners to work together more effectively when caring for pregnant women. The CYMRC recognises the importance of these systems for strengthening communication between GPs and LMCs on maternal pertussis booster vaccination referrals. To help facilitate referrals, LMCs should be able to notify GPs when a patient is in their care and wishes to be referred for their booster vaccination. LMCs should also be able to see when the vaccination has been administered. Once the shared maternity record is available for viewing by pregnant women, GPs could also use the system to assist with recalling their patients in the third trimester for a booster vaccination.

3. Equity issues for Māori and Pacific infants and infants living in deprived areas

Analyses from section B in this report show Māori and Pacific infants are over-represented in pertussis hospitalisations and mortality. Other recent analyses corroborate these findings and show that, at 6 months of age, Māori and Pacific infants have the highest disease incidence and the lowest coverage. A similar trend is seen among infants aged under 6 months living in the most deprived areas in New Zealand (Kiedrzynski 2015).

The higher hospitalisation rates among Māori and Pacific infants aged under 6 months observed in this report partly reflect pertussis immunisation coverage inequities in Māori and Pacific infants under 6 months (see Kiedrzynski et al 2015). Although overall immunisation coverage has improved for Māori and Pacific infants aged 8 months and 2 years (Health Quality & Safety Commission 2015), improvements are still needed to ensure Māori and Pacific infants receive all three doses from their primary pertussis vaccination course on time.

For these infant populations, immunisation timeliness is affected by a number of barriers, such as a lack of transport, that restrict parents' ability to access the vaccination through general practices. These barriers could be addressed by the adoption of a broad range of service delivery models, such as outreach immunisation services that deliver the vaccines to these groups in their local community. For Māori and Pacific peoples, the development of targeted and culturally appropriate resources that resonate with pregnant women, and Māori and Pacific non-governmental organisations (NGOs) and health providers could help improve immunisation uptake.

4. Minimising transmission among those in close contact with young infants

Immunising health care workers is a reasonably cost-effective way to limit pertussis transmission, particularly among newborns and neonates in clinical and community settings. Immunising health care workers with booster doses every 10 years is recommended in the current *Immunisation Handbook* by the Ministry of Health (Ministry of Health 2014a). Immunising health care workers could be a useful complementary prevention strategy to adopt, particularly in times of epidemics. Individual DHBs are currently responsible for deciding which health care workers should be immunised and for funding those immunisations. Many DHBs offer pertussis booster vaccinations selectively to staff working in close contact with children aged under 12 months. However, vaccinating DHB health care workers is not guided by any national policies, and there is some variability in the frequency with which DHBs offer the vaccinations. Some DHBs currently recommend booster doses every 5 years and others recommend doses every 10 years.

5. Providing no-cost immunisation

The CYMRC is aware that some pregnant women have been referred to their general practice by their LMC to receive their free Tdap booster vaccination for pertussis, but were told by their general practice they need to have a consultation in order to receive the vaccination. These consultations are not always free and, in some instances, have led to pregnant women not having the vaccination to avoid the consultation fee. Having no-cost immunisation plays an important role in pregnant women's decision to get immunised (Litmus Ltd 2015).

The CYMRC recognises that general practices may be requesting women to have a consultation prior to receiving the pertussis booster vaccination because these women may not have seen their GP for some time. Some of the consultation feedback from the CYMRC's stakeholders suggested having a fully funded free third trimester consultation with GPs available to all pregnant women. A fully funded GP visit could remove any remaining cost barrier experienced by pregnant women as well as help establish relationships for post-natal care and ongoing family health care.

6. Maximising coverage – using national policies to drive local goals

Over the last 5 years, New Zealand has made excellent gains in equitable immunisation coverage and now almost 95 percent of infants are immunised by 8 months of age. These gains are mainly the result of changes in policy and practice following the Government's decision to place child immunisation targets within the national health targets and set Better Public Services targets for government agencies.

Immunisation targets are currently transitioning to being included in the new Integrated Performance Incentive Framework (IPIF). The aim of the IPIF is to support the health system to address issues of access, equity, quality, safety and the cost of health services (Ashton 2015). The IPIF programme shifts the performance improvement focus from primary health organisations (PHOs) to the whole-of-health system. The IPIF provides a framework that links national system-level measures (set by the Ministry of Health) with various local-level measures elected by DHBs for their contribution to the system-level measures (Ashton 2015). The CYMRC believes the IPIF is important for improving immunisation timeliness and coverage inequities that exist among Māori and Pacific peoples, and deprived populations at 6 months of age.

The IPIF aligns strongly with the value and high performance theme of the draft Health Strategy currently out for consultation. Action 8 of the draft health strategy roadmap of actions refers to building on the IPIF work to date to develop and implement a health outcome-focused framework for the whole health system (Ministry of Health 2015c). Local alliances that have been forming since 2013 are pivotal to helping develop the IPIF and facilitating the development of integrated models of primary care (Ashton 2015).

C. Recommendations

National policy and practice recommendations

The CYMRC expects the health system to deliver high-quality equitable services that are culturally competent, health literate, and meet the health needs and aspirations of pregnant women and their whānau.

1. The Ministry of Health should make equitable coverage of the pertussis booster vaccination during pregnancy a quality improvement measure, or target, for DHBs.
2. The Ministry of Health should record pertussis booster vaccinations given to pregnant women in the National Immunisation Register and develop a national system for transferring the information to the infant's immunisation health record at birth.[3]
3. The Ministry of Health should deliver a suite of education resources for pregnant women, LMCs and other primary health care service providers, informing them of the benefits of maternal pertussis immunisation.
4. The Ministry of Health and DHBs should include a maternal immunisation topic in the DHB Funded Pregnancy and Parenting Information and Education service specifications, to ensure antenatal classes provide information on pertussis booster vaccinations to expectant parents.
5. A national system should be developed that helps facilitate pertussis booster vaccination referrals and improves two-way communication between GPs and LMCs. This system should:
   a. facilitate the safe[4] and appropriate recall of pregnant women for their third trimester immunisation
   b. allow GPs and other immunisation providers to notify LMCs when the immunisation has been provided.
6. The Ministry of Health should support health providers to address barriers to immunisation service access for pregnant Māori and Pacific women and their whānau.

Local recommendations for DHBs, PHOs, LMCs and NGOs

1. All health providers in a general practice setting (ie, practice nurses and GPs) who confirm a pregnancy should initiate a plan to safely recall the pregnant woman for a pertussis booster vaccination in the third trimester.
2. LMCs in contact with pregnant women in the third trimester should ensure those women:
   a. are aware that a pertussis booster vaccination in the third trimester can protect young infants from pertussis
   b. understand where they can go to receive a pertussis booster vaccination in their region, and are offered the vaccination, or referred to an appropriate immunisation provider.
3. All health providers should ensure that the pregnant women they are in contact with are aware of the need for a pertussis booster vaccination in the third trimester.
4. General practices and PHOs should support the development of integrated primary care services that enable equitable and no-cost access to a pertussis booster vaccination for pregnant women in the third trimester.
5. DHBs and PHOs should establish policies that offer regular pertussis booster vaccinations to clinical and community health care workers in contact with neonates and newborns.
6. All health providers, including LMCs, should address barriers to immunisation service access for pregnant Māori and Pacific women and their whānau.

3 After the point of information transfer, the antenatal pertussis immunisation should be considered the 'first' immunisation on the child's immunisation record and be included in the parents' copy of the Well Child/Tamariki Ora My Health Book.

4 The 'safe' recall of pregnant women should take into account those pregnant women who have experienced a miscarriage or a stillbirth before the point of recall.

Best practice in community messaging

1. Parents and caregivers should continue to immunise infants on time with the primary course of pertussis vaccinations listed in the National Immunisation Schedule (with doses at 6 weeks, 3 months and 5 months of age).
2. All pregnant women should receive a pertussis booster vaccination in their third trimester in order to protect their young infants from pertussis. This booster should be delivered in every pregnancy.

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Appendix: Statistical significance testing

Introduction

Inferential statistics are used when it is necessary to use a sample to draw conclusions about the population as a whole (eg, weighing 1000 newborn babies to estimate the average birth weight of all babies in New Zealand). Any measurement based on a sample, however, will always differ from that of the underlying population, simply because of chance. Similarly, in assessing whether the risk of a particular condition (eg, sudden infant death syndrome) is different between two groups (eg, babies whose mothers smoked or did not smoke during pregnancy), the possibility that any differences seen arose simply by chance must always be considered (Craig et al 2008).

Statisticians have developed a range of measures to try to quantify the role chance plays when samples are used to make inferences about the population as a whole. Of these, one that is used in this report is the confidence interval. A 95 percent confidence interval suggests that if you were to randomly sample from the same population 100 times, in 95 times out of 100 the confidence interval would include the true value. In general, if the 95 percent confidence intervals of two samples overlap, there is no statistically significant difference between them. If the 95 percent confidence intervals do not overlap, they are thought to be statistically different (Webb et al 2005).

The use of statistical significance testing in this report

Descriptive statistics: The data presented in this report are derived from administrative data sets (eg, National Mortality Collection, EpiSurv) that capture information on all of the events (eg, deaths, hospital discharges) occurring during a particular period. Such data sets can thus be viewed as providing information on the entire population, rather than a sample. As a consequence, 95 percent confidence intervals are not required to quantify the precision of the estimate (eg, the number of pertussis deaths during 2002–14, although small, is not an estimate, but rather reflects the total number of deaths from pertussis during this period). Therefore, 95 percent confidence intervals are not provided for any of the data presented in this report where the intention is purely to describe the number of deaths occurring in a particular category (eg, number of deaths), on the basis that the numbers presented reflect the total population under study.

Measures of association: In considering whether statistical significance testing is ever required when using total population data, Rothman (2002) notes that if one wishes only to consider descriptive information (eg, rates) relating to the population in question (eg, New Zealand during 2002–14), then statistical significance testing is probably not required (as per the argument above). If, however, one wishes to use total population data to explore causal associations more generally, then the same population can be considered a sample of a larger super-population, for which statistical significance testing may be required. For example, the fact that mortality from pertussis is higher for children of Pacific ethnic groups might be used to draw conclusions about the impact of ethnicity on disease risk more generally. Similarly, the strength of any observed associations is likely to vary over time (eg, in updating 5-year pertussis hospitalisation data from 2005–11 to 2006–12, rate ratios for Māori infants are likely to fluctuate in line with variations in the underlying rates, even though the data include all hospitalisations for the 7-year period).

Therefore, whenever measures of association (ie, rate ratios) are presented, 95 percent confidence intervals are provided, so that the reader can assess the extent to which the associations presented may have arisen by chance (Rothman 2002). Examples of such measures of association would include an exploration of differences by deprivation or DHB.

Child and Youth Mortality Review Committee

"...Unuhia i te rito o te harakeke..."
"...taken away too early..."

Child and Youth Mortality Review Committee

"...Unuhia i te rito o te harakeke..."
"...taken away too early..."

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Immunisation Handbook

2014

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***Immunisation Handbook 2014* – sixth edition**

The *Immunisation Handbook* was first published in 1996 and was reprinted in 2000 with the inclusion of the Immunisation Standards. Since then further updated versions have been published in 2002, 2006, 2011 and 2014.

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.

Additional copies of this publication can be ordered from the Ministry of Health, phone (04) 496 2277.

Citation: Ministry of Health. 2014. *Immunisation Handbook 2014*. Wellington: Ministry of Health.

Published in May 2014 by the Ministry of Health
PO Box 5013, Wellington 6145, New Zealand

ISBN: 978-0-478-42779-0 (print)
ISBN: 978-0-42780-6 (online)
ISBN: 978-0-478-42782-0 (ebook)
HP 5839

This document is available at www.health.govt.nz

Foreword

It is appropriate to begin the *Handbook* by extending the Ministry'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 last edition of the *Handbook*, the management and purchasing of vaccines has transferred from the Ministry of Health to PHARMAC. Since July 2012 PHARMAC has been responsible for considering any changes to the National Immunisation Schedule vaccines, including the eligibility criteria, funding of new vaccines, and managing the supply of vaccines needed for localised and national disease outbreaks. PHARMAC recently approved funding for varicella, meningococcal conjugate and hepatitis A vaccines for individuals most at risk from these diseases. The rotavirus vaccine will be introduced to the National Immunisation Schedule in 2014 and is expected to significantly reduce the burden of rotavirus disease, particularly in young infants.

Immunisation coverage has significantly improved since it became a national Health Target. As at December 2013, 93 percent of 2-year-olds were fully immunised for the October to December 2013 quarter. Large gains have consistently been made for Māori children in this age group, with an increase from 85 percent in 2010 to 91 percent in December 2013. And in the Human Papillomavirus (HPV) Immunisation Programme equity has consistently been achieved for young Māori and Pacific women. Eight district health boards have achieved the HPV immunisation coverage target of 60 percent of 12-year-old girls having received all three HPV doses.

At a population level, the effects of increasing immunisation coverage are clearly discernable, 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 pneumococcal 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. 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
Acting 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 2014*. 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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Acknowledgements

The Ministry of Health (the Ministry) appreciates the time and commitment of those involved in the updating and rewriting of the *Immunisation Handbook 2014*.

The Ministry wishes to specifically acknowledge: Don Bandaranayake, Emma Best, Robert Booy, Harriette Carr, Steve Chambers, Felicity Dumble, Keith Grimwood, Helen Heffernan, Simon Hoare, David Holland, Darren Hunt, the Immunisation Advisory Centre, the Institute of Environmental Science and Research, Chris James, Bryn Jones, Tomasz Kiedrzynski, Min Lo, Peter McIntyre, Ryan McLane, Andrea McNeill, Chris Millar, Diana Murfitt, Lisa Oakley, Helen Petousis-Harris, Stewart Reid, Stephen Ritchie, Loretta Roberts, Allison Ross, Andi Shirtcliffe, Mishra Suryaprakash, Lesley Voss and Rachel Webb.

The Ministry would especially like to acknowledge the work of Vikki Cheer, the *Handbook* medical writer.

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Commonly used abbreviations

23PPV	23-valent pneumococcal polysaccharide vaccine
Ab	antibody
ACC	Accident Compensation Corporation
AEFI	adverse event following immunisation
AFP	acute flaccid paralysis
AIDS	acquired immunodeficiency syndrome
BCG	Bacillus Calmette-Guérin vaccine
BSE	bovine spongiform encephalopathy
CARM	Centre for Adverse Reactions Monitoring
CRS	congenital rubella syndrome
CSF	cerebrospinal fluid
DHB	district health board
DNA	deoxyribonucleic acid
DT	diphtheria tetanus vaccine
DTaP	paediatric 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
Hep B	hepatitis B
HHE	hypotonic-hyporesponsive episode
Hib	*Haemophilus influenzae* type b
HIV	human immunodeficiency virus
HPV	human papillomavirus
HZ	herpes zoster
HZV	herpes zoster vaccine
ICD	International Classification of Diseases
IG	immunoglobulin
IgG	immunoglobulin G
IM	intramuscular
IMAC	Immunisation Advisory Centre
IPV	inactivated polio vaccine
IV	intravenous
ITP	idiopathic thrombocytopenic purpura (also known as immune thrombocytopenia)
IVIG	intravenous immunoglobulin
LMC	lead maternity carer
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
MSD	Merck Sharp & Dohme (New Zealand) Limited
NIR	National Immunisation Register
NZBS	New Zealand Blood Service

NZPSU	New Zealand Paediatric Surveillance Unit
OMP	outer membrane protein
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
PHARMAC	Pharmaceutical Management Agency
PHO	primary health organisation
PPV	pneumococcal polysaccharide vaccine
PRP	polyribosylribitol phosphate
PTAC	Pharmacology and Therapeutics Advisory Committee
RCT	randomised controlled trial
RIG	rabies immunoglobulin
RV1	rotavirus vaccine (monovalent)
RV5	rotavirus vaccine (pentavalent)
SC	subcutaneous
SUDI	sudden unexpected death in infancy
TB	tuberculosis
Td	adult tetanus diphtheria vaccine
Tdap	adult tetanus, diphtheria and acellular pertussis vaccine
TIG	tetanus immunoglobulin
TT	tetanus toxoid
UK	United Kingdom
US	United States of America
VAPP	vaccine-associated paralytic poliomyelitis
vCJD	variant Creutzfeldt-Jakob disease
VV	varicella vaccine
VZV	varicella zoster virus
WHO	World Health Organization
ZIG	zoster immunoglobulin

Introduction

The purpose of the *Immunisation Handbook 2014* (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 printing, from published and unpublished literature.

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

Changes to the *Handbook* in 2014

All chapters have been updated and revised since the 2011 edition. In addition:

- the disease chapters have been reordered alphabetically
- there is a new 'Key information' box at the beginning of each disease chapter
- each disease chapter has the same sequence of sections, and many sections have the same sequence of subsections (for example, section 17.4 discusses rotavirus vaccines and subsection 17.4.2 the efficacy and effectiveness of rotavirus vaccines; similarly, section 21.4 discusses varicella vaccines and subsection 21.4.2 the efficacy and effectiveness of varicella vaccines)
- the content from the 'Passive immunisation' chapter has been moved to chapter 1
- 'Vaccination questions and concerns' has been moved from the end to the beginning of the *Handbook* (now chapter 3)
- there is a new chapter called 'Immunisation of special groups' (chapter 4), which provides recommendations for during pregnancy and lactation, infants with special immunisation considerations, immune-deficient individuals, immigrants and refugees, before travel, and those with occupational and lifestyle risk factors

- there is a new chapter for zoster (chapter 22)
- the 'History of the schedule' sections from each disease chapter have been removed, and the content added to Appendix 1
- Appendix 3 ('Immunisation standards') and Appendix 4 ('Authorisation of vaccinators') have been updated to include pharmacist vaccinators
- there is a new 'The cold chain: vaccine storage, transport and destruction' appendix (Appendix 6), which incorporates much of the cold chain information (previously in chapter 2)
- the 'Medicines Act' appendix has been removed and its content added to Appendix 6
- the 'Measles specimen collection' and the 'Management of exposure to varicella during pregnancy and care of the newborn' appendices have been removed and their content merged into the relevant disease chapters.

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 2.7 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.health.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 Pharmaceutical 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 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.health.nz) for changes to funding decisions, and the online edition of the *Immunisation Handbook* (www.health.govt.nz/immunisation) for the latest immunisation information. There may also be locally funded immunisation programmes in response to a specific need.

Changes to the National Immunisation Schedule in 2014

Table 1 shows the 2014 Schedule. All children transfer to the new Schedule from 1 July 2014, although the date the new vaccines are available may be later than 1 July while existing vaccine stocks are used up. There are no changes to the ages of the routine immunisation events.

The changes to the Schedule in 2014 are as follows.

1. Rotavirus vaccine (RV5, RotaTeq) is introduced at ages 6 weeks, 3 and 5 months (see chapter 17: 'Rotavirus'). Note that RV5 is an orally administered vaccine.
2. The 13-valent pneumococcal vaccine (PCV13, Prevenar 13) replaces the 10-valent pneumococcal conjugate vaccine (PCV10, Synflorix) at age 6 weeks, and at ages 3, 5 and 15 months (see chapter 15: 'Pneumococcal Disease').
3. All vaccines on the Schedule are funded for revaccination following immunosuppression (see chapter 4 and the relevant disease chapters).
4. Funded quadrivalent human papillomavirus vaccine (HPV4, Gardasil) may now be administered to girls from age 9 years; however, the usual Schedule remains at age 12 years (school year 8) (see chapter 9: 'Human papillomavirus').
5. Women with rubella antibody levels of <10 IU/mL are considered to be non-immune to rubella. This is a change from the previous recommendation of <15 IU/mL (see chapter 18: 'Rubella').

6. DTaP-IPV-HepB/Hib (paediatric diphtheria, tetanus, acellular pertussis, polio, hepatitis B and Hib vaccine, Infanrix-hexa) and DTaP-IPV may be administered to children aged under 10 years for catch-up immunisation. This is a change from the previous recommendation of age 7 years (see Appendix 2: 'Planning immunisation catch-ups' and the relevant disease chapters).

7. Tdap (adult tetanus, diphtheria and acellular pertussis vaccine) may be administered to children aged under 18 years for catch-up immunisation (funded from age 7 to under 18 years) (see Appendix 2: 'Planning immunisation catch-ups' and the relevant disease chapters).

8. All vaccines on the National Immunisation Schedule are funded for (re-)vaccination of individuals following significant immunosuppression. The timing and number of doses should be discussed with the individual's specialist.

Table 1: National Immunisation Schedule, commencing 1 July 2014*

Note: For ease of reading throughout the *Handbook*, vaccine trade names have been written in the standard font and as proper nouns.

Antigen(s)	**DTaP-IPV-HepB/Hib**	**PCV13**	**RV5**	**MMR**	**Hib**	**DTaP-IPV**	**Tdap**	**HPV**	**Td**	**Influenza**
Brand	Infanrix-hexa	Prevenar 13	RotaTeq	MMR II	Act-HIB	Infanrix-IPV	Boostrix	Gardasil	ADT Booster	Influvac and Fluarix
Manufacturer	GSK	Pfizer	MSD	MSD	Sanofi-aventis	GSK	GSK	bioCSL / MSD	bioCSL	Abbott and GSK
6 weeks	●	●	●							
3 months	●	●	●							
5 months	●	●	●							
15 months		●		●	●					
4 years				●		●				
11 years							●			
12 years (girls only)								● 3 doses		
45 years									●	
65 years									●	● annually

Key: D = diphtheria; T = tetanus; aP = acellular pertussis; IPV = inactivated polio vaccine; Hib = *Haemophilus influenzae* type b; Hep B = hepatitis B; PCV13 = 13-valent pneumococcal conjugate; RV5 = rotavirus vaccine (pentavalent); MMR = measles, mumps and rubella; d = adult diphtheria; ap = adult acellular pertussis; HPV = human papillomavirus; Td = adult tetanus and diphtheria vaccine.

* The date the new vaccines are released for use may be later than 1 July 2014 while existing stocks are used up.

2014 changes to targeted programmes for special groups

Vaccines funded for special groups are described in Table 2 below. New programmes and changes to existing programmes for 2014 are as follows.

1. Hepatitis A vaccine (see chapter 7) will be funded for:
   - transplant patients
   - children with chronic liver disease
   - close contacts of hepatitis A cases.
2. Hepatitis B vaccine (see chapter 8) will continue to be funded for household or sexual contacts of individuals with chronic hepatitis B infection, and for babies born to mothers with chronic hepatitis B infection (HBsAg positive). In addition, hepatitis B vaccine will be funded for:
   - HIV-positive patients
   - hepatitis C-positive patients
   - patients following immunosuppression (see also section 4.3)
   - transplant patients
   - dialysis patients.
3. Babies born to mothers with chronic hepatitis B infection (HBsAg positive) require hepatitis B immunoglobulin and hepatitis B vaccine at birth, preferably within the first 12 hours. However, both may be given up to seven days after birth. This is a change from the previous recommendation of up to 10 days after birth. These babies also require serological testing (anti-HBs and HBsAg) at age 9 months. This is a change from the previous recommendation for serological testing at age 5 months. (See chapter 8.)
4. Human papillomavirus vaccine (HPV, see chapter 9) will be funded for:
   - individuals aged under 26 years with confirmed HIV infection
   - transplant patients.

5. Meningococcal conjugate vaccines, MenCCV and MCV4-D (see chapter 12), will be funded for:
   - individuals pre- or post-splenectomy or with functional asplenia
   - individuals with HIV, complement deficiency (acquired, including monoclonal therapy against C5, or inherited) or pre- or post-solid organ transplant
   - close contacts of meningococcal cases
   - bone marrow transplant patients
   - individuals following immunosuppression.
6. Pneumococcal conjugate vaccine, PCV13 (see chapter 15) will be funded for:
   - high-risk children who have previously received four doses of PCV10
   - (re-)vaccination for children aged under 18 years: with HIV; who are post-haematopoietic stem cell transplant (HSCT) or chemotherapy; who are pre- or post-splenectomy or with functional asplenia; who are pre- or post-solid organ transplant, renal dialysis and other severely immunosuppressive regimens.
7. Pneumococcal polysaccharide vaccine, 23PPV (see chapter 15), will be funded for:
   - individuals who are pre- or post-splenectomy or with functional asplenia
   - high-risk children aged under 18 years.
8. Varicella vaccine (see chapter 21) will be funded for the following groups:
   - non-immune patients:
     - with chronic liver disease who may in future be candidates for transplantation
     - with deteriorating renal function prior to transplantation
     - prior to solid organ transplant
     - prior to any elective immunosuppression
   - patients at least two years after bone marrow transplantation, on advice of their specialist

- patients at least six months after completion of chemotherapy, on advice of their specialist
- HIV-positive individuals with mild or moderate immunosuppression who are non-immune to varicella, on advice of their HIV specialist
- individuals with inborn errors of metabolism at risk of major metabolic decompensation, with no clinical history of varicella
- household contacts of paediatric patients who are immune compromised, or undergoing a procedure leading to immune compromise, 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 immune compromised or undergoing a procedure leading to immune compromise, where the household contact has no clinical history of varicella.

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

Table 2: Funded vaccines for special groups

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

Vaccine	Individuals eligible for funded vaccine
Hepatitis A vaccine (see chapter 7)	Hepatitis A vaccine is recommended for: · transplant patients · children with chronic liver disease · close contacts of hepatitis A cases.
Hepatitis B vaccine and hepatitis B immunoglobulin (HBIG) (see chapter 8)	Babies of mothers with chronic hepatitis B infection need both hepatitis B vaccine and HBIG at birth. Hepatitis B vaccine is also recommended for: · household and sexual contacts of people with chronic hepatitis B infection · HIV-positive patients · hepatitis C-positive patients · patients following immunosuppression* · transplant patients · dialysis patients.

Vaccine	Individuals eligible for funded vaccine
Hib (see chapter 6)	Individuals of any age, pre- or post-splenectomy, or children aged under 18 years with functional asplenia should be offered Hib vaccine.
HPV (see chapter 9)	HPV vaccine should be offered to: · individuals aged under 26 years with HIV infection · transplant patients.
Influenza vaccine (see chapter 10)	Annual immunisation should be offered to all individuals 65 years and older and those aged under 65 years (including infants and children aged 6 months and older) with certain medical conditions. Pregnant women are also eligible for funded vaccine.
Meningococcal conjugate vaccines (see chapter 12)	Meningococcal conjugate vaccines, MenCCV and MCV4-D, should be offered to: · individuals pre- or post-splenectomy or with functional asplenia · individuals with HIV, complement deficiency (acquired, including monoclonal therapy against C5, or inherited) or pre- or post-solid organ transplant · close contacts of meningococcal cases · bone marrow transplant patients · individuals following immunosuppression.*
Pertussis vaccine (see chapter 14)	Recommended for women during pregnancy from 28 to 38 weeks' gestation.
Pneumococcal conjugate (PCV13) and pneumococcal polysaccharide (23PPV) vaccines (see chapter 15)	PCV13 for: · high risk children who have previously received 4 doses of PCV10 · (re-)vaccination for children aged under 18 years: with HIV; who are post-haematopoietic stem cell transplant (HSCT) or chemotherapy; who are pre- or post-splenectomy or with functional asplenia; who are pre- or post-solid organ transplant, renal dialysis and other severely immunosuppressive regimens. 23PPV for: · individuals who are pre- or post-splenectomy or with functional asplenia · high-risk children aged under 18 years.

Vaccine	Individuals eligible for funded vaccine
BCG (Bacillus Calmette-Guérin) (see chapter 20)	Neonatal BCG is recommended for infants at increased risk of tuberculosis (TB). Other children aged under 5 years at risk of TB exposure are also eligible.
Varicella vaccine (see chapter 21)	Recommended for: · 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* · patients at least two years after bone marrow transplantation, on advice of their specialist · patients at least six months after completion of chemotherapy, on advice of their specialist · HIV-positive individuals with mild or moderate immunosuppression who are non-immune to varicella, on advice of their HIV specialist · individuals with inborn errors of metabolism at risk of major metabolic decompensation, with no clinical history of varicella · household contacts of paediatric patients who are immune compromised, or undergoing a procedure leading to immune compromise, 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 immune compromise, where the household contact has no clinical history of varicella.

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

For more information, see section 2.7 (adult vaccination), chapter 4: 'Immunisation of Special Groups' and the individual disease chapters.

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)
- hepatitis A, hepatitis B, Hib, HPV, 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 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. Further information on eligibility can be found on the Ministry of Health website (www.health.govt.nz/eligibility).

Note that non-resident girls aged under 18 years can only receive funded HPV vaccine if they are staying in New Zealand for longer than nine months. See section 4.4 for more information about immigrant and refugee immunisation.

1 General immunisation principles

1.1 Immunity and immunisation

Immunity is the biological state of being able to protect oneself from infection and disease. The immune system is a complex network of organs, cells and molecules interacting with the rest of the body as well as the environment. It includes innate (non-specific, non-adaptive) mechanisms and acquired (specific, adaptive) systems.

One of the immune system's primary functions is to identify and remove infectious organisms, thereby preventing disease. It does this by recognising molecular fragments of microbes, called antigens. Immunity can be achieved either actively, by exposure to the disease or vaccination, or passively via antibody transfer *in utero* and through breast milk, or by injecting serum that contains antibodies.

The essential goal of active immunisation is to prime and prepare the immune system so that it can respond rapidly and specifically to the wild organism, thereby preventing (or attenuating) disease and, ideally, colonisation and infection.

1.1.1 Disease transmission, herd immunity and immunisation coverage

Vaccines are given to people to protect them against disease. They provide not only individual protection for some diseases but also population-wide protection by reducing the incidence of diseases and preventing them spreading to vulnerable people. Some of these population-wide benefits only arise with high immunisation rates, depending on the infectiousness of the disease and the effectiveness of the vaccine.

The basic reproduction number (R_0) 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 people.

If a significant proportion of the population are immune, then the chain of disease transmission is likely to be disrupted. This is called herd immunity. 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 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 eradicated. The greater the proportion of the population that is immune to the infection, the lower the R_0 will be. For example, data from an Australian study[2] indicates that an HPV (human papillomavirus) vaccine programme with 70 percent coverage in young women may lead to the near disappearance of genital warts from the heterosexual population, and the authors suggest that the R_0 for HPV types 6 and 11 (causing genital warts) has fallen to below 1 (see the herd immunity discussion 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
Smallpox	5–7	80–85
Tetanus	Not applicable	Not applicable
Tuberculosis	Not defined	Not defined
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 tremendous 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 probably varies greatly 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.

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

Immunisation coverage

High immunisation coverage is important to protect not only the health of an individual but, for most vaccines, the health of the community as well. High coverage reduces the spread of disease to those who have not been vaccinated because of medical reasons (eg, children with leukaemia while receiving treatment), or because of age (eg, infants who are too young to respond to some vaccines).

New Zealand's target for immunisation coverage is for at least 95 percent of children to be fully immunised by age 8 months, and then at age 2 years. This target is based on the need for:

- on-time immunisation coverage, particularly three doses of pertussis-containing vaccine for babies and the first dose of measles vaccine at age 15 months
- high population immunity, particularly to prevent measles transmission, one of the most infectious vaccine-preventable diseases.

For the three months ending 31 December 2013, 91 percent of New Zealand children were fully immunised by age 8 months and 93 percent were fully immunised by age 2 years.

1.1.2 Innate and specific immunity

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.

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 specific immunity and immune memory.

Specific immunity

B lymphocytes (B cells) and T lymphocytes (T cells), which come in a range of subsets with different functions, are responsible for specific immune responses. Plasma cells, a subset of B cells, secrete antibodies that play a vital role in killing microbes, such as viruses and bacteria, and inactivating toxins. Memory B cells are long lived and if stimulated by re-exposure to a microbial antigen can rapidly proliferate and secrete large amounts of antibody long after the original infection or vaccination has occurred.

Some T lymphocyte subgroups, such as T helper lymphocytes, have a role in directing the specific immune response, while others, such as cytotoxic T lymphocytes, have a role in killing pathogens, either directly or by killing host cells that have become infected. Another subset of T cells reside as memory T cells and can also be reactivated upon repeat exposure.

Vaccine-induced immunity follows a similar process, with the development of specific immunity and memory, but it is designed to produce maximal protective immunity with minimal systemic or local reactions.

1.1.3 Active and passive immunity

Active immunity

Active immunity is generated by the host's specific immune system, following exposure either to a microbe or to a microbial antigen (such as a surface protein or toxin).

The primary immune response, following first exposure to a microbe or antigen, is evidenced by plasma cells secreting first immunoglobulin M (IgM) and then immunoglobulin G (IgG). This first response is slow and peaks after around 30 days. The secondary immune response, which follows subsequent exposure to the same microbe or antigen, results in a more rapid response by plasma cells, which secrete very large amounts of IgG highly specific to the microbe or antigen. The secondary response peaks in four to seven days. Although the T-cell responses are also important for protection, it is usually the level of antibodies directed against a microbe or antigen that is measured in order to quantify an immune response.

Passive immunity

Passive immunity does not depend on the recipient's immune response for protection and is only temporary, lasting weeks to months. Passive immunity can be provided by the injection of human immunoglobulin, which is derived from pooled donated blood and contains high titres of antibodies to hepatitis B, cytomegalovirus, varicella, tetanus toxin, etc. In addition, preparations of specific high-titre immunoglobulin, derived from the blood of donors with especially high levels of antibodies, such as hepatitis B immunoglobulin (HBIG), zoster immunoglobulin (ZIG, for use after exposure to varicella or zoster), rabies immunoglobulin (RIG) and tetanus immunoglobulin (TIG), are available for use in people who have recently had an exposure to one of these organisms. Recommendations for the use of immunoglobulins are outlined in the relevant specific disease sections of this *Handbook*, and in section 1.5.

Another example of passive immunity is the passing of protective antibodies from mothers to their infants, both by placental transfer and via breast milk. Maternal antibodies play an important role in early protection against a range of diseases and in attenuating (weakening) infections so that infants can generate their own active immunity without serious illness. A baby born prematurely has a lower concentration of antibodies, and therefore a shorter duration of protection than a full-term infant, and if born before 28 weeks' gestation will have few or no maternal antibodies.

1.1.4 How vaccines work

Vaccines are live microbes that have been attenuated (weakened), whole microbes that have been killed so that they cannot replicate or cause disease, or fragments of the disease-causing microbe.

Administration of a vaccine elicits an immune response that begins with the innate, non-specific cells of the immune system recognising the vaccine antigens. The cells of the innate immune system then stimulate the cells of the adaptive immune system (T and B lymphocytes). Immune memory can last for many years, often for life. Protective levels of antibodies may wane, and a booster dose of vaccine can stimulate the memory cells into developing more antibodies.

Vaccination with killed microbes or with fragments of the microbe commonly requires three or more successive doses over a period of some months to generate effective immune responses. In contrast, a single vaccination with a highly immunogenic vaccine, particularly a live attenuated vaccine, is usually sufficient to generate long-term immune memory. If a further dose (a booster) is given some months or years later, a greater and longer-lasting secondary response can be stimulated, reinforcing and extending the immunological memory for that microbe.

1.2 Classification of vaccines

Vaccines are an antigenic preparation used to produce active immunity to a disease and may be classified in the following way. (See also Table 1.2.)

1.2.1 Live attenuated vaccines

To produce a live vaccine, such as MMR or varicella, the wild or disease-causing virus is attenuated (weakened), traditionally by repeated culture in the laboratory, or nowadays for new live vaccines, by genetic engineering, such as with rotavirus vaccines. The virulence properties of the virus are reduced so that it does not cause disease in healthy individuals. The attenuated vaccine virus multiplies to a limited extent in host tissue and induces an immune response similar to wild virus infection in the majority of subjects. Live vaccines are generally very effective and induce long-lived immunity.

In some instances (eg, varicella vaccine in adults), more than one dose may be needed because effective replication of the vaccine virus, and hence immunity, does not always result from the first dose.

1.2.2 Killed and inactivated vaccines

The term 'killed' is generally used for bacterial vaccines and the term 'inactivated' for viral vaccines. These vaccines are prepared by treating the whole cell or virus with chemicals that cause inactivation. Generally these organisms remain intact and whole. They generate an immune response (to a broad range of antigens) but cannot cause an infection because they are dead and so cannot reproduce.

1.2.3 Subunit vaccines

Subunit vaccines are developed using only the antigens known to elicit protective immunity. They can be further categorised as follows.

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 hepatitis B and HPV, are made using a gene from the (disease-causing) pathogen as an antigen, which generates a protective immune response. The gene is inserted into a cell system capable of producing large amounts of the protein of interest. For example, the gene for the hepatitis B surface antigen is inserted into yeast cells, which replicate and produce large amounts of the hepatitis B surface antigen. 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, 4vMenPV and 23PPV, see chapters 12 and 15). Polysaccharide vaccines are poorly immunogenic. They produce low affinity antibodies (which do not bind well to the antigen) and, because they do not elicit T-cell responses, immune memory does not develop. Multiple priming doses (even a single dose) can cause hyporesponsiveness in both children and adults to further doses (see section 12.4.2).

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, and immune memory.

Examples of carrier proteins and vaccines that use them are:

- tetanus toxoid (TT), used in one of the meningococcal C conjugate vaccines (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 (OMP), 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.

Other subunit vaccines

Another subunit vaccine is acellular pertussis vaccine, which is prepared from purified fragments of *Bordetella pertussis*. Outer membrane vesicle vaccines (OMV), such as the meningococcal B vaccines, are made from 'chunks' of the outer membrane of the cell. They contain a range of antigens.

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) · meningococcal ACYW-135 Conjugate: · pneumococcal (10- and 13-valent) · *Haemophilus influenzae* type b · meningococcal C and ACYW-135 Recombinant: · hepatitis B · human papillomavirus Other subunit: · pertussis, acellular · influenza

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

1.3 Vaccine ingredients

In addition to the antigen, a vaccine may contain a range of other substances (eg, an adjuvant and a preservative). Traces of residual components from the manufacturing process may also be present in the vaccine.

1.3.1 Adjuvants

Adjuvants are substances that enhance the immune response to an antigen by 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).

Previously the only adjuvants licensed for human use were aluminium salts such as aluminium hydroxide and aluminium phosphate. Other adjuvants now in use include oil-in-water emulsions (MF59, Novartis; AS03, GSK), a bacterial endotoxin (AS04, GSK) and one that uses immunopotentiating reconstituted influenza virosomes. Most non-live vaccines require an adjuvant, and most vaccines still use aluminium adjuvants.

See chapter 3 for further information on vaccine content.

1.3.2 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 no longer used in vaccines on the New Zealand National Immunisation Schedule.

1.3.3 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).

1.3.4 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.

1.3.5 Residuals

Residuals are traces of substances that remain in the vaccine as an inevitable consequence of the manufacturing process, and because the concentrations are so low there is no reason to remove them. Regulatory bodies vary as to which trace substances must be specified. Some manufacturers choose to list all of them. Residuals may include virus-inactivating agents (such as formaldehyde), antibiotics and other substances used in the manufacturing process, such as egg protein and gelatin.

1.4 Contraindications to vaccination

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 or consultant paediatrician.

1.4.1 General contraindications

Anaphylaxis to a previous vaccine dose or any component of the vaccine is an absolute contraindication to further vaccination with that vaccine. **For more detail on anaphylaxis, see section 2.4.**

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

1.4.2 Precautions

Acute febrile illness

Minor infection without significant fever or systemic upset is not a reason to defer immunisation. The decision to administer or delay immunisation because of a current or recent acute illness depends on the severity of the illness and the aetiology of the disease. All vaccines can be administered to people with minor acute illness (eg, diarrhoea or mild upper respiratory tract infections), but should be postponed if the individual has a fever over 38°C.

Reaction to a previous dose

Careful consideration will be needed depending on the nature of the reaction. If in doubt about the safety of future doses, seek specialist advice. A confirmed anaphylactic reaction to a previous dose is a contraindication to further doses of that vaccine.

Allergy to vaccine components

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 2.4).

Egg allergy, including anaphylaxis, is not a contraindication to MMR vaccine. Anaphylaxis to a prior dose of MMR is a contraindication to a further dose. Egg allergy, including anaphylaxis, is no longer considered a contraindication to influenza vaccination. However, a history of egg anaphylaxis warrants the first dose of influenza vaccine to be given in a supervised medical setting (see section 10.6.2).

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. If an individual has had anaphylaxis to any component contained in a vaccine, seek specialist advice.

Thrombocytopenia or bleeding disorders

Intramuscular vaccines should be administered with caution to individuals with thrombocytopenia or a bleeding disorder, since a haematoma may occur following intramuscular administration. Vaccine administration should be coordinated with clotting factor replacement therapy, where appropriate. A 23-gauge or smaller needle should be used and firm pressure applied to the injection site (without rubbing) for at least two minutes.

In the past, the subcutaneous route was recommended for people with significant bleeding disorders, but guidelines are now moving to recommend the intramuscular route, providing the vaccine is administered by someone familiar with the individual's bleeding risk. With the exception of hepatitis B vaccines, most Schedule vaccines may be given subcutaneously, but there is a risk of reduced immunogenicity and increased local reactions with subcutaneous administration. (See section 2.3 for information on vaccine administration.)

Recent receipt of another vaccine, blood or immunoglobulin product

If two different live parenteral virus vaccines are given within four weeks of each other, the antibody response to the first may interfere with the response to the second. They may be given on the same day without interference. There are no dose interval restrictions for inactivated/subunit vaccines (see section 2.6.1 and chapter 3). 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 (see Table 1.3). Note that this **does not apply to rotavirus vaccine, which is a non-parenteral vaccine**.

Table 1.3: Suggested intervals between immunoglobulin (IG) product administration or blood transfusion and MMR or varicella vaccination (does not apply to rotavirus vaccine)

Indications or product	Route	Dose		Interval (months)[a]
		U or mL	mg IgG/kg	
Tetanus prophylaxis (as TIG)	IM	250 U	10	3
Hepatitis A prophylaxis (as IG)				
· contact prophylaxis	IM	0.02 mL/kg	3.3	3
· international travel[c]	IM	0.06 mL/kg	10	3
Hepatitis B prophylaxis (as HBIG)	IM	0.06 mL/kg	10	3
Rabies prophylaxis (as RIG)	IM	20 IU/kg	22	4
Varicella prophylaxis (as ZIG)	IM	125 U/10 kg (max 625 U)	20–40	5
Measles prophylaxis (as IG):				
· standard	IM	0.25 mL/kg	40	5
· immunocompromised host	IM	0.50 mL/kg	80	6
RSV-prophylaxis (palivizumab monoclonal antibody)[b]	IM		15 mg/kg (monoclonal)	None

Continued overleaf

Indications or product	Route	Dose		Interval (months)[a]
		U or mL	mg IgG/kg	
Cytomegalovirus immunoglobulin[d]	IV	3 mL/kg	150	6
Blood transfusion:				
· washed RBCs	IV	10 mL/kg	Negligible	0
· RBCs, adenine saline added	IV	10 mL/kg	10	3
· packed RBCs	IV	10 mL/kg	20–60	5
· whole blood	IV	10 mL/kg	80–100	6
· plasma/platelet products	IV	10 mL/kg	160	7
Replacement (or therapy) of immune deficiencies (as IVIG)	IV		300–400	8
Therapy for ITP (as IVIG)	IV		400	8
Therapy for ITP	IV		1000	10
Therapy for ITP or Kawasaki disease (as IVIG)	IV		1600–2000	11

Key: MMR = measles, mumps, rubella; MMRV = measles, mumps, rubella, varicella; TIG = tetanus immunoglobulin; IM= intramuscular; IG = immunoglobulin; HBIG = hepatitis B immunoglobulin; RIG = rabies immunoglobulin; ZIG = zoster immunoglobulin; RSV = respiratory syncytial virus; IV = intravenous; RBCs = red blood cells; IVIG = intravenous immunoglobulin; ITP = immune (formerly termed 'idiopathic') thrombocytopenic purpura.

Notes

a These intervals should provide sufficient time for decreases in passive antibodies to allow for an adequate response to measles vaccine. Physicians should not assume that individuals are fully protected against measles during these intervals. Additional doses of IG or measles vaccine may be indicated after exposure to measles.

b Monoclonal antibodies may interfere with the immune response to vaccines. Seek specialist advice.

c Immunoglobulin is not available or recommended in New Zealand for pre-travel use.

d Cytomegalovirus immunoglobulin is not available in New Zealand.

Source: Adapted from American Academy of Pediatrics. 2012. Active and passive immunization. In: Pickering LK, Baker CJ, Kimberlin DW, et al (eds). *Red Book: 2012 report of the Committee on Infectious Diseases* (29th edition). Elk Grove Village, IL: American Academy of Pediatrics, Table 1.9.

1.5 Passive immunisation

Passive immunisation involves administering pre-formed antibody as human immune globulin 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 the immune globulins (immunoglobulins) for the New Zealand Blood Service (NZBS). Their sterile solutions of immunoglobulin are prepared by fractionating large pools of plasma collected from blood donors to the 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 either 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.

1.5.1 Preparations available in New Zealand

Immunoglobulin products available in New Zealand include: human normal immunoglobulin for intramuscular (IM) use, specific immunoglobulin for intramuscular use, human normal immunoglobulin for intravenous use (IVIG) and human normal immunoglobulin for subcutaneous use. All of these products have an excellent safety record in both Australia and New Zealand.

Human Normal Immunoglobulin-VF for intramuscular use

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 2 mL and 5 mL 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.

Specific immunoglobulin for intramuscular use

There are a number of specific human immunoglobulin preparations for IM use 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 from the NZBS, commercial products from alternative donor sources may be supplied.

Other products are held in a limited number of centres for national use. For example, rabies immunoglobulin (RIG) is held at NZBS sites in Auckland, Christchurch and Wellington. These products can be accessed following discussion with an NZBS medical officer.

Human normal immunoglobulin for intravenous use

The current human normal immunoglobulin for intravenous use in New Zealand is Intragam P, produced by CSL Behring Australia. 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).

It is 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 tetanus immunoglobulin. Because the level of immunoglobulin in each batch varies, consultation with a medical officer at the NZBS is recommended prior to issuing a prescription.[3]

Human normal immunoglobulin for subcutaneous use

Human normal immunoglobulin for subcutaneous use (Evogam) is produced by CSL Behring Australia. It is a sterile solution containing 16 g per 100 mL of total human plasma 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 are aggregates. The distribution of the IgG subclasses closely resembles that found in normal human plasma.

The pH value of the ready-to-use solution is 6.6. It contains 2.25 g of glycine in each 100 mL 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.

It 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.

Accessing immunoglobulin or contacting the NZBS

The 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 writing to:

New Zealand Blood Service
Private Bag 92071
Auckland 1142

or (during normal office hours) by:

telephone: (09) 523 2867
fax: (09) 523 5754.

1.5.2 Indications for use

Passive immunisation

For advice on the use of immunoglobulin products and specific dosages of these products, please contact a medical officer at the 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). 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 8.5.3 and 8.8.1), tetanus (section 19.5.3) and varicella zoster (section 21.8.2).

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 used by patients at home. This avoids the need for 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.[4] 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.

1.5.3 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 the light. If the product appears turbid or to contain 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, and 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 1.5.6.[4]

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, it is advisable to administer it in divided doses at different sites.

The subcutaneous product, Evogam, is normally given using an infusion pump. Information on infusion rates is provided in the medicine's data sheet.

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. (Refer to Table 1.3, in section 1.4.2, for the suggested intervals between immunoglobulin product administration or blood transfusion and MMR or varicella live virus vaccines.) If possible, immunoglobulins or other blood products should be deferred for at least three weeks after the administration of a live vaccine.

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 hepatitis B surface antigen (HBsAg) positive mothers.

Passive transfer of antibodies and interference with serological testing

Serological testing after the administration of immunoglobulin may detect the transfused antibodies for several months after administration. Serological testing after immunoglobulin should therefore be discussed with an expert.

1.5.4 Duration of effect

The estimated half-life of *intramuscular* human normal immunoglobulin is 27 ± 7 days (mean ± standard deviation [sd]).[4] 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).[4]

The estimated half-life of *subcutaneous* human normal immunoglobulin is 55 days (range 14–165 days).[4]

1.5.5 Contraindications and precautions

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 concentrated gammaglobulin may cause a local inflammatory reaction, which can be misinterpreted as a positive allergic reaction. Such 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.[3]

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 2.3).

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 2.4).

1.5.6 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 the 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.[3, 4]

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.

There have been occasional reports of renal failure following infusion of IVIG. These largely relate to sucrose-containing products. Intragam P, the product available in New Zealand, does not contain sucrose, but patients should be adequately hydrated prior to its 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.

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 section 1.4.2 and Table 1.3). 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.

(See sections 1.6 and 2.5 for further information about adverse events and reporting.)

1.6 Safety monitoring of vaccines in New Zealand

1.6.1 The approval of vaccines for use in New Zealand

All medicines and vaccines have risks and benefits. Before a medicine or vaccine is approved for use it must be tested in clinical trials to determine its effectiveness. Information about potential risks is known 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.

As the use of a medicine or vaccine increases, more 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 be available for distribution by the manufacturer or supplier.

Most countries have a safety monitoring system, which includes a voluntary spontaneous reporting scheme, to help identify any possible safety concerns. In New Zealand, Medsafe 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 benefit/risk 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 Spontaneous reporting

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 (AEFI) to the Centre for Adverse Reactions Monitoring (CARM), which is part of the New Zealand Pharmacovigilance Centre. Pharmaceutical companies also submit adverse event reports.

Data published by the WHO shows that New Zealand has one of the highest spontaneous reporting rates per capita in the world. It has been estimated that, in general, only around 10 percent of all adverse reactions are reported. However, it is not necessary for all adverse reactions to be reported for a potential safety signal to be spotted.

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 section 2.5 for details about what information should be reported to CARM.

1.6.3 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.

1.6.4 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.

1.6.5 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).

In New Zealand it is less likely that any new rare side-effects to vaccines will be detected because the number of people immunised is small compared to the number immunised in 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.

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. In some circumstances a longer timeframe between immunisation and reaction onset has been considered where there is a scientific basis to support it.[5]

Another approach to assessing vaccine safety is to compare 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.[6] Table 1.4 shows the number of coincidental events that might be expected as background rate events within one day, one week and six weeks after receipt of a hypothetical vaccine.

Table 1.4: Predicted numbers of coincident, temporally associated events after a single dose of a hypothetical vaccine, based on background incidence rates

	Number of coincident events since a vaccine dose			Baseline rate used for estimate
	Within 1 day	Within 7 days	Within 6 weeks	
Guillain-Barré syndrome (per 10 million vaccinated people)	0.51	3.58	21.50	1.87/100,000 person-years (all ages; UK Health Protection Agency data)
Optic neuritis (per 10 million female vaccinees)	2.05	14.40	86.30	7.5/100,000 person-years in US females
Spontaneous abortions (per 1 million vaccinated pregnant women)	397	2780	16,684	Based on data from the UK (12% of pregnancies)
Sudden death within 1 hour of onset of any symptoms (per 10 million vaccinated people)	0.14	0.98	5.75	Based on UK background rate of 0.5/100,000 person-years

Source: Black S, Eskola J, Siegrist C-A, et al. 2009. Importance of background rates of disease in assessment of vaccine safety during mass immunisation with pandemic H1N1 influenza vaccines. *The Lancet* 374(9707): 2115–22.

1.6.6 Seriousness of adverse events following immunisation (AEFI)

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.*

CARM considers a report to be serious 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.

Because a report is defined as serious based on what is reported, it is possible to have both serious and non-serious reports for the same event/person.

There is a risk of serious allergic reactions with all medicines and vaccines, and with some foods. With vaccines the risk of anaphylaxis is estimated to be around one to three reactions per one million doses administered. All vaccinators are trained and equipped to treat anaphylaxis if it does occur. This is the main reason people are asked to wait for 20 minutes following any immunisation, and why there is at least one health professional and one other adult with CPR training on-site.

See section 2.4 for information about preventing, recognising and treating anaphylaxis and section 2.5 for the AEFI reporting process.

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2 Processes for safe immunisation

Who can administer a vaccine?

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

- 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 ('authorised vaccinator').

Since 2012, pharmacists have been able to administer influenza vaccine due to a reclassification of the vaccine by the Medicines Classification Committee. It is the vaccine's medicine classification that gives a pharmacist (who meets the conditions of the classification) the authority to administer the vaccine. A pharmacist vaccinator must successfully complete a vaccinator training course approved by the Ministry of Health and comply with the immunisation standards of the Ministry of Health.

In early 2014, meningococcal, Tdap and zoster vaccines were also reclassified as being able to be given by a trained pharmacist vaccinator. It is anticipated that future reclassification of other vaccines will widen the range of vaccines that a pharmacist vaccinator is able to administer. (See Appendix 4: 'Authorisation of vaccinators and criteria for pharmacist vaccinators administering vaccines'.)

2.1 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 Appendix 6 and the *National Guidelines for Vaccine Storage and Distribution*[1] for detailed vaccine storage, transportation and destruction information.

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 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 monthly basis.
All immunisation providers who offer immunisation services must achieve Cold Chain Accreditation (CCA), including public health units, pharmacies, travel clinics, hospital wards, clinics and departments, and pharmacies.
Each immunisation provider must have a written cold chain management policy in place and ensure their policy is reviewed and updated annually.
If the vaccine refrigerator temperature goes outside the recommended +2°C to +8°C range: · refer to Appendix 6 and the *Annual Cold Chain Management Guide and Record* · label the vaccines 'not for use' and leave them in your refrigerator – keep the refrigerator door closed · download the data logger and check for inconsistencies or temperature fluctuations · contact your local immunisation coordinator for advice and further actions, as required · document the steps and actions you have taken · if you are recalling or re-immunising children or adults, inform the Ministry of Health's National Immunisation Programme by emailing immunisation@moh.govt.nz or by contacting the Manager Immunisation directly.

2.2 Informed consent

2.2.1 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 and Privacy Act 1993).

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.

2.2.2 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 risks 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 National Immunisation Register). 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).

2.2.3 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.

2.2.4 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 National Immunisation Register (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.

Information for parents, guardians and health care providers

Health care providers should offer information without individuals or parents/guardians having to ask for it. The depth of information offered or required will 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, as well as 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 2.8 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, it is good practice to 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 to order, view or download 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 [code 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'.

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 professional 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 local immunisation coordinator (a list and contact details are available at www.immune.org.nz).

2.2.5 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.

2.2.6 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 2001 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).

2.3 Vaccine administration

The 'Immunisation standards for vaccinators' and the 'Guidelines for organisations 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 Appendix 6 and the *National Guidelines for Vaccine Storage and Distribution*).[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 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.

2.3.1 Pre-vaccination checklist

Prior to immunisation with *any* vaccine, the vaccinator should ascertain if the vaccinee (child or adult):

- is unwell on that day
- has a fever over 38°C
- has ever had a severe reaction to any vaccine
- has any severe allergies to vaccine components (eg, gelatin, egg protein, neomycin)
- has appropriate spacing between doses of the same vaccine (what/when was the last vaccination?)
- is pregnant (if applicable) or planning pregnancy
- has an undiagnosed or evolving neurological condition (for pertussis-containing vaccines only).

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 will also need to advise the individual/parent/guardian they will need to remain for 20 minutes post-vaccination.

2.3.2 Additional precautions for live vaccines

Prior to immunisation with a *live* vaccine, the vaccinator should know whether the vaccinee (child or adult):

- has lowered immunity (eg, due to leukaemia, cancer, HIV – see section 4.3)
- is taking corticosteroids (eg, prednisone) or other immunosuppressive drugs (see section 4.3)

- has had a live parenteral or intranasal vaccine within the last four weeks – if in doubt, check the individual's immunisation status on the NIR (if applicable)
- has had an injection of immunoglobulin or a blood transfusion within the last 11 months (see section 1.4.2 and Table 1.3)
- who is receiving a varicella vaccine lives with someone with a disease or treatment that lowers immunity; advise the vaccinee that if a post-immunisation rash occurs, they should be isolated from the immunosuppressed individual (see section 21.7)
- is pregnant (if applicable) or planning pregnancy (see section 4.1).

2.3.3 Conditions that are not contraindications to immunisation

The following conditions are not contraindications to the immunisation of children and adults (see chapter 3 for further detail):

- mildly unwell, with a temperature less than 38°C
- asthma, hayfever, 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 (HHE, see section 2.4.2)
- 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; immunisation with MMR does not pose any extra risks to those already immune to one or all of the three diseases)

- prematurity in 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, which is no longer a contraindication to MMR vaccine (see section 11.6.3)
- family history of vaccine reactions
- family history of seizures
- family history of sudden unexplained death in infancy (SUDI)
- child's mother or household member is pregnant.

See section 1.4.1 for information on general contraindications to immunisation, or the relevant disease chapter section for more specific vaccine contraindications.

2.3.4 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 vitally 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 2.2: 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.	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.
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.

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.

Needle angle, gauge and length (see Table 2.3)

All schedule vaccines (with the exception of MMR, which is 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.

Table 2.3: Needle gauge and length, by site and age

Age	Site	Needle gauge and length	Rationale
Intramuscular injection			
Birth	Vastus lateralis	23–25 G x 16 mm	
6 weeks	Vastus lateralis	23–25 G x 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 x 25 mm	A 25 mm needle will ensure deep IM vaccine deposition.
15 months–3 years	Deltoid or Vastus lateralis	23–25 G x 16 mm 23–25 G x 25 mm	The vastus lateralis site remains an option in young children when the deltoid muscle bulk is small and multiple injections are necessary.
3–7 years	Deltoid	23–25 G x 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 x 25 mm	
Older children (7 years and older), adolescents and adults	Deltoid[b]	23–25 G x 16 mm, or 23–25 G x 25 mm, or 21–22 G x 38 mm	Most adolescents and adults will require a 25 mm needle to effect deep IM deposition.
	Vastus lateralis[a]	21–22 G x 38 mm	
Subcutaneous injection			
Subcutaneous injection	Deltoid	25–26 G x 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.

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 x 16 mm needle; for 60–90 kg use a 23–25 G x 25mm needle; for >90 kg use a 21–22 G x 38 mm needle. For adolescent and adult males, a 23–25 G x 25 mm needle is sufficient.[3, 4]

2.3.5 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 and older – the choice will be based on the vaccinator's professional judgement
- the deltoid muscle for older children, adolescents and adults.

In infants and young children aged under 15 months, the deltoid muscle does not provide a safe IM injection site due to the superficiality of the radial nerve and the deltoid muscle being insufficiently developed to absorb medication adequately.

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.

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.

2.3.6 Infant vaccination (vastus lateralis)

Infants aged under six months do not need to be grasped or restrained as firmly as toddlers. At this age, excessive restraint increases their fear as well as muscle tautness. An infant can be placed lying on his or her back on the bed, or in the cuddle (semi-recumbent) position on the parent's/guardian's lap. Placing the infant on the bed minimises delay between injections and makes the injection process easier, although some vaccinators believe the cuddle position offers better psychological support and comfort for both the infant and the parent/guardian.

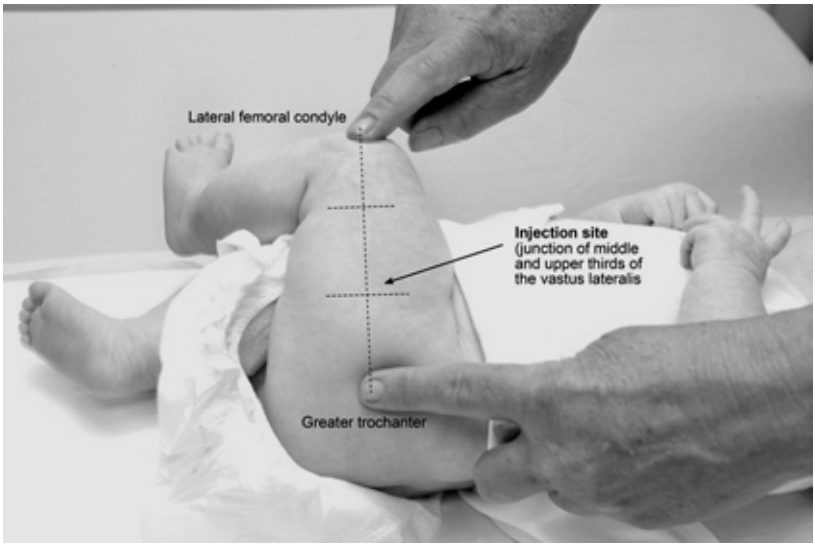
Ideally, the parent/guardian should be asked if they wish to hold the infant or child for the injections. Some will prefer not to be involved with the procedure – some do not even wish to be present. If the parent/guardian is helping to hold the infant or child, ensure they understand what is expected 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 2.3.13 for soothing measures).

To locate the injection site, undo the nappy, gently adduct the flexed knee and (see Figure 2.1):

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 2.1: 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.

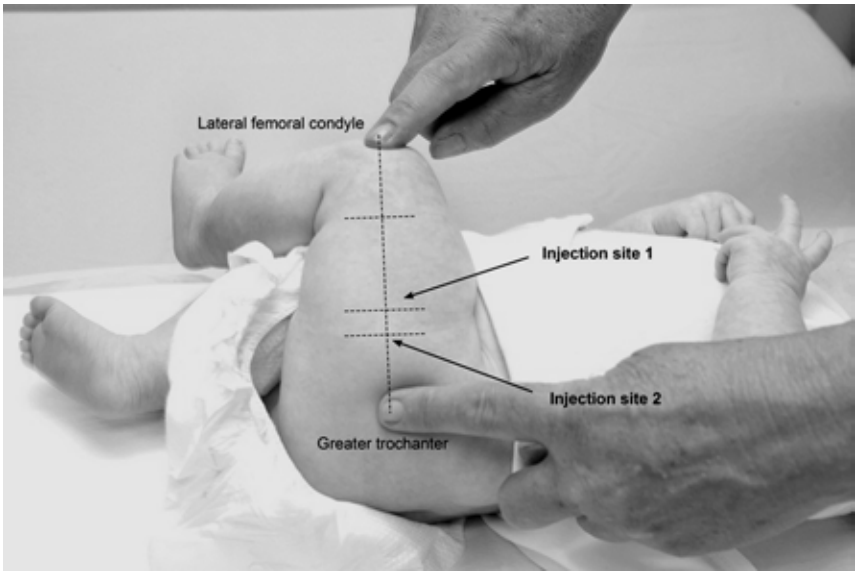
Multiple injections in the same muscle

In general, the best-practice recommendation is only one injection per site (eg, vastus lateralis), although with the introduction of new vaccines and the need for best protection (eg, catch-ups), two injections in one muscle may be required. Unless the manufacturer's data sheet states otherwise, this is considered safe and acceptable.

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 it is necessary for two vaccines to be given in the same limb, the vastus lateralis is preferred because of its greater muscle mass (see Figure 2.2). 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.

Figure 2.2: Diagram showing suggested sites for multiple injections in the lateral thigh



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.

If all scheduled vaccines are not administered concurrently, there is no minimum interval necessary between visits (ie, it could be the next day). However, there must be at least four weeks between:

- doses of the same vaccine
- two live parenteral or intranasal vaccines (note: this does not apply to rotavirus vaccine).

2.3.7 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.

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 2.3 and 2.4).

Figure 2.3: Photo showing cuddle positions for vastus lateralis or deltoid injections in children

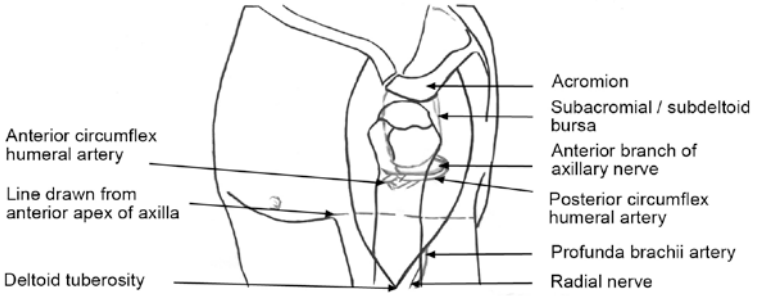
Figure 2.4: Photo showing the straddle position for vastus lateralis or deltoid injections in children

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.

2.3.8 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 arm may damage the nerve) (see Figure 2.5).

Figure 2.5: Line drawing showing surface landmarks and structures potentially damaged by intramuscular injection in the upper limb



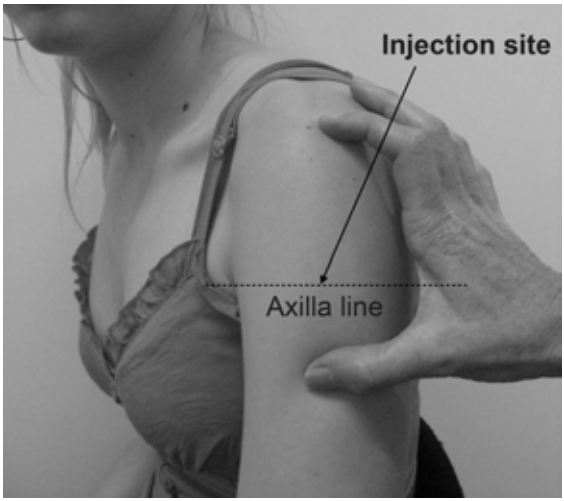
Reproduced with permission: Cook IF. 2011. An evidence based protocol for the prevention of upper arm injury related to vaccine administration (UAIRVA). *Human Vaccines* 7(8): 845–8.

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).[5]

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 2.6).

Figure 2.6: Diagram showing how to locate the deltoid site



If multiple injections in the deltoid are required, the sites should be separated by at least 2 to 3 cm.[6]

2.3.9 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 section 1.4.2 for information about thrombocytopenia and bleeding disorders.

2.3.10 Intradermal injections

The intradermal injection technique for BCG vaccine requires special training, and should only be performed by a gazetted BCG vaccinator. (See chapter 20 and the *Technical Guidelines for Mantoux Testing and BCG Vaccination 1996*[7] [or the current edition].)

Some other non-funded vaccines (eg, Intanza, an influenza vaccine) are administered by the intradermal route. Vaccinators should refer to the manufacturer's data sheet for instructions on administration.

2.3.11 Oral vaccine administration

The rotavirus vaccine is administered orally. Administer the dose by gently squeezing the liquid into the infant's mouth, towards the inner cheek, until the dosing tube is empty. **Do not inject oral vaccines.**

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

2.3.12 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 2.4) 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 2.4: Common vaccine responses

Vaccine	Common vaccine responses
DTaP- or Tdap-containing vaccine	Localised pain, redness and swelling at injection site. Mild fever. Being grizzly and unsettled – this may persist for 24–48 hours. Drowsiness. Extensive limb swelling after the 4th dose of a DTaP-containing vaccine.
Hepatitis B	Very occasionally soreness and redness at the injection site. Mild fever.
Hib	Localised pain, redness and swelling at the injection site. Mild fever.
MMR	Discomfort at injection site. 5–12 days after vaccination: · mild fever with faint rash (not infectious) · head cold and/or runny nose · cough and/or puffy eyes · swelling of salivary glands.
Adult Td	Localised discomfort, redness and swelling at the injection site.
Influenza	Mild fever. Occasional discomfort, redness and swelling at the injection site.
Pneumococcal	Pain at the injection site. Mild fever.
HPV	Localised discomfort, redness and swelling at the injection site. Heavy arm. Mild fever. Nausea. Dizziness. Headache.
Rotavirus	Diarrhoea may occur after the first dose.

2.3.13 Recommendations for fever and pain management

Fever

General fever-relieving measures include:

- giving extra fluids to drink (eg, more breastfeeds or water)
- reducing clothing if the baby is hot
- placing a cold, wet cloth on the injection site to help relieve some of the discomfort.

The use of paracetamol during paediatric immunisation (including influenza vaccine) may affect the antibody response.[8] 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.[9]

Using age-appropriate distraction has been shown to reduce pain and distress.[9] 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. For children aged over 12 months, tactile stimulation may create 'white noise'. Paediatric and adult studies found rubbing or applying pressure to the injection site before and during injection reduced pain.[10] Vibration devices can also be used.[11] Do not rub the injection site after the injection as it increases the risk of vaccine reactogenicity.

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.[12]

For infants aged under 12 months, giving a sugar solution immediately before the injection provides pain relief and may last for up to 10 minutes.[9] Rotavirus vaccines contain sucrose at a similar concentration and volume to the sugar solution doses shown to reduce pain, although rotavirus vaccines have not been directly evaluated.

Give the rotavirus vaccine 1–2 minutes before the other immunisations. Do not give additional sucrose if giving a rotavirus vaccine. The infant can then be breastfed or held comfortably while the immunisations are given.

For infants and children, the use of a topical anaesthetic cream or patch has been found to be effective for immunisation pain management.[9] 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.

Only use antipyretic analgesics such as paracetamol for relief of post-vaccination pain and significant discomfort. Because they may affect the antibody response,[8] antipyretic analgesics should not be used before immunisations or for fever prevention.

2.4 Anaphylaxis

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.

2.4.1 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 2.5.

Table 2.5: Signs and symptoms of anaphylaxis

	Signs and symptoms	Severity
Early warning signs (within a few minutes)	Dizziness, perineal burning, warmth, pruritis, 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	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 2.8).

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 2.6). 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 2.6: 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

2.4.2 Distinguishing a hypotonic-hyporesponsive episode (HHE) from anaphylaxis

Hypotonic-hyporesponsive episode (HHE) is the sudden onset of pallor or cyanosis, limpness (muscle hypotonia), and reduced responsiveness or unresponsiveness occurring after vaccination, where no other cause is evident, such as a vasovagal episode or anaphylaxis.[13] The episode usually occurs 1 to 48 hours after vaccination and resolves spontaneously. Adrenaline is not recommended for HHE because these children do not have respiratory and circulatory problems.

In the reported cases, full recovery has occurred and there have been no long-term sequelae.[14]

HHE is a recognised serious reaction to immunisation and should be reported to the Centre for Adverse Reactions Monitoring (CARM; see section 2.5).

2.4.3 Avoidance of anaphylaxis

To help avoid 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.

2.4.4 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 2.7) 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 2.7 and 2.8).

Table 2.7: Emergency equipment

An emergency kit should contain:

- adrenaline* 1:1000 (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 x 25 mm, 22 G x 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).

The following drugs are used only under the direction of a medical practitioner:

- antihistamine injection
- hydrocortisone injection (available on Medical Practitioner Supply Order).

2.4.5 Emergency management

IM injection of 1:1000 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 2.8: Initial anaphylaxis response/management

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

ASSESS – Lie the person down in the recovery position. If they are unconscious, place them in the recovery position and institute standard procedures for basic life support (airway, breathing, circulation). If cardiorespiratory arrest occurs, administer age-appropriate CPR and life-support measures.

ADMINISTER ADRENALINE by deep intramuscular injection – dosage: 1:1000 (adrenaline 1:1000 = 1 mg/mL).

Adrenaline dosage for 1:1000 formulation is 0.01 mL/kg up to a maximum of 0.5 mL.

If weight is unknown, use the following guidelines:

- Infants aged under 1 year: 0.05–0.1 mL
- Infants aged under 2 years: 0.1 mL
- Children 2–4 years: 0.2 mL
- Children 5–10 years: 0.3 mL
- Adolescents ≥11 years: 0.3–0.5 mL
- Adults: 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.

2.4.6 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, the individual must be accompanied by the attending health professional so that treatment can be continued during transfer.

Hydrocortisone and antihistamines 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 include:

- phenergan: 0.5 mg/kg orally or 0.25 mg intravenous, to inhibit delayed histamine reactions
- 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, either via online reporting (https://nzphvc-01.otago.ac.nz/carm-adr/reporting.php) or by downloading, completing and posting the reporting form to CARM, as described below.

2.5 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.

Health professionals are professionally and ethically responsible for reporting serious or *unexpected* adverse events that occur after the administration of all medicines, including vaccines. Serious events are defined as those that significantly affect an individual's health, including reactions suspected of causing:

- death
- danger to life
- hospitalisation
- prolongation of hospitalisation
- interruption of productive activity in an adult recipient
- increased investigational or treatment costs
- birth defects.

Some providers are able to report events through their practice management system. Reports can also be completed online (https://nzphvc-01.otago.ac.nz/carm-adr/reporting.php), or the form can be downloaded and printed using the above link, completed and mailed to:

Freepost 112002
The Medical Assessor
Centre for Adverse Reactions Monitoring (CARM)
PO Box 913
Dunedin, 9710

or faxed to:

(03) 479 7150.

The information required in the reporting form covers:

- the individual's details
- vaccine(s) administered
- which vaccine, if in a series (eg, primary series, 6-week event)
- vaccine(s) batch number(s)
- date of onset of symptoms
- type and duration of adverse event
- treatment required
- outcome, if known (reporting should not be delayed while awaiting outcome information).

2.5.1 What should be reported?

Health professionals/vaccinators should report any serious or unexpected AEFI (regardless of whether or not they consider the event to have been caused by the vaccination), such as those described in Table 2.9 below.

Individuals or parents/guardians should be encouraged to notify vaccinators of any AEFI which 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 IMAC (0800 IMMUNE / 0800 466 863) to notify on their behalf.

CARM prefers reports from health professionals – doctors, other prescribers, pharmacists and nurses. When consumers report to CARM, the individual's health practitioner should be involved, where possible.

Table 2.9: AEFIs to be reported

Timeframe	Event
Within 24 hours of vaccination	Anaphylactic reaction (acute hypersensitivity reaction) Anaphylaxis Persistent inconsolable screaming (more than three hours) Hypotonic-hyporesponsive episode (HHE) Fever >40^{o}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 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

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

2.5.2 CARM assessment of causality

Each report received by CARM is evaluated by a medical assessor to determine the likelihood of an association between the adverse event and the medicine.

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.

2.6 General immunisation practices

2.6.1 Spacing of doses

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

Spacing of doses of the same vaccine

The immune response to a series of vaccines depends on the time interval between doses. A second dose of the same vaccine given less than three weeks from the first dose may result in a reduced immune response. Therefore, the general rule is for a minimum of four weeks between doses of a primary series, unless there are specific recommendations for a rapid schedule by the manufacturer. It is not necessary to repeat a prior dose if the time elapsed between doses is more than the recommended interval.

A minimum interval of four months between priming dose(s) and the booster dose allows affinity maturation of memory B cells, and thus higher secondary responses.

Spacing of different vaccines

Unless the manufacturer makes 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 or live vaccine.

Where two or more parenterally or intranasally administered *live* vaccines are given at different visits, a minimum interval of four weeks is recommended. This is to avoid the response to the second vaccine being diminished due to interference from the response to the first 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 may 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.

2.6.2 Vaccination of children with inadequate vaccination records

Children *without a documented history of vaccination* are recommended to have a full course of vaccination appropriate for their age. In cases of doubt, it is much better to provide an unnecessary dose than to miss out a needed dose.

2.6.3 Catch-up programmes for unimmunised or partially immunised children

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

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, medical officer of health, public health service or IMAC.

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

2.7 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 2.10. 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 2.10: 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 (women only)	3 doses*

* Women who were under age 20 years when they commenced HPV vaccination are currently funded to complete the three-dose course, even if they are older than 20 years when they complete it.

See Table 2.11 for a checklist for adult vaccination, 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, of immune-deficient individuals, of immigrants and refugees, for travel, and for those with occupational and lifestyle risk factors.

Table 2.11: Checklist for adult vaccination, excluding travel requirements

Vaccine (relevant chapter)	Recommended and funded for adults ≥18 years	Recommended but not funded for adults ≥18 years
Hib (chapters 4 and 6)	Pre- or post-splenectomy	
Hepatitis A (chapter 7)	Transplant patients Close contacts of hepatitis A cases	Individuals with hepatitis C infection
Hepatitis B (chapter 8)	Household and sexual contacts of people with chronic hepatitis B infection Individuals: · undergoing renal dialysis · with hepatitis C infection · who are HIV positive · following immunosuppression[a] · who are solid organ and bone marrow transplant recipients · with chronic liver disease, and prior to liver transplant · who are haemodialysis patients	Hepatitis B vaccine for non-immune adults at risk
HPV (chapters 4 and 9)	Women who started their immunisation course before age 20 years[b] Individuals aged under 26 years with HIV infection Transplant patients	Individuals aged under 26 years who are immune compromised Men who have sex with men

Vaccine (relevant chapter)	Recommended and funded for adults ≥18 years	Recommended but not funded for adults ≥18 years
Influenza (chapter 10)	Annual influenza vaccine for: · individuals aged 65 years and older · pregnant women · individuals aged under 65 years who meet the chronically ill criteria	Annual influenza vaccine
MMR (chapters 11, 13 and 18)	Any individual susceptible to any one of these three diseases	
Meningococcal conjugate (chapters 4 and 12)	For individuals: · pre- or post-splenectomy or with functional asplenia · with HIV, complement deficiency (acquired, including monoclonal therapy against C5, or inherited) or pre- or post-solid organ transplant · who are close contacts of meningococcal cases · bone marrow transplant patients · following immunosuppression[a]	Young adults in communal accommodation Laboratory personnel routinely exposed to *N. meningitidis*
Pneumococcal conjugate and polysaccharide (chapters 4 and 15)	23PPV for individuals pre- or post-splenectomy or with functional asplenia	PCV13 for adults pre- or post-splenectomy or with functional asplenia (ideally before the funded 23PPV) PCV13 followed by 23PPV for those at risk PCV13 followed by 23PPV for those aged ≥65 years
IPV (chapter 16)	Any unvaccinated or partially-vaccinated individual	

Vaccine (relevant chapter)	Recommended and funded for adults ≥18 years	Recommended but not funded for adults ≥18 years
Td, Tdap vaccine (chapters 5, 14 and 19)	Td for susceptible individuals; boosters at 45 and 65 years[c] Tdap for pregnant women from 28 to 38 weeks' gestation	Tdap instead of Td vaccine for individuals who are likely to be in contact with infants aged under 12 months
Varicella (chapter 21)	Non-immune individuals: · with chronic liver disease · with deteriorating renal function before transplantation · prior to solid organ transplant · prior to any elective immunosuppression[a] Patients at least 2 years after bone marrow transplant Patients at least 6 months after completion of chemotherapy HIV-positive patients who are non-immune to varicella, with mild or moderate immunosuppression Individuals with inborn errors of metabolism at risk of major metabolic decompensation, with no clinical history of varicella Household contacts of paediatric patients who are immune compromised or undergoing a procedure leading to immune compromise, 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 immune compromised, or undergoing a procedure leading to immune compromise, where the household contact has no clinical history of varicella	Non-immune individuals

Vaccine (relevant chapter)	Recommended and funded for adults ≥18 years	Recommended but not funded for adults ≥18 years
Zoster (chapter 22)		Adults aged 50 years and older

Notes

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

b Women who were under age 20 years when they commenced HPV vaccination are currently funded to complete the three-dose course, even if they are older than 20 years when they complete it.

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

2.8 The National Immunisation Register and School-Based Vaccination System

2.8.1 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 will collect 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, the high-risk pneumococcal, meningococcal and pre- and post-splenectomy programmes, and BCG vaccine)
- collects information about influenza immunisations and high-risk adolescent and adult immunisations (from 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 2.2.3).

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 number (NHI), 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
- 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 the Centre for Adverse Reactions Monitoring (CARM).

More information about privacy and informed consent can be found in section 2.2 and Appendix 3. Further information about the NIR can be found on the Ministry of Health website (www.health.govt.nz/nir).

2.8.2 The School-Based Vaccination System

The School-Based Vaccination System (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 patient management system (PMS) or direct enter on to the NIR.

2.9 Documentation and insurance

2.9.1 Documentation and record keeping

Accurate documentation (including information on the NIR and SBVS) 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 or SBVS, 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 2.5).

The vaccinator should also complete the relevant sections in the *Well Child Tamariki Ora 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 patient management system.

2.9.2 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.

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3 Vaccination questions and 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 varicella vaccine 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 parenteral vaccines, live and inactive vaccines, or two inactive vaccines.

What steps are required if the Schedule is interrupted?

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:

- hepatitis B vaccine given at birth to babies born to HBsAg-positive mothers – this dose does not count as part of a catch-up
- the three-dose course of rotavirus vaccine should be started by age 15 weeks and completed by age 8 months and 0 days; if a partially vaccinated infant reaches age 8 months before the third dose is given, the first or second doses already given will offer them some protection against disease
- MMR given prior to age 12 months – infants who receive MMR prior to age 12 months still require two further MMR doses at ages 15 months and 4 years

- protein conjugate/polysaccharide 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, varicella) 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, and that close follow-up may be required.

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

Proceeding with the Schedule after an adverse event following immunisation (AEFI) depends on the nature of the event and the likelihood that it was caused by the vaccine. 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, PO Box 913, Dunedin, using the prepaid postcard HP3442, or via online reporting (https://nzphvc-01.otago.ac.nz/carm-adr/) (see section 2.5: '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 the Immunisation Advisory Centre, 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 the 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 on hepatitis B). These babies may be at higher risk of some of these diseases, so vaccinating them on time is important. For rotavirus vaccine, it is best to vaccinate preterm infants as they leave hospital because of vaccine virus shedding in the stool. However, if discharge is not anticipated before age 15 weeks, which is the upper age limit for giving dose one, then giving rotavirus vaccine in hospital is acceptable (see sections 4.2.1 and 17.5.3).

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 hepatitis B vaccine (HBvaxPRO, 5 µg), which should be given at or as close as possible to birth (preferably within 12 hours).

If HBIG and/or hepatitis B vaccine 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 8.5.3).

A baby at higher risk of tuberculosis is offered a Bacillus Calmette-Guérin (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?

Children who are healthy have an immune system that functions optimally. Eating a healthy diet, getting adequate sleep and exercise, and minimising stress will help keep the immune system healthy. However, none of the above confer the disease-specific immunity that vaccination provides (see also section 3.3.4).

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 section 1.4 on general contraindications to vaccination, 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. 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 guidelines (www.apagbi.org.uk/sites/default/files/images/Final%20Immunisation%20apa.pdf).

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 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) and 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.

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

Yes. 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. Check the vaccine data sheet for the list of components.

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. Most importantly, children with illnesses or treatment that causes immunosuppression should not 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 measles, mumps and rubella (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 a contact of a vaccinee. Internationally, there have been only 10 documented cases of attenuated varicella vaccine virus causing disease in contacts, particularly immune-compromised contacts (see chapters 11, 13 and 18 for MMR and chapter 21 for varicella).

3.2 Addressing false beliefs about immunisation

This section provides information to help understand concerns about immunisation.

3.2.1 Introduction

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.

In New Zealand, as elsewhere, there are 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, 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 rational 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.

In any discussion it may help to acknowledge that science does not always have all the answers. 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 2.2 on informed consent, and section 1.6 on the safety monitoring of vaccines in New Zealand).

Understanding anti-immunisation

It is useful to understand that people tend to take on board what makes sense to them and what supports their belief system and to ignore information that does not. The internet makes it very easy to access information that is appealing. 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.[1]

If a parent is concerned about immunising their child, determining their concerns and addressing them can be helpful. As a health professional, you should challenge poor information.

Until recently, anti-immunisation information was propagated mainly via print media. Now, the internet has online magazines and websites dedicated to disseminating myths about immunisation, and social media such as Facebook and Twitter also contribute. Although the source of information has changed, the general themes have not.

An important paper published in 1998 summarised the core arguments presented by those opposed to vaccination.[2] The reporting of anti-immunisation arguments by the press frequently contains words and phrases such as:

- 'cover-up' – information is suppressed to keep the true facts hidden
- 'excavation of the facts' – scientific evidence against immunisation and medical experts who oppose immunisation can be found if searched for
- 'unholy alliance for profit' – doctors, pharmaceutical companies and the government collude for the sake of the profits made from the sale of vaccines
- 'towards totalitarianism' – government uses the law to force immunisation as the first step towards increased state control
- 'us and them' – caring, concerned friends and parents against doctors, pharmaceutical companies and bureaucrats
- 'poisonous cocktails' – vaccines are toxic and made from undesirable products
- 'the cause of idiopathic illnesses' – many illnesses of unknown cause are blamed on vaccines
- 'back to nature' – natural (disease) is better than man-made (vaccine).

These themes have been consistent since the first use of the smallpox vaccine over 200 years ago. Most false beliefs have an origin that can be traced and may even contain some element of truth.

3.2.2 False beliefs based on fallacies

Beliefs based on falsehoods or fallacies about immunisation have existed since Benjamin Jesty and Edward Jenner used cowpox to prevent smallpox in the 18th century. During the past 100 years many new vaccines have been developed, and each generation is associated with misperceptions, which often result in children being inappropriately denied vaccination.

Such beliefs have always tended to flourish where there is a limited understanding of science. Also, the dissemination of contradictory information and conspiracy theory has been facilitated by new technologies such as the internet and text messaging. The media will respond to controversy and tend to give equal weight to both sides of the arguments, ignoring the robust science that supports immunisation programmes. There are many examples in the medical literature of negative press coverage and a subsequent reduction in vaccine uptake, followed by a resurgence of disease.

Over the past two centuries, controversies about immunisation have tended to fall into several categories. Although the details may change, the themes remain the same. Table 3.1 summarises some suggested responses to concerns about immunisation. (For more information, see the relevant sections of this chapter.)

Table 3.1: Summary of suggested responses to concerns about immunisation

Concern	Response
The disease is not serious	Healthy children can and do still die from these diseases, and many more would do so if it were not for vaccination.
The disease is uncommon	The disease is common in unimmunised populations and can easily recur and spread if immunisation rates drop.
The vaccine is ineffective	Studies showing the effectiveness of a vaccine are needed before a vaccine is introduced.
The vaccine is unsafe	As with effectiveness, the safety of a vaccine is rigorously tested before, and after, its introduction.
Other methods of disease prevention such as homeopathy are preferable to immunisation	There is no body of scientific evidence that supports homeopathy or other methods for preventing the diseases.

Adapted from: Bedford H, Elliman D. 2000. Concerns about immunisation. *British Medical Journal* 320: 240–3.

3.3 Addressing misconceptions about immunisation

This section looks at a number of the common and longstanding misconceptions about immunisation. Many additional issues may arise, and new evidence is constantly emerging, so it may be helpful to contact the Immunisation Advisory Centre (0800 IMMUNE / 0800 466 863) for more detailed information on specific concerns. There are also some suggestions at the end of this section for locating helpful commentary and rebuttals to new myths and concerns as they arise.

3.3.1 Idiopathic ills

There are many claims that vaccines cause long-term adverse effects, such as chronic immunological and neurological disorders. Examples of these disorders are autism, attention deficit disorders, asthma and eczema, chronic fatigue syndrome and other autoimmune disorders. There have been many studies addressing these issues and they consistently demonstrate that vaccines are not responsible for any increased risk in these sorts of disorders. The most prominent claims in recent years are summarised below.

Claim: Vaccines cause autism

Response

There is no evidence that the MMR vaccine causes autism.[3, 4] Extensive scientific research has been devoted to this topic, resulting in an increasing body of evidence that childhood vaccination is unrelated to the development of autism.

In 1998 a British physician announced he had found a virus from measles vaccines lingering in the intestines of 12 autistic children, which he believed was related to autism. No subsequent studies following his study have been able to reproduce his results. In 2004 *The Lancet* published a retraction submitted by 10 of the 13 original authors of the 1998 study. The authors stated that there was no connection between the MMR vaccine and the bowel disease/autism syndrome.

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. *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.[5] Studies exonerating the MMR vaccine continue to be published.

Claim: Vaccines cause asthma and allergic disease

Response

There are often claims that childhood vaccines have a role in the development of allergic disease. There have been many studies of different design that 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.[6]

It is especially important that children with asthma be given all recommended vaccines, as catching a disease like pertussis or influenza can worsen asthma.[7] In New Zealand, influenza vaccination is particularly recommended for children with asthma because of this risk.

The possibility that MMR vaccine can cause allergic diseases has been raised. In 2005 and 2012 a Cochrane Systematic Review of the literature on vaccines for measles, mumps and rubella found no evidence that MMR increases allergic disease.[3, 8]

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.[4]

Claim: Vaccines cause cot death

Response

Sudden unexplained 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.[9] 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.[9] Some studies, including the New Zealand Cot Death Study, found a lower rate of SUDI in immunised children.[10] This is consistent with a Scandinavian study, which found that some cases of SUDI were probably caused by undiagnosed pertussis.[11] A large case-control study showed no increased risk of SUDI associated with immunisation,[12] and a meta-analysis of nine case-control studies further suggested that immunisation is protective against SUDI.[13] Consistent findings from several studies using a range of methods invalidate claims that associate vaccination with SUDI or cot death.

Claim: Immunisations 'overload' or 'overwhelm' the infant immune system

Response

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. 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.

Furthermore, 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 3000 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.[14]

From birth, an infant's immune system responds to various microbial challenges in the environment. The infant is also able to generate an effective immune response to most vaccines; for example, infants born to mothers infected with hepatitis B virus are mostly protected against infection after receiving the hepatitis B vaccine given at birth (along with hepatitis B immunoglobulin) and at age 6 weeks, 3 months and 5 months.

Eighty-five to ninety-five percent of infants immunised against pertussis, diphtheria, tetanus, poliomyelitis (polio), Hib, pneumococcus and hepatitis B in the first six months of life develop protective vaccine-specific antibodies. Conjugation of a vaccine antigen to a carrier protein (eg, Hib or pneumococcal conjugate vaccine) enables the infant to develop a specific immune response using helper T-cells, and therefore a specific T-cell memory. In contrast, infants and children aged under 2 years do not develop such protective immune responses following infection with wild organisms (eg, *H. influenzae* and *S. pneumoniae*).

3.3.2 Poisonous chemical cocktails

Claim: Vaccines contain toxic chemicals, viruses and cells

Response

Vaccine production is highly regulated, requiring extensive testing during manufacture and of the final product (see section 1.6). The testing standards are rigorous and internationally regulated by independent authorities. The manufacturer must show that each dose is safe, refined and potent enough to be effective. The sophistication of this testing continues to improve, and modern technology enables the detection of single molecules of viral DNA or RNA.

There have been occasions when vaccines have become contaminated with unwanted viruses: avian leucosis virus in yellow fever vaccines, SV40 in polio vaccines in the 1950s, and pestivirus in some Japanese vaccines in the 1980s. Most recently, due to new technology, rotavirus vaccines have been found to contain DNA fragments of porcine viruses. In March 2010 the United States (US) Food and Drug Administration (FDA) temporarily suspended the use of RV1 (Rotarix) after porcine circovirus (PCV) was identified in commercial vaccine lots.[15] Fragments of the PCV genome were also later identified in RV5 (RotaTeq). The FDA later resumed the use of RV1 and continues to support the safety profile of both vaccines.[16]

Any potentially toxic substances (eg, formaldehyde) present in vaccines are only permitted in trace amounts, too small to cause any harm, and usually in lower amounts than naturally occur during environmental exposure. The chances of modern vaccines becoming contaminated with harmful residuals is extremely low and the probability of detecting such contamination very high.

The rubella vaccine virus can only be grown in cell lines of human origin. A cell line is an 'immortal' self-replicating group of cells that can be maintained indefinitely in the laboratory, providing a safe, standardised medium for growing vaccine viruses. Both the rubella vaccine cell line and the rubella vaccine virus were derived from fetal tissue in the 1960s. Once vaccine virus has been cultivated in cells, it is separated from cellular material and purified. If any cellular material remains in the vaccine, it is only in minute traces.

During the early stages of the HIV epidemic it was suggested that an early polio vaccine was cultivated in chimpanzee cells contaminated with the precursor of HIV-1, simian virus. It was claimed that the use of this polio vaccine resulted in the transfer of the virus to humans, and was the source of HIV. No chimpanzee tissue was involved in the production of this vaccine. Also, supplies of the early polio vaccine were discovered in freezers and tested in several laboratories, none of which found that HIV, or chimpanzee DNA, was present in the vaccine. Thus it has been convincingly demonstrated that polio vaccine was not the source of HIV.[17]

Claim: Vaccines contain aluminium, which is a neurotoxin

Response

Aluminium is one of the most abundant elements on earth and has been used in vaccines for more than 70 years. An average daily exposure to aluminium is about 10–15 mg, most of which comes from foods. Humans and other mammals are constantly exposed to aluminium compounds, and as a consequence aluminium compounds are found in the blood of all humans and animals. Normally, aluminium compounds are excreted through the urine.

Aluminium compounds are used in some vaccines as an adjuvant (something that helps stimulate an immune response). Aluminium adjuvants have a long-established safety record, with a low incidence of reported adverse events. Minor reactions occur fairly often, but there have been very few serious reactions. Local reactions are more likely if the injection is delivered into the subcutaneous tissue rather than deep into the muscle.

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.[18]

Claim: Vaccines contain mercury, which is a dangerous toxin

Response

None of the vaccines on the New Zealand National Immunisation Schedule contain thiomersal, including the current influenza vaccines.

Thiomersal (also known as thimerosal) is a mercury-based preservative used in some vaccines and other pharmaceutical products, such as antiseptics.

Mercury is a naturally occurring element found in the Earth's crust, soil, water and the air and is released into the environment by volcanic eruptions, weathering of rocks and the burning of coal. Once released, mercury can find its way through the food chain via fish and other animals. At high levels it is toxic.

Some forms of mercury pose a greater health risk than others. For example, mercury vapour is extremely dangerous, whereas amalgam, used in dental fillings, has not been shown to pose any health risk. Ethyl mercury found in thiomersal has significantly less potential for toxicity than methylmercury (found in the food chain) because it is rapidly eliminated from the body and does not build up in tissues.

Thiomersal continues to be used in vaccines in many countries. The WHO's Global Advisory Committee on Vaccine Safety (GACVS) has concluded that 'there is currently no evidence of mercury toxicity in infants, children or adults exposed to thiomersal-containing vaccines' and that 'there is no reason to change current immunisation practices with thiomersal-containing vaccines on the grounds of safety'.

3.3.3 Vaccines are ineffective

Claim: Vaccine immunity is temporary

Response

The duration of immunity varies with different diseases and different vaccines. Lifelong immunity is not always provided by either natural infection or vaccination. The recommended timing of vaccine doses aims to achieve the best immune protection to cover the period in life when vulnerability to disease is highest.

- For many diseases immunity wanes following natural infection.
- The duration of immunity provided by vaccines varies depending on a range of factors, particularly the vaccine itself.
- Live vaccines generally induce longer-lived immunity than subunit vaccines.
- Subunit vaccines frequently require primary courses and boosters.
- Polysaccharide vaccines do not generate long-lived memory cells.
- If the interval between doses is too short, the duration of immunity can be affected, which is why minimum intervals are required.
- In the very young and the very old, immune persistence can be more limited.
- Some vaccines, such as tetanus vaccine administered to anyone and protein conjugate polysaccharide vaccines administered to those aged under 2 years, provide immunity where suffering from the disease does not.

Claim: Natural immunity is better than vaccine-induced immunity

Response

The duration of immunity following vaccination may be shorter than the duration of immunity induced by the disease (but not always). However, both are protective, and if immunity following immunisation wanes, booster doses can be given. Natural immunity and vaccine-induced immunity are both the result of the natural responses of the body's immune system.

More importantly, those who suffer 'natural' disease run the risks of serious illness, disability and death to acquire their immunity. In contrast, the acquisition of vaccine-derived immunity is a much lower risk. However, several doses of vaccine, along with booster doses, may be necessary to attain and maintain good levels of immunity, and immunisation does fail in a small proportion of vaccinees.

For some organisms (eg, Hib in children aged under 2 years, HPV and tetanus at any age), the immunity following vaccination is better than that following infection. The Hib vaccine stimulates immune memory in infants in a way that the disease does not, and tetanus can be caused by a small amount of toxin that is insufficient to generate an immune response. In 1995 a 40-year-old man developed tetanus for a second time. He had failed to complete the recommended immunisation course after recovering from an earlier episode of tetanus (see chapter 19).

Claim: Immunisation has played a minimal role, if any, in controlling disease

Response

Improvements in living standards, in particular clean water, had a great impact on health during the 19th century. Apart from sanitation and clean water, no other public health intervention has had as great an impact on the decline of infectious diseases as immunisation.

Improvements in living conditions and medical care have reduced the chance 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 measles, mumps and rubella vaccine (MMR) schedule given between 14 and 16 months and at age 6 years.[19]

Healthy children living in ideal conditions remain at risk of death and disability from infections that can be prevented by immunisation. Smallpox vaccination led to the elimination of smallpox, and polio vaccination has eradicated polio from most countries. This could not have occurred through improvements in living standards alone.

Another example of the impact of immunisation was seen in New Zealand, and elsewhere, following the introduction of the Hib vaccine in 1994. This led to a decline in Hib disease of approximately 95 percent – unrelated to any other change (see chapter 6). Conversely, when pertussis immunisation coverage dropped in England, Japan and Sweden in the 1970s, there were dramatic increases in pertussis disease and deaths.

There are many examples of resurgence of disease when immunisation is halted for some reason, or when whole communities are unimmunised. Examples include the following.

- There were 13 outbreaks of measles among Amish populations, who do not accept vaccination, in the US between 1985 and 1994, with 1200 cases and nine deaths.[20]
- A 10-month-long measles outbreak occurred in 1999 among an unimmunised community in the Netherlands, with 2961 cases and three deaths.
- There was a rubella outbreak in 2004 and 2005 in an unimmunised community in the Netherlands, which resulted in 309 laboratory-confirmed cases; 23 were pregnant women, with at least nine infant deaths and nine infants severely disabled by congenital rubella syndrome (CRS). The outbreak spread to Canada, where there were 214 cases, including five pregnant women.[21]
- Recent measles epidemics and outbreaks in New Zealand have started within unimmunised families or communities and spread through pockets of low immunisation coverage. The largest outbreak in 2011 mainly affected Auckland, with 489 confirmed or probable cases.[22] 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 school children. The outbreak officially ended in July 2012.

The role of immunisation is discussed in more detail in each chapter, but its overall impact on vaccine-preventable diseases has been well established. If high enough immunisation coverage could be attained, it may be possible to eliminate measles, mumps, rubella and Hib from New Zealand.

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

Response

No vaccine is 100 percent effective and some immunised children will get the disease. 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. Forgetting 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).

3.3.4 Healthy lifestyle alternatives

Claim: Immunisation is unnatural

Response

The claim that immunisation is harmful simply because it is artificial is not based on evidence or biological first principles. Some claim that the immune system was not designed to be exposed 'directly' to an antigen, in the manner of an injection. The immune system is extremely well equipped to respond to foreign antigens entering via a range of different routes in the body. Foreign protein is taken up and processed by the immune system very well when injected into muscle. The specific immune response occurs in lymph nodes regardless of the antigen's mode of entry. An example is the injectable polio vaccine, which has been shown to work just as well as the oral vaccine (which enters the body in the same way as the infection).

Claim: A healthy lifestyle will protect children from disease

Response

A healthy lifestyle alone does not result in the necessary specific immune response occurring rapidly enough to protect a child from a potentially serious infection. Only immunisation or being infected by the organism can do this. Immunisation poses far less risk than natural infection because it is very unlikely to cause an illness, while those suffering natural infection are very likely to become ill.

The living arrangements of a person (eg, overcrowding, inadequate sanitation and hygiene) will affect the likelihood of exposure to infection. While those in good health will be less likely to suffer a severe illness or complications as a consequence of infection, a healthy lifestyle does not provide secure protection against infectious disease or its complications. Most hospitalisations in New Zealand for vaccine-preventable diseases are in previously healthy children.

Claim: Breastfeeding protects against infection

Response

Although breastfeeding reduces the frequency and severity of gut, respiratory and ear infections, there are many infections for which no protection has been demonstrated. The protection from breastfeeding is multifactorial, including passive immunity, which is dependent on the mother's level of circulating antibodies, so it varies from woman to woman and is of brief duration. Breastfeeding is not an alternative to immunisation, and both contribute to the health of children. Of particular note is the fact that breastfeeding does not protect against pertussis infection.[23]

Claim: Homeopathic immunisation prevents infection

Response

Some homeopaths do not support conventional immunisation and state that homeopathic preparations can prevent disease. There is no evidence that homeopathic 'immunisation' provides any protection against infectious diseases. The United Kingdom (UK) Faculty of Homeopathy supports conventional immunisation.[24]

Claim: Infectious diseases are not serious, and are needed for normal development

Response

The morbidity and mortality resulting from vaccine-preventable diseases is detailed in each disease chapter. Some people claim that measles is important for normal development and that after the illness children have a leap in physical and mental development. There is no evidence to support this, and given the serious impact of measles on a child's health it is not surprising that a child who has recovered will appear to have much more energy than during the illness. On the other hand, there is evidence that a child has reduced immunity for weeks to months after measles, and during this time the child is more likely to get other infections.

For information for parents and guardians, including a comparison of the effects from disease and possible side-effects of vaccines, see the Ministry of Health resource *Childhood Immunisation* (HE1323; available from www.healthed.govt.nz or your local authorised resource provider) and the Resources page of the Immunisation Advisory Centre website (www.immune.org.nz).

3.3.5 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. They can be a source of new information that may help to address a concern and ask a question. While the format is often colloquial, the writers are respected scientists who volunteer commentary against the abuse of science and evidence-based medicine.

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 lifestyle choices. The topics covered are:

- pregnancy and lactation
- infants with special immunisation considerations
- immune-deficient and immunosuppressed individuals of all ages
- immigrants and refugees
- travel
- occupational and lifestyle risk.

Note: Vaccinators are advised to regularly check the Pharmaceutical Schedule and any online updates (www.pharmac.health.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 18.5.2) and varicella (see section 21.5.3).

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

Varicella

Varicella vaccine 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 the varicella vaccine 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.

Influenza vaccine

The influenza vaccine is recommended and funded for pregnant women, and may be offered to women at any stage of pregnancy, as soon as the annual influenza vaccine becomes available (see section 10.5). A 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] There is no evidence that influenza vaccine prepared from inactivated virus causes harm to the fetus or to the neonate.[2]

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. A review of adverse event reports and medical records for women who received Tdap in pregnancy did not identify any concerning patterns in maternal, infant or fetal outcomes.[3]

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 Lactation and post-partum

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. (Note that post-partum Tdap may be locally funded in some regions, so vaccinators are advised to check local guidelines.)

Varicella

Varicella vaccine is recommended (but not funded) for all susceptible adults. Women who are non-immune with healthy babies can receive varicella vaccine after delivery.

Varicella vaccine for the mother is recommended (and funded) after delivery if the baby is immune compromised 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 vaccination is due, the scheduled 6-week vaccines, with the exception of rotavirus vaccine (see below), should be given at the appropriate chronological age.

Rotavirus vaccine

Rotavirus vaccine is an exception to the above recommendation. It is best to vaccinate preterm infants as they leave hospital because of vaccine virus shedding in the stool. However, if discharge is not anticipated before age 15 weeks, which is the upper age limit for giving dose one, then giving rotavirus vaccine in hospital is acceptable. If standard universal precautions are maintained, administration of rotavirus vaccine to hospitalised infants, including hospitalised preterm infants, would be expected to carry a very low risk for transmission of vaccine viruses.[4] Subsequent doses must be at least four weeks apart, with the third dose given before age 8 months and 0 days.

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 hepatitis B vaccine) as soon as possible after birth (see section 8.5.3). 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 to July 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 (PCV13 and 23PPV)

- PCV13 should be given as per the Schedule at ages 6 weeks, 3, 5 and 15 months.
- For preterm infants who develop chronic lung disease, give 23PPV 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.

Note that there is a potential risk of apnoea with PCV13 and other scheduled vaccines 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,[5] but do not avoid or delay immunisation.

4.2.2 Infants with congenital heart disease (CHD)

- Some children with CHD 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.

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

Note: Varicella vaccine is funded for susceptible household contacts of transplant patients. **Refer to the Pharmaceutical Schedule (www.pharmac.health.nz) for the number of funded doses and any changes to funding decisions.**

Age	Immunisation/serology	Comments
6 weeks	Usual Schedule: DTaP-IPV-HepB/Hib (Infanrix-hexa), PCV13 (Prevenar 13) and RV5 (RotaTeq)	Do not start earlier than age 6 weeks.
3 months	Usual Schedule, plus MenCCV (NeisVacC)	
5 months	Usual Schedule, plus MenCCV (NeisVacC)	
7 months	MMR (MMR II)	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 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 Hep B vaccine, 4 weeks apart (HBvaxPRO; use the 10 µg adult dose).
12 months	PCV13 (Prevenar 13)	
	MMR (MMR II)	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 at the discretion of the specialist.
	MenCCV (NeisVacC)	
13 months	DTaP-IPV-HepB/Hib (Infanrix-hexa)	
	MMR (MMR II)	MMR should not be given within 1 month of predicted transplant.

Continued overleaf

Age	Immunisation/serology	Comments
13 months (continued)	Hep A (Havrix Junior)	If Hep A and Hep B are due at the same time, consider using combined Hep A-Hep B 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. Give a booster after 3 years, then 5-yearly.
6 months post-transplant	Hep B (HBvaxPRO), plus anti-HBs serology before and 1 month after the initial Hep B series	3 doses of Hep B vaccine (5 µg). If Hep B was not previously given, and anti-HBs is negative, give 3 doses of Hep B vaccine (10 µg). If there is an inadequate immune response to the initial 3-dose Hep B series, give a further 3 doses (10 µg).
	23PPV	If at least 24 months old and not given pre-transplant. Revaccinate once after 5 years.
4 years	Usual Schedule: DTaP-IPV (Infanrix-IPV) and MMR (MMR II)	MMR can only be given if pre-transplant.
From age 9 years	HPV vaccine	3 doses at 0, 2 and 6 months. Funded for boys and girls post-transplant. If given early to girls, they do not require the usual Schedule doses in year 8 (age 12 years).
11 years	Usual Schedule: Tdap (Boostrix)	
Annually	Influenza (Influvac or Fluarix)	Recommended for patients (funded) and all family members (not funded). For patients (at any age) and family members aged under 9 years, give 2 doses 4 weeks apart in the first year, and 1 dose in subsequent years.

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, with the addition of age-appropriate pneumococcal polysaccharide, meningococcal conjugate, influenza and varicella 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 hepatitis B vaccine and hepatitis B immunoglobulin (HBIG) (see section 8.5.3).

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 is an oral, live, attenuated viral vaccine, which should not be given when severe combined immune deficiency (SCID) has been diagnosed; its use in milder immune deficiency may cause prolonged shedding of the vaccine virus, but it is unlikely to harm the patient.

BCG, being a live bacterial vaccine against tuberculosis, 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 anti-tumour necrosis factor (anti-TNF) therapies (eg, infliximab) during pregnancy, BCG vaccination should be delayed until the infant is at least 8–9 months old.[6]

(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 and are also eligible to receive funded meningococcal, varicella and influenza vaccines. (See the HIV discussion 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.

- Infants with cystic fibrosis or other chronic lung diseases are eligible for funded influenza vaccine from age 6 months (see section 10.5) and funded pneumococcal polysaccharide vaccine from age 2 years (see section 15.5).
- Infants with metabolic and endocrine disorders (eg, congenital diabetes or adrenal insufficiency) should receive rotavirus vaccine to avoid electrolyte disturbance through gastroenteritis. Infants with diabetes are eligible for influenza vaccine from age 6 months (see section 10.5) and pneumococcal polysaccharide vaccine from age 2 years (see section 15.5), both funded. Varicella vaccine is funded for infants with inborn errors of metabolism at risk of major metabolic decompensation (see section 21.5); and is recommended for a variety of endocrine disorders – discuss with the specialist.
- Infants with sickle cell disease (not trait) should be treated as for functional asplenia (see section 4.3.4).
- Infants with haemoglobinopathy, or with cochlear implants or intracranial shunts, are eligible for funded pneumococcal polysaccharide vaccine from age 2 years (see section 15.5).
- Infants with Down syndrome are eligible for funded pneumococcal polysaccharide vaccine from age 2 years (see section 15.5). These infants may also be eligible for funded influenza vaccine; for example, if they have congenital heart disease (see section 10.5).
- Infants who may be exposed to tuberculosis are eligible for BCG vaccine (see sections 4.4 and 20.5). However, if the infant's mother received anti-TNF therapies (eg, infliximab) during pregnancy, BCG vaccination of the infant should be delayed until age 8 to 9 months[6] (see section 20.6).

4.3 Immune-deficient 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 general contraindications and precautions (section 1.4) and the vaccine data sheets.

> 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 safety and effectiveness of vaccines in individuals with immune deficiency are determined by the nature and degree of immunosuppression.[7] 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[7] (see section 4.3.2). Secondary disorders of the immune system 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.[7]

Live parenteral vaccines (these include MMR, varicella and BCG) should not in general be given to individuals who are severely immunosuppressed because of the risk of disease from vaccine strains. Subunit and inactivated vaccines should be administered, because the risk of adverse reactions is not increased in immunosuppressed individuals but the response of immunodeficient or immunosuppressed individuals to these inactivated vaccines may be inadequate.

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 they are at increased risk of infection 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

Immunologically 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 immunosuppressed 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.[8] There is no risk of transmission of MMR vaccine viruses to the immunocompromised individual.

Varicella vaccine can be given safely to the household contacts of immunosuppressed individuals. However, where a vaccinee (household contact) develops a vesicular rash, then that individual should be isolated from the immunosuppressed individual for the duration of the rash. Varicella vaccine is funded for household contacts of patients who are immunocompromised or undergoing a procedure leading to immunocompromise.

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.[7] Most of these individuals will be on intravenous immunoglobulin (IVIG) replacement therapy, which provides passive protection against most vaccine-preventable infections.

Hib, PCV13 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 recommended 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.[9]

Below is a summary of the appropriate immunisations for individuals with primary immune deficiencies, adapted from the *Red Book: 2012 Report of the Committee on Infectious Diseases*.[7] Seek specialist advice. (See also Table 1.3 in section 1.4.2.)

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 is contraindicated.
- MMR and VV vaccines 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.

T lymphocyte deficiencies (cell mediated and humoral)

Complete defects (eg, severe combined immune deficiency [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 and varicella vaccines 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 and meningococcal vaccines are recommended.
- There are no specific contraindications or precautions.

Phagocytic function deficiencies

Chronic granulomatous disease (CGD), leukocyte adhesion defect, myeloperoxidase deficiency

All routine vaccines are probably effective.

- Influenza vaccine is recommended.
- BCG is contraindicated.
- Live viral vaccines are safe in CGD[8] 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 immunosuppression.

The ability of individuals with secondary immune deficiency to develop an adequate immunological response depends on when immunosuppression occurs and the severity of the immunosuppression.

Before commencing a therapy that would be expected to cause significant immunosuppression, a full vaccination history should be obtained.

If circumstances permit, such as prior to commencing immunosuppressive therapy for rheumatological disease or prior to solid organ transplant, vaccination should be completed and additional non-routine vaccines (eg, varicella) 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. When immunosuppressive therapy is discontinued, immune recovery usually takes between 3 and 12 months.

Influenza vaccine is recommended for immunosuppressed individuals before each influenza season, and after completion of chemotherapy for malignant neoplasm three to four weeks after chemotherapy is discontinued, once both the peripheral granulocyte and lymphocyte counts are $>1.0 \times 10^9$/L. 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.[9]

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 vaccine to individuals on corticosteroids. Table 4.2 provides a summary of the guidelines for individuals on high-dose corticosteroids.

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 daily or on alternate days 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[10]
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: Immunisation Advisory Centre

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. 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; azathiaprine ≤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.

Table 4.3: Immunotherapy agents for immune-mediated inflammatory disease

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 **Anti-TNF DMARDS** Adalimumab Etanercept Infliximab	Cyclo-phosphamide

When these agents are used singly

Source: Immunisation Advisory Centre

Commencement of such treatments is often planned (elective), and the opportunity should be taken to ensure patients are up to date with their routine vaccinations *(*including HPV from age 9 years). If immediate treatment is required it should not be delayed to allow for vaccination. Live viral vaccines (MMR and varicella) should only be given if the patient is non-immune, is not severely immunocompromised and is ≥4 weeks prior to commencement of immunosuppressive therapy. Varicella vaccine may be given at a shorter interval at the discretion of the specialist.

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. 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 chapter 11) and varicella vaccine (funded; see the 'Household contacts' discussion in section 4.3.1, or chapter 21), and annual influenza vaccination is recommended (not funded).

Vaccination after chemotherapy

Those who have received routine immunisations prior to cancer diagnosis do not need full re-immunisation. Booster dose(s) of a diphtheria/tetanus/pertussis containing vaccine, hepatitis B, polio (IPV) and pneumococcal vaccines (PCV13 and 23PPV) should be given, starting not less than three months after chemotherapy has ended, when the lymphocyte count is >1.0 x 10^9/L. Live viral vaccines should be delayed for at least six months after chemotherapy, but MMR and varicella vaccine should then be given to seronegative patients. The interval may need to be extended according to the intensity and type of therapy, radiation therapy, receipt of blood products or immunoglobulin (see Table 1.3 in section 1.4.2), underlying disease and other factors. For children aged under 18 years, suggested age-appropriate schedules and worksheets are available at: www.starship.org.nz/media/199142/children_off_cancer_therapy_may_2013_final.pdf

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 (GVHD). Some recipients acquire the immunity of the donor, but others lose all serological evidence of immunity. Complete re-immunisation is recommended, starting with inactivated vaccines 12 months after bone marrow transplant.

Routine Schedule immunisations should be given for children aged under 10 years, but from the 10th birthday Tdap should be given. Pneumococcal vaccines (PCV13 and 23PPV), meningococcal (conjugate C and quadrivalent conjugate), hepatitis B and a booster dose of Hib and IPV are all recommended.

Healthy survivors of bone marrow transplant can be given MMR and varicella vaccine not less than two years after transplant. A second dose of MMR vaccine (and varicella vaccine if aged 13 years and older) should be given four weeks or more after the first dose, unless serological response to measles (and varicella) is demonstrated after the first dose. The vaccines should not be given to individuals suffering from GVHD 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 at: www.starship.org.nz/media/199142/children_off_cancer_therapy_may_2013_final.pdf

Chronic kidney disease (CKD)

Immune response and duration of protection after immunisation decreases with advancing kidney disease, so routine Schedule and other recommended vaccines should be given as soon as 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.[11]

Patients should receive routine Schedule vaccines and annual influenza vaccine. Live viral vaccines are considered safe for individuals with CKD and minimal immune compromise, but they are generally not recommended for individuals on immunosuppressive medicines because of the risk of disseminated disease from the vaccine virus.[12] However, a number of small studies suggest that the risk of disseminated varicella vaccine-related disease is small and can be managed with antiviral therapy, and that varicella immunisation is a significantly lower risk for immunosuppressed individuals than community-acquired disease.[10]

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 (the High Risk Pneumococcal Programme, for children aged under 5 years), a Hib booster, conjugate meningococcal vaccines and annual influenza vaccine are recommended.

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

There is no relationship between immunisation and deterioration of renal function or a reduction in the efficacy of dialysis.[11]

A recommended immunisation schedule and worksheet for paediatric CKD stage 4–5 and dialysis patients is available at the Starship website (www.starship.org.nz).

Solid organ transplants

An accelerated immunisation schedule is recommended for individuals likely to be listed for solid organ transplant (see Table 4.1 for infant recommendations). Specialist advice should be sought in these situations.

Individuals older than 12 months who have been scheduled for solid organ transplantation should receive MMR and varicella vaccines at least four weeks before the transplant. 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.

In patients undergoing organ transplantation, pneumococcal vaccine (funded for children aged under 18 years) 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. (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+ >14%) and rotavirus (infants only). Asymptomatic children who are not severely immune compromised 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 hepatitis B vaccine) should be discussed with the individual's specialist.

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

Table 4.4 summarises the additional vaccine recommendations (funded and unfunded) and schedules for HIV-positive individuals.

Table 4.4: Additional vaccine recommendations (funded and unfunded) for HIV-positive individuals

Note: HIV-positive individuals should receive the routine Schedule vaccines, including rotavirus vaccine, but see the MMR recommendations in the table below. HPV vaccine may be given from age 9 years (females and males). BCG should not be given. **Funded vaccines are in the shaded rows, however vaccinators are advised to refer to the Pharmaceutical Schedule (www.pharmac.health.nz) for the number of funded doses and any changes to funding decisions.**

Age at diagnosis	Vaccine (trade name)	Recommended vaccine schedule
Infants aged under 12 months	PCV13 (Prevenar 13) and 23PPV (Pneumovax 23)	PCV13[a] at ages 6 weeks, 3, 5 and 15 months (usual childhood Schedule) 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. 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 (Influvac or Fluarix)	Annual immunisation 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
Infants aged under 12 months (continued)	MenCCV (NeisVacC) 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.
Children aged 12 months to under 5 years	PCV13 (Prevenar 13) and 23PPV (Pneumovax 23)	The PCV13,[a,c] age-appropriate catch-up schedule is: · children aged ≥12 months[d] who have completed the age-appropriate primary course of PCV10 require 1 dose of PCV13[c] · if commencing immunisation at ages 12 months or older, give 2 doses of PCV13,[c] 8 weeks apart. 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 (Influvac or Fluarix)	Annual immunisation. In previously unvaccinated children, give 2 doses 4 weeks apart, then 1 dose in each subsequent year.
	MMR (MMR II)	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] (Varilrix)	If CD4 lymphocyte percentage is ≥15%: · give 2 doses (starting 4 weeks after the 2nd MMR), at least 3 months apart.

Continued overleaf

Age at diagnosis	Vaccine (trade name)	Recommended vaccine schedule
Children aged 12 months to under 5 years (continued)	MenCCV (NeisVacC) 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.
Children aged 5 to under 18 years	PCV13 (Prevenar 13)	1 dose of PCV13.[c,f]
	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 or Fluarix)	Annual immunisation. Regardless of age, if previously unvaccinated, give 2 doses[g] 4 weeks apart. Then give 1 dose in each subsequent year.
	MMR (MMR II)	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] (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.

Continued overleaf

Age at diagnosis	Vaccine (trade name)	Recommended vaccine schedule
Children aged 5 to under 18 years (continued)	MCV4-D (Menactra)	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.
Adults aged 18 years and older	PCV13 (Prevenar 13) and 23PPV (Pneumovax 23)	1 dose of PCV13.[c,f] 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 or Fluarix)	Annual immunisation. If previously unvaccinated, give 2 doses[g] 4 weeks apart. Then give 1 dose in each subsequent year.
	MMR (MMR II)	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[e] (Varilrix)	If no history of varicella disease or immunisation and CD4 lymphocyte count is ≥200 cells/mm^3: · give 2 doses at least 3 months apart.
	Hepatitis B (HBvaxPRO)	If previously unvaccinated, give 3 doses, at 0, 1 and 6 months.[h]
	MCV4-D (Menactra)	Give 2 doses of MCV4-D 8 weeks apart, then 1 dose every 5 years.[c]
Males and females with confirmed HIV infection aged under 26 years	HPV4 (Gardasil)	Give 3 doses at 0, 2 and 6 months.[i]

a PCV13 replaces PCV10 (Synflorix) on the Schedule.

b Give MCV4-D at least 4 weeks after PCV13.

c If 23PPV has already been given (prior to any doses of PCV13), wait at least 1 year 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 Give varicella vaccine on the advice of an HIV specialist.

f PCV13 is registered for children aged under 5 years and adults aged 50 years and older. There is emerging but limited efficacy data for PCV13 use outside of these age ranges. However, PCV13 can also be used for older children and adults with high-risk conditions.

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

h Consider screening for seroconversion after vaccination (see section 8.5.5).

i Registered for use from age 9 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.

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, the following vaccines are recommended and/or funded as soon as the asplenic condition is recognised. The immunisation schedules are age-dependent and are provided in Table 4.5 below.

- Pneumococcal conjugate and polysaccharide vaccines are funded for asplenic children (see also chapter 15). If children have commenced immunisation with PCV10, they can complete it with PCV13. Pneumococcal conjugate and polysaccharide vaccines are recommended for asplenic adults, but only polysaccharide vaccines are funded (see also chapter 15).
- Meningococcal conjugate vaccine is funded for all asplenic individuals (see also chapter 12). Meningococcal C conjugate vaccine (MenCCV; NeisVacC) 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 (not funded) from 6 months of age (see also chapter 10).
- Varicella vaccine is recommended (not funded) for individuals from 12 months of age (see also chapter 21).

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 4.5: 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. **Funded vaccines are in the shaded rows, however vaccinators are advised to refer to the Pharmaceutical Schedule (www.pharmac.health.nz) for the number of funded doses and any changes to funding decisions.**

Age at diagnosis	Vaccine (trade name)	Recommended vaccine schedule
Infants aged under 12 months with functional asplenia or pre-[a] or post-splenectomy	PCV13 (Prevenar 13) and 23PPV (Pneumovax 23)	PCV13[b] at age 6 weeks, 3, 5 and 15 months (usual childhood Schedule), 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. 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 (NeisVacC) 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[c] 8 weeks apart, then a booster dose after 3 years, then 5-yearly.
	Influenza (Influvac or Fluarix)	Annual immunisation from age 6 months. In the first year, give 2 doses 4 weeks apart, then 1 dose in each subsequent year.

Age at diagnosis	Vaccine (trade name)	Recommended vaccine schedule
Children aged 12 months to under 18 years with functional asplenia or pre-[a] or post-splenectomy	PCV13 (Prevenar 13) and 23PPV (Pneumovax 23)	PCV13,[b,d] age-appropriate catch-up schedule: · children aged >12 months[e] who have completed the primary course of PCV10 require 1 dose of PCV13[b] · previously unimmunised children aged ≥12 months to under 5 years require 2 doses of PCV13,[d] 8 weeks apart · children aged 5 years to under 18 years[f] require 1 dose of PCV13.[d] 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 (NeisVacC) and MCV4-D (Menactra)	If aged 12–23 months at diagnosis, give 1 dose of MenCCV, followed by MCV4-D[c] 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[c] 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 (Act-HIB)	If aged 12–15 months, give 1 dose at age 15 months as per the National Immunisation Schedule. If aged 16 months to under 5 years and has not received a single Hib dose after age 12 months, give 1 dose. If aged 5 years and older, give 1 dose, even if fully vaccinated.
	Influenza (Influvac or Fluarix)	Annual immunisation. In previously unvaccinated children aged under 9 years, give 2 doses 4 weeks apart, then 1 dose in each subsequent year.

Age at diagnosis	Vaccine (trade name)	Recommended vaccine schedule
Children aged 12 months to under 18 years (continued)	Varicella (Varilrix or Varivax)	If no history of varicella disease or immunisation, give 2 doses at least 6 weeks apart.
Adults ≥18 years, pre-[a] or post-splenectomy or with functional asplenia	PCV13 (Prevenar 13)	1 dose of PCV13.[d,f]
	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.[c,g]
	Hib[h] (Act-HIB)	Give 1 dose regardless of previous vaccination history.
	Influenza (Influvac or Fluarix)	Annual immunisation.
	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 PCV13 replaces PCV10 (Synflorix) on the Schedule.

c Give MCV4-D at least 4 weeks after PCV13.

d If 23PPV has already been given (prior to any doses of PCV13), wait at least 1 year 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 PCV13 is registered for children aged under 5 years and adults aged 50 years and older. There is emerging but limited efficacy data for PCV13 use outside of these age ranges. However, PCV13 can be used for high-risk older children and adults.

g 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.

h Hib vaccine is not funded for adults with functional asplenia.

Source: Starship Children's Health.

Antimicrobial prophylaxis

The effectiveness of antimicrobial prophylaxis in asplenic children has been proven only for sickle cell disease, but it is recommended for all such children aged under 5 years and for at least one to two years after splenectomy. Monthly benzathine penicillin injections have been shown to reduce episodes of pneumococcal bacteraemia in asplenic children as compared with rates observed in untreated children. Oral penicillin daily also reduces the incidence of severe bacterial infection by 84 percent in asplenic children, compared with the rates observed in placebo-treated controls.

It is reasonable to extrapolate this data to other asplenic children with a high risk of bacteraemia (eg, asplenic children with malignancies, thalassaemia, etc). There is less agreement regarding the use of chemoprophylaxis in children who have been splenectomised following trauma.

Chemoprophylaxis is recommended for:

- asplenic/hyposplenic children aged under 5 years
- older asplenic children for at least two years post-splenectomy.

There are no studies that help decide the age at which chemoprophylaxis should be discontinued. This decision has to be made according to clinical judgement.

The recommended dosage is:

- aged under 5 years: 125 mg bd (twice daily) oral penicillin
- aged 5 years and older: 250 mg bd oral penicillin.

An alternative recommended by some experts is amoxycillin 20 mg/kg per day (up to a maximum of 500 mg).

Parents/guardians should be advised that all febrile illnesses are potentially serious and that they should seek immediate medical help in these circumstances. Individuals should be hospitalised if bacteraemia is a possibility. In hospital, the usual treatment would be cefotaxime, ceftriaxone, or another regimen effective against *S. pneumoniae*, *H. influenzae* type b and *N. meningitidis*.

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.

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. 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 a developing country may have received BCG, three doses of DTwP and OPV 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 or MMR vaccine. Many countries, including European countries, do not have hepatitis B vaccine 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). Documented vaccine doses should be taken into account when planning a catch-up programme that complies with the Schedule.

Details of immunisation schedules of other countries can be found at the WHO website (http://apps.who.int/immunization_monitoring/globalsummary/schedules).

4.4.2 Tuberculosis

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.

It is important that all refugee children with suspected TB be appropriately investigated. If they 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 tuberculosis 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.

4.4.3 Hepatitis B

The Pacific Islands and most of Asia (except Japan and India) are regions with a high prevalence of chronic hepatitis B infection. If a member of an immigrant or refugee family is found to have chronic hepatitis B 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 hepatitis B 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 adults. Because adult chickenpox can be severe, if there is no history of chickenpox, varicella vaccine 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) can be obtained from the Centers for Disease Control and Prevention (www.cdc.gov/travel) or the WHO (www.who.int/ith/en/).

4.6 Occupational and lifestyle risk

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 4.6 are recommended for certain occupational groups and in Table 4.7 for those with lifestyle 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 2.7 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*).

Table 4.6: Recommended vaccines, by occupational group

Occupation	Recommended vaccines
Health care workers	
Medical, nursing, 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

Continued overleaf

Occupation	Recommended vaccines
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)
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)

Continued overleaf

Occupation	Recommended vaccines
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)
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)

Continued overleaf

Occupation	Recommended vaccines
Sewerage workers, plumbers or other workers in regular contact with untreated sewage	IPV Hepatitis A
Sex workers	Hepatitis B (if susceptible) HPV

Table 4.7: Recommended vaccines for those with lifestyle risk factors

Lifestyle 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 (MCV4-D) 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).
Funded immunisation 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. At ages 45 and 65 years: Td (administration not funded). During pregnancy (from 28 to 38 weeks' gestation): 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 ESR for toxin detection. Transmission is by respiratory tract droplets, or by direct contact with skin lesions or contaminated articles. Humans are the only known host for diphtheria, and the disease is spread by close personal contact with a case or carrier. 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.

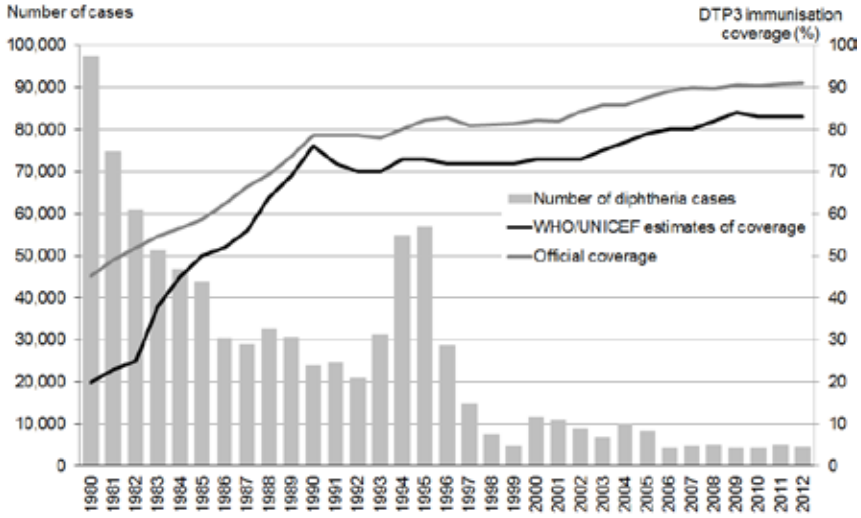
The major complication of diphtheria is respiratory obstruction, although the majority of deaths are due to the effects of diphtheria toxin on various organs. Of particular importance are the effects of the toxin on the myocardium (leading to myocarditis and heart failure), peripheral nerves (resulting 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).

Figure 5.1: Diphtheria global annual reported cases and DTP3* immunisation coverage, 1980–2012



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

Source: World Health Organization. *Immunization Surveillance, Assessment and Monitoring*. URL: www.who.int/immunization_monitoring/data/data_subject/en/index.html

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.[1] Diphtheria remains endemic in these countries, as well as in countries in Africa, Latin America, Asia, the Middle East and parts of Europe, where childhood immunisation coverage with diphtheria toxoid-containing vaccines is suboptimal.[2]

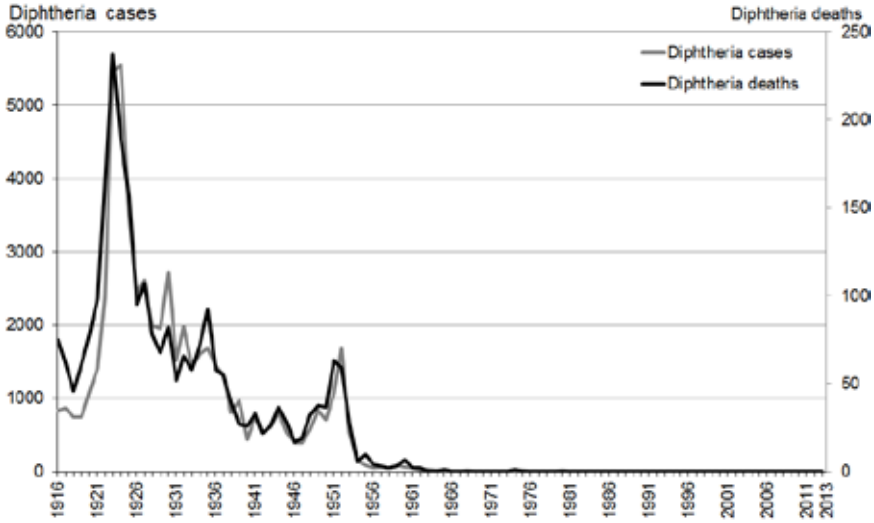
Diphtheria is rare in developed countries such as New Zealand due to active immunisation with diphtheria toxoid-containing vaccine. However, continuing endemic cutaneous diphtheria in indigenous communities has been reported from the US, Canada and Australia. Small diphtheria outbreaks still occur in developed countries.[3] These often appear to be caused by unvaccinated or partially vaccinated individuals travelling to endemic countries.[4, 5, 6]

The overall case fatality rate for 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.[7]

5.3.2 New Zealand epidemiology

Diphtheria infection was common in New Zealand until the 1960s (see Figure 5.2). In 2009 a case of toxigenic diphtheria was reported in an adult male who developed a cutaneous infection after being tattooed in Samoa. A secondary case of toxigenic cutaneous diphtheria was subsequently identified in a fully immunised 11-year-old household contact.[8] The last case of toxigenic respiratory diphtheria was reported in 1998.[9]

Figure 5.2: Number of cases of diphtheria and diphtheria mortality, 1916–2013



Source: Ministry of Health and the Institute of Environmental Science and Research

The 2005–07 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.[10] 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 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
- 10 µg of purified polyribosyl-ribitol-phosphate capsular polysaccharide (PRP) of *Haemophilus influenzae* type b (Hib), covalently bound to 20–40 µg tetanus toxoid (T), 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, bioCSL): 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 and sodium hydroxide.

Other vaccines

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

- DTaP-IPV: Quadracel (Sanofi-aventis NZ Ltd)
- Tdap: Adacel (Sanofi-aventis NZ Ltd)
- Tdap-IPV: Boostrix-IPV (GSK) and Adacel Polio (Sanofi-aventis NZ Ltd).

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 and reduces carriage and therefore transmission.[11] To prevent major community outbreaks, it has been suggested that 70 percent or more of the childhood population must be immune to diphtheria.[12, 13] 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 given. 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.[14]

Despite this, there has been minimal disease in developed countries, suggesting that antibody levels may not be a reliable guide to protection and that other factors may be operating.[15] 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.[16]

The duration of protection after Tdap boosters is unknown, but the results of an ongoing Australian study have shown that five years after the Tdap booster dose, 94.4 percent of adults had seroprotective levels of antibodies, compared with 93.7 percent who received Td vaccine.[17]

5.4.3 Transport, storage and handling

Transport according to the *National Guidelines for Vaccine Storage and Distribution*.[18] 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, hold at room temperature for up to eight hours.

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 2.3).

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 immunoglobulins.

5.5 Recommended immunisation schedule

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. 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).

Dose intervals between Td and Tdap

No minimum interval between Td and Tdap is required,[19, 20, 21] unless Tdap is being given as part of a primary immunisation course.

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). 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

No minimum interval between Td and Tdap is required,[19, 20, 21] 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.[3] 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.[22]

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.

Tdap boosters are also funded for pregnant women, from 28 to 38 weeks' gestation (see section 14.5).

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 (Re-)vaccination

Diphtheria toxoid-containing vaccine is funded for (re-)vaccination of children following immunosuppression. See also sections 4.2 and 4.3.

5.6 Contraindications and precautions

5.6.1 Contraindications

See section 1.4 for general contraindications for all vaccines. 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, including DTaP-IPV-HepB/Hib.

5.7 Expected responses and adverse events following immunisation (AEFI)

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.[23] However, local and systemic reactions do occur with diphtheria toxoid-containing vaccine, especially when the infant vaccine is used in older children and adults.

See also sections 14.7 and 19.7 for expected responses and adverse events following immunisation 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. If *C. diphtheriae* or *C. ulcerans* is isolated, it should be sent to the Institute of Environmental Science and Research (ESR) reference laboratory to determine whether it is a toxigenic strain. 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, be given antimicrobial prophylaxis and have their immunisation status updated.

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.

5.8.2 Vaccination

All 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

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 *Communicable Disease Control Manual 2012*[24] or the *Control of Communicable Diseases Manual*.[25]

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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.
Funded vaccines	DTaP-IPV-HepB/Hib (Infanrix-hexa). Hib-PRP-T (Act-HIB).
Funded immunisation schedule	At age 6 weeks, 3 months and 5 months: DTaP-IPV-HepB/Hib. At age 15 months: Hib-PRP-T. For eligible high-risk individuals.
Vaccine efficacy/ effectiveness	Hib disease has been almost eliminated in countries where Hib vaccine is used.
Public health measures	All contacts should have their immunisation status assessed and updated as appropriate. Rifampicin prophylaxis should be administered to contacts 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.

6.2 Clinical features

Transmission is by inhalation of respiratory tract droplets or by direct contact with respiratory tract secretions. Before the introduction of the vaccine, *H. influenzae* type b (Hib) caused 95 percent of *H. influenzae* invasive disease in infants and children. 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. The incubation period of the disease is unknown, but is probably from two to four days.

Prior to immunisation, the most common presentations of Hib invasive disease in New Zealand were meningitis and epiglottitis. Meningitis tends to occur in younger children aged between 3 months and 3 years, while epiglottitis usually occurs in children aged between 2 and 4 years. 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.

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. Immunisation against Hib does not protect against infections due to other *H. influenzae* types or NTHi strains.

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).

H. influenzae type b and NTHi strains also cause diseases (including pneumonia and septicaemia) in the elderly.

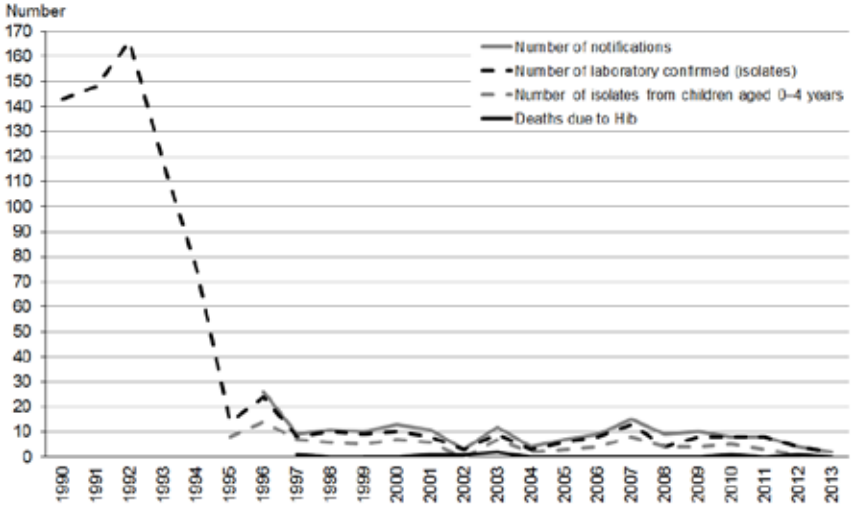
6.3 Epidemiology

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 184 countries having introduced Hib onto their schedules by the end of 2012 (this includes four countries that have introduced Hib in part of the country), or 96 percent of all 191 WHO member states.[1]

6.3.1 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).

Figure 6.1: Number of culture-positive cases of *Haemophilus influenzae* type b invasive disease, 1990–2013



Source: Institute of Environmental Science and Research

From 2000 to 2012, 54 laboratory-confirmed cases of invasive Hib were reported in children aged under 5 years.[2] Of the 54 cases, nine were reported as having received Hib immunisation appropriate for their age and 41 had either received no Hib immunisation or were incompletely immunised for their age. The immunisation history of the remaining four cases was unknown. There were no laboratory-confirmed cases of invasive Hib in children aged under 5 years in 2013.

In summary, of the small number of children who have developed Hib infection in New Zealand since the Schedule change in 2000 (see Appendix 1, section A1.3.2), most had either received no Hib vaccines or were incompletely vaccinated for their age.

6.4 Vaccines

The only way to reliably protect against Hib disease is immunisation. Antibodies to PRP (polyribosylribitol phosphate), 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 1.2.3). 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): 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 (Act-HIB, Sanofi-aventis NZ Ltd): contains 10 µg of purified Hib capsular polysaccharide conjugated to 18–30 µg of inactivated tetanus toxoid; other components (excipients) include trometamol, sucrose and sodium chloride.

Other vaccines

Hib-PRP-T (Hiberix, GSK) is also registered (approved for use) and is available (marketed) in New Zealand. It contains 10 µg of purified Hib capsular polysaccharide conjugated to 30 µg of inactivated tetanus toxoid. Other components (excipients) include lactose in the vaccine and sterile saline solution in the diluent.

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,[3, 4, 5] including New Zealand. Hib vaccines are highly effective after a primary course of two or three doses.[6, 7, 8] 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.[9]

6.4.3 Transport, storage and handling

Transport according to the *National Guidelines for Vaccine Storage and Distribution*.[10] 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 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, hold at room temperature for up to eight hours.

Hib-PRP-T vaccine (Act-HIB) 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 2.3).

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. A primary course of Hib-PRP-T as DTaP-IPV-HepB/Hib (Infanrix-hexa) vaccine is given at ages 6 weeks, 3 months and 5 months, and a booster of Hib-PRP-T (Act-HIB) is given at age 15 months.

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. The Hib PRP-T vaccine has been shown to be immunogenic in adults.

Hib-PRP-T vaccine (Act-HIB) is funded for older children and adults pre- or post-splenectomy; one dose of vaccine is recommended (see also section 4.3.4). Hib-PRP-T vaccine is approved for use (registered) in individuals aged under 5 years; use of Hib-PRP-T vaccine in children older than 5 years and adults will be outside current licensure, and parents/guardians and individuals must be fully informed of this. There are not expected to be any safety concerns for use in older age groups.

(Pneumococcal, meningococcal, influenza and varicella 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 vaccine is funded for (re-)vaccination of children following immunosuppression. (See also sections 4.2 and 4.3.)

6.6 Contraindications and precautions

See section 1.4 for general contraindications for all vaccines. See section 14.6 for contraindications and precautions to DTaP-IPV-HepB/Hib vaccine.

Hib-PRP-T vaccines should not be administered to individuals:

- who developed anaphylaxis to any component of the vaccine
- who developed anaphylaxis after a previous Hib injection.

Significant hypersensitivity reactions to Hib vaccines appear to be extremely rare.

6.7 Expected responses and adverse events following immunisation (AEFI)

See section 14.7 for expected responses and adverse events following immunisation 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.[11]

6.7.2 Adverse events following immunisation

A meta-analysis of trials of Hib vaccination from 1990 to 1997 found that serious adverse events were rare.[12] 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.[13]

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*).[14]

6.8.1 Management of contacts

All contacts should have their immunisation status assessed and updated, as appropriate. Note that the prophylaxis for Hib is different from that for meningococcal disease (see chapter 12).

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.

Rifampicin recommendations

Chemoprophylaxis with rifampicin is recommended for the following contacts of an index case of Hib:

- all household contacts, regardless of age, who live in a home where there are one or more children aged under 5 years, and who are 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 5 years other than the index case
- occupants of households where all contacts aged 12 months to under 5 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 *Communicable Disease Control Manual 2012*[14] or the *Control of Communicable Diseases Manual*.[15]

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7 Hepatitis A

Key information

Mode of transmission	The hepatitis A virus (HAV) is spread through the 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 immune compromised. There is no carrier state.
Vaccines (registered and available)	Monovalent inactivated HAV vaccine (Havrix; Avaxim). Combined inactivated HAV-recombinant hepatitis B surface antigen protein vaccine (Twinrix). Combined HAV-purified *Salmonella typhi* Vi polysaccharide vaccine (Hepatyrix; Vivaxim).
Funded vaccine indications	HAV vaccine (Havrix) is recommended and funded for: · transplant patients · children with chronic liver disease · close contacts of hepatitis A cases.
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, immunoglobulin (IG) is recommended · age 12 months through 40 years, vaccination is recommended · age ≥41 years, IG is recommended.

7.1 Virology

Hepatitis A virus (HAV) is an 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 immune compromised (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

In developing countries the disease is virtually confined to early childhood and is not an important cause of morbidity. Almost all adults in these countries are immune. In developed countries the infection is less common in childhood and only 20–40 percent of adults are immune.

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. These continents and countries include the Pacific, Africa, Asia (except Japan), Eastern Europe, the Middle East, South and Central America, Mexico and Greenland. Others also at greater risk of contracting HAV are people who have oral–anal sexual contact, illegal drug users, those with chronic liver disease or blood-clotting disorders (or who receive clotting factor concentrates), 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 1.8 per 100,000 in 2012.[1] This fall in rate is attributable to the use of HAV vaccination in travellers and a reduction in HAV prevalence overseas. In 2013, 91 cases were notified compared to 82 in 2012. From 2000 to 2013, between 22 and 43 percent of notified cases required hospitalisation.

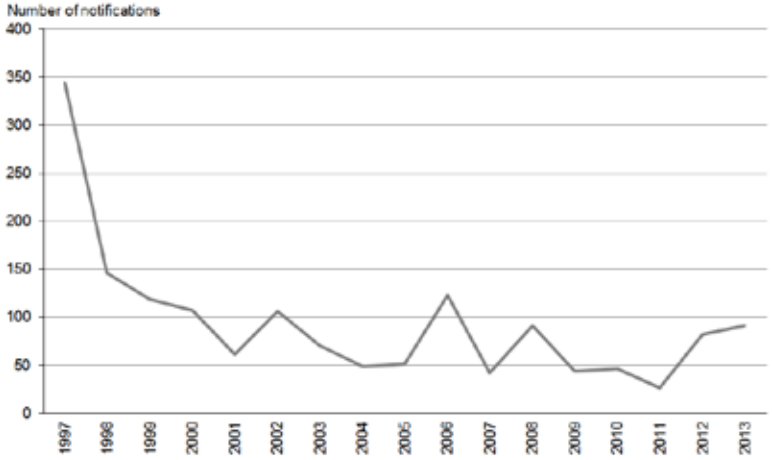
Age was recorded for all cases in 2012, with the highest rates occurring in the 5–9 years age group (21 cases, 7.2 per 100,000 population), followed by the 1–4 years age group (13 cases, 5.2 per 100,000) and the 10–14 years age group (10 cases, 3.5 per 100,000). Ethnicity was recorded for 80 (97.6 percent) cases. The Middle Eastern/Latin American/African ethnic group had the highest notification rate (5 cases, 13.2 per 100,000), followed by the Asian ethnic group (53 cases, 13.0 per 100,000). One person-to-person outbreak occurred in 2012, involving 30 cases.[1]

Of the 76 cases with travel information recorded, 38 (50 percent) had travelled overseas during the incubation period of the disease. The countries most frequently visited included India (14 cases), Fiji (5 cases), Samoa (5 cases), Pakistan and Singapore (3 cases each).[1]

Hepatitis A outbreaks continue to occur, the most recent in Ashburton in 2013. Transmission was through person-to-person spread in homes and early childhood centres. A mass vaccination of preschool children was implemented to curb the spread.

Figure 7.1 illustrates the overall national downward trend since a peak of notifications in 1997. There have been no deaths with hepatitis A as the primary cause since 2002.

Figure 7.1: Hepatitis A notifications, by year, 1997–2013



Source: Institute of Environmental Science and Research

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 hepatitis B (HBV) vaccine and two HAV and typhoid combined vaccines.

The HAV vaccines are manufactured from cell-culture-adapted hepatitis A propagated in human fibroblasts. The HAV preparation is formalin-inactivated and adsorbed onto an aluminium adjuvant (aluminium hydroxide).

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.

Havrix (GSK) contains 1440 EU (enzyme-linked immunosorbent assay [ELISA] units) of inactivated HAV adsorbed onto aluminium hydroxide. Havrix Junior contains 720 EU of inactivated HAV. Other components and residuals include aluminium hydroxide, 2-phenoxyethanol, polysorbate 20, phosphate salts, sodium chloride and formaldehyde.

Other vaccines

Inactivated HAV vaccine

- Avaxim (Sanofi-aventis NZ Ltd) contains 160 antigen units of inactivated HAV; other components and residuals include neomycin, bovine serum albumin, phenoxythanol and formaldehyde.

Combined HAV and HBV vaccine

- Twinrix (GSK) contains 720 EU of inactivated HAV and 10 µg of recombinant DNA hepatitis B surface antigen (HBsAg) vaccine. The Twinrix Junior preparation contains half these amounts. The vaccines are adsorbed onto aluminum adjuvants. Other components and residuals include aluminium hydroxide, aluminium phosphate, sodium chloride, formaldehyde, neomycin sulphate, polysorbate 20, phosphate buffer 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 1440 EU of HAV and 25 µg of purified *Salmonella typhi* Vi polysaccharide; other components and residuals include aluminium hydroxide, sodium chloride, formaldehyde, polysorbate 20, trometamol and neomycin.
- Vivaxim (Sanofi-aventis NZ Ltd) contains 160 antigen units of HAV and 25 µg of purified *Salmonella typhi* Vi polysaccharide; other components and residuals include sodium chloride, sodium phosphate, aluminium hydroxide, phenoxyethanol, formaldehyde, neomycin and bovine serum albumin.

7.4.2 Efficacy and effectiveness

HAV vaccines are highly immunogenic in both adults and children, with 90–100 percent of recipients developing protective antibody levels one month after the first dose.[2]

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.[2, 3] 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.[2]

Duration of immunity

Antibodies to HAV vaccine have been shown to persist in vaccinated adults for at least 15 years after vaccination, and up to 10 years in vaccinated children and adolescents. Mathematical models estimate that following completion of a two-dose series, protective levels of antibody will persist for 25 years or longer.[2]

7.4.3 Transport, storage and handling

Transport according to the *National Guidelines for Vaccine Storage and Distribution*.[4] 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 infants (see section 2.3).

Co-administration with other vaccines

The US Advisory Committee on Immunization Practices (ACIP) has reported that limited data from studies in adults indicates that simultaneous administration of HAV vaccine with any one of the diphtheria, poliovirus (oral and inactivated), tetanus, typhoid (both oral and intramuscular), cholera, Japanese encephalitis, rabies or yellow fever vaccines does not decrease the immune response to either vaccine or increase the frequency of reported adverse events. Studies indicate that hepatitis B virus (HBV) vaccine can be administered simultaneously with HAV vaccine without affecting either vaccine's immunogenicity or increasing the frequency of adverse events.[5]

When HAV vaccine is administered concurrently with other vaccines, it should be given in a separate syringe and needle at a different injection site.

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.health.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 carriers of hepatitis B and C · other chronic liver disease.
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 · sewerage 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 Refer to the *Communicable Disease Control Manual*[6] 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.[2]

Chronic carriers of hepatitis B and C

Studies have shown that in these individuals, super-infection with HAV leads to increased morbidity and mortality.

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.[7, 8]

Travellers

HAV vaccine is recommended (but not funded), and if given prior to departure to the continents and countries specified in section 7.3.1 is likely to provide protection. After one dose in healthy people, protective levels of antibody have been demonstrated by two weeks, and 95–100 percent of people vaccinated will seroconvert by four weeks. Immunoglobulin is no longer available or recommended 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:

- illicit drug users (who account for 30 percent of cases in communities during outbreaks)[2]
- men who have sex with men
- individuals who are travelling to areas of high endemicity.

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 below. See the manufacturers' data sheets for more information.

Table 7.2: Hepatitis A-containing vaccines: by age, dose and schedule

Note: Havrix and Havrix Junior are funded for eligible individuals (Table 4.1).

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[a]
2 years–adult	Avaxim	160 antigen units	0.5	2	0 and 6–36 months
≥16 years	Havrix 1440	1440 EU	1	2	0 and 6–12 months[a]
Hepatitis A–Hepatitis B combined vaccine					
1–15 years	Twinrix Junior	360 EU of HAV and 10 µg of HBsAg	0.5	3[b]	0, 1 and 6 months; or 0, 7, 21 days plus a booster at 1 year
≥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	1440 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[c]
≥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 6–12 months[c]

Continued overleaf

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 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.[9]

b See the manufacturer's data sheet for a two-dose schedule of Twinrix (adult dose) for children.

c If the individual remains at risk from typhoid fever, a single dose of the typhoid vaccine is recommended every 3 years.

7.6 Contraindications and precautions

7.6.1 Contraindications

The usual general contraindications to immunisation apply to HAV vaccine (see section 1.4). Administration of HAV vaccine should be delayed in individuals suffering from acute severe febrile illness. HAV vaccine should not be administered to people with a history of a severe reaction to a prior dose of HAV vaccine or to a vaccine component.

7.6.2 Precautions

The safety of HAV vaccine during pregnancy and while breastfeeding has not been determined. However, because HAV vaccine is produced from inactivated HAV, the risk to the developing fetus and infant is expected to be extremely low. Therefore, the risk associated with vaccination during pregnancy and while breastfeeding should be weighed against the risk of HAV. As a precaution, HAV vaccines should be used during pregnancy and while breastfeeding only when clearly needed, such as when travelling to a country where HAV is endemic.

In individuals with an impaired immune system, adequate anti-HAV antibody titres may not be obtained after a single dose.

7.7 Expected responses and adverse events following immunisation (AEFI)

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.[10] Similar responses are seen with HAV–HBV combination vaccines, and HAV–typhoid combination vaccines.

7.7.2 Adverse events following immunisation

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.[10]

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

HAV vaccination is the preferred method for controlling outbreaks, or for post-exposure prophylaxis. HAV vaccine may be used for post-exposure prevention of infection if given within two weeks of exposure.[11] The US Advisory Committee on Immunization Practices (ACIP) recommends HAV vaccine for post-exposure prophylaxis in healthy persons aged 12 months t0 40 years.[12] Human IG may be given to infants aged under 12 months and adults aged 41 years and older, and to other vulnerable groups. IG is not usually offered if more than two weeks have elapsed since the onset of exposure to the index case.

See Table 7.3 below for immunoprophylaxis recommendations.

Newborn infants of infected mothers

Perinatal transmission is rare. If the mother develops symptoms two weeks before to one week after delivery, the infant may be given IG (0.02 mL/kg), although its efficacy in these circumstances has not been established. The mother may breastfeed. Specific advice should be sought from a paediatrician or infectious diseases physician.

Early childhood workers, children and household contacts

Prevention of spread in these circumstances requires educating people about the modes of spread. For example, HAV can survive on objects in the environment for up to several weeks.

Immunisation should be considered for unimmunised children aged 12 months and older and unimmunised adult workers aged 40 years and under in the same room as the index case. In addition, new workers appointed or children admitted up to six weeks after the outbreak should be vaccinated prior to entry. Infants aged under 12 months and workers aged 41 years and older may be offered IG. Household contacts of confirmed cases should also be protected. Minimal contact in schools is not considered a high-risk situation.

Community-wide outbreaks of hepatitis A infection

HAV vaccine is effective in controlling community-wide epidemics and common-source outbreaks of HAV infection.[13] 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.

Table 7.3: Recommendations for post-exposure immunoprophylaxis of Hepatitis A virus (HAV)

Time since exposure	Age of patient	Recommended prophylaxis
2 weeks or less	Younger than 12 months	IG, 0.02 mL/kg[a]
	12 months through 40 years	HAV vaccine[b]
	41 years or older	IG, 0.02 mL/kg[a] but HAV vaccine[b] can be used if IG is unavailable[a]
	People of any age who are immune compromised or have chronic liver disease	IG, 0.02 mL/kg[a]
More than 2 weeks	Younger than 12 months	No prophylaxis
	12 months or older	No prophylaxis, but HAV vaccine may be indicated for ongoing exposure[b]

a IG (immunoglobulin) should be administered deep into a large muscle mass. Ordinarily no more than 5 mL should be administered in one site in an adult or large child; lesser amounts (maximum 3 mL in one site) should be given to small children and infants.

b See Table 7.2 for hepatitis A vaccine dosage and scheduling.

Source: Adapted from: American Academy of Pediatrics. 2012. Hepatitis A. In: Pickering LK, Baker CJ, Kimberlin DW, et al (eds). *Red Book: 2012 report of the Committee on Infectious Diseases* (29th edition). Elk Grove Village IL: American Academy of Pediatrics, Table 3.13.

For more details on control measures, refer to the *Communicable Disease Control Manual*[6] or the *Control of Communicable Diseases Manual.*[14]

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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 vaccine	Hep B (HBvaxPRO). DTaP-IPV-HepB/Hib (Infanrix-hexa).
Funded immunisation schedule	At ages 6 weeks, 3 months and 5 months: DTaP-IPV-HepB/Hib. Babies born to HBsAg-positive mothers: Hep B plus HBIG at birth, then the usual childhood schedule. Serological testing (anti-HBs and HBsAg at age 9 months). Unvaccinated children aged under 18 years: 3 doses of Hep B, at 0, 1 and 6 months (an accelerated schedule is available). Eligible adults: 3 doses of Hep B, at 0, 1 and 6 months (an accelerated schedule is available).
Vaccine efficacy/ effectiveness	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 (HCC).

8.2.1 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 variable[2]).

The common symptoms of acute hepatitis B illness are fever, jaundice, malaise, anorexia, nausea, vomiting, myalgias and abdominal pain. Jaundice develops usually 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 acute liver failure (less than 1 percent), of whom almost half will die or require emergency liver transplantation.

8.2.2 Chronic HBV infection

The main burden of HBV disease occurs in people with chronic HBV infection. These chronically infected people are identified by persistence of hepatitis B surface antigen (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. This asymptomatic chronic infection stimulates persistent immune responses that may eventually (decades later) lead to cirrhosis, which itself increases the risk of development of hepatocellular carcinoma.

Chronically infected people 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 the rate of viral replication is lower, HBeAg may be absent from the blood, and HBV DNA levels are usually lower. People who have cleared HBeAg and remain HBsAg positive are termed carriers; this is a subset of chronic HBV infection.

8.2.3 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.[3]

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,[4] 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 Burden of chronic disease and geography

Almost half the world's population have been exposed to the hepatitis B virus (HBV), and an estimated 400 million people have chronic infection and remain at risk of developing hepatocellular carcinoma and cirrhosis. 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 (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.[5, 6]

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 Andean Latin America.[5] 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 had been infected by age 15 years.[7, 8] Even after the introduction of universal hepatitis B vaccine 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.[9, 10, 11]

Acute HBV infection

Only acute hepatitis B is a notifiable disease in New Zealand. Therefore notification rates do not describe the burden of chronic hepatitis B infections.

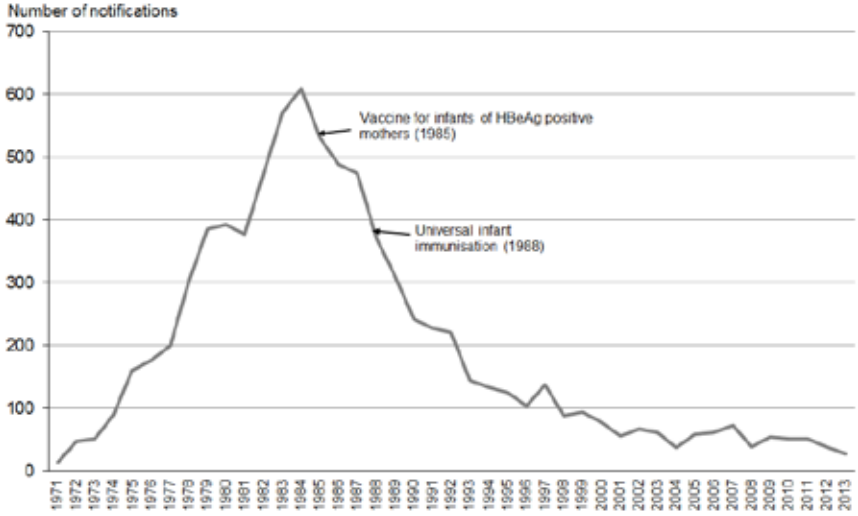
The HBV notification rate in 2012 was 0.9 per 100,000 population, which is a small decrease from the 2011 rate (1.2 per 100,000).[12] The highest notification rate was in the 40–49 years age group (2.4 per 100,000, 15 cases), followed by the 50–59 years age group (1.4 per 100,000, 8 cases). There were no notified cases in children aged under 15 years. The notification rate was higher for males (1.1 per 100,000 population, 25 cases) than for females (0.6 per 100,000, 14 cases).

Ethnicity was recorded for 38 (97.4 percent) cases.[12] Of the ethnic groups with more than five cases reported in 2012, the highest notification rate was among the Asian (1.7 per 100,000, 7 cases) ethnic group, followed by the Māori (1.2 per 100,000, 8 cases) and European or Other (0.7 per 100,000, 20 cases) ethnic groups. The most common risk factors reported by hepatitis B cases in 2012 were:

- being overseas during the incubation period for this disease
- sexual contact with a confirmed case or person with chronic HBV infection
- household contact with a confirmed case or person with chronic HBV infection.

Hepatitis B notifications have declined from 609 cases in 1984 to 28 cases in 2013 (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, 1971–2013



Source: Ministry of Health and the Institute of Environmental Science and Research

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 the risk of early horizontal transmission.[13]

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.[14] 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 (HCC) 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 HCC 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, who would have been eligible to receive funded hepatitis B vaccine in childhood.[15]

Strategy for prevention

In 1988 New Zealand was one of the first countries to introduce universal infant hepatitis B immunisation. At the end of 2013 approximately 93 percent of New Zealand children aged 2 years had completed a primary course of hepatitis B vaccine, which confers lifelong immunity in approximately 95 percent of vaccinees.

The Hepatitis Foundation of New Zealand[16] recommend that the following individuals be screened for HBV – people who:

- are over age 25 years and of Māori, Pacific or Asian ethnicity
- are contacts of HBsAg-positive people or people with chronic HBV infection
- live with someone who has HBV
- have had unprotected sexual contact with an HBV-infected person
- have received a tattoo using unsterile equipment
- have a mother or a close family member who has HBV infection.

Screening for HBsAg is also part of routine antenatal care.

8.4 Vaccines

8.4.1 Available vaccines

A number of HBV-specific monovalent and combination vaccines that contain HBV vaccine are licensed (approved for use) and available (marketed) in New Zealand, all of which contain HBsAg that has been synthesised by genetically modified yeast or bacterial cells.

Funded vaccines

The hepatitis B-containing vaccines funded as part of the Schedule are:

- Hep B (HBvaxPRO, MSD): contains either 5 µg, 10 µg or 40 µg of hepatitis B surface antigen per dose; it does not contain a preservative
- 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

Other hepatitis B-containing vaccines licensed and available are:

- Hep B: Engerix-B (GSK)
- HAV-Hep B (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. Immunity is strongly correlated with post-vaccination serum anti-HBs antibody levels of ≥10 IU/L. 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 produce adequate antibody levels after a further booster dose of vaccine or a full second course.

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 8.5.5).

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, 17] 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 (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 above 10 IU/L is considered protective. Once a seroprotective level is reached after the primary vaccination course, booster doses of vaccine are unnecessary.[18, 19] Children who are given booster doses up to 12 years after the primary series show strong anamnestic (secondary) responses, indicating the boost was likely to have been unnecessary.

There is evidence from Taiwan,[20] Alaska[21] and Hawaii[22] that boosters of hepatitis B vaccine 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.[23] 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.[24, 25]

8.4.3 Transport, storage and handling

Transport hepatitis B vaccines according to the *National Guidelines for Vaccine Storage and Distribution*.[26] 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, hold at room temperature for up to eight hours.

8.4.4 Dosage and administration

The dose of DTaP-IPV-HepB/Hib (Infanrix-hexa) is 0.5 mL administered by intramuscular injection (see section 2.3).

The dose of Hep B vaccine varies according to the age of the individual (see Table 8.2 for Hep B [HBvaxPRO] dosage and scheduling information). Hep B vaccine is administered by intramuscular injection. In special circumstances Hep B vaccine may be given intradermally to increase the immune response (see 'Non-responders to vaccination' in section 8.5.5).

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

8.5.1 Recommendations

Individuals recommended to have a primary course of hepatitis B vaccine are described in Table 8.1.

Table 8.1: Hepatitis B vaccine recommendations, funded and unfunded

Note: Funded conditions are in the shaded rows. See the Pharmaceutical Schedule (www.pharmac.health.nz) for the number of funded doses and any changes to the funding decisions.

Recommended and funded
Babies of mothers with acute or chronic HBV infection (HBsAg positive) – require a birth dose plus the primary series (HBIG is also given to these babies at birth)
Children aged under 18 years
Household and sexual contacts of people with chronic HBV infection
Those undergoing renal dialysis[a,b]
Adults with hepatitis C infection (who should also receive hepatitis A vaccine, although this is not currently funded)
Individuals who are HIV positive[a]
Individuals following immunosuppression[a,c]
Solid organ and bone marrow transplant recipients[a,b]
Adults with chronic liver disease, and prior to liver transplant, who should receive hepatitis B vaccine early in the course of their illness[b]
Adult haemodialysis patients[a]

Continued overleaf

Recommended, not funded
Adults at occupational risk (see section 4.6)
Adults at risk of infection by sexual exposure: · sexual partners of people with acute HBV infection · 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
Household and sexual contacts of people with acute HBV infection
Individuals with haemophilia and other regular recipients of blood products
Prison inmates
Current or recent injecting drug users
Migrants from HBV endemic countries[d]
Individuals with developmental disabilities
Travellers to HBV endemic regions[d]

a See also section 4.3.

b The 40 µg dose of hepatitis B vaccine is recommended for adult dialysis patients or for adult liver or kidney transplant patients. See Table 8.2.

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

d See the CDC website for countries with high hepatitis B prevalence (wwwnc.cdc.gov/travel/yellowbook/2014/chapter-3-infectious-diseases-related-to-travel/hepatitis-b). Consider combined Hep A and B vaccination for travellers to these regions.

8.5.2 Immunisation schedule

The hepatitis B vaccine doses and immunisation schedules vary according to the age of the individual. These are summarised in Table 8.2 below.

Newborn babies

For babies born to HBsAg-positive mothers, a birth dose of 5 µg of Hep B vaccine plus hepatitis B immunoglobulin are recommended, plus the usual childhood Schedule at ages 6 weeks, 3 and 5 months. See section 8.5.3 for more detailed information, including serological testing at age 9 months.

Infants

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. If a course of immunisation is interrupted for any reason, it may be resumed without repeating prior doses (see Appendix 2).

Adolescents

Hepatitis B vaccine is recommended and funded for everyone aged under 18 years. If the hepatitis B vaccine is not given during the first year of life, three doses of vaccine are recommended (follow the manufacturer's recommendations). A two-dose accelerated regimen for adolescents aged 11–15 years, with the second dose four to six months after the first, is useful to improve compliance in this age group. See also Appendix 2 for catch-up schedules.

Adults

For adults, the vaccine manufacturers recommend three doses of 10 µg hepatitis B vaccine spaced at zero, one and six months. (Note that three 40 µg doses are recommended for certain high-risk adults; see section 8.5.3.) Shorter intervals between the second and third doses lead to lower antibody levels but equivalent seroconversion and therefore adequate protection.

In healthy adults, a two-dose schedule separated by six months,[27] a three-dose schedule given over three weeks,[28] and various other accelerated schedules have led to seroconversion rates equivalent to those obtained when following the usual recommended schedule. In general, three doses separated by four-week intervals are recommended, but the doses may be delivered at weekly intervals if more rapid protection is needed.

Table 8.2: Summary of funded hepatitis B vaccine doses and immunisation schedules

Note: Funded conditions are in the shaded rows. See the Pharmaceutical Schedule (www.pharmac.health.nz) for the number of funded doses and any changes to the funding decisions.

Who	Vaccine	Dose	Volume (mL)	Number of doses	Schedule
Babies born to HBsAg-positive mothers	Hep B (HBvaxPRO)	5 µg	0.5	1	As close to birth as possible, then continue with usual childhood schedule, plus serological testing at 9 months of age
Babies born to HBsAg-negative mothers (usual childhood schedule)	DTaP-IPV-HepB/Hib (Infanrix-hexa)	10 µg (hepatitis B component)	0.5	3	6 weeks, 3 months, 5 months
Children/ adolescents 1 to under 18 years	Hep B (HBvaxPRO)	5 µg	0.5	3	0, 1 and 6 months
Accelerated schedule for adolescents 11–15 years	Hep B (HBvaxPRO)	10 µg	1.0	2	0, 4–6 months
Eligible adults ≥18 years	Hep B (HBvaxPRO)	10 µg[a]	1.0	3	0, 1 and 6 months[b]

a 40 µg is the recommended dose for adult dialysis patients or for adult liver or kidney transplant patients.

b Check the manufacturer's data sheet for accelerated immunisation schedules.

8.5.3 Special cases

Babies of HBsAg mothers

The routine schedule for these infants is a birth dose 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 (see section 8.5.5). 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 hepatitis B immunoglobulin (HBIG) neonatal, at or as close as possible to birth
- a birth dose of hepatitis B vaccine (HBvaxPRO, 5 µg), which should be given at or as close as possible to birth (preferably within 12 hours).

If HBIG and/or hepatitis B vaccine 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 hepatitis B vaccine 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.[29] 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.[29]

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.

The National Immunisation Register (NIR) collects data (with parental consent) on those babies who receive HBIG and hepatitis B vaccine at birth.

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 'Infants' in section 8.5.2

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, early in her pregnancy, the woman should be referred to a specialist for ongoing care.

Give the baby hepatitis B protection as follows.

At age	Action to be taken
Birth	Give hepatitis B immunoglobulin 100–110 IU neonatal and hepatitis B vaccine 5 µg
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 1 to 3 further doses of hepatitis B vaccine at least 4 weeks apart. Recheck serology 4 weeks after each dose to determine if further doses are necessary (ie, if anti-HBs is still ≤10 IU/L). If there is no seroconversion after the third further dose of hepatitis B vaccine, discuss with a specialist.

All other vaccines should be administered as per the Schedule.

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 (ALT), 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 also 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 an estimated 8 percent are HBsAg positive, with the majority 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 sections 1.5 and 8.8.1 for more information about passive immunisation and HBIG.

Pregnancy and breastfeeding

Hepatitis B vaccine may be given during pregnancy and while breastfeeding. Acute hepatitis B 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).

Preterm and low birthweight infants

Infants of HBsAg-positive women

Preterm and low birthweight infants of HBsAg-positive women should be managed as above, regardless of birthweight or gestation.

Preterm infants of HBsAg-negative women

Infants of HBsAg-negative women who were born at less than 37 weeks' gestation, or who are less than 2000 grams should be vaccinated as per the usual childhood schedule above (at ages 6 weeks, 3 and 5 months) and follow-up serological testing is not indicated.

Some low birthweight or preterm infants may have a reduced response to hepatitis B vaccine at birth.[30] However, by the chronological age of 1 month, all medically stable preterm infants, regardless of initial birthweight or gestational age, are as likely to respond to hepatitis B vaccine as are term and larger infants.[29] Because New Zealand's Schedule starts at age 6 weeks, low birthweight and preterm infants are expected to respond to hepatitis B vaccine.

Adult dialysis or adult liver or kidney transplant patients

These adults may have a reduced response to hepatitis B vaccine, so the higher-dose (40 ug) formulation is recommended and funded. See also section 8.5.5 for information about post-vaccination serology.

Management of blood and body fluid exposures (BBFE)

Recommendations following a needle-stick injury are covered in Appendix 7, but the principles relating to hepatitis B are as follows.

- Needle-stick recipient is immune (anti-HBs antibody [Ab] >10 IU/L), regardless of source status
  - No specific intervention is required for hepatitis B.
- Unknown source status
  - If the recipient has a history of being vaccinated but has anti-HBs Ab <10 IU/L, give another dose of hepatitis B vaccine – unless they have ever previously had a recorded anti-HBs Ab ≥10 IU/L.
  - If recipient has been incompletely vaccinated but has had two doses more than four months previously, give a third dose.

- Source HBsAg positive
  - If the recipient was previously vaccinated and is anti-HBs Ab <10 IU/L, give another dose of hepatitis B vaccine and HBIG.
  - If the recipient was not previously vaccinated, give HBIG and commence the three-dose vaccination course.
  - If the recipient has been incompletely vaccinated, give the next vaccine dose and HBIG.
- Source HBsAg negative
  - No specific intervention is required in this case. However, vaccination would often be indicated on the basis that the recipient is at higher risk, as demonstrated by being exposed on this occasion.

8.5.4 (Re-)vaccination

Hepatitis B vaccine is funded for (re-)vaccination of patients following immunosuppression. See also section 4.3.

8.5.5 Serological testing

Serological markers of infection

The antigens described in section 8.1 and their associated antibodies are serological markers of HBV infection or vaccination. At least one serological marker is present during the different phases of infection (Table 8.3). The antigens and their respective antibodies include:

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 8.3: Interpretation of serology for hepatitis B virus 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
–	–	–	+	Immune if concentration is ≥10 IU/L. 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.

Source: Adapted from: Van Damme P, Ward J, Shouval et al. 2013. Hepatitis B vaccines. In: Plotkin SA, Orenstein WA, Offit PA (eds). *Vaccines* (6th edition). Elsevier Saunders, Table 15.1.

See the *Communicable Disease Control Manual 2012*[31] for recommendations for HBV case and contact management.

Pre-vaccination screening: screening for chronic infection

Screening should be part of the informed consent procedure before administering hepatitis B vaccine (see sections 2.3 and 8.3.2), other than in infancy and early childhood. The purpose of pre-vaccination screening is to avoid giving vaccine to those who are chronically HBV infected or are already immune.

In general, those at higher risk of chronic HBV infection should be encouraged to undergo pre-vaccination screening, while those at low risk may be vaccinated without prior screening. Vaccinating a person who is chronically HBV infected does not prevent the future diagnosis, nor does it cause an increase in adverse reactions. Globally, pre-vaccination serological testing is not recommended as routine practice.

Pregnancy

All pregnant women should receive antenatal screening for hepatitis B infection by testing for HBsAg. All HBsAg-positive pregnant women should also be tested for HBeAg and have their HBV DNA level measured early in pregnancy. A referral to a specialist with an interest in hepatitis B and/or the high-risk obstetric team should be made, because anti-viral treatment maybe indicated. Infants of HBsAg-positive mothers should be given hepatitis B immunoglobulin (HBIG) and hepatitis B vaccine as close as possible to birth, preferably within 12 hours. HBIG can only be given up to seven days post-delivery (see section 8.5.3). Babies born to mothers who received oral antiviral therapy must still receive the recommended neonatal HBIG/vaccine schedule (see section 8.5.3). All other vaccines are administered as per the Schedule.

Other high-risk groups

Adults in population groups at high risk of chronic HBV infection (eg, Māori, Pacific and Asian people; see the Hepatitis Foundation recommendations in section 8.3.2) should be screened for chronic HBV infection. All identified HBsAg-positive individuals can be offered counselling about the risks of transmission to others and the importance of avoiding or minimising other causes of liver damage, such as excessive alcohol consumption. All HBsAg-positive individuals should be offered follow-up under the Hepatitis Foundation Hep B Follow-up Programme to enable early diagnosis and treatment of the complications of severe liver disease and hepatocellular carcinoma (HCC). Vaccination is recommended (and funded) for household and sexual contacts of people with chronic HBV infection.

Testing post-vaccination

Routine measurement of anti-HBs antibody levels after vaccination is not normally recommended. The exception may be for those at increased risk of disease, in which case seroconversion should be demonstrated. Such groups include:

- babies of HBsAg-positive mothers (see section 8.5.3)
- some occupational groups in contact with blood, body fluids and tissue

- people with chronic disease, such as diabetics, haemodialysis patients,[32] chronic liver disease and coeliac disease[33]
- HIV-infected people[34, 35, 36, 37, 38]
- immune-compromised individuals[39, 40]
- sexual partners or needle-sharing partners of HBsAg-positive people.[36, 37, 38]

For previously vaccinated individuals at increased risk without a documented seroconversion, it is recommended that a booster dose of hepatitis B vaccine be given and antibodies measured four weeks later. Most vaccinees will develop a high anti-HBs titre, usually >100 IU/L. Those who fail to achieve a titre of 10 IU/L should have the course of three doses of vaccine completed. If they have not achieved a titre of >10 IU/L, they should be considered a non-responder and treated according to the protocol outlined below.

Vaccinated individuals 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, 41]

Non-responders to vaccination

Individuals who fail to achieve an anti-HBs level of ≥10 IU/L following a recent series of three doses of vaccine are recommended a further three doses of hepatitis B vaccine, separated by four-week intervals, with anti-HBs checked one to two months later. These doses are funded for children aged under 18 years, and for individuals aged 18 years and older who are household and/or sexual contacts of people with chronic HBV infection (see section 8.5.1).

Persistent non-responders with no immunodeficiency who have completed the primary series and a full second course 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.

An intradermal injection of reduced doses of routine hepatitis B vaccine,[42, 43] intramuscular injection of double doses of routine hepatitis B vaccine[44, 45] and intramuscular injection of double doses of combined hepatitis A and B vaccine[46] have all been shown to stimulate protective responses in a proportion of individuals who have not responded to a three-dose series, but it is not possible to recommend one approach over the others.

8.6 Contraindications and precautions

The general contraindications to all vaccines apply to hepatitis B vaccine (see section 1.4). The only specific contraindication to hepatitis B vaccine 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 adverse events following immunisation (AEFI)

See section 14.7 for expected responses and adverse events following immunisation 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 Adverse events following immunisation

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.[47] These studies have documented no increased risk of multiple sclerosis,[48, 49] diabetes, chronic fatigue syndrome,[50] encephalomyelitis or hair loss.[51] Rarely, transient thrombocytopenia[52] and myalgia and arthralgia[53, 54] have been reported after hepatitis B vaccine.

8.8 Public health measures

The elimination of hepatitis B virus (HBV) transmission is now a realistic public health goal,[55] especially with the proven effectiveness and safety record of hepatitis B vaccine.[56]

Large increases in hepatitis B vaccine coverage and the inherently long interval of time to achieve vaccine-related reductions in HBV acute and chronic disease can undermine support for hepatitis vaccination in the face of seemingly urgent competing priorities. However, it is important to ensure vaccination programmes are maintained for the at-risk populations.

> It is a legal requirement that all cases of acute hepatitis B infection be notified immediately on suspicion 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 8.5.3.

8.8.1 Passive immunisation

Hepatitis B immunoglobulin (HBIG) is prepared from donated blood plasma and contains high levels of anti-HBs antibody (see section 1.5). It is given after exposure to HBV and provides passive anti-HBs antibody protection against acute and chronic HBV disease. HBIG prophylaxis is ideally given in combination with the hepatitis B vaccine 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, see Table 8.4) 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.

Table 8.4: Hepatitis B immunoglobulin (HBIG) doses

Age	HBIG dose
Neonates (under 1 month)	100–110 IU*
1 month to 4 years	200 IU
5 to 9 years	300 IU
10 years to adult	400 IU

* The HBIG presentation for neonates may be 100 or 110 IU units.

The following individuals should receive HBIG and the hepatitis B vaccine:

- infants born to mothers with chronic HBV infection (HBsAg positive) (see section 8.5.3)
- non-immune individuals who have been accidentally inoculated, or who have contaminated the eye, mouth, fresh cuts or abrasions of the skin with blood from a known HBsAg-positive person – those individuals who suffer such accidents should wash the contaminated area thoroughly and seek medical advice from the local medical officer of health, the local hospital infection control officer or an occupational health service (see section 8.5.3 and Appendix 7)

- susceptible household and sexual contacts of those with acute hepatitis B infection – HBIG should be given within seven days of the onset of clinical disease in the index case (commence vaccination at the same time; the local medical officer of health can assist with contact tracing and HBIG administration)
- sexual and household contacts of chronically infected people who are not already immune or infected – these people should be vaccinated (funded) but need not receive HBIG.

For more details on control measures, refer to the *Communicable Disease Control Manual 2012*[31] or the *Control of Communicable Diseases Manual*.[57]

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9 Human papillomavirus (HPV)

Key information

Mode of transmission	Skin-to-skin contact with a person with HPV infection.
Links to cancer	High-risk HPV types (predominantly HPV16 and 18) are the most important risk factor for the development of cervical cancer and play an important role in other anogenital and oropharyngeal cancers in both women and men. Low-risk HPV types (predominantly 6 and 11) cause genital warts.
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. Genital warts have a prevalence of 1–10%. There were 180 cervical cancer registrations in New Zealand in 2010 (1.8% of female cancer registrations) and 52 deaths (1.3% of female cancer deaths). HPV is linked to about 99.7% of cervical cancers and to about 50% of vulvar, 65% of vaginal, 35% of penile, 95% of anal and about 60% of oropharyngeal cancers.
Funded vaccine	HPV4 (Gardasil) is a recombinant subunit vaccine containing virus-like particles from HPV types 16, 18, 6 and 11.
Funded immunisation schedule	HPV4 vaccine is funded for: · girls and young women aged under 20 years · individuals aged under 26 years with HIV infection · transplant patients.

Continued overleaf

Vaccine efficacy/ effectiveness	The incidence of HPV infection, pre-cancerous lesions and genital warts is significantly reduced in immunised populations (in women and men). There is some evidence for herd immunity (reductions in genitals warts in unimmunised populations).
Adverse events to vaccine	Syncope (fainting) is a known injection reaction in adolescent girls.
Cervical cancer prevention measures	HPV immunisation. Regular cervical screening. Safe 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 wart (eg, common, palmar, plantar or anogenital). More than 40 HPV types can infect the anogenital tract.[1, 2]

On the basis of their causal link to cancer, HPVs are divided into low-risk and high-risk types. High-risk types include 16, 18, 31, 33, 45, 52 and 58, with types 16 and 18 most frequently associated with cervical cancer. High-risk HPV types are also associated with anal cancer, vulvar cancer, vaginal cancer, penile cancer and HPV-positive oropharyngeal cancer. Low-risk types include 6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81 and 89. They are predominantly associated with non-malignant lesions, such as genital warts (especially types 6 and 11), and can also cause recurrent respiratory papillomatosis.

9.2 Clinical features

9.2.1 Infection

Infection results from skin-to-skin contact 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. 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.

9.2.2 Cervical cancer

There is rapid clearance of HPV in the first 6 to 12 months, with 80–90 percent clearance by two years. Following this, there is a very small fraction of persistent infection that progresses to cervical intraepithelial neoplasia (CIN2+).

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 99 percent of 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.[3, 4]

9.2.3 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]

9.2.4 Other cancers

HPV infection is also responsible for other cancers in women and men. Data from the US cancer registry indicates that HPV is linked to about 50 percent of vulvar, about 65 percent of vaginal, about 35 percent of penile, about 95 percent of anal and about 60 percent of oropharyngeal cancers (see Table 9.1).[5]

9.2.5 Respiratory papillomatosis

Perinatal transmission of HPV virus can cause laryngeal infection in infants, which in rare cases can result in recurrent respiratory papillomatosis.

9.3 Epidemiology

9.3.1 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.[6]

New Zealand data

Data from the NZ Youth 2012 survey 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. Approximately 17 percent of sexually active students don't use or only sometimes use a condom or other contraception. This proportion was higher among younger students and students from areas with high levels of deprivation.[7]

9.3.2 Acquisition of HPV

Infection with oncogenic serotypes of HPV is common, with an estimated 70–80 percent of sexually active women becoming infected at some stage. Approximately 28 percent of women have acquired infection with at least one HPV serotype within one year of beginning sexual activity, increasing to nearly 50 percent after three years.[8, 9] Mixed infection is common, with 20–30 percent of women concurrently infected with several serotypes.

Most episodes of infection are eradicated 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.[10, 11]

The consequences of HPV infection are commonly detected by cytological examination of cervical epithelial cells. Cervical screening programmes can identify the early changes associated with HPV infection (eg, squamous atypia or CIN1) in about one-third of infected women. In the overwhelming majority of these women the abnormalities resolve within five years of acquisition, with clearance of HPV infection.

9.3.3 HPV-related cancer

Cervical cancer

Approximately 15 HPV oncogenic serotypes are responsible for most cases of cervical cancer: HPV16 is responsible for about 60 percent and HPV18 for about 10 percent of cervical cancers worldwide, with types HPV31, HPV33 and HPV45 being the next most likely causes.

In approximately 15 percent of women with persistent HPV16 infection, CIN3 or cervical cancer develops about 7 to 15 years after acquiring the infection. The risk of cancer in women with persistent infection due to HPV18 is approximately 10 percent, while the risk due to persistent infection with all other oncogenic serotypes is less than 5 percent.

The incidence of cervical cancer in developed nations is approximately 10–15 per 100,000 women aged 20–70 years, with an annual mortality of approximately 5–8 per 100,000.

Table 9.1 shows data from the US cancer registry and provides estimates of the percentage of cancers attributable to HPV.

Table 9.1: Estimated average annual percentage and number of cancers attributable to HPV, by anatomical site and sex, United States, 2004–2008

Site	Average annual number*	Percentage attributable to HPV	
		%	Range
Cervix	11,967	96	(95–97)
Vulva	3136	51	(37–65)
Vagina	729	64	(43–82)
Penis	1046	36	(26–47)
Anus:			
· female	3089	93	(86–97)
· male	1678	93	(86–97)
Oropharynx:			
· female	2370	63	(50–75)
· male	9356	63	(50–75)

* Data is from population-based cancer registries that participate in the US National Program of Cancer registries and/or the Surveillance, Epidemiology, and End Results Program, and meet criteria for high data quality.

Adapted from: Centers for Disease Control and Prevention. 2012. Human papillomavirus-associated cancers – United States, 2004–2008. *Morbidity & Mortality Weekly Report* 61(15): 258–61. URL: www.cdc.gov/mmwr/preview/mmwrhtml/mm6115a2.htm (accessed 3 September 2013).

New Zealand cervical cancer registrations

The most recent data available for New Zealand cancer registrations is for 2010.[12] There were 180 cases of cervical cancer (1.8 percent of female cancer registrations) and 52 deaths (1.3 percent of female cancer deaths). Ethnic disparities in registrations and mortality remained from 1999 through to 2010. Although disparity in mortality reduced, mortality remained significantly higher in Māori women.

Other cancers

HPV16 and 18 are linked to other cancers in women and men, including vulval, vaginal, penile, anal and oropharyngeal cancers. Table 9.1 (above) provides estimates from the US of the percentage of cancers attributable to HPV.

9.3.4 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.[13, 14] In Scandinavian countries the reported rates are as high as 10 percent.[15]

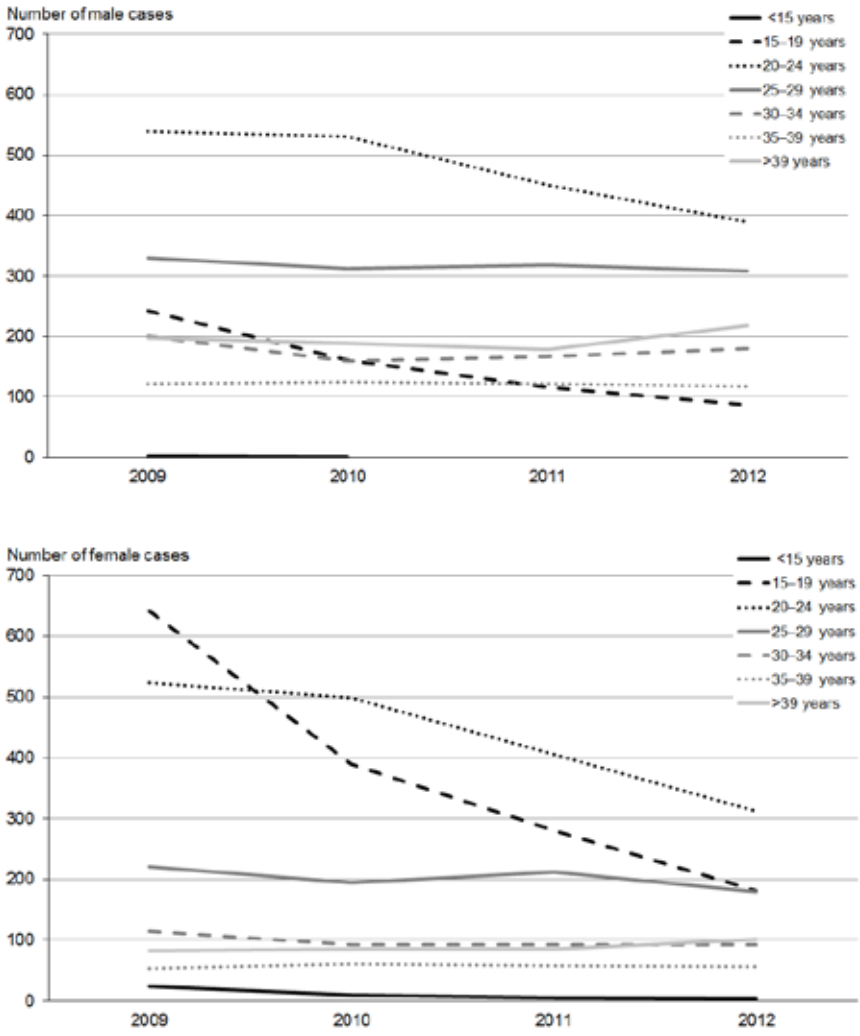
New Zealand genital warts trends 2009–2012

From 2009 to 2012 genital warts clinical case counts reported by sexual health clinics (SHCs) decreased by 32.3 percent (from 3294 to 2231 cases) and case counts reported by family planning clinics (FPCs) by 52.1 percent (from 532 to 255 cases).[16] In SHCs there was a decrease in diagnoses in all ethnic groups. In FPCs the number of diagnoses in every ethnic group decreased between 2009 and 2010 but remained stable in the following years.

The decrease was most notable in women aged 15–19 years, although decreases also occurred in men in the same age group and in men and women aged 20–24 years (Figure 9.1). These decreases follow the 2008 introduction of HPV vaccine onto the Schedule for girls aged 12 years, and a catch-up programme for young women born on or after 1 January 1990 (see Appendix 1).

This data supports the findings of ecological studies in Auckland and Australia, which observed a decline in the proportion of new clinical patients diagnosed with genital warts in populations targeted by immunisation programmes.[17, 18]

Figure 9.1: Number of genital warts (first presentation) in sexual health clinics, by sex and age group, 2009–2012



Source: Institute of Environmental Science and Research

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. HPV4 (Gardasil, bioCSL/MSD) contains HPV types 6, 11, 16 and 18, and HPV2 vaccine (Cervarix, GSK) contains HPV types 16 and 18.

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 present in HPV4 are produced by genetically engineered yeast cells, while the L1 proteins present in HPV2 are produced by insect cells infected with genetically engineered baculovirus.

Funded HPV vaccine

HPV4 vaccine (Gardasil, bioCSL/MSD) 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.

Other vaccines

HPV2 vaccine (Cervarix, GSK) is approved for use in girls and young women aged 10–45 years. HPV2 contains:

- 20 µg of HPV16 L1 VLP and 20 µg of HPV18 L1 VLP
- a novel adjuvant composed of 500 µg of aluminium hydroxide and 50 µg 3-deacylated monophosphoryl lipid A (MPL); other components include sodium chloride and sodium dihydrogen phosphate dihydrate.

9.4.2 Efficacy and effectiveness

Immunogenicity

Immunisation with three doses of HPV4 vaccine (Gardasil) 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 clearance of natural infection.

Effects on disease

Cervical and other cancers

No studies have 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 (CIN2/3 or adenocarcinoma *in situ*) require treatment to prevent progression to invasive cancer. However, protection against CIN2/3 or adenocarcinoma *in situ* is widely accepted as a surrogate for protection against invasive cancer. HPV vaccines are highly effective in preventing these HPV16- and 18-related precancerous lesions in females.[2, 19]

Studies in males have shown that HPV4 vaccine is efficacious against anal HPV infection and associated pre-cancerous lesions.[20, 21, 22]

Genital warts

Australia has been using HPV vaccine longer than any other country, and vaccine uptake has been relatively high. Between 2007, when HPV4 vaccination was initiated, and 2010 there has been a profound reduction in new cases of genital warts and in Melbourne a near elimination among the vaccinated population and reductions in rates in their sexual partners.[23] Other countries, including New Zealand, have also had a significant reduction in new cases of genital warts (see section 9.3.4).

Duration of protection

As vaccination programmes have only been in place for a maximum of seven years, the duration of protection is not yet known. There is no evidence of waning immunity at this time and no indication to date for booster doses.

The immunogenicity of both HPV4 (Gardasil) and HPV2 (Cervarix) vaccines has been established to be robust and long-lasting.[24, 25, 26, 27] Anamnestic responses have been demonstrated out to 8.5 years. In younger women, two doses appear to be as immunogenic as three doses in older women, but the duration of immunity from two doses remains to be established.[28]

Cross-protection

Both vaccines are highly efficacious against vaccine-type infection and related outcomes. Some cross-protection against non-vaccine oncogenic HPV types has been noted, particularly for the HPV2 vaccine.

As non-vaccine types are responsible for around one-third of cervical cancers, the issue of cross-protection may be an important one. Data so far suggests that HPV4 vaccine offers cross-protection against CIN grade 2 or worse caused by HPV31 (70 percent) and some cross-protection for HPV33 and 45, but these numbers are not large enough to reach significance. HPV2 vaccine appears to have greater cross-protection against CIN grade 2 or worse caused by HPV33, which is the fourth most prevalent type after HPV16, 18 and 45.[29]

Herd immunity

Australia has seen a reduction in the prevalence of vaccine-type HPV infections in unvaccinated young men after the introduction of the vaccine to young women, supporting the role of herd immunity.[17, 23] In a study of data from a sexual health clinic in Melbourne, 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 1.1.1) had fallen below one. This reduction in genital warts cases in women and men aged under 21 years 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 genital warts national surveillance network.

Models to assess the impact of HPV vaccination against cervical cancer for the most effective community protection support vaccinating at an early age (prior to sexual debut) and vaccinating men, particularly if coverage for women is relatively low.[30]

Previous exposure to HPV

A retrospective analysis of the HPV4 vaccine's pivotal efficacy trial data (Future I and Future II) 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 course of the trial.[31] The study showed a 46.2 percent reduction after cervical surgery of any HPV-related disease (95% CI: 22.5–63.2) and 35.5 percent reduction after diagnosis of vaginal or vulvar disease (95% CI: 20.1–86.3).

This data suggests that the vaccine may have a role in reducing the incidence of subsequent HPV disease in women who already have HPV disease. This study was in a subgroup of women who were vaccinated before they had their first treatment for HPV-related disease.[32] Further studies will be needed to see if similar results are seen in women who receive HPV vaccination after treatment for HPV-related disease.

While awaiting further data, 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, and there may be some benefit.

9.4.3 Transport, storage and handling

Transport according to the *National Guidelines for Vaccine Storage and Distribution*.[33] Store in the dark at +2°C to +8°C. Do not freeze.

9.4.4 Dosage and administration

The dose of HPV4 is 0.5 mL, administered by intramuscular injection in the deltoid area (see section 2.3).

Co-administration with other vaccines

Data available indicates no interference when HPV4 is administered concurrently with other adolescent vaccines, including Tdap and hepatitis B.[34] Influenza vaccine and Tdap vaccine may be administered concurrently with HPV4 or at any time interval before or after the administration of HPV4.

9.5 Recommended immunisation schedule

Three doses of HPV4 vaccine are recommended at 0, 2 and 6 months. There does not appear to be any reduction in efficacy if the intervals between the doses are longer than recommended. A shortened schedule may be used if necessary, with a four-month interval between the first and third doses (eg, 0, 1 and 4 months).

In New Zealand, HPV4 is registered for use in women aged 9–45 years and in men aged 9–26 years. Recommendations for HPV4 vaccine are described below, and summarised in Table 9.2.

9.5.1 Funded HPV4 vaccine

Girls and young women aged under 20 years

HPV4 vaccine is funded for girls and young women aged under 20 years. The optimal age for administration is 11–13 years, as most in this age group would be naïve to all HPV types. The decision to vaccinate older age groups who may have already commenced sexual activity should follow an assessment of the potential benefits of vaccination – based on their likely previous HPV exposure and future risks.

Individuals aged under 26 years with confirmed HIV infection

HPV4 vaccine is funded for individuals aged under 26 years with confirmed HIV infection. HPV4 vaccine is safe and immunogenic in HIV-infected men.[35]

Those with confirmed HIV infection are more at risk of HPV infection.[36] HIV-infected individuals who are co-infected with HPV are less likely to clear the HPV infection.[36, 37] A direct relationship has been identified between low CD4 cell count and an increased risk of cervical cancer in HIV-infected women.[38] See also section 4.3.

Transplant patients

In view of the increased risk from persistent HPV infection, HPV4 is funded for transplant patients. See also section 4.3.

9.5.2 Recommended but not funded

HPV4 vaccine is recommended but not funded for the following groups.

Immune-compromised individuals

Those who are immune compromised are more likely to develop a persistent HPV infection and to subsequently progress to HPV-related disease.[39, 40] There are no clinical trials as yet demonstrating the efficacy of HPV vaccine in immune-compromised individuals, but these are not live vaccines so there are no safety concerns.

Men who have sex with men

Men who have sex with men (MSM) are at higher risk for HPV infection, anal cancer and high-grade anal intraepithelial neoplasia (HGAIN). Studies in MSM have shown that HPV4 vaccine is efficacious against anal HPV infection and associated pre-cancerous lesions.[20, 21, 22] Currently MSM are deriving no herd immunity benefit from vaccination programmes that target only women.[17]

Boys and young men aged under 20 years

The US Food and Drug Administration licensed HPV4 vaccine for boys and men aged 9–26 years in 2009 for the prevention of genital warts. Since this time there has been additional data from the pivotal trials in males to support the use of the vaccine in preventing anal cancer precursor lesions.[21] The optimal age for administration is 11–13 years, as most in this age group would be naïve to all HPV types.

The decision to vaccinate older age groups who may have already commenced sexual activity should follow an assessment of the potential benefits of vaccination – based on their likely previous HPV exposure and future risks. Including boys and men in a routine vaccination programme is likely to increase the benefit to the population in terms of both HPV-related cancer outcomes and genital warts.

Other groups to consider

Women previously exposed to HPV

Women who have received treatment for HPV-related cervical, vulval or vaginal disease can still be offered HPV vaccination. They may receive some benefit from HPV vaccination in terms of future recurrence of disease.[31, 32] They should be advised that vaccination is not treatment and will not hasten the resolution of existing disease.

Women and men aged 20 years and older

Immunisation should be completed before the onset of sexual activity. However, women and men who have begun sexual activity may still benefit from vaccination.

The data from the pivotal studies for both HPV2 and HPV4 has demonstrated potential benefit to 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.[41] However, pre-vaccination testing for cervical cytological abnormalities or for HPV infection is not recommended.

Women who have genital warts should still be offered vaccination but advised that vaccination is not treatment and will not hasten the resolution of existing warts.

Many women and men aged 20 years and older will have passed the period of highest risk of acquisition of HPV infection. However, history-taking may identify women and men in this age group for whom vaccination is likely to be beneficial, and they may choose to purchase the vaccine.

Table 9.2: Summary of HPV vaccine recommendations, funded and unfunded

Note: Funded conditions are in the shaded rows. See the Pharmaceutical Schedule (www.pharmac.health.nz) for the number of funded doses and any changes to the funding decisions.

Recommended and funded – HPV4 vaccine
Girls and young women aged under 20 years[a]
Individuals aged under 26 years with confirmed HIV infection[b]
For use in transplant patients[b]
Recommended, not funded
Individuals aged under 26 years who are immune compromised
Men who have sex with men, as early as possible prior to, or after, sexual debut
Boys and young men aged under 20 years

a Women who were under age 20 years when they commenced HPV vaccination are currently funded to complete the 3-dose course, even if they are older than 20 years when they complete it.

b See also section 4.3.

9.6 Contraindications

The general contraindications that apply to all immunisations are also relevant to HPV (see section 1.4). HPV4 contains HPV proteins produced by genetically engineered yeast cells. It should not, therefore, be given to people with a history of an immediate hypersensitivity to yeast.

9.7 Expected responses and adverse reactions following immunisation (AEFI)

Syncope (fainting) occurs frequently in adolescents following HPV vaccination, but this is an injection reaction, not a reaction to the vaccine.[1, 42] Serious adverse effects are rare. Both 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.[43] Post-marketing surveillance systems globally continue to monitor the safety of HPV vaccination programmes.[44, 45, 46]

Mild to moderate pain is experienced by over three-quarters of vaccinees but severe pain is very uncommon (approximately 3 percent of vaccinees). Swelling and erythema occur in about one-quarter of vaccinees. Vaccination is not associated with any increased risk of systemic adverse effects. There do not appear to be any adverse effects related to vaccination during pregnancy or while breastfeeding.

9.8 Cervical cancer prevention measures

HPV immunisation is part of a three-pronged approach to cervical cancer prevention that also includes regular cervical screening and safe sex approaches.

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 cervical 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, during early adolescence or even in childhood.

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

A successful HPV immunisation programme will reduce the prevalence of HPV infection in women and thus the incidence of cervical cancer. However, it 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 Safe sex approaches

To minimise the risk of HPV infection (plus other sexually transmitted infections), practitioners should remind individuals of safe 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.

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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 immune compromised.
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	Trivalent inactivated split virion vaccines (Influvac; Fluarix).
Funded immunisation schedule	Recommended and funded for: · those aged 65 years and older · pregnant women · those aged under 65 years with high-risk conditions · children aged under 5 years who have been hospitalised for respiratory illness or have a history of significant respiratory illness.
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.
Precaution	Individuals who have had a confirmed anaphylactic reaction to egg protein may still be able to receive influenza vaccine, but should do so under specialist supervision. There may be an increased risk of fever and febrile convulsions with concomitant PCV13 and influenza vaccine in children aged 6–59 months.
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 are from the family Orthomyxoviridiae, and are classified by their antigenic differences into influenza virus 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.

Examples of influenza A viruses include H1N1, H2N2 and H3N2, which have caused previous epidemics and pandemics. Influenza B is associated with widespread outbreaks and epidemics. Influenza C virus is associated with sporadic cases of mild upper respiratory infection.

10.1.1 Antigenic drift

Influenza A and B viruses undergo frequent small changes (mutations) in the DNA coding regions responsible for H and N surface antigens. Over time, these mutations accumulate so that a new virus variant emerges. This is known as antigenic drift and is responsible for annual influenza outbreaks and the need to reformulate influenza vaccines. New variants are described by their type, geographic site of isolation, culture number and year of isolation; for example, the H3N2 virus A/Wellington/1/2004.

10.1.2 Antigenic shift

Influenza A viruses can also significantly change the DNA coding regions responsible for H and N surface antigens, causing a completely new virus subtype to emerge. This is known as antigenic shift and is largely responsible for pandemics. These new subtypes typically result from the adaption of an avian influenza virus to human virus DNA coding regions, or the reassortment of human and avian influenza virus genes.

10.2 Clinical features

Influenza is contagious, with a reproductive number estimated at 1.4–4[1] (see section 1.1.1). The virus is transmitted by 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.[2]

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 relatively 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.

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.

10.3 Epidemiology

10.3.1 New Zealand epidemiology

The impact of influenza in New Zealand over the past 20 seasons, since the sentinel surveillance systems commenced, has been substantial in terms of GP 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 Māori and Pacific ethnic groups. Future considerations to prevent influenza-related hospitalisations, particularly among young children, could include a childhood immunisation programme.

Influenza surveillance

New Zealand experiences the typical temperate climate epidemiology for influenza, and although influenza activity can occur throughout the year, the peak incidence is usually around the winter months (Figure 10.1). Ongoing surveillance of influenza is carried out by the four regional virus diagnostic laboratories, and by the Institute of Environmental Science and Research (ESR) virology laboratory. The regional virus diagnostic laboratories report respiratory virus diagnoses to ESR.

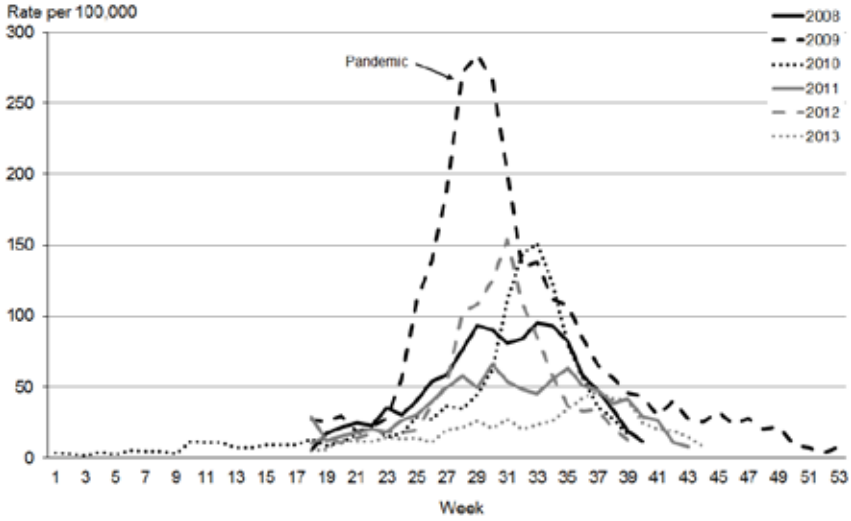
Sentinel general practice surveillance, as part of the WHO Global Program for Influenza Surveillance, operates nationally during the 'influenza season' from May through September each year. Sentinel general practices, distributed at approximately 1:50,000 population, record the daily number of consultations that fit a case definition for an influenza-like illness (ILI) and collect respiratory samples for virus. Weekly consultation and virus detection data is forwarded by regional coordinators to ESR. The surveillance data and virology laboratory data are compiled weekly onto the ESR website (www.esr.cri.nz). During periods of Pandemic Alert, the surveillance system is enhanced by the inclusion of additional sentinel general practices and other sites.

In addition to the influenza surveillance systems described above, the SHIVERS study (Southern Hemisphere Influenza, Vaccine Effectiveness, Research and Surveillance) is collecting New Zealand data to help better understand the burden of disease and how to prevent its spread. Two new surveillance systems have been established in Auckland – one hospital-based and one general practice-based. Data from SHIVERS is available on the ESR website, including reports on mild to severe acute respiratory disease.

Weekly reports

The national weekly consultation rate is used to describe the overall level of ILI activity, using a set of threshold values: a weekly rate of 50–249 consultations per 100,000 patients is considered indicative of normal (baseline) seasonal influenza activity; 250–399 indicates higher than expected activity; while 400 and over indicates an epidemic level of disease. Figure 10.1 shows the national weekly ILI consultation rates from 2008 to 2013. In 2013 the weekly consultation rates were below the baseline level of activity.[3]

Figure 10.1: National weekly consultation rates for influenza-like illness, 2008–2013

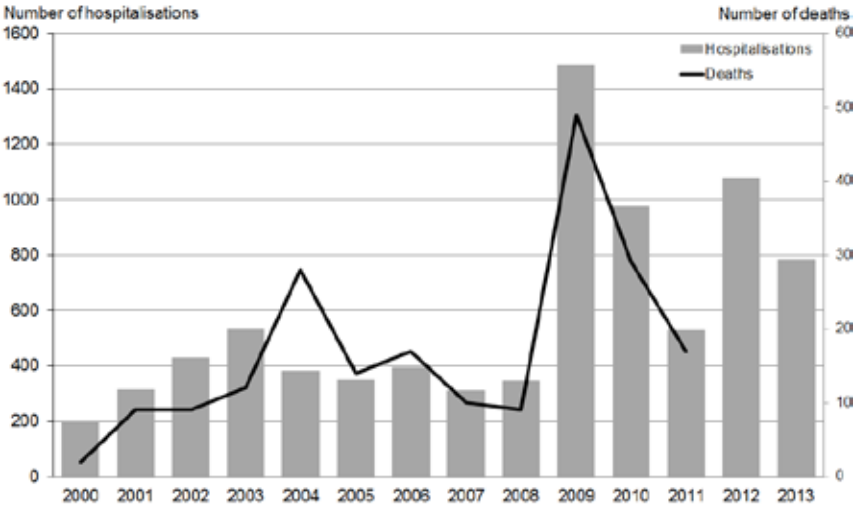


Source: Institute of Environmental Science and Research

Hospitalisations and deaths

In 2013 there were 782 hospitalisations for influenza, fewer than in 2012 (1076) (Figure 10.2). There were 205 deaths during the period 2000 to 2011: nine were children aged under 5 years, 126 were adults aged 65 years and older and one was a pregnant woman.

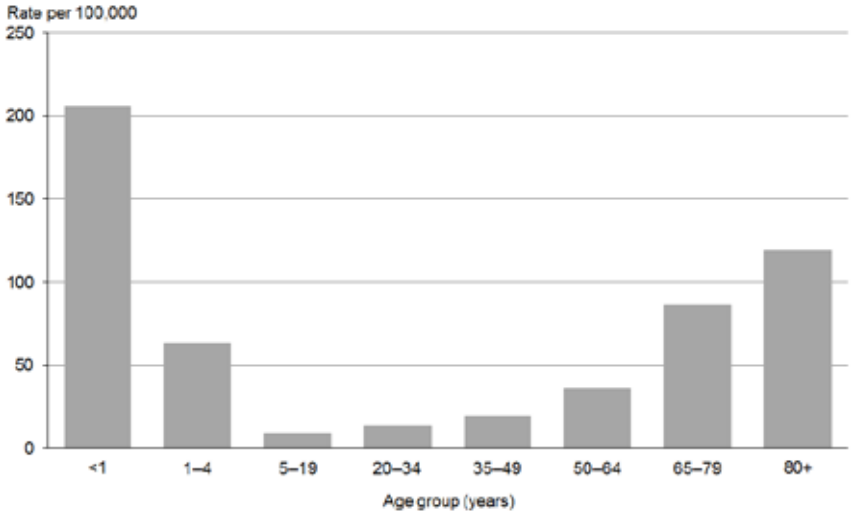
Figure 10.2: Hospitalisations for influenza, 2000–2013, and mortality, 2000–2011



Source: Institute of Environmental Science and Research (hospitalisations) and the Ministry of Health (mortality)

SHIVERS hospitalisation data[4] from the Auckland and Counties Manukau DHBs showed high hospitalisation rates in the very young and elderly populations (Figure 10.3), as well as for Pacific peoples, Māori and those from low-income groups.

Figure 10.3: Age-specific influenza hospitalisation rates among residents from Auckland and Counties Manukau DHBs (SHIVERS data), 29 April–29 December 2013



Source: Institute of Environmental Science and Research

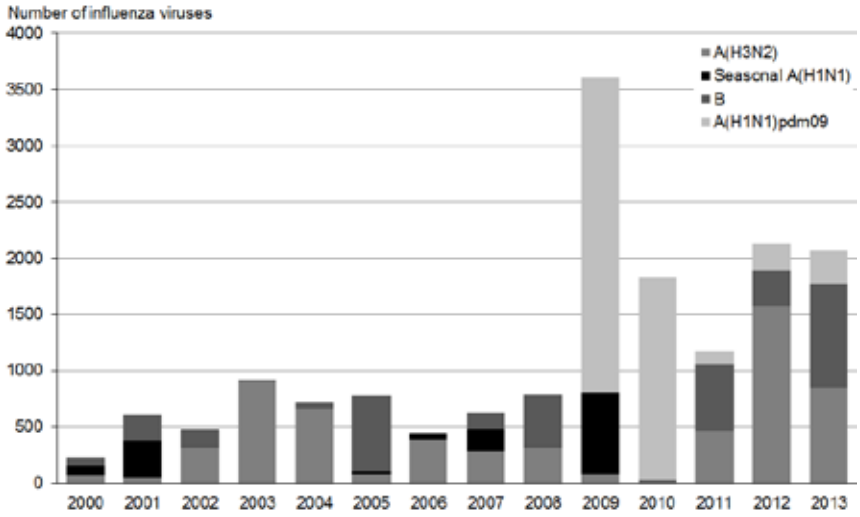
Hospital data for pneumonia and influenza includes both those cases coded as influenza and cases diagnosed with pneumonia that are secondary to, or a complication of, influenza. The primary diagnosis coded is pneumonia, but this underestimates the burden of disease associated with influenza.

Previous modelling data suggests that for every death attributable to influenza, a further 7.7 deaths are associated with complications of influenza.[5] Overseas modelling has found a similar patterns of under-diagnosis, with a factor of 3.7 for the Netherlands[6] and 10 for the UK.[7]

Circulating influenza strains

In 2013 a total of 2066 viruses were typed and subtyped. Of these, influenza B was the predominant strain (45 percent of all typed and subtyped viruses), then influenza A(H3N2) (41 percent) and the 2009 pandemic strain, A(H1N1)pdm09 (15 percent); see Figure 10.4.

Figure 10.4: Influenza viruses, by type, 2000–2013

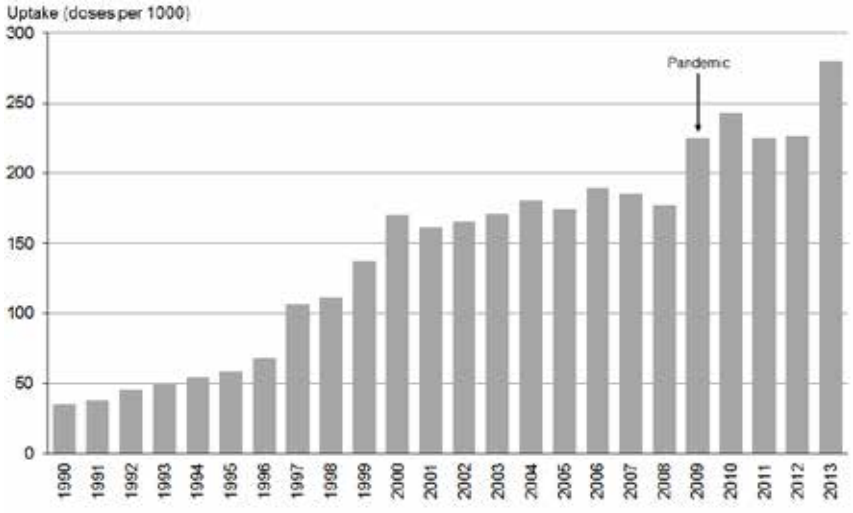


Source: Institute of Environmental Science and Research

10.3.2 Influenza immunisation uptake

The number of influenza vaccine doses distributed in 2013 was higher than in previous years, including 2010 (the year after the pandemic) (see Figure 10.5). Funded vaccine uptake for individuals aged 65 years and older was 70 percent, a small increase from 2012 (65 percent).

Figure 10.5: Influenza vaccine uptake, 1990–2013



Funded vaccine for individuals aged 65 years and older was introduced in 1997. Funded vaccine for individuals aged under 65 years with certain medical conditions was introduced in 1999.

Source: Institute of Environmental Science and Research

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 very low, but it has steadily increased from 45 percent in 2010 to 58 percent in 2013.

10.3.3 Pandemic influenza A(H1N1)pdm09

A new influenza pandemic caused by a novel strain (ie, not covered in previous vaccines) of influenza A(H1N1) commenced in 2009. The pandemic strain became the predominant cause of influenza in New Zealand, with 3211 confirmed cases reported between 1 April and 31 December 2009, including 48 deaths. It was estimated that 30 percent of New Zealanders (1.3 million) had immunity to A(H1N1)pdm09 by March 2010, and an estimated 18 percent (800,000) were infected with the virus during the first wave, including one child in every three.[8]

Risk factors for severe H1N1 disease included obesity, pregnancy,[9] diabetes mellitus and Pacific or Māori ethnicity.[8]

10.3.4 Avian influenza associated with human cases

Human infections and outbreaks following interspecies transmission of avian influenza viruses have been reported since 1997. Most cases have been associated with direct or indirect contact with infected birds.

Avian influenza is a rare disease in humans but requires close monitoring. In New Zealand, illness due to highly pathogenic avian influenza virus (HPAI) is a notifiable disease. Further information can be found on the Ministry of Health website (www.health.govt.nz).

Avian influenza A virus subtypes H5N1, H7N9 and H9N2 have caused human infections, with the H5N1 subtype established in domestic poultry throughout Southeast Asia, and in wild birds or domestic poultry in Europe and Africa. The H5N1 virus is highly pathogenic, with a mortality rate of over 50 percent. There has been no evidence of ongoing person-to-person transmission. Human infections with H7N9 virus were first reported in China in March 2013, with a mortality rate of approximately one-third of cases. At the time of writing, there was no evidence of ongoing person-to-person transmission.

Monitoring, surveillance and response for new pandemic strains are in place. See section 10.8.3.

10.4 Vaccines

Annual influenza vaccination for those at risk of complications of infection is the single most important measure for preventing influenza infection and mortality. The National Influenza Specialist Group (NISG) is responsible for New Zealand's annual Influenza Communication Campaign (www.influenza.org.nz). This campaign includes an influenza kit for health care professionals and a national education and communication programme.

Funded vaccines

The trivalent inactivated split virion influenza vaccines funded in New Zealand are:

- Influvac (Abbott Laboratories (NZ) Ltd), containing 15 µg of each of the three recommended influenza strains; other components and excipients include potassium chloride, potassium phosphate monobasic, sodium phosphate-dibasic dihydrate, sodium chloride, calcium chloride and magnesium chloride
- Fluarix (GSK), containing 15 µg of each of the three recommended influenza strains; other components and excipients include saccharose, d-alpha-tocopheryl acid succinate and traces of formaldehyde and gentamicin sulphate.

Other vaccines

Other influenza vaccine brands registered and available in New Zealand are:

- Fluvax (bioCSL), Intanza (Sanofi-aventis NZ Ltd, registered for those aged 18–59 years) and Vaxigrip (Sanofi-aventis NZ Ltd).

10.4.1 Vaccine preparations

Influenza vaccine preparations vary by their type, the number of influenza strains contained in the vaccine and their delivery systems. The adjuvanted and live attenuated vaccines have improved efficacy, particularly for some groups, but the safety data needs to be further assessed.

Vaccine types

Inactivated influenza vaccines (split virion or subunit vaccines)

The trivalent inactivated vaccines (TIV) available in New Zealand are inactivated split virion vaccines prepared from virus grown in the allantoic cavity of embryonated eggs. The virus is purified, disrupted and inactivated with beta-propiolactone or formaldehyde.

Inactivated quadrivalent influenza vaccines are not yet registered in New Zealand, but will be used in the US[10] and in some European countries for the 2013/14 influenza season and in Australia in 2014 to improve strain matching.

Live attenuated influenza virus vaccines

Live attenuated influenza virus (LAIV) vaccines (trivalent and quadrivalent) are a new technology licensed for use in North America for healthy non-pregnant individuals aged 2–49 years and in Europe for children aged 2–18 years. At the time of writing, LAIV vaccines were not registered in New Zealand.

Adjuvanted vaccines

Adjuvants enhance the immune response to an antigen. There are three new adjuvants licensed (internationally) for use in influenza vaccines: two oil-in-water emulsions, and a third that uses immunopotentiating reconstituted influenza virosomes.[11]

Vaccines with these adjuvants have modestly improved immune responses, but may also cause more local and systemic reactions than unadjuvanted vaccines.[11] At the time of writing, influenza vaccines containing these adjuvants were not registered and/or available in New Zealand.

Number of strains

Trivalent vaccines

The majority of influenza vaccines are trivalent, containing three influenza strains. The strains vary each year depending on the prevailing virus subtypes. The current trivalent vaccines used in New Zealand contain two influenza A strains (eg, H1N1, H3N2) and one prevailing B strain. The WHO recommends the strains for inclusion in September/October of each year, following the southern hemisphere strain selection meeting. Strain selection may differ from that of the northern hemisphere.

Since 2010 the H1N1 component of the trivalent vaccine has been the 2009 pandemic strain.

Quadrivalent vaccines

Quadrivalent vaccines contain four influenza strains (currently two A strains and two B strains). Since four influenza strains co-circulate each year in New Zealand (see section 10.3.1), a quadrivalent vaccine would likely be beneficial to improve the vaccine strain match with circulating strains. Quadrivalent vaccines are not yet registered in New Zealand.

Monovalent pandemic H1N1 vaccine

A monovalent vaccine directed against the A(H1N1)pdm09 strain was approved for use in New Zealand in January 2010. This vaccine was prepared in mammalian cells rather than eggs. The vaccine was offered to specific target groups (including front-line health care workers) as part of the national pandemic response. Its use became redundant once the 2010 trivalent seasonal vaccine (containing the pandemic strain) became available.

Vaccine delivery systems

Intramuscular

With the exception of the intradermal vaccine described below, the seasonal influenza vaccines available in New Zealand are all delivered by intramuscular injection.

Intradermal

Intradermal vaccines are generally recognised as offering similar immune responses in healthy subjects[12] and possibly more efficient immune responses,[13] particularly in the older adult population.[14]

The intradermal vaccine (Intanza, Sanofi-aventis NZ Ltd) registered in New Zealand has a prefilled microinjection device that delivers vaccine into the dermis of the skin. The needle is 90 percent shorter than needles used for intramuscular administration. Compared to intramuscular vaccines, the intradermal vaccine has a similar immune response, with a slightly higher rate of injection site reactions.[11, 15]

Intranasal mists

Live attenuated influenza vaccines (LAIV), delivered by intranasal spray, induce stronger immune responses than TIVs by mimicking natural influenza infection and evoking both mucosal and systemic immunity, and including broader cellular immune responses.[16]

10.4.2 Efficacy and effectiveness

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.

The current data for vaccine efficacy and effectiveness of TIV vaccines is summarised in Table 10.1.

Infants and children

The evidence for vaccine efficacy and effectiveness in infants and children is varied. Maternal influenza vaccination 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 to 3 months.[17] 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,[18] 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.[19]

There is wide variability in the estimates of effectiveness of annual influenza vaccination against influenza-like illness in nursing home residents (0–80 percent).[11] Vaccination has been demonstrated to prevent hospitalisation and death in these groups,[19, 20, 21, 22] but a 2010 Cochrane review concluded that there was insufficient evidence to support influenza vaccine effectiveness in the elderly.[23] 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.[24]

Pregnant women

Pregnant women are at increased risk of hospitalisation from influenza-related cardiorespiratory disorders during the second and third trimesters, and this was especially apparent in the 2009 pandemic.[25] Influenza vaccination is expected to have the same efficacy in healthy pregnant women as in other healthy adults.

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%[17, 26]
Healthy children aged under 2 years	Efficacy against laboratory-confirmed influenza	Insufficient data[27, 28]
	Effectiveness against laboratory-confirmed influenza	66% (9–88)[29]
Healthy children aged 6–35 months	Effectiveness against laboratory-confirmed influenza	66% (29–84)[29]
Healthy children aged under 16 years	TIV vaccine efficacy in prevention of laboratory-confirmed influenza in randomised controlled trials	59% (41–71)[27]
Healthy adults aged 18–65 years	Effectiveness against influenza-like illness*	30% (17–41)[30]
	Efficacy against influenza symptoms*	73% (54–84)[30]
	Efficacy against laboratory-confirmed influenza	59% (51–67)[28]
Those aged 65 years and older	Effectiveness in preventing influenza, influenza-like-illness, hospitalisations, complications and mortality	Inconclusive due to poor quality of studies[23]
Those aged 65 years and older	Effectiveness against non-fatal and fatal complications	28% (26–30)[24]
	Effectiveness against influenza-like illness	39% (35–43)[24]
	Effectiveness against laboratory-confirmed influenza	49% (33–62)[24]

* From age 16 years.

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.[31] Benefits from influenza vaccination have been observed for both diabetes[32] and chronic obstructive pulmonary disease.[33] 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.[34]

Herd immunity

There is some evidence to suggest that herd immunity can be achieved, particularly by vaccinating children, if immunisation coverage is very high (greater than 80 percent).[35, 36, 37] Some studies suggest that herd immunity may also be achieved in nursing homes if immunisation coverage of residents is greater than 80 percent.[38] Vaccinating health care workers is likely to be an effective strategy, particularly for nursing homes.[39]

Duration of immunity

Because influenza strains continually shift, 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.[11, 40]

Protection due to live attenuated influenza vaccines has been demonstrated to persist beyond a year.[41, 42]

10.4.3 Transport, storage and handling

Transport according to the *National Guidelines for Vaccine Storage and Distribution*.[43] Store at +2°C to +8°C. Do not freeze. Influvac should be stored in the dark.

10.4.4 Dosage and administration

The funded trivalent seasonal influenza vaccine should be administered by intramuscular or subcutaneous injection (see section 2.3). The contents of the syringe must be shaken thoroughly before use. For administration instructions for the intradermal vaccine, see the manufacturer's data sheet.

Individuals aged 9 years and older

Individuals aged 9 years and older receive a single 0.5 mL intramuscular dose of 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 6–35 months are given a 0.25 mL dose (see Table 10.2 and the manufacturer's data sheet for the dose in children).

Table 10.2: Recommended influenza vaccine doses in children

Age	Dose	Number of doses
6–35 months	0.25 mL	1 or 2*
3–8 years	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.

There is limited data on which to base the recommendations, but the aim is to reduce reactions, particularly febrile reactions (which are increased in young children), while maintaining an adequate immune response.

Immunosuppressed or immune-deficient individuals

Regardless of their age, previously unvaccinated immunosuppressed or immune-deficient individuals are recommended to receive two doses of influenza vaccine, four weeks apart. One dose is then given in each subsequent year. (See section 4.3.)

When to vaccinate

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 activity. The vaccine can be given even when influenza virus activity has been identified, because protective antibody levels develop from four days to two weeks after immunisation.[44] The vaccine should be administered annually to maintain immunity and to provide protection against new strains.

Co-administration with other vaccines

Influenza vaccine can be administered with other vaccines, such as pneumococcal polysaccharide vaccine 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.[45, 46] 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

Influenza vaccine should be given annually because protective antibody levels wane with time and the prevailing strains may change between years and may not have been included in the previous year's vaccine. See Table 10.3 for a summary of the funded and unfunded recommendations for influenza immunisation.

10.5.1 Funded influenza immunisation

Funded influenza immunisation is available for the following groups. To encourage early uptake of the vaccine, funded immunisation is available only until the end of July each year.

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.

Pregnancy and breastfeeding

Influenza vaccine is safe to administer during any stage of pregnancy or while breastfeeding. Pregnant women are at greater risk from complications associated with influenza illness. Pregnant women with co-existing medical conditions are at even greater risk of severe influenza-related morbidity. 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.

There is no evidence that influenza vaccine prepared from inactivated virus causes damage to the fetus. The seasonal influenza vaccine is strongly recommended, and funded, for women who will be pregnant during the influenza season, usually May to September. The seasonal influenza vaccine is normally given in the second and third trimesters but should be offered to women who are or will be in the first trimester when influenza is expected to be circulating.

Because there is no registered vaccine for children aged under 6 months, vaccination during maternal pregnancy is highly recommended to improve maternal fetal passive antibody transfer. Influenza vaccination of pregnant women has been shown to significantly decrease influenza in their newborn babies.[16, 25, 26, 47] Breastfeeding is also strongly recommended, to deliver passive immunity to the infant.[16]

Children

Influenza vaccine is funded for children 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.

- 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. (See also section 4.3.)

10.5.2 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.

Table 10.3: Influenza vaccine recommendations

Note: Funded conditions are in the shaded rows. See the Pharmaceutical Schedule (www.pharmac.health.nz) for the number of funded doses and any changes to the funding decisions.

Recommended and funded
All individuals aged 65 years and older.
Individuals aged 6 months to 64 years who: · have cardiovascular disease (ischaemic heart disease, congestive heart disease, 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, excluding basal and squamous skin cancers if not invasive · have other conditions (autoimmune disease, immunosuppression, HIV infection, transplant recipients, neuromuscular and central nervous system diseases, haemaglobinopathies, children on long-term aspirin) · are pregnant · are children aged under 5 years who have been hospitalised for respiratory illness or have a history of significant respiratory illness.
Recommended but not funded
Individuals with asthma not requiring regular preventive therapy
Asplenic and immune-deficient individuals
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

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 monsoon, 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

10.6.1 Contraindications

See section 1.4 for general contraindications for all vaccines.

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.

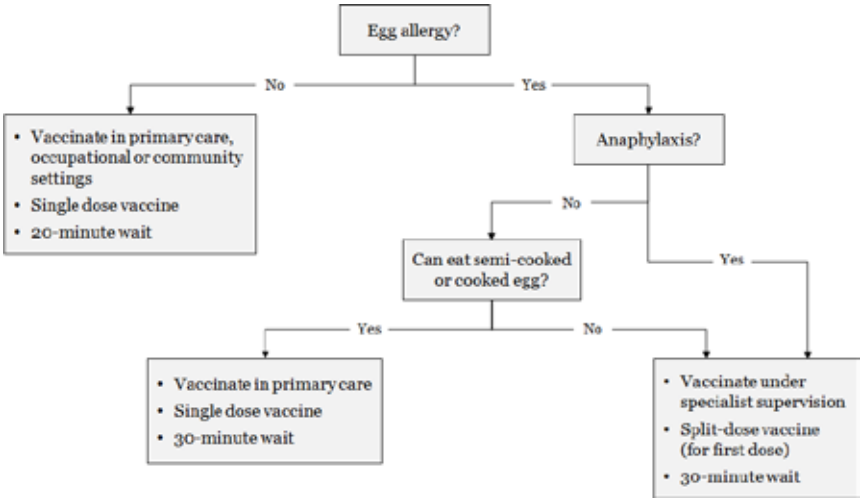
10.6.2 Precautions

Known egg allergy

Non-anaphylactic egg allergy is not a contraindication to influenza vaccination. A history of anaphylaxis to egg has been considered a contraindication to influenza vaccination. However, there is increasing evidence that it can be given safely.[48, 49] Reported cases of anaphylaxis after influenza vaccination in egg-allergic individuals all occurred over 20 years ago, at a time when vaccine egg (ovalbumin) content was much higher than it is now.

For extra safety, for patients with definite previous egg anaphylaxis and who cannot tolerate any egg ingestion, the available vaccine with the lowest egg content (not exceeding 1.0 µg per dose) should be chosen and administered in hospital using a split-dose protocol (10 percent dose given, wait at least 30 minutes then give remainder of dose),[50] as shown in Figure 10.6.

Figure 10.6: Influenza vaccination of the egg-allergic individual



Adapted from: Australasian Society of Clinical Immunology and Allergy Inc. 2010. *Guidelines for Medical Practitioners: Influenza vaccination of the egg-allergic individual*. URL: www.allergy.org.au/health-professionals/papers/influenza-vaccination-of-the-egg-allergic-individual (accessed 8 October 2013).

History of Guillain Barré syndrome

There appears to be a small increase in the risk of Guillain-Barré syndrome (GBS) following seasonal influenza vaccination (less than one additional case per million doses administered). This risk is substantially less than the risk of developing severe complications from influenza infection.[11, 30] There is also more risk of developing GBS from wild-type influenza (4–7 cases per 100,000 persons) than from the inactivated vaccine strains.[10]

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.

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.[45, 46] Separation of the vaccines by two days can be offered, but is not essential. (See also section 15.6.2.)

10.7 Expected responses and adverse events following immunisation (AEFI)

Influenza vaccine is well tolerated. Placebo-controlled trials have shown that influenza vaccine may cause systemic reactions (eg, fever, malaise, myalgia) in only 1 percent of adults.[51, 52, 53] Systemic reactions are more likely in children not previously exposed to the vaccine or virus, starting 6 to 12 hours after immunisation and persisting for one to two days.[54]

In early 2010 there were reports of children in both Australia and New Zealand who had received the seasonal 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 recipients, but these effects are usually mild. Analysis by gender of 14 studies has revealed that females (both young and elderly) report significantly more local reactions.[55] There were no gender differences in seroconversion.

In 2010 an association, probably related to the adjuvant, between one H1N1 pandemic vaccine (not used in New Zealand) and narcolepsy was found. There is now data from a number of countries, which together supports a temporal link.[56, 57] However, it is possible that the onset of narcolepsy may be confounded by other factors (such as genetic predisposition, H1N1 influenza and/or other environmental factors).[56, 58, 59] Further data is required to confirm the strength of this association and the size of the risk, and to identify the underlying biological mechanisms.[60]

See section 10.6.2 for information on egg allergy.

10.8 Public health measures

Using influenza signs and symptoms in the diagnosis of influenza is of limited value. The most sensitive diagnostic method is 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.

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

Vaccination of contacts during an outbreak is not immediately effective because of the short incubation period of influenza (one to three days), shorter than the time to mount an immune response following vaccination (up to two weeks). Antiviral drugs are approximately 80 percent effective in reducing influenza symptoms and should be considered for unimmunised or recently immunised contacts at high risk. 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.

10.8.3 Pandemics

At the time of a pandemic, the 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*[61] describes the key phases of a pandemic and the actions and responsibilities within each phase.

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11 Measles

Key information

Mode of transmission	By direct contact with infectious droplets or, less commonly, 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 immunoglobulin 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	Measles-mumps-rubella vaccine (MMR II) is a live attenuated vaccine.
Funded immunisation 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 after 1968 with no documented history of 2 doses of measles-containing vaccine after age 12 months · individuals with no documented measles IgG antibody.
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.

11.1 Virology

Measles 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 or, less commonly, by airborne spread. Measles is one of the most highly communicable of all infectious diseases, with an approximate basic reproductive number of 12–18 in developed countries[2] (see section 1.1.1). 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 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 immunoglobulin 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 (see Table 11.1 in section 11.7.2), and include otitis media, pneumonia, croup and diarrhoea. Encephalitis has been reported in 1 in every 1000 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 immune thrombocytopenic purpura (ITP or thrombocytopenia).

Sub-acute sclerosing panencephalitis (SSPE), a rare degenerative central nervous system disease resulting from persistent measles virus infection, is fatal. SSPE typically occurs 7 to 10 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 1000. Measles is particularly severe in the malnourished 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

Measles is the most common vaccine-preventable cause of death among children throughout the world. The disease is highly infectious in non-immune communities, with epidemics occurring approximately every second year.

In 2000 the estimated global measles mortality was 535,000 deaths (95% CI: 347,200–976,400). In 2008 all WHO member states endorsed a target of a 90 percent reduction in measles mortality by 2010, compared to 2000 levels. By 2010 the global measles mortality had decreased by 74 percent to 139,300 (95% CI: 71,200–447,800). India accounted for 47 percent of estimated measles mortality in 2010, and the WHO African region accounted for 36 percent.[5]

Measles elimination

Indigenous cases of measles, mumps and rubella have been eliminated from Finland over a 12-year period using a two-dose measles, mumps and rubella vaccine (MMR) schedule given between 14 and 16 months and at age 6 years.[6] The WHO region of the Americas eliminated indigenous transmission of measles in 2002.[7]

In October 2005 the Regional Health Assembly of the Western Pacific Region of WHO endorsed a target that by 2012 measles would be eliminated from the Western Pacific Region. In 2012 measles incidence in the region declined to a record low of six cases per million population.[8] As at March 2013, 33 out of 37 countries may have interrupted endemic measles virus transmission,[9] meaning that the virus cannot spread within the population (unless it is imported).

In May 2012 the 194 member states of the World Health Assembly endorsed the *Global Vaccine Action Plan 2011–2020*,[10] which aims to eliminate measles in at least four WHO regions by 2015 and in five WHO regions by 2020.

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 – although hospitalisation data does not support this figure) and 1997 (2169 cases identified).

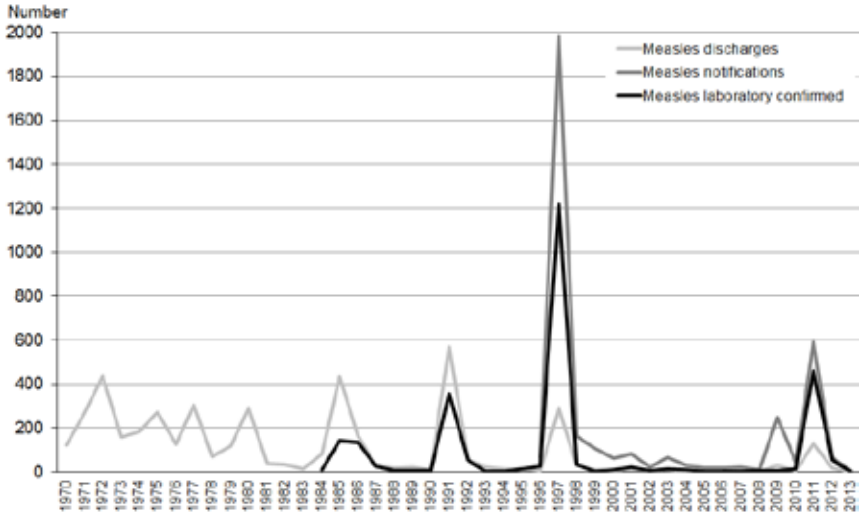
Smaller outbreaks continue to occur, the most recent in 2009 (248 cases notified, 205 of which were due to three outbreaks) and 2011[11] (597 cases notified, 560 of which were due to six outbreaks). The largest outbreak in 2011 mainly affected Auckland, with 489 confirmed or probable cases. It started 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 school children. The outbreak officially ended in July 2012.[12]

In 2012, 68 cases of measles were notified (1.5 per 100,000) and 55 (80.9 percent) were laboratory confirmed. This was a significant decrease from 2011 (597 cases; 13.6 per 100,000). Of the 68 cases, 57 (83.8 percent) had a known vaccination status. Of these, 40 were not vaccinated, including 20 cases aged under 15 months (not eligible for the first dose of MMR vaccine). Ten cases had received one dose of vaccine and seven cases had received two doses.[13]

Measles cases significantly decreased again in 2013, with four hospitalisations (20 hospitalisations in 2012), eight notifications and three laboratory-confirmed cases.

Figure 11.1 shows hospital discharges, notifications of measles and laboratory-confirmed cases.

Figure 11.1: Hospital discharges from measles, 1970–2013, notifications, 1996–2013, and laboratory-confirmed cases, 1984–2013



Source: Ministry of Health and the Institute of Environmental Science and Research

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.[14] If this coverage level is achieved and maintained, the length of time between epidemics will increase and may lead to the elimination of measles.

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

The funded MMR vaccine (MMR II, MSD), is a sterile lyophilised preparation of:

- 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.
- The reconstituted vaccine also contains sorbitol, sodium phosphate, sucrose, sodium chloride, hydrolysed gelatin, recombinant human albumin, fetal bovine serum and neomycin. The vaccine contains no preservative.

Other vaccines

Another MMR vaccine registered (approved for use) and available (marketed) in New Zealand is:

- Priorix (GSK), which contains Schwartz strain measles, RA 27/3 rubella, and RIT 4385 mumps strain derived from the Jeryl Lynn strain.

A quadrivalent measles, mumps, rubella and varicella vaccine (MMRV, see chapter 21) is also registered and available:

- 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).

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.[15] 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 six months and older.[16] This was a systematic review of clinical trials and studies, and 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.

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 any of the three components of the vaccine, most commonly mumps. A meta-analysis of the measles vaccine found no evidence of secondary vaccine failure in the US-manufactured vaccine currently used in New Zealand.[17]

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.[18] The antibody avidity also decreased over time, by 8 percent for measles and 24 percent for mumps.[19]

Waning of both the concentration and the avidity of antibodies might contribute to measles and mumps infections in individuals who have received two doses of MMR. New Zealand will have to consider the possibility that further doses of MMR in adults may be required in the future. Information from Finland and elsewhere will assist decision-making as to whether adult booster doses of MMR are required.

See section 21.4.2 for efficacy and effectiveness data for the varicella vaccine.

11.4.3 Transport, storage and handling

Transport according to the *National Guidelines for Vaccine Storage and Distribution*.[20] Store in the dark 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 in the dark at +2°C to +8°C for up to eight hours.

See section 21.4.3 for MMRV vaccine information.

11.4.4 Dosage and administration

The dose of MMR is all of the reconstituted vaccine (approximately 0.5 mL) administered by subcutaneous injection in the deltoid area of the upper arm, to all age groups (see section 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.

11.5 Recommended immunisation schedule

11.5.1 Children

MMR vaccine is recommended irrespective of a history of measles, mumps, 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. In an outbreak situation, children aged 6–14 months may be offered MMR vaccine. Children who receive MMR vaccine when aged under 12 months will still require two further doses administered after age 12 months (see section 11.8.3).

MMR vaccine is recommended irrespective of a history of measles, mumps, rubella infection or measles immunisation. There are no known ill effects from vaccinating children, even if they have had serologically confirmed infection with any of the viruses.

11.5.2 Adolescents and adults

Two doses of MMR (at least four weeks apart) are recommended and funded for any adolescent or adult who is known to be susceptible to one or more of the three diseases.

Adults born before 1969 should be considered to be immune to measles as circulating virus and disease was prevalent prior to the introduction of measles vaccine in 1969.

Adults born after 1968

All individuals born after 1968 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 after 1968 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 Immunosuppression

MMR is contraindicated in immunosuppressed children (see section 4.3). They can be partially protected from exposure to infection by ensuring that all contacts are fully immunised, including hospital staff and family members. There is no risk of transmission of MMR vaccine viruses from a vaccinee to the immune-compromised individual.

MMR vaccination at 12 months of age is recommended for children with HIV infection who are asymptomatic and who are not severely immune compromised (see the HIV discussion in section 4.3.3). MMR is contraindicated in children with severe immunosuppression from HIV because vaccine-related pneumonitis (from the measles component) has been reported.[3] Discuss vaccination of children with HIV infection with their specialist.

11.5.4 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 medical officer of health and the Ministry of Health based on local epidemiology.

11.5.5 Pregnancy and breastfeeding

MMR vaccine is contraindicated during pregnancy. Pregnancy should be avoided for four weeks after MMR vaccination.

MMR vaccine can be given to breastfeeding women.

(See also sections 4.1 and 18.5.2.)

11.5.6 Travel

The US reported[21] that of the 251 cases of measles reported from 2001 to 2004, 177 (71 percent) were in US residents, and of these 100 were preventable. Forty-three percent of these preventable cases were associated with international travel; the rest acquired the disease in the US. Travel was also linked to the measles outbreaks in New Zealand in 2011[11] and 2014. Because international travel is an important factor in reintroducing measles into a country, a measles-containing vaccine should be considered for those travelling overseas if they have not previously been adequately vaccinated.

11.6 Contraindications and precautions

11.6.1 Contraindications

The general contraindications that apply to all immunisations are relevant to MMR vaccines (eg, children with an acute febrile illness should have their immunisation deferred; see section 1.4).

Anaphylaxis following a previous dose of MMR vaccine or any of its components is a contraindication to a further dose of MMR. Children who have anaphylaxis after MMR should be serologically tested for immunity and referred to, or discussed with, a specialist if non-immune to rubella or measles.

Individuals in whom MMR is contraindicated include:

- those with proven anaphylaxis (but not contact dermatitis) to neomycin
- immunosuppressed children (ie, children 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)
- children who have received another live parenteral or intranasal vaccine, including Bacillus Calmette-Guérin (BCG), within the previous four weeks (see chapter 20). Note: this does not apply to rotavirus vaccine
- pregnant women
- individuals who have received immunoglobulin or a blood transfusion during the preceding 11 months (see Table 1.3 in section 1.4.2 for the length of time to defer measles vaccine after specific blood products)
- children with HIV infection who are severely immune compromised.[3]

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 immune thrombocytopenic purpura (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] after MMR vaccine (see chapter 18).

Tuberculin skin testing (Mantoux) is not a prerequisite for measles vaccination. Antituberculous therapy should be initiated before administering MMR vaccine to people with untreated tuberculous infection (latent) or disease (active). Tuberculin skin testing, if otherwise indicated, can be done on the day of vaccination. Otherwise testing should be postponed for four to six weeks, because measles vaccination may temporarily suppress tuberculin skin test reactivity.[3]

11.6.3 Egg allergy

Egg allergy, including anaphylaxis, is **not** a contraindication to measles-containing vaccines. Various studies have confirmed these children can be vaccinated safely.[3, 22, 23] Other components of the vaccine (eg, gelatin)[24] may be responsible for allergic reactions.

11.7 Expected responses and adverse events following immunisation (AEFI)

11.7.1 Expected responses

A fever of 39.4°C or more occurs in 5–15 percent of children and generally lasts one to two days. Rash occurs in approximately 5 percent of children 6 to 12 days after immunisation. A placebo-controlled study has shown that fever and/or rash in most cases are unrelated to immunisation, and only rash in 1.6 percent and high fever in 1.4 percent of cases could be attributed to MMR; these fevers were most likely nine or 10 days after immunisation and the rash occurred in the second week.[25]

The mumps vaccine may produce parotid and/or submaxillary swelling in about 1 percent of vaccinees, most often 10 to 14 days after immunisation. The rubella vaccine can cause a mild rash, fever and lymphadenopathy between two and four weeks after immunisation. There were no persisting sequelae associated with the administration of three million doses of MMR to 1.5 million children in Finland.[25, 26]

Febrile seizures occur in approximately 1 in 3000 children, 6 to 12 days after immunisation. Parents/guardians should be advised that along with other cooling measures, they can give the child an age-appropriate dose of paracetamol if there is fever greater than 39°C (see section 2.3.13 for more detail on the use of paracetamol and other antipyretics). Children with a history of seizures should be given MMR, but the parents/guardians should be warned that there may be a febrile response and encouraged to use cooling measures and/or antipyretics if fever develops. After re-immunisation, reactions are expected to be clinically similar but much less frequent, since most vaccine recipients are already immune. No unusual reactions have been associated with MMR re-immunisation.[25]

11.7.2 Adverse events following immunisation

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.[27] Following immunisation with both measles and rubella vaccines, live virus has been isolated rarely from pharyngeal secretions.[28, 29] There have been no confirmed cases of disease transmission from MMR vaccine viruses.

MMR vaccine is the only childhood vaccine with an elevated risk of immune thrombocytopenic purpura (ITP), which occurs in approximately 1 in 30,000 doses, 15 to 35 days after immunisation. 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).[30] 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.[31, 32, 33, 34]

Central nervous system symptoms following measles vaccine are reported to occur in approximately 1 in 1 million children. In most cases this seems to be a chance occurrence not caused by the vaccine. An analysis of claims for encephalitis following measles vaccine in the US found clustering of events at eight to nine days after immunisation.[35] This clustering supports, but does not prove, the claim that the vaccine causes encephalitis, albeit rarely and at a lower rate than the wild virus illness. For comparison, the rate of encephalitis following measles disease is approximately 1 in 1000.

MMR containing the Urabe strain of mumps was withdrawn internationally in 1992 following a UK study that found a 1 in 11,000 risk of mumps vaccine meningitis. MMR containing the Urabe strain was used in New Zealand from 1991 until it was withdrawn in 1992. Aseptic meningitis occurs in 1 in 800,000 doses following administration of the Jeryl Lynn strain of mumps vaccine,[36, 37] which is used in New Zealand. For comparison, aseptic meningitis occurs in 15 percent of cases of mumps.

Arthritis or arthralgia occurs after both the rubella disease and vaccine, especially in adults. About 15 percent of adult women and fewer than 1 percent of children get joint symptoms about two to four weeks after immunisation. There is no evidence to suggest that rubella vaccine leads to chronic long-term arthritis: two large controlled studies found no evidence,[38, 39] while another study did find a slight increase in arthritis risk following rubella vaccine, but this was of borderline statistical significance.[40] 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.[41]

Table 11.1 shows the complications associated with contracting measles, mumps and rubella, and from receiving MMR vaccine.

Table 11.1: Complications from contracting measles, mumps and rubella diseases compared with MMR vaccine adverse effects

Measles complications	
Otitis media, pneumonia, diarrhoea	1/10–100
Encephalitis, probably resulting in brain damage	1/1000
Death	1–3/1000
Mumps complications	
Meningitis	1/7
Orchitis	1/5 post-pubertal males
Nerve deafness	1/15,000
Death	1.8/10,000

Continued overleaf

Rubella complications	
Congenital rubella: cataracts, deafness, cardiac malformations and brain damage. Some abnormality of the fetus will be detectable in 85 percent of women infected in the first eight weeks of pregnancy (see Table 18.1).	
Vaccine adverse effects	
Rashes, fever, local reactions, parotid swelling	1/7
Febrile seizures	400/1,000,000
Transient joint symptoms – children	1/35
Thrombocytopenia	33.3/1,000,000
Encephalitis	1/1,000,000
Aseptic meningitis	<1/100,000

11.7.3 Adverse outcomes not linked to MMR

There have been multiple epidemiological studies published from the UK,[42] Finland[43] and elsewhere[44, 45] confirming that there is no link between MMR vaccine and the development of autism in young children. A Japanese case-control study assessed the relationship between autistic spectrum disorder and general vaccinations, including MMR, in a genetically similar population. In this study, MMR vaccination and increasing the number of vaccine injections were not associated with an increased risk of autistic spectrum disorder (see section 3.3.1 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.

11.8.1 Diagnosis

A single case of measles should be considered an outbreak and result in a suitable outbreak response. Although practitioners should have a low index of suspicion for notification, it is important that all suspected clinical cases be laboratory confirmed or epidemiologically linked to a confirmed case.

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, blood should be taken for serological confirmation and a nasopharyngeal and throat swab taken for viral identification by PCR. For instructions on measles specimen collection and transport, see the National Measles Laboratory website (www.measles.co.nz).

Further specimens for viral culture, detection of measles virus by PCR or further serological tests should be taken in consultation with the laboratory. The timing and choice of samples in relation to the onset of symptoms is important. For further information, contact the local medical officer of health or infectious diseases physician. More detailed information is available from the National Measles Laboratory.

11.8.2 Prophylaxis

MMR vaccine

There is some 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]

Normal immunoglobulin (IG) prophylaxis for contacts

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, IG is given to attenuate disease and should be given as soon as possible, up to a maximum of six days after exposure.

Normal immunoglobulin is recommended for the following contacts of measles cases as soon as possible after exposure:

- immune-compromised or immune-deficient children
- pregnant women
- immune-competent children aged under 15 months beyond 72 hours after exposure
- people outside the 72-hour window for MMR who have not had a history of measles infection or vaccination.

The recommended doses of IG are:

- immune-competent infants aged under 15 months should receive 0.6 mL/kg intramuscularly, to a maximum volume of 5 mL
- pregnant women, immune-competent adults and immune-compromised or immune-deficient children should receive 0.6 mL/kg intramuscularly, to a maximum dose of 15 mL, recommended as three 5 mL injections.

Prophylaxis with intravenous immunoglobulin

Intravenous immunoglobulin (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 section 1.5 for more information about passive immunisation).

The recommended dose of intravenous immunoglobulin is 0.15 g/kg. See the guidance from the Health Protection Agency for further information (www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1238565307587).

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

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 catching 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).

Acceptable presumptive evidence of immunity is:

- anyone born before 1 January 1969
- documentation of immunity or previous infection
- children aged 12 months to under 4 years who have documentation of 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.

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.

11.8.4 Recommendations for vitamin A for infants and children with measles infection

In developing countries the use of vitamin A has been associated with decreased morbidity and mortality.[46, 47] All infants and children hospitalised with measles should receive vitamin A (subject to its availability). Measles may occur in children recently arrived from developing countries, where vitamin A deficiency may be more prevalent than in New Zealand. If a child with measles has a condition causing fat malabsorption (cystic fibrosis, short bowel syndrome and cholestasis), an immune deficiency or malnutrition (including adolescents with eating disorders), the case should be discussed with a paediatrician and vitamin A may be recommended.

Vitamin A treatment in hospital at the time of measles infection can reduce the risk of fatality and eye complications and should be considered particularly in cases with severe or complicated measles, immune deficiency, malabsorption, malnutrition or documented vitamin A deficiency.

Vitamin A is administered once daily for two days at the following doses:

- 200,000 IU for children aged 12 months or older
- 100,000 IU for infants aged 6–11 months
- 50,000 IU for infants aged under 6 months.

In children with clinical signs of vitamin A deficiency, a third dose should be given four to six weeks following the diagnosis of measles.

For more details on control measures, refer to the *Communicable Disease Control Manual 2012* [48] or the *Control of Communicable Diseases Manual*.[49]

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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 rifampicin, ceftriaxone or ciprofloxacin eradicates *N. meningitidis* from mucosal surfaces within 24 hours, and the case is no longer considered infectious.
Suspected cases	Administer antibiotics as soon as possible (prior to transport to hospital). Notify all suspected cases as soon as possible.
Available vaccines	Meningococcal group C conjugate (MenCCV): Meningitec, NeisVacC. Quadrivalent meningococcal conjugate (MCV4-D): Menactra. Quadrivalent meningococcal polysaccharide (4vMenPV): Mencevax ACWY, Menomune ACYW-135.
Funded vaccine indications	MCV4-D or MenCCV for individuals: · pre- or post-splenectomy or with functional asplenia · with HIV, complement deficiency (acquired, including monoclonal therapy against C5, or inherited) or pre- or post-solid organ transplant · who are close contacts of meningococcal cases · who are bone marrow transplant patients · following immunosuppression.
Vaccine efficacy/ effectiveness	Meningococcal conjugate vaccines are preferred over polysaccharide vaccines because they allow vaccination in younger children and are associated with the development of herd immunity.
Precaution	Individuals with a history of Guillain-Barré syndrome who are considering immunisation with MCV4-D.
Management of close contacts	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 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 non-specific or rapidly fatal.

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 through your nearest public hospital. 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 is a form of gram-negative sepsis and frequently presents with sudden onset of fever and rash. Septic shock may rapidly ensue. Meningitis occurs when blood-borne organisms seed the meninges, and may be part of a sepsis syndrome, or present more with isolated signs of bacterial meningitis. 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) at least 6-hourly Children: 25–50 mg/kg IV (or IM) at least 6-hourly
Amoxycillin	Adults: 1–2 g IV (or IM) Children 50–100 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.

Asymptomatic colonisation of the upper respiratory tract by *N. meningitidis* occurs in more than 10 percent of individuals and may be higher during epidemics and in household contacts of an index case. Smoking, passive smoking, crowding and upper respiratory tract infections increase carriage.

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.

12.3 Epidemiology

12.3.1 General

Those particularly at risk of meningococcal disease are children aged under five years, although all age groups can be infected. There is a higher case fatality rate in adults. The presentation may be non-specific in young infants.

Close contacts of primary cases of meningococcal infection are at increased risk of developing infection, such as within families,[1] 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.[2, 3, 4] 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) who develop the disease usually do so 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 rifampicin, ceftriaxone or ciprofloxacin is necessary to reliably eradicate nasopharyngeal carriage and hence relax infection prevention and control precautions (see section 12.8.1).

Serogroup A disease

Group A disease is rare in New Zealand (the last large outbreak was in 1985/86) but it can cause massive outbreaks of disease, such as the regular epidemics in the sub-Saharan Africa meningitis belt, where attack rates may approach 1000–2000 cases per 100,000 people per year. There have been outbreaks of meningococcal disease associated with the Hajj pilgrimage, and meningococcal vaccination is recommended before travel.[5] Documented evidence of vaccination is required by the Saudi Arabian Ministry of Health for anyone going to the Hajj pilgrimage.

Serogroup B disease

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. A very large epidemic of group B meningococcal disease, caused by a single subtype (B:4:P1.7b,4), occurred in New Zealand between 1991 and 2007, with a peak incidence of 200 cases per 100,000 children aged under 12 months in 2001. The epidemic disproportionately affected Māori and Pacific people.

Serogroup C disease

Group C meningococci have been occasionally associated with small clusters of meningococcal disease cases in schools and universities, and in 2011 there was a more widespread outbreak in Northland.

Other serogroups

Sporadic cases, particularly in the elderly, are seen often in individuals presenting with non-specific febrile illnesses and pneumonia.

12.3.2 New Zealand epidemiology

Incidence and mortality

In 2012 the rate was 1.9 cases per 100,000 population, with a total of 85 cases notified (74 confirmed)[6] (Table 12.3).

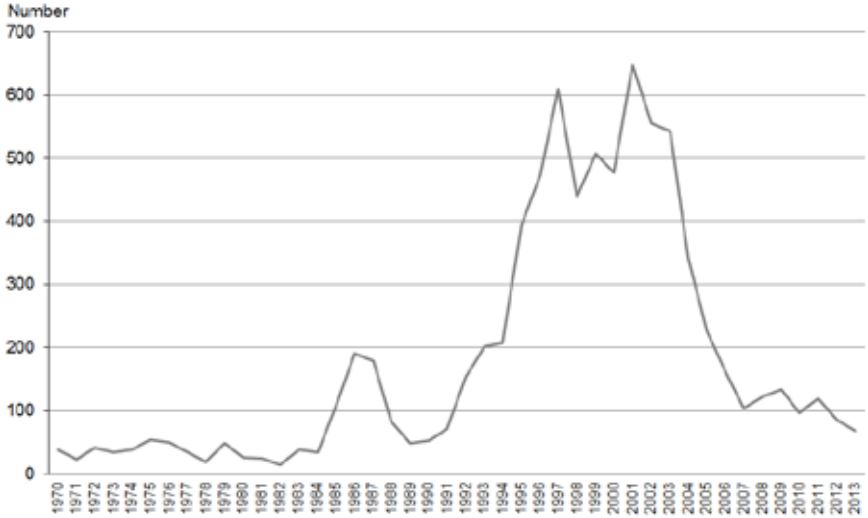
Table 12.3: Notified cases and rates of meningococcal disease, 2008–2012

Year	Number	Rate/100,000 population
2008	122	2.9
2009	133	3.1
2010	97	2.2
2011	119	2.7
2012	85	1.9

Source: Lopez L, Sexton K. 2013. *The Epidemiology of Meningococcal Disease in New Zealand in 2012*. URL: https://surv.esr.cri.nz/PDF_surveillance/MeningococcalDisease/2012/2012AnnualRpt.pdf (accessed 10 September 2013), Table 1.

The annual number of notified cases of meningococcal disease in New Zealand since 1970 is shown in Figure 12.1. There were 68 notifications in 2013.

Figure 12.1: Notified cases of meningococcal disease, 1970–2013

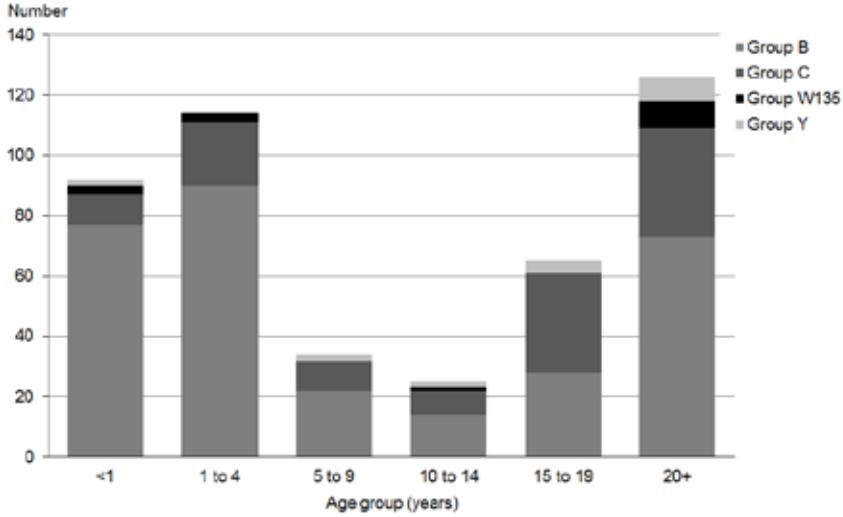


Source: Institute of Environmental Science and Research

Meningococcal infection rates remain consistently higher in Māori and Pacific people compared with the total population. Māori had the highest disease rate in 2012 (4.5 per 100,000), followed by Pacific people (3.7) and European or Other (1.4). The highest disease rate by age group was for Māori children aged under 12 months (49.0 per 100,000).[6]

In 2012 the highest age-specific disease rates were among those aged under 1 year (19.8 per 100,000 population, 12 cases) and 1–4 years (5.6 per 100,000 population, 14 cases), with a secondary peak in the notification rate for those aged 15–19 years (4.8 per 100,000 population, 15 cases).[6] Figure 12.2 shows the age distribution of the 456 strain-typed cases from 2008 to 2012. Group B strains were the most prevalent in all age groups except for the age 15–19 years group, in which Group C strains were the most prevalent.

Figure 12.2: Age distribution among strain-typed meningococcal disease cases, 2008–2012 cumulative data



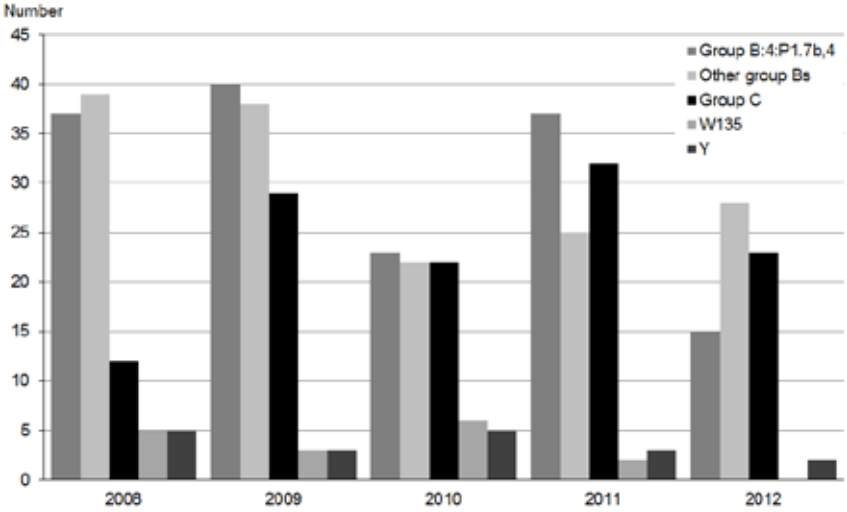
Source: Institute of Environmental Science and Research

Six fatalities occurred in 2012, a case fatality rate of 7.1 percent. Two fatalities were due to group B strains (one from the epidemic strain) and four were due to group C strains.[6]

Strain types

Group B strains were the most prevalent in 2012, causing over 60 percent of the confirmed cases. The group B strain (B:4:P1.7b,4) responsible for the epidemic caused 22.1 percent of all meningococcal disease in 2012. The number of cases of meningococcal disease caused by group C strains has increased since 2007 (Figure 12.3), particularly the group C:P1.5-1,10-8 strain.[6]

Figure 12.3: Groups and dominant subtypes among strain-typed meningococcal disease cases, 2008–2012



Source: Institute of Environmental Science and Research

Between 2008 and 2012, the number of cases due to strains targeted by the MeNZB vaccine (B:4:P1.7b,4) fell from 46 to 15. In contrast, the number of cases due to strains targeted by the group C conjugate vaccine significantly increased between 2008 and 2011 (from 12 to 32) and then decreased in 2012 to 23 cases. The trends in cases due to strains targeted by the quadrivalent vaccine (A, C, W135 and Y) are being driven by the increase in group C disease. Of the 25 cases in 2012 caused by strains targeted by the quadrivalent meningococcal vaccine, only two were caused by non-group C strains.[6]

Meningococcal conjugate group C vaccination is not on the New Zealand Schedule at present, but this recommendation could change if the incidence of group C meningococcal disease increases. In 2012 the group C rate was 0.51 per 100,000 population (23 cases). The UK had a total population rate of 2.10 per 100,000 when the group C meningococcal vaccination was introduced in 1999.[7] In Australia the rate was 1.10 per 100,000 when the vaccine was introduced in 2003.

12.4 Vaccines

12.4.1 Introduction

Meningococcal vaccination programmes have been revolutionalised by the development of conjugate vaccines (firstly against group C but now also quadrivalent ACYW135 is available), which allow vaccination in younger children and are associated with the development of herd immunity when used widely (see section 1.2.3 for more information about conjugate vaccines). The inclusion of other serogroups (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.

Group B vaccines have been harder to develop because the group B capsule is poorly immunogenic and vaccines have been subtype specific. More recently, a recombinant group B vaccine has been developed, which covers a broad range of group B subtypes, but B group vaccines are not available in New Zealand at present.

The monovalent (C) and quadrivalent 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 the infant age group. Polysaccharide vaccines may still be useful and can offer three to five years' protection in adults, but they are generally regarded as inferior to conjugate vaccines.

The meningococcal vaccines registered (approved for use) and available (marketed) in New Zealand are summarised in Table 12.4 below.

Table 12.4: Meningococcal vaccines registered and available in New Zealand

Name (manufacturer)	Vaccine type
NeisVac-C (Baxter Healthcare Ltd)	Meningococcal group C conjugate (MenCCV)
Meningitec (Pfizer NZ Ltd; distributed by Te Arai BioFarma Ltd)	Meningococcal group C conjugate (MenCCV)
Menactra (Sanofi-aventis NZ Ltd)	Quadrivalent meningococcal conjugate (MCV4-D)
Mencevax ACWY (GSK)	Quadrivalent meningococcal polysaccharide (4vMenPV)
Menomune ACYW-135 (Sanofi-aventis NZ Ltd)	Quadrivalent meningococcal polysaccharide (4vMenPV)

Funded vaccines

No meningococcal vaccine is included on the routine Schedule, but in special circumstances, under the auspices of the medical officer of health and the Ministry of Health, meningococcal group C conjugate and quadrivalent meningococcal conjugate vaccines are recommended and funded (see section 12.5).

Two meningococcal conjugate vaccines are funded for certain at-risk groups.

- Meningococcal group C conjugate vaccine MenCCV (NeisVac-C, Baxter Healthcare 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-aventis NZ Ltd) 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

Group C vaccines

Meningococcal group C conjugate vaccine MenCCV (Meningitec, Pfizer NZ Ltd) is also registered and available in New Zealand. It contains 10 µg of polysaccharide derived from the group C capsule, conjugated to 15 µg of diphtheria CRM_{197} protein. Other components include aluminium phosphate and sodium chloride.

Group A vaccines

There are no monovalent group A vaccines registered and available in New Zealand; group A strains are contained in the quadrivalent conjugate and polysaccharide vaccines.

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 (OMVs) 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 shortlived 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. The recombinant vaccine (4CMenB, Bexsero) contains four components from the group B bacteria: three different group B surface proteins plus detoxified OMV from the New Zealand group B epidemic strain. The vaccine has large-scale clinical trial data to support its use, and licensure has been granted in Europe, Australia and Canada. The cost effectiveness of this vaccine is currently being determined, and at the time of writing it has not been included in any funded schedules.

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.[8]

Quadrivalent meningococcal polysaccharide vaccines

There are two quadrivalent meningococcal polysaccharide vaccines (4vMenPV) registered and available in New Zealand (Mencevax ACWY, GSK; and Menomune ACYW-135, Sanofi-aventis NZ Ltd). Both contain 50 µg of each polysaccharide derived from the capsules of group A, C, Y and W135 *N. meningitidis* strains.

Like other unconjugated polysaccharide vaccines, 4vMenPVs are less effective in children aged under 2 years and are approved for use only in children over this age.

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. Data from that programme indicates that a booster dose in the second year of life is important for sustained protection following infant vaccination. Some countries (eg, Australia) have introduced conjugate group C meningococcal vaccine as a single dose in the second year of life, with subsequent significant reductions in disease incidence.[9]

The conjugate vaccines containing tetanus toxoid (TT) as the carrier protein appear to be more immunogenic, with longer persistence of bactericidal antibodies.[10, 11] Two studies showed that serum bactericidal titres at five years were higher in children whose primary vaccination used the TT conjugate.[12, 13]

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 efficacy was at least 83 percent in children who had received the conjugate vaccine from age 5 months to 18 years.[14] However, the vaccine offered little protection one year after the last dose in infants who were immunised only in the first six months of life.

Protective efficacy against carriage by adolescents of group C one year after the 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 adults older than age 25 years, also unvaccinated.[16] At the same time there is 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.

The optimal vaccine schedule in New Zealand (where we do not have a universal programme) is not known. In view of waning immunity, some experts recommend boosters every three to five years for individual protection.

Quadrivalent meningococcal conjugate vaccines

Immunisation against meningococcal disease with quadrivalent meningococcal conjugate vaccine is recommended in the US for all adolescents (at age 11 or 12 years and a booster at age 16 years). Individuals at high risk for meningococcal disease and underlying medical conditions may be given two doses, eight weeks apart, with boosters every five years if the risk condition persists (first booster given after three years if aged under 7 years at the time of the primary course).[18]

Because there is little group A meningococcal disease in New Zealand for the general population, there does not appear to be any major additional advantage over C conjugate vaccines, except for individuals travelling countries with different serotype predominance, such as Saudi Arabia (to the Hajj) or sub-Saharan Africa.

An early 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.[19] There was no published data for evidence of the effectiveness in older adults identified at the time of writing.

The MCV4-D vaccine was poorly immunogenic in infants aged under 6 months,[20] and it is currently registered in New Zealand for children from 9 months of age.

Quadrivalent meningococcal polysaccharide vaccines

Protective levels of antibody are usually achieved within seven to 10 days of vaccination with quadrivalent polysaccharide vaccines (4vMenPV).[21] Immunity, as determined by antibody levels, lasts approximately three years, although in young children there may be a more rapid decline.

The effectiveness of 4vMenPV against disease due to group A or C *N. meningitidis* has been 85–100 percent in outbreaks involving children over the age of 2 years and adults. There is no similar efficacy data for protection against disease due to groups Y and W135.

In response to a meningococcal group C epidemic in Canada in the early 1990s, about 1.6 million doses of 4vMenPV were administered to people aged 6 months to 20 years. The overall field effectiveness of the vaccine was 79 percent (higher in teenagers and lower in children aged under 5 years).[22] The epidemic waned both in provinces that vaccinated and in those that did not. A subsequent case-control study found a good level of protection (77 percent) was provided over a five-year period by a single dose of the polysaccharide vaccine in individuals aged 6 years and over, but in those aged 2 to 5 years only short-term protection was achieved.[23]

Revaccination with and hyporesponsiveness to polysaccharide vaccines

Revaccination with polysaccharide vaccines results in a reduced antibody response compared with the primary immunisation.[24] In addition, following repeated vaccination with 4vMenPV, immunological hyporesponsiveness to the serogroup C component may be seen in both children and adults. This hyporesponsiveness can be partially overcome with meningococcal conjugate vaccines,[18, 21] although additional doses of a conjugate vaccine may be required in young children.[24] There is little response to the serogroup C component of the 4vMenPV before 18 months of age and little response to serogroup A before 3 months of age.[24]

12.4.3 Transport, storage and handling

Transport meningococcal conjugate and polysaccharide vaccines according to the *National Guidelines for Vaccine Storage and Distribution*.[25] Store at +2°C to +8°C. MCV4-D should be protected from light. Do not freeze.

Quadrivalent meningococcal polysaccharide vaccines

These vaccines must be reconstituted with the supplied diluent and used as soon as possible.

12.4.4 Dosage and administration

Meningococcal group C conjugate vaccine

Each MenCCV dose is 0.5 mL, administered by intramuscular injection (see section 2.3). See Table 12.6 for a suggested meningococcal schedule for healthy children.

- NeisVacC: see sections 4.2 and 4.3 for schedules for high-risk children. 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.
- Meningitec: For healthy infants aged under 12 months, three doses are given at least four weeks apart, with the first dose given not earlier than age 6 weeks. A booster is given at, or after, age 12 months. For healthy children, adolescents and adults, one dose is given.

MenCCVs can be administered concurrently with other scheduled vaccines, in separate syringes and at separate sites.[26, 27]

Quadrivalent meningococcal conjugate vaccine

MCV4-D is registered in New Zealand for individuals aged 9 months to 55 years. Each 0.5 mL dose is administered by intramuscular injection (see section 2.3). 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 sections 4.2 and 4.3 for schedules for high-risk individuals and Table 12.6 for a suggested meningococcal schedule for healthy children.

MCV4-D can be concurrently administered with other vaccines in separate syringes and at separate sites,[28, 29, 30, 31] 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.

Quadrivalent meningococcal polysaccharide vaccines

For those aged 2 years and older, a single dose of 0.5 mL is administered by subcutaneous injection (see section 2.3).

12.5 Recommended immunisation schedule

Meningococcal conjugate vaccines are preferred to polysaccharide vaccines in all instances.

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 12.5 below. 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 12.5.

Table 12.5: Meningococcal group C conjugate (MenCCV) and quadrivalent meningococcal vaccine (MCV4-D) recommendations

Note: Funded conditions are in the shaded rows. See the Pharmaceutical Schedule (www.pharmac.health.nz) for the number of funded doses and any changes to the funding decisions.

Recommended and funded
MenCCV and MCV4-D are recommended and funded for individuals: · who are pre- or post-splenectomy or with functional asplenia[a,b] · with HIV, complement deficiency (acquired, including monoclonal therapy against C5, or inherited) or who are pre- or post-solid organ transplant[b] · who are close contacts of meningococcal cases · who are bone marrow transplant patients[b] · following immunosuppression.[b,c]
Recommended but not funded
MenCCV and MCV4-D are recommended,[d] but not funded, for individuals: · who are laboratory workers regularly handling meningococcal cultures · who are travelling to high-risk countries (see the WHO website), or before the Hajj · 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).

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 Quadrivalent meningococcal polysaccharide vaccines are another option for individuals aged 2 years and older.

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 is the preferred vaccine for travel, with 4vMenPV as an alternative option. 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.

12.5.2 Recommendations for non-high-risk children

Given the absence of a universal programme, for the protection of non-high-risk children the meningococcal schedule in Table 12.6 below is advised. The predominant meningococcal strains in New Zealand in childhood are B and C. There is no vaccine currently available for B. For those who are likely to travel, the quadrivalent vaccine is preferable because of the differing serotype patterns between countries.

Table 12.6: Suggested meningococcal schedule for non-high-risk children (not funded)

Note: Vaccine immunity is not long-lasting. This suggested schedule is not expected to protect individuals through all of childhood, but is pragmatically focused on offering protection during the ages of highest risk. This schedule does not apply to epidemic situations.

Age at presentation	Vaccine options (trade name)	Number of doses
<12 months	MenCCV (NeisVac-C; Meningitec)	2 or 3 doses[a] (primary course) plus a booster after 12 months of age
12 months to 2 years	MenCCV (NeisVac-C; Meningitec) or MCV4-D (Menactra)	1 MenCCV or 2 MCV4-D[a,b] doses
Early adolescence	MenCCV (NeisVac-C; Meningitec) or MCV4-D (Menactra)	1 dose
Late adolescence	MenCCV (NeisVac-C; Meningitec) or MCV4-D (Menactra)	1 dose

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.

12.6 Contraindications and precautions

12.6.1 Contraindications

The general contraindications that apply to all vaccines also apply to meningococcal conjugate and polysaccharide vaccines (see section 1.4).

12.6.2 Precautions

There is a precaution for individuals with a history of Guillain-Barré syndrome who are considering immunisation with MCV4-D. See section 12.7.2.

12.7 Expected responses and adverse events following immunisation (AEFI)

Frequent adverse reactions after meningococcal conjugate and polysaccharide vaccines include localised pain, irritability, headache and fatigue.[32] Fever is reported by 2 to 5 percent of adolescents who receive either MCV4-D or 4vMenPV.

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.[21] 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.[33] 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.[21]

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.[34] 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).

Guillain-Barré syndrome

In 2005, shortly after MCV4-D (Menactra) was licensed in the US, several cases of Guillain-Barré syndrome (GBS) were reported to the US Vaccine Adverse Event Reporting System (VAERS).[18] Because the risk of GBS following vaccination was unknown, the Food and Drug Administration (FDA) considered a previous history of GBS to be a contraindication to MCV4-D, and the contraindication was added to the vaccine data sheet. The US Advisory Committee on Immunization Practices (ACIP) also added precautionary language to its vaccine information statement.

Large safety studies, during which over 2 million doses of MCV4-D were administered, found there was no risk of GBS after MCV4-D in the general population. This data was extrapolated to conclude that people with a history of GBS are not at higher risk than they are after other vaccines that have no association with GBS.[35]

In June 2010, after reviewing the safety studies, the ACIP removed its precaution for individuals with a history of GBS because the benefit of vaccination outweighs the risk for recurrent GBS in these individuals.[18] However, a history of GBS continues to be listed as a contraindication/precaution in the MCV4-D data sheet.

This information should be discussed with individuals with a history of GBS who are considering immunisation with MCV4-D.

12.7.3 Quadrivalent meningococcal polysaccharide vaccine

Generalised reactions to 4vMenPV are rare, but are more common in children than in adults. Up to 80 percent of recipients will have some local reaction, but most reactions are minor.[36] Approximately 10 percent of recipients will develop local reactions at the injection site within 24 hours of the injection.

The Canadian campaign delivered over a million doses of 4vMenPV, with reported allergic reactions in 9.2 per 100,000 doses, anaphylaxis in 0.1 per 100,000 doses, and neurological reactions in 0.5 per 100,000 doses; there were no reports of long-term sequelae or of encephalopathy, meningitis or encephalitis.[37]

12.7.4 Meningococcal vaccinations during pregnancy

The available data does not suggest that giving meningococcal vaccine to pregnant women causes any adverse effects. Nevertheless, as with any vaccine in pregnancy, careful consideration of the risks and benefits of immunisation to the mother and fetus is needed. Maternal antibodies will protect the newborn for the first few months, and the subsequent response to the vaccine is not altered.[38]

12.8 Public health measures

Invasive meningococcal disease must be notified on suspicion to the local medical officer of health.

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. Three to five millilitres of blood should be taken in an EDTA anticoagulant tube (usually with a purple top).

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.

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.[39] 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).

12.8.1 Chemoprophylaxis for contacts

Recommended antibiotics

The recommended antibiotics are rifampicin, ceftriaxone or ciprofloxacin.

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.

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.[40]

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.[39] Ciprofloxacin is not generally recommended for pregnant and lactating women or for children aged under 18 years.[41] Consult the manufacturer's data sheet for appropriate use and dosage of ciprofloxacin in children.

Use of group C meningococcal vaccines for close contacts

Close contacts of cases of group C meningococcal disease may be offered a group C-containing meningococcal vaccine (see section 12.5). See below for the use of the vaccines for the control of outbreaks.

12.8.2 Outbreak control

When there is an outbreak of meningococcal disease of a specific vaccine group, the medical officer of health and Ministry of Health assess the epidemiology of the cases as follows.

- Organisation outbreak: two or more cases of the same serogroup occurring within a four-week period at the same day care, school, sports group, social group, nursing home, university, etc.
- Community outbreak: three or more confirmed cases of the same serogroup within a three-month period and an age-specific incidence or specific community population incidence of approximately 10 per 100,000, where there is no other obvious link between the cases (not absolute).

When there is an organisation or community outbreak, an immunisation programme may be recommended and funded for a defined population.

For more details on control measures, refer to the *Communicable Disease Control Manual 2012*[39] or the *Control of Communicable Diseases Manual*.[42]

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13 Mumps

Key information

Mode of transmission	Airborne droplets or direct contact with infected respiratory tract secretions or urine.
Incubation period	About 16 to 18 days, ranging from 12 to 25 days.
Period of communicability	From 7 days before the onset of parotitis until 9 days after the onset of illness.
Funded vaccine	A live-attenuated vaccine (MMR II), containing measles, mumps and rubella viruses.
Funded immunisation schedule	Children at ages 15 months and 4 years. Adults who are susceptible to one or more of measles, mumps and rubella.
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.

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.[1]

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.

Classic mumps, an acute viral illness, is characterised by fever, headache, and swelling and tenderness of one or more parotid (salivary) glands. At least 30 percent of mumps infections in children are asymptomatic. Patients may have no involvement of salivary glands but still experience involvement of other organs (eg, orchitis or meningitis).

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 6000, the latter being a more realistic estimate.

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. Pancreatitis, neuritis, arthritis, mastitis, nephritis, thyroiditis and pericarditis may also occur. Mumps in the first trimester of pregnancy may increase the rate of spontaneous abortion, but there is no evidence that it causes fetal abnormalities.

The period of communicability ranges from seven days before the onset of parotitis until nine days after the onset of illness. Exposed non-immune individuals should be considered infectious from 12 to 25 days after exposure.

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 are subclinical, while those affected in adulthood are more likely to experience severe disease. The peak incidence is in late winter and spring.

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 2013, 23 cases of mumps were notified, compared to 26 notifications in 2012 (17 were laboratory confirmed) and 51 notifications in 2011 (24 were laboratory confirmed). The 2012 mumps notification rate was 0.6 per 100,000 population, a significant decrease from 2011 (1.2 per 100,000).[2]

13.4 Vaccines

13.4.1 Available vaccines

Mumps vaccine is one of the components of the live attenuated measles-mumps-rubella (MMR) and measles-mumps-rubella-varicella (MMRV) vaccines, considered in sections 11.4 and 21.4. The MMR and MMRV vaccines registered (approved for use) and available (marketed) in New Zealand contain the Jeryl Lynn mumps strain. The more reactive Urabe strain was used in New Zealand for a short time from 1991 until it was withdrawn in 1992 (see also section 11.7.2).

Funded vaccine

MMR vaccine funded as part of the Schedule is MMR II (MSD), which contains further attenuated Enders' Edmonston (Moraten) strain measles, RA 27/3 rubella, and Jeryl Lynn mumps. See section 11.4.1 for more information.

There is no single-antigen mumps vaccine available in New Zealand (see sections 11.4.1 and 21.4.1 for information on other vaccines).

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.[3]

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. A third dose of MMR vaccine has been used safely and effectively during mumps outbreaks in highly immunised populations.[4] 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.[5]

See section 11.4.2 for information on the duration of immunity from MMR vaccine.

13.4.3 Transport, storage and handling

Transport according to the *National Guidelines for Vaccine Storage and Distribution*.[6] Store in the dark 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 in the dark 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 in the deltoid area to all age groups (see section 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.

13.5 Recommended immunisation schedule

13.5.1 Children

Two doses of mumps vaccine as MMR are recommended at age 15 months and age 4 years.

Approximately 5 percent of children fail to be protected by the first dose; of these, nearly all will be protected by the second (see section 11.4.2). 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. 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.

13.5.2 Older children and adults

MMR is recommended and funded for older children and adults who are known to be susceptible to one or more of the three diseases (two doses, four weeks apart).

13.5.3 Immunosuppression

MMR is contraindicated in children who are immunosuppressed (see sections 1.4 and 4.3). They can be partially protected from exposure to infection by ensuring that all contacts are fully immunised, including hospital staff and family members. There is no risk of transmission of MMR vaccine viruses from a vaccinee to the immune-compromised individual.

MMR vaccination at 12 months of age is recommended for children with HIV infection who are asymptomatic and who are not severely immune compromised (see section 4.3).

MMR is contraindicated in children with severe immune suppression from HIV because vaccine-related pneumonitis (from the measles component) has been reported.[7] Discuss vaccination of children with HIV infection with their specialist.

13.5.4 Pregnancy and breastfeeding

MMR vaccine is contraindicated during pregnancy. Pregnancy should be avoided for four weeks after MMR vaccination.

MMR vaccine can be given to breastfeeding women.

13.6 Contraindications and precautions

See also sections 1.4, 11.6 and 18.6.

13.6.1 Contraindications

Anaphylaxis to a previous dose of MMR, MMRV or any of the vaccine components (including neomycin and gelatin) is a contraindication to a further dose of MMR or MMRV.

MMR vaccine should not be given to women who are pregnant, and pregnancy should be avoided for four weeks after immunisation.

13.6.2 Precautions

Egg allergy, including anaphylaxis, is **not** a contraindication to measles-containing vaccines. See section 11.6.3 for more information, and section 11.6.2 for further precautions.

13.7 Expected responses and adverse events following immunisation (AEFI)

See section 11.7.

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.

All suspected mumps cases should be laboratory confirmed. See Appendix 8 for the specimens required for laboratory confirmation of mumps, or discuss these with the local laboratory.

When an outbreak of mumps occurs, all susceptible people (ie, those who have no previous history of mumps and have not received the mumps or MMR vaccine) should be offered MMR vaccine. The mumps vaccine given after exposure has not been shown to be effective in preventing infection, but immunisation will provide protection against future exposure. 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.

Parents/guardians should be advised that children who are cases should be excluded from early childhood services or school until five days after the onset of illness, at which time they cease to be infectious. Previously immunised (pre-exposure) contacts need not be excluded from early childhood services or school.

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.

Consider advising exclusion of susceptible contacts from school, early childhood services or work for 25 days after last exposure to the infectious case, if there are other susceptible people present.[8] If a susceptible contact is vaccinated following exposure, they still need to be excluded (for the current outbreak) for 25 days. The vaccine given after exposure has not been shown to be effective in preventing infection, but immunisation will provide protection against future exposure. Contacts immunised prior to exposure do not need to be excluded.

For more details on control measures, refer to the *Communicable Disease Control Manual 2012*[8] or the *Control of Communicable Diseases Manual*.[9]

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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, erythromycin), infectivity lasts until 5 days of antibiotics have been taken.
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).
Funded immunisation 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 (no minimum interval is required between Td and Tdap, unless Tdap is being given as part of a primary immunisation course). During pregnancy (from 28 to 38 weeks' gestation): Tdap.
Vaccine efficacy/ effectiveness	84 percent efficacy after the 3-dose primary course in infants, lasting up to age 6 years. Immunity (derived from both natural infection and immunisation) wanes over time.
Precautions	Children with an evolving neurological disorder. Very premature babies have shown evidence of apnoea, bradycardia and desaturations with combination DTaP vaccines.
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 polymerase chain reaction (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 1.1.1). 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.

The above description is of the clinical presentation in a non-immune child, but it does vary 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, the clinical 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, not infrequently for more than four weeks, is the cardinal feature in adults.[4] 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 have evidence of recent *B. pertussis* infection.[3, 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 that recent *B. pertussis* infection was present 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]

In adults, cough is worse at night and often paroxysmal. Adults describe being awoken by a choking sensation. Post-tussive vomiting and whoop are infrequent. A scratchy throat and sweating attacks are common.

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. Young infants have always been particularly vulnerable to pertussis disease. For example, in the US during the 1940s pertussis resulted in more infant deaths than measles, diphtheria, poliomyelitis and scarlet fever combined.[13]

14.3.1 Global burden of disease

Pertussis mortality

Pertussis mortality rates have always been highest in the first year of life.[13, 14] 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 deaths are under-reported. It is estimated that in the developed world 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]

Pertussis morbidity

The majority of national epidemiological data on pertussis is collected via passive notification systems. The proportion of pertussis cases that are notified is estimated to vary between 6 and 25 percent. As well as underestimating disease incidence, passive notification systems are biased: a larger proportion of more clinically severe cases are notified and the proportion of cases that are notified may decrease with increasing age.[17]

Since the introduction of mass immunisation, countries with consistently low pertussis incidence rates have had consistently high immunisation coverage 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. This contrasts with the increase in time between epidemics that has occurred with 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 current pertussis epidemic (see below), there have been three deaths in children: two in infants aged under 6 weeks and one in an unimmunised preschooler.

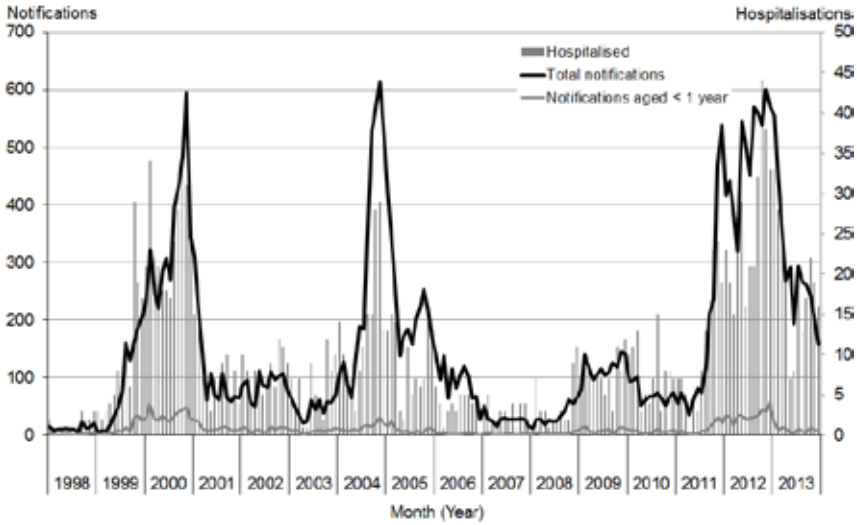
Pertussis morbidity in New Zealand

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

Three epidemics have occurred since pertussis became a notifiable disease, with an epidemic peak annual number of notified cases of 4140 in 2000, 3485 in 2004, and 5902 in 2012 (see Figure 14.1).[37] Although pertussis notifications fell in 2013, they still remained well above those seen in 2010 and 2011.[38]

Figure 14.1: Pertussis notifications and hospitalisations, 1998–2013

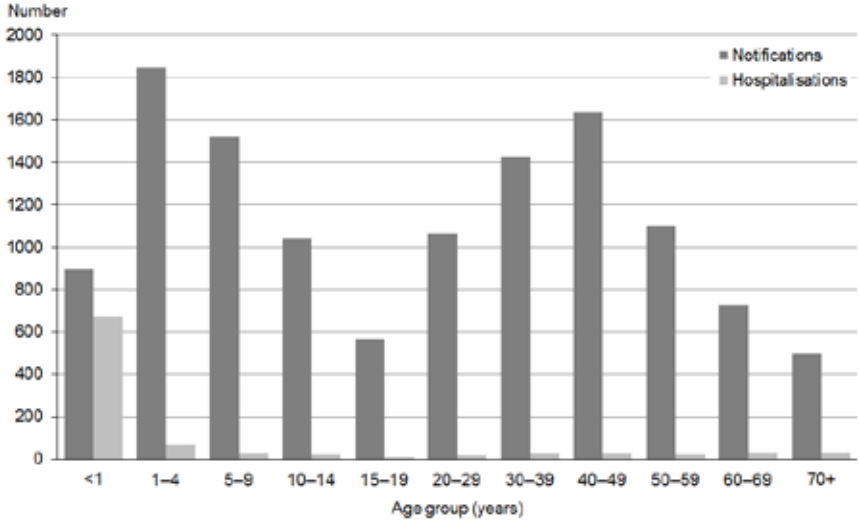


Note: Includes confirmed, probable and suspect cases, and notifications still under investigation.

Source: Institute of Environmental Science and Research

Since pertussis became notifiable, the annual proportion of notified cases aged 30 years or older has increased from 23 percent (in 1997) to 48 percent in 2013. However, the highest proportion of hospitalised cases continues to be in infants aged under one year. Of the 898 notified cases in infants from 2010 to 2013, 673 (75 percent) were hospitalised (Figure 14.2).

Figure 14.2: Age distribution of notified and hospitalised pertussis cases, 2010–2013 cumulative data



Source: Institute of Environmental Science and Research (notifications) and the Ministry of Health (hospitalisations)

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).[39, 40, 41]

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 1000) was higher for Māori (1.49; relative risk 2.29 [95% CI: 1.77–2.96]) and Pacific people (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 1000).[42]

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 1000; relative risk 4.81 [95% CI: 2.99–7.75]).[42]

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:

- DTaP-IPV: Quadracel (Sanofi-aventis NZ Ltd)
- Tdap: Adacel (Sanofi-aventis NZ Ltd)
- Tdap-IPV: Boostrix-IPV (GSK) and Adacel Polio (Sanofi-aventis NZ Ltd).

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.[43] 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.[44]

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.[45, 46, 47]

Clinical trial data suggests that acellular pertussis vaccines, while effective, may be less effective than some whole-cell vaccines in preventing whooping cough.

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.[48] 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. 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]

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.[50] 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.[51] However, the duration of protection is unknown.

14.4.3 Transport, storage and handling

Transport according to the *National Guidelines for Vaccine Storage and Distribution*.[52] 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, hold at room temperature for up to eight hours.

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 2.3).

Co-administration with other vaccines

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

14.5 Recommended immunisation schedule

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. 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

No minimum interval is required between Td and Tdap,[53, 54, 55] unless Tdap is being given as part of a primary immunisation course.

14.5.2 Pregnancy

Pregnant women should receive a dose of Tdap (funded) from 28 to 38 weeks' gestation. This should be given during each pregnancy.[56] (See also section 4.1.)

14.5.3 (Re-)vaccination

Pertussis-containing vaccine is funded for (re-)vaccination of children following immunosuppression. (See also sections 4.2 and 4.3.)

14.5.4 Recommended but not funded

Tdap is recommended but not funded by the Ministry of Health 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.

14.6 Contraindications and precautions

14.6 1 Contraindications

See section 1.4 for general contraindications for all vaccines. 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 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.

DTaP-IPV-HepB/Hib

Immunisation at the usual chronological age is recommended for all preterm babies. Very premature babies and those with chronic disease have shown evidence of apnoea, bradycardia and desaturations with combination DTaP vaccines.[57] These infants would usually still be in hospital at the time of vaccination and would be vaccinated under medical supervision.

14.7 Expected responses and adverse events following immunisation (AEFI)

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 sudden unexplained death in infancy (SUDI).[58, 59, 60, 61, 62, 63, 64, 65] Similar to previous studies, the New Zealand Cot Death Study found a lower rate of SUDI in immunised children.[66] 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-IPV-HepB/Hib vaccine

DTaP-IPV-HepB/Hib (Infanrix-hexa) is generally well tolerated in infants aged under 2 years, including preterm (24 to 36 weeks' gestation) and/or low birthweight (820–2020 grams) infants.[67, 68]

A higher incidence of local symptoms is associated with administration of DTaP-IPV-HepB/Hib booster dose in the second year of life than following the primary doses.[44] 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.

Expected responses and adverse events following immunisation with DTaP-IPV-HepB/Hib vaccine are as follows (see the manufacturer's data sheet for more information).

In ≥10 percent of vaccine recipients there is:

- loss of appetite
- irritability
- restlessness
- abnormal crying
- pain, redness and swelling at the injection site
- fever (>38°C)
- fatigue.

In ≥1 percent and <10 percent of vaccine recipients there is:

- vomiting
- diarrhoea
- local swelling and induration at the injection site (≥50 mm)
- fever (>39.5°C).

14.7.2 DTaP-IPV vaccine

Expected responses and adverse events following immunisation with DTaP-IPV (Infanrix-IPV) are as follows (see the manufacturer's data sheet for more information).

In ≥10 percent of vaccine recipients there is:

- loss of appetite
- irritability
- restlessness
- abnormal crying
- pain, redness and swelling at the injection site
- fever (>38°C)
- headache
- malaise/fatigue.

In ≥1 percent and <10 percent of vaccine recipients there is:

- nausea
- vomiting
- diarrhoea
- local swelling and induration at the injection site (≥50 mm).

14.7.3 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.[69, 70, 71] Administration of Tdap to pregnant women did not identify any concerning patterns in maternal, infant, or fetal outcomes.[72]

Expected local responses following immunisation of adolescents with Tdap include:[73]

- pain in 75 percent of recipients, of which 5 percent is severe (defined as spontaneously painful and/or preventing normal everyday activities)
- swelling at the injection site in 21 percent (of which 3 percent is ≥50 mm)
- redness at the injection site in 23 percent (of which 2 percent is ≥50 mm).

Expected systemic reactions following immunisation of adolescents with Tdap include:[73]

- fever >38°C (5 percent)
- headache, fatigue or gastrointestinal symptoms of sufficient severity to interfere with or prevent normal activity:
  - headache (16 percent)
  - fatigue (14 percent)
  - gastrointestinal symptoms: nausea, vomiting, diarrhoea and/or abdominal pain (10 percent).

14.7.4 Adverse events associated with pertussis vaccines

The incidence of major adverse events following primary pertussis immunisation is summarised in Table 14.1.

Table 14.1: Incidence (per 100,000 doses) of major adverse reaction following acellular pertussis vaccine

Event following immunisation	Timing	Incidence per 100,000 doses
Persistent (>3 hours) inconsolable screaming	0–24 hours	44
Seizures	0–2 days	7
Hypotonic-hyporesponsive episode (HHE)	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. 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.

Neither a hypotonic-hyporesponsive episode (HHE) nor seizures are associated with long-term consequences for the child[74, 75, 76] (see section 2.4.2). Children who have febrile seizures after pertussis immunisation do not have an increased risk of subsequent seizures or neurodevelopmental disability.[77] It is safe to give acellular pertussis vaccine after an HHE has occurred following a previous dose.[78]

14.8 Public health measures

14.8.1 Improving pertussis control

The goal of the pertussis immunisation programme is to protect those most vulnerable to severe disease; that is, infants in the first year of life. Infants can be protected either directly, by immunisation in early infancy, or indirectly, by immunisation of others with whom the infant may come into contact and hence be exposed to *B. pertussis*.[79] The 'cocoon strategy' is the term used to describe the protection of infants by immunising those who are potential sources of *B. pertussis*.[79]

The field effectiveness of the cocoon strategy is yet to be demonstrated. Reinforcement and/or improvement of the current infant immunisation series (direct protection) remains the highest priority for New Zealand. More complete and timely delivery of the current immunisation series would reduce infant pertussis disease burden.[80] All children attending early childhood services should be fully vaccinated for their age.

Data on the protective effects of indirect strategies is currently incomplete. Because of low coverage and the short duration of protection, plus the unknown efficacy for the protection of infants, universal adult pertussis immunisation is a lower priority at present. Targeted immunisation of adult groups who have the most contact with young and vulnerable infants is considered a more appropriate strategy. Three identified groups are (1) pregnant women, new mothers, family, and close contacts of newborns; (2) health care workers; and (3) early childhood workers. Vaccination during pregnancy is recommended and funded during pertussis epidemics (see section 14.5.2).

Of the three target refinement groups, selective immunisation of health care workers is the most readily justified and least costly. Health care workers are at increased risk of pertussis and can transmit pertussis to other health care workers and to patients.[81] Outbreaks in maternity wards, neonatal units and outpatient settings have been described.[82] Fatalities occur as a result of such nosocomial spread.[83]

Immunisation cannot be used to control an 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 the airborne route, non-vaccinated health care personnel looking after pertussis cases should wear a mask.

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 several 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. Erythromycin has been shown 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.[84, 85, 86] 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 14.2), even if six to eight weeks have elapsed since the onset of cough.[87]

In New Zealand, azithromycin and erythromycin are funded for the treatment of pertussis. Azithromycin is the recommended treatment.

Macrolide use during pregnancy, lactation and in the neonatal period is associated with an increased risk of pyloric stenosis.[88, 89] With erythromycin, the risk increases with decreasing age and increased duration of treatment.[90] The risk is presumed to be lower with azithromycin, although there are case reports of 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.[84, 91, 92]

Table 14.2: 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, 1600 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.

Cases should be excluded from early childhood services, school, or community gatherings until:

- they are well enough to attend, *and*
- either they have received five days of antibiotics, *or* exclude them for three weeks from the date of onset of the coughing paroxysms (at which point they are unlikely to be infectious) or until the end of their coughing (whichever comes first).

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 *Communicable Disease Control Manual 2012*.[93]

A contact can be defined as someone who has been in close proximity (within one metre)[94] 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.[93]

Those most at risk from pertussis and who are therefore high-priority contacts for public health follow-up are:

- infants, especially those aged under 6 months
- children and adults who live with, or spend time around, infants, 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).

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.[95]

Any contacts, high priority or otherwise, should be advised to avoid attending early childhood services, school, work or community gatherings if they become symptomatic. 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.

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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 immune compromised.
Funded vaccines	13-valent protein conjugate vaccine, PCV13 (Prevenar 13): for all children aged under 5 years. PCV13: for high-risk children who have previously received 4 doses of PCV10; for (re-)vaccination of children aged under 18 years with HIV, who are post-haematopoietic stem cell transplant (HSCT) or chemotherapy, who are pre- or post-splenectomy or with functional asplenia, who are pre- or post-solid organ transplant, renal dialysis and other severely immunosuppressive regimens. 23-valent polysaccharide vaccine, 23PPV (Pneumovax 23): for individuals who are pre-or post-splenectomy or with functional asplenia; for high-risk children aged under 18 years.
Funded immunisation schedule	Children who have started with PCV10 can continue with PCV13. Healthy children aged under 5 years: PCV13 at ages 6 weeks, 3, 5 and 15 months. High-risk children aged under 5 years: standard PCV13 schedule, plus 1 dose of 23PPV at age 2 years or older (with at least 8 weeks between the last PCV13 and the 23PPV). If risk persists, revaccinate once with 23PPV, 5 years after the first 23PPV. Eligible children aged 5 to under 18 years: 1 dose of PCV13 followed 8 weeks later with 1 dose of 23PPV. Revaccinate once with 23PPV, 5 years after the first 23PPV. Eligible adults: a maximum of 3 doses of 23PPV in their lifetime, a minimum of 5 years apart.

Vaccine efficacy/ effectiveness	For pneumococcal conjugate vaccines: reductions in pneumococcal disease and carriage 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 6–59 months. Due to the potential risk of apnoea, PCV13 should be used with caution in very premature babies, but do not avoid or delay immunisation.

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. 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.

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.[1] 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* invasive 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 (blood, pleural fluid or cerebrospinal fluid). Clinically, these are cases of meningitis and bacteraemic pneumonia, especially in the very young, and *S. pneumoniae* is often the cause of bacteraemia with no obvious primary site of infection.

Local mucosal or non-invasive infection is common, such as otitis media, especially in children, and sinusitis and pneumonia (without bacteraemia) in all age groups. Rarely, *S. pneumoniae* may cause invasive disease such as endocarditis and deep infection in sites such as joints, the peritoneal cavity or the fallopian tubes. The incubation period of *S. pneumoniae* infection is variable but may be as short as one to three days.

Along with the very old and very young, patients with underlying conditions have the highest rates of disease.

15.3 Epidemiology

15.3.1 New Zealand epidemiology

Pneumococcal disease occurs throughout the year, but is more common in the autumn and winter months.[2] The risk of disease is highest in infants,[3, 4] especially Māori and Pacific infants, and in elderly people.

Invasive isolates from cases of IPD are serogrouped and serotyped at the Institute of Environmental Science and Research (ESR). IPD became a notifiable disease in October 2008 with direct laboratory notification to public health units, which, along with ESR laboratory serotyping, allows accurate national surveillance of all IPD in New Zealand. Detailed surveillance information can be found on the ESR Public Health Surveillance website (www.surv.esr.cri.nz/surveillance/IPD.php).

ESR laboratory-based surveillance provides an estimate of the coverage of IPD isolates by available vaccine serotypes. During the two years (2006–2007) prior to the introduction of PCV7, 82 percent of cases in children aged under 5 years were due to serotypes contained in PCV7, 84 percent to PCV10 serotypes and 94 percent to PCV13 serotypes.[5] The relative importance of serotypes varies by age group and year by year. See Table 15.1 for a summary of serotypes contained in the pneumococcal vaccines.

Table 15.1: Summary of pneumococcal vaccine serotype content

Vaccine	Serotypes
PCV13	Includes: · serotypes 4, 6B, 9V, 14, 18C, 19F, 23F (previously contained in PCV7) · plus serotypes 1, 5, 7F (previously 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.

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, and in July 2011 was replaced by the 10-valent pneumococcal conjugate vaccine (PCV10, Synflorix). The 13-valent pneumococcal conjugate vaccine (PCV13, Prevenar 13) replaced PCV7 for high-risk individuals in July 2011 and replaced PCV10 for all children in July 2014.

The effect of PCV7 on IPD has been well-documented internationally, with significant reductions in vaccinated children and indirect effects on unvaccinated individuals (ie, a herd immunity effect; see the herd immunity discussion below).

15.3.2 New Zealand epidemiology since the introduction of PCV

There have been dramatic reductions in the incidence of IPD in the vaccine-eligible age groups in New Zealand since the introduction of PCV7. The rate of IPD in New Zealand children aged under 2 years has decreased by 80 percent since the introduction of PCV7: from an average annual rate of 100.8 per 100,000 for 2004–2007 to 20.4 per 100,000 in 2013.[4] The impact on IPD caused by PCV7 serotypes in this age group is even greater, with a 98 percent decrease from an average rate of 83.1 per 100,000 in 2006/07 to 1.6 per 100,000 in 2012 (note that the 2012 rate was calculated based on two cases only).[6]

There was one case caused by a PCV7 serotype in a child aged under 2 years in 2013.[7] The rate of IPD has also significantly decreased in children aged 2 to 4 years, for all-cause IPD and IPD caused by PCV7 serotypes.

Figure 15.1 and Table 15.2 show the rates of IPD by age group and vaccine serotype since the introduction of PCV7. See also the herd immunity section below for the effect on IPD in those age groups who were not eligible for funded vaccine.

Notification rates for IPD since 2011 (with the change to PCV10)

The IPD rate for children aged under 2 years for 2013 (20.4 per 100,000 population, 25 cases) was a significant decrease from the 2012 rate (30.8 per 100,000 population, 44 cases). During 2013 the highest rates were for individuals aged 65 years and older (30.8 per 100,000 population, 188 cases) and children aged under 2 years. The notification rate for all ages for 2013 (10.9 per 100,000 population, 482 cases) was a non-significant decrease from the 2012 rate (11.1 per 100,000 population, 489 cases).[7]

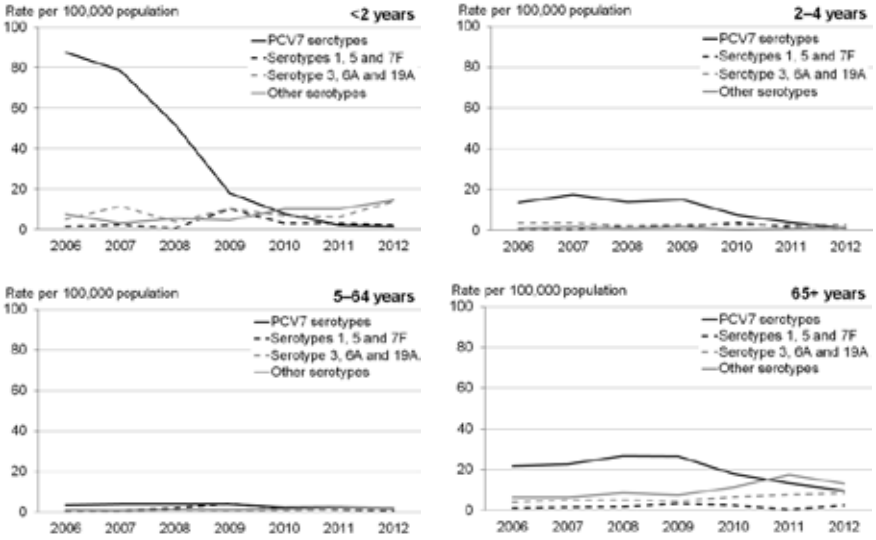
Disease caused by PCV7 and PCV10 vaccine serotypes

PCV7 serotypes accounted for just 20 percent of IPD cases across all age groups in 2013, with only one case due to a PCV7 type in children aged under 5 years.[7] The additional three serotypes in PCV10 accounted for further 16 percent of IPD cases. Cases of the PCV10 type 7F increased 86 percent between 2012 and 2013 (37 to 69 cases), with the result that 7F was the second most common serotype among IPD cases in 2013. However, the increase in type 7F cases in 2013 occurred wholly in those aged 5 years and older and were therefore not eligible to receive PCV10.

Disease caused by non-PCV10 vaccine serotypes

Serotype 19A was the most common type among IPD cases in 2013, although cases due to 19A actually decreased from 80 in 2012 to 75 in 2013.[7] The second most common non-PCV10 serotype in 2013 was type 22F. However, there was little change in cases of 22F disease between 2012 and 2013 (40 to 41 cases).

Figure 15.1: Rates per 100,000 of invasive pneumococcal disease by vaccine coverage, age group and year, 2006–2012



Notes: PCV7 was introduced in 2008 and PCV10 in 2011. IPD became a notifiable disease in 2008.

Source: Institute of Environmental Science and Research

Table 15.2: Decrease in rates of culture-positive invasive pneumococcal disease due to PCV7 serotypes between 2006–2007 and 2012, by age group

Age group	Rate of IPD due to PCV7 serotypes per 100,000 population		Percentage reduction between time periods
	2006–2007	2012	
<2 years	83.1	1.6*	98
<5 years	43.2	1.3*	98
5–64 years	3.6	1.9	46
≥65 years	22.2	9.5	57
All ages	8.6	2.9	66

* Rate should be interpreted with caution as it relates to fewer than five children.

Source: Institute of Environmental Science and Research

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 hospitalisations due to pneumonia.[8, 9] Other impacts, such as on acute otitis media, are less clear and more difficult to measure accurately.[10]

In New Zealand there is some evidence from South Auckland that the introduction of PCV7 has been associated with fewer admissions for pneumonia in young children.[11] However, there are ethnic disparities, with impacts more apparent for Pacific infants and less so for Māori in pneumonia hospitalisation. This is in contrast to IPD data, where there has been a reduction in disease in Māori children aged under 2 years but not in Pacific children (Māori: decrease from 86.6 per 100,000 in 2009 to 43.3 per 100,000 in 2012; Pacific: increase from 64.0 per 100,000 in 2009 to 83.0 per 100,000 in 2012).[6, 12]

Herd immunity

There is good evidence for the indirect 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 New Zealand,[6] the US (for both adult pneumonia and IPD in adults),[13, 14, 15] England and Wales,[16] the Netherlands,[17] Norway[18] and Denmark.[19] These herd effects are likely to be due to decreased nasopharyngeal carriage of vaccine types in immunised children resulting in reduced transmission to unimmunised children and adults. Although most of the data available is for the indirect effect on IPD, there is also evidence of an all-age effect on non-bacteraemic pneumonia.[20] Early data from Norway[21] and Canada[22] 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.

The herd effects of adding PCV7 to the New Zealand schedule in 2008 were evident by 2012, with significant reductions in IPD due to PCV7 types in all age groups, not just those that were eligible for routine infant immunisation (Figure 15.1 and Table 15.2).[6] The rate of IPD due to PCV7 serotypes in the 65 years and older age group decreased 57 percent, from an average of 22.2 per 100,000 population in 2006–2007 to 9.5 per 100,000 in 2012, while in the 5–64 years age group there was a 46 percent decrease over the same time period (3.6 to 1.9 per 100,000).

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.[6] Introduction of pneumococcal conjugate vaccination has reduced the circulation of resistant pneumococcal serotypes elsewhere.[23] In New Zealand, trends for *S. pneumoniae* resistance to betalactams (penicillin and cefotaxime) and multi-resistance over the last 10 years have varied; the 2012 rate of penicillin resistance (meningitis interpretation) of 17.2 percent was within the range of rates recorded for other years during the last decade (14–22 percent).

In 2012 ESR surveillance shows that PCV7 serotypes now account for a smaller proportion (44 percent) of the penicillin-resistant isolates than previous years, and the non-PCV10 type 19A, accounts for a larger proportion (39 percent). However, this increase in the proportion of penicillin-resistant isolates that are type 19A is due to 19A causing a greater proportion of IPD cases rather than penicillin resistance becoming more common among this serotype.[6]

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 polysaccharide is coupled to a carrier protein. The protein conjugate induces increased production of antibodies, immunological memory and maturation of the antibody response (see section 1.2.3).

Funded vaccines

The *S. pneumoniae* vaccines funded as part of the Schedule are:

- the 13-valent protein conjugate vaccine PCV13 (Prevenar 13, Pfizer NZ Ltd), for all infants and for high-risk children aged under 5 years, and those aged under 18 years pre- or post-splenectomy or with functional asplenia, or who are eligible for (re-)vaccination.
- the 23-valent polysaccharide vaccine 23PPV (Pneumovax 23, MSD), for eligible adults and children aged 2 years and older.

PCV13

Each 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 pneumococcal purified capsular polysaccharides for serotype 6B. Each serotype is individually conjugated to non-toxic diphtheria CRM_{197} protein and adsorbed onto aluminium phosphate (0.565 mg). Each dose contains succinic acid, polysorbate 80, aluminium phosphate and sodium chloride in water for injections.

23PPV

23PPV includes 23 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. Each dose contains 25 µg of each capsular polysaccharide antigen, dissolved in isotonic saline solution, with phenol (0.25 percent) added as a preservative, and no adjuvant.

Other vaccines

The 10-valent pneumococcal conjugate vaccine previously used on the Schedule is still registered and available in New Zealand.

- PCV10 (Synflorix, GSK) contains 1 µg of pneumococcal polysaccharide serotypes 1, 5, 6B, 7F, 9V, 14 and 23F (conjugated to Protein D, an immunogenic protein from non-typeable *H. influenzae*), and 3 µg of pneumococcal polysaccharide serotypes 4, 18C, 19F (conjugated to Protein D, diphtheria toxoid carrier protein and tetanus toxoid carrier protein, respectively), adsorbed

onto aluminium phosphate. Each dose also contains sodium chloride in water for injection. PCV10 contains no preservative.

Another 23-valent pneumococcal polysaccharide vaccine registered and available in New Zealand is:

- 23PPV (Pneumo 23, Sanofi-aventis NZ Ltd), which contains the same serotypes as the funded 23PPV vaccine; each dose also includes ≤1.25 mg of phenol as a preservative in a buffered solution of sodium chloride, disodium phosphate dihydrate and sodium dihydrogen phosphate dihydrate.

15.4.2 Efficacy and effectiveness

13-valent pneumococcal conjugate vaccine (PCV13)

Immunogenicity

Immunogenicity studies for PCV13 showed high levels of functional antibody not inferior to those induced by PCV7 for the common serotypes, and a comparable antibody response for the additional serotypes (including 19A).[24, 25, 26, 27]

Impact on nasopharyngeal colonisation

A randomised double-blind trial in healthy infants compared the impact of PCV13 versus PCV7 on nasopharyngeal colonisation and immunogenicity.[28] Infants were randomised to receive either PCV7 or PCV13 at ages 2, 4, 6 and 12 months. PCV13 significantly reduced nasopharyngeal colonisation of the additional PCV13 serotypes 1, 6A, 7F and 19A; the cross-reacting serotype 6C; and the common PCV7 serotype 19F. It was comparable with PCV7 for all other common serotypes, except for serotype 5 where there were too few events to draw inference. Following the introduction of PCV13, reductions in nasopharyngeal colonisation by vaccine serotypes have been seen in early observational data from Alaska,[29] Italy[30] and France (in children with acute otitis media).[31]

PCV13 effectiveness

In an open-label clinical trial, Alaskan native children aged under 5 years were offered PCV13 as appropriate for age and prior history of PCV7 vaccination.[32] Following the introduction of PCV13, IPD caused by

PCV13 serotypes declined significantly from 31 to 7 cases. No cases of IPD caused by PCV13 serotypes occurred among children who received PCV13 vaccine (3680 person-follow-up years). There were seven PCV13 serotype cases among children who had not received the vaccine (5007 person-follow-up years). There were 52 all-type IPD cases in the study population in the period before the study (399 per 100,000) and nine cases after the study commenced (107 per 100,000).

Early data from the UK suggests that in children aged under 2 years, IPD due to PCV13 serotypes had halved one year after the vaccine was introduced.[33] Similarly, following the introduction of PCV13 vaccine in Norway,[21] the US[34] and Canada,[22] early data indicates reductions in IPD caused by PCV13 serotypes.

PCV7 was introduced to the Apulia region in Italy in 2006 and was replaced by PCV13 in 2010.[35] Comparing hospitalisation risk ratios for the pre-PCV years to the vaccination period, PCV effectiveness against vaccine-type IPD was 84.3 percent (95% CI: 84.0–84.6). There was an overall reduction in the number of pneumococcal disease-related hospitalisations, particularly for pneumococcal pneumonia (RR: 0.43, 95% CI: 0.21–0.90).

In the United States, PCV7 was licensed in 2000 and PCV13 in 2010. In a study of claims data for otitis media visit rates and related complication rates in children aged 6 years or younger, there was an overall downward trend in otitis media-related healthcare visits from 2001 to 2011.[36] In children aged under 2 years, there was a significant reduction in otitis media visit rates in 2010–2011, which coincided with the availability of PCV13.

Use of pneumococcal conjugate vaccines in older children and adults

PCV13 is safe and immunogenic when administered to healthy older children, regardless of previous PCV7 vaccination.[37] In the US and Europe, PCV13 licensure was extended in 2013 to older children aged 6–18 years. One dose is recommended in the US for children at risk of pneumococcal disease.[38]

There is little data on the effectiveness of pneumococcal conjugate vaccines in adults. PCV13 is immunogenic in adults aged over 50 years,[39] including adults aged over 70 years.[40] It is at least as immunogenic as 23PPV. Some studies suggest that 23PPV attenuates the immune

response to subsequent doses of PCV13.[40, 41] This attenuation is not seen if PCV13 is given before 23PPV.

Based on immunogenicity data, pneumococcal conjugate vaccines are likely to be effective at preventing pneumococcal disease in older children and adults, but data from ongoing clinical trials is needed before the precise role of these vaccines is defined for adults. However, priming adults with conjugate vaccines prior to any doses of 23PPV vaccine seems well supported. PCV13 is registered in New Zealand for adults aged 50 years and older. There are not expected to be any safety concerns in using PCV13 in ages outside of its registration.

Pneumococcal polysaccharide 23-valent vaccine (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 developed countries.

23PPV efficacy

Assessment of the efficacy of pneumococcal vaccination depends on whether immune-competent or immune-compromised 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.[42] 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.[43] However, a 2012 review of data from elderly populations concluded that that low

protection was possible but differences in study designs prevent definitive conclusions.[44]

15.4.3 Transport, storage and handling

Transport according to the *National Guidelines for Vaccine Storage and Distribution*.[45] Store at +2°C to +8°C. Do not freeze.

15.4.4 Dosage and administration

The dose of PCV13 and 23PPV is 0.5 mL, administered by intramuscular injection (see section 2.3). 23PPV can also be administered by subcutaneous injection (see section 2.3), but there is an increased likelihood of injection site reactions.[46] (See also section 1.4.2.)

Co-administration with other vaccines

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 2.3). The exception is the quadrivalent meningococcal conjugate vaccine MCV4-D, which should be given at least four weeks after PCV13. (See section 12.4.4.)

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 6–59 months. Separation of the vaccines by two days can be offered, but is not essential. Systemic reactions have been noted in adults aged over 65 years. (See sections 15.6.2 and 15.7.2.)

Recent evidence[47] suggests that herpes zoster vaccine can be concomitantly delivered with 23PPV, despite earlier research to the contrary. (See section 22.4.4.)

15.5 Recommended immunisation schedule

See Table 15.5 for an overall summary of pneumococcal vaccination recommendations.

15.5.1 Healthy children

A primary course of PCV13 vaccine is given at ages 6 weeks, 3 months and 5 months, followed by a booster dose at age 15 months. Children who have started their immunisation course on PCV10 can complete it with PCV13.

Where a previously unimmunised healthy child presents late for pneumococcal vaccination, the age-appropriate catch-up schedules in Appendix 2 should be followed.

15.5.2 High-risk children aged under 5 years

PCV13 and 23PPV are funded for the high-risk children aged under 5 years listed in Table 15.3 below. See Table 15.5 for the funded vaccine recommendations and schedules for high-risk children, and sections 4.2 and 4.3 for more information.

Table 15.3: Children aged under 5 years at high risk of pneumococcal disease (funded)

PCV13 and 23PPV are funded for high-risk children aged under 5 years:
· on immunosuppressive therapy or radiation therapy, including children immunosuppressed following organ transplantation
· with primary immune deficiencies
· with HIV infection
· with renal failure and/or nephrotic syndrome
· with intracranial shunts
· with cochlear implants
· with cerebrospinal fluid leaks
· receiving corticosteroid therapy for more than two 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 are preterm infants with chronic lung disease
· with cardiac disease, with cyanosis or failure
· with diabetes
· with Down syndrome
· who are pre-or post-splenectomy, or with functional asplenia*

* See also section 4.3.4 and the individual disease chapters for meningococcal conjugate, Hib, influenza and varicella vaccine recommendations for asplenic children.

PCV13

A primary course of PCV13 vaccine is given to all children at ages 6 weeks, 3 months and 5 months, followed by a booster dose at age 15 months. High-risk children who have started their immunisation course with PCV10 may complete it with PCV13. High-risk children who have previously received four doses of PCV10 may receive one dose of PCV13. (See Table 15.5.)

23PPV

One dose of 23PPV is given from age 2 years, and at least eight weeks after the last dose of PCV13. If the risk persists, revaccination once with 23PPV is recommended five years after the first 23PPV. (See Table 15.5.)

15.5.3 Older children and adults at higher risk of pneumococcal disease

Older children and adults[48] at higher risk of pneumococcal disease include those in Table 15.4 below. (See Table 15.5 for vaccine recommendations (funded and unfunded) and schedules.)

Table 15.4: Older children and adults at higher risk of pneumococcal disease

Older children and adults at higher risk of pneumococcal disease are:
· individuals of any age who are pre-or post-splenectomy or with functional asplenia*
· immune-competent individuals at increased risk of pneumococcal disease or its complications because of chronic illness (eg, chronic cardiac, renal, liver or pulmonary disease, diabetes or alcoholism)
· individuals with cerebrospinal fluid leak
· immune-compromised individuals at increased risk of pneumococcal disease (eg, those with nephrotic syndrome, multiple myeloma, lymphoma and Hodgkin's disease, or those who are immunosuppressed following organ transplantation)
· individuals with HIV infection
· individuals who have had one episode of invasive pneumococcal disease
· individuals with cochlear implants
· individuals aged 65 years and older.

* See also section 4.3.4 and the individual disease chapters for meningococcal conjugate, Hib, influenza and varicella vaccine recommendations for asplenic individuals.

PCV13

One dose of PCV13 is recommended for older children and adults at higher risk of pneumococcal disease.

23PPV

One dose of 23PPV is recommended for older children and adults at higher risk of pneumococcal disease. Revaccination with polysaccharide vaccine (23PPV) is recommended after five years in children and adults belonging to high-risk groups, including post-splenectomy, who frequently exhibit a poor immune response.[49] A maximum of three 23PPV doses is recommended in a lifetime.

15.5.4 (Re-)vaccination

Age-appropriate pneumococcal conjugate vaccine is funded for (re-)vaccination of children aged under 18 years:

- with HIV
- who are post-haematopoietic stem cell transplant (HSCT) or chemotherapy
- who are pre- or post-splenectomy, or with functional asplenia
- who are pre- or post-solid organ transplant, renal dialysis and other severely immunosuppressive regimens.

(See also sections 4.2 and 4.3.)

15.5.5 Summary of pneumococcal vaccine schedules

Table 15.5 below summarises the pneumococcal vaccine recommendations (funded and unfunded) and schedules.

Table 15.5: Summary of pneumococcal vaccine recommendations (funded and unfunded) and schedules

Note: Funded vaccines are in the shaded rows. See the Pharmaceutical Schedule (www.pharmac.health.nz) for the number of funded doses and any changes to the funding decisions.

National Immunisation Schedule (funded)	
Children aged <5 years	PCV13, at age 6 weeks, 3, 5 and 15 months, or age-appropriate catch-up schedule (see Appendix 2).
High-risk children aged under 5 years (funded)	
Children aged <5 years who meet the high-risk pneumococcal immunisation criteria[a]	PCV13,[b] at age 6 weeks, 3, 5 and 15 months or age-appropriate catch-up schedule, as follows: · 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 · children aged ≥12 months[c] who have completed the primary course of PCV10 require 1 dose of PCV13[b] · previously unimmunised high-risk children aged ≥12 months require 2 doses of PCV13,[b] 8 weeks apart. 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.
High-risk children aged 5 to under 18 years (funded and unfunded)	
Children aged 5 to <18 years with functional asplenia or who are pre- or post-splenectomy,[a,d] or who meet the PCV (re-) vaccination criteria	1 dose of PCV13.[b,e] Followed by 1 dose of 23PPV at least 8 weeks after the PCV13 dose. Revaccinate once with 23PPV, 5 years after the 1st 23PPV.

Continued overleaf

Children aged 5 to <18 years with other high-risk conditions	1 dose of PCV13.[b,e] 1 dose of 23PPV at least 8 weeks after the PCV13 dose. Revaccinate once with 23PPV, 5 years after the 1st 23PPV.
High-risk adults aged ³ 18 years (funded and unfunded)	
Adults (≥18 years) who are pre- or post-splenectomy[a,d] or with functional asplenia	1 dose of PCV13.[b,e] 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.
Recommended but not funded	
Adults ≥18 years with high-risk conditions	1 dose of PCV13.[b,e] Give a maximum of 3 doses of 23PPV in a lifetime. 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.
Adults ≥65 years with no risk factors	1 dose of PCV13.[b,e] 1 dose of 23PPV, given at least 8 weeks after PCV13.

a See also section 4.3.4 and the individual disease chapters for meningococcal conjugate, Hib, influenza and varicella vaccine recommendations for asplenic individuals.

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

c There are no safety concerns, regardless of the interval between the last dose of PCV10 and the first dose of PCV13.

d Where possible, the vaccines should be administered at least 14 days before splenectomy.

e PCV13 is registered for children aged under 5 years and adults aged 50 years and older. There is emerging but limited efficacy data for PCV13 use outside of these age ranges. However PCV13 can also be used for older children and adults with high-risk conditions.

15.6 Contraindications and precautions

15.6.1 Contraindications

See section 1.4 for general contraindications for all vaccines. 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

PCV13

- Systemic reactions (chills, rash and myalgia) may occur when PCV13 and influenza vaccine are administered at the same time (see section 15.7.2). PCV13 has been associated with increased risk of fever over 39°C and febrile convulsions when co-administered with inactivated influenza vaccine in infants and young children (see section 15.7.2). Febrile convulsion history is not a contraindication to PCV13 immunisation. Parents/guardians can be encouraged to use cooling measures and/or antipyretics (see section 2.3.13) if a child with a history of febrile convulsions develops a fever after immunisation. If a child aged under 5 years needs both PCV13 and influenza vaccines, separation of vaccines by two days can be offered. If the child has a history of febrile convulsions, separation of the vaccines is recommended.
- PCV13 should be used with caution in very premature babies (born at under 28 weeks' gestation) as there is a potential risk for apnoea. 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,[50] but do not avoid or delay immunisation.
- 23PPV should not be given to children aged under 2 years due to the reduced immune response associated with polysaccharide vaccines (see section 1.2.3).

15.7 Expected responses and adverse events following immunisation (AEFI)

Always check the manufacturers' data sheets if further information is required.

15.7.1 Expected responses

PCV13

The most commonly reported adverse reactions are injection-site reactions, fever, irritability, decreased appetite, and increased and/or decreased sleep.[51] 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.[51]

23PPV

Local discomfort, erythema and induration lasting a couple of days are expected responses.[52] Revaccination is not associated with an increase in systemic events.[53, 54] A large study compared hospitalisation rates after first or repeat vaccination and found no significant difference.[55] Therefore, it appears that revaccination may be safely given, with a small increased risk of self-limiting, large local reactions.

15.7.2 Adverse events following immunisation

PCV13

Rare events (≥0.01 percent and <0.1 percent) include hypersensitivity reactions, including face oedema, dyspnoea, bronchospasm, febrile seizures and hypotonic-hyporesponsive episode. Very rare events (<0.01 percent) include urticaria or urticaria-like rash, erythema multiforme, and hypersensitivity, including anaphylaxis.

During the 2010/11 influenza season in the US, PCV13 co-administered with inactivated influenza vaccine was associated with increased risk of fever over 39°C and febrile convulsions in children aged 6 to 59 months.[56] Concomitant administration of PCV13 with inactivated influenza vaccine doubled the incidence risk ratio from 2.4 and 2.5, respectively, to 5.9 when given together in this age group. The bioCSL-manufactured influenza vaccines that were associated with febrile events in the southern hemisphere in 2010 (see section 10.7) were not recommended for this age group in the US. The study does not note which brands of influenza vaccines were used.

PCV13 has been evaluated when co-administered with trivalent influenza vaccine in adults aged 65 years and older. Systemic reactions were more common (chills, rash and myalgia) after administration of both vaccines, but were low in severity. No serious events were vaccine related.[57]

23PPV

Adverse events requiring a GP consultation occur in approximately 8 per 1000 vaccinations, and more severe adverse events in 1 per 100,000.[58]

15.8 Public health measures

Invasive pneumococcal disease is a notifiable condition, and if confirmed, the laboratory undertaking the testing must notify the local medical officer of health.

Antimicrobial prophylaxis is not indicated for close contacts of cases of invasive pneumococcal disease. 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.

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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 the immune compromised).
Global burden of disease	Endemic in Afghanistan, Nigeria and Pakistan. Outbreaks are still frequent (see www.polioeradication.org/Dataandmonitoring.aspx).
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).
Funded immunisation 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, 2 doses of IPV 4 weeks apart, followed by a third dose 6 months later.
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.[1]

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 immunosuppressed 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.[2]

16.3 Epidemiology

16.3.1 Global burden of disease

In the pre-vaccination era, cases of poliomyelitis occurred sporadically and in epidemics in developed countries of 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.

In 2012 the lowest number of new polio cases (223), from the lowest number of countries, were reported than at any previous time in history.[1] Cases increased in 2013 (385), mainly due to an outbreak in the Horn of Africa (207 cases) affecting previously polio-free countries (Somalia, Kenya, Ethiopia and South Sudan). Cases have also emerged in Syria, and a comprehensive outbreak response has been implemented there. Polio remains endemic in Afghanistan, Nigeria and Pakistan. Compared to 2012 there were 28 percent fewer cases in these endemic countries in 2013 (157 cases).[3]

Vaccine-associated paralytic poliomyelitis (VAPP) with OPV

After receiving oral poliomyelitis vaccine (OPV), most infants excrete the polio vaccine virus for about six weeks. Their family and other contacts are exposed to the vaccine virus and the contacts may 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) from 7 to 30 days after vaccination in the recipient and from 7 to 60 days in the contact of a vaccine recipient. The immunosuppressed are more likely to suffer VAPP, whether they receive vaccine or acquire infection as a contact.

VAPP presenting in New Zealand can only occur from contact with people vaccinated in countries still using OPV. The risk of importing wild-type or neurovirulent oral vaccine-derived strains means that maintaining high inactivated poliomyelitis vaccine (IPV) coverage in New Zealand is essential.

Once the wild virus became uncommon and restricted to specific countries, 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.[4]

16.3.2 Global poliomyelitis eradication

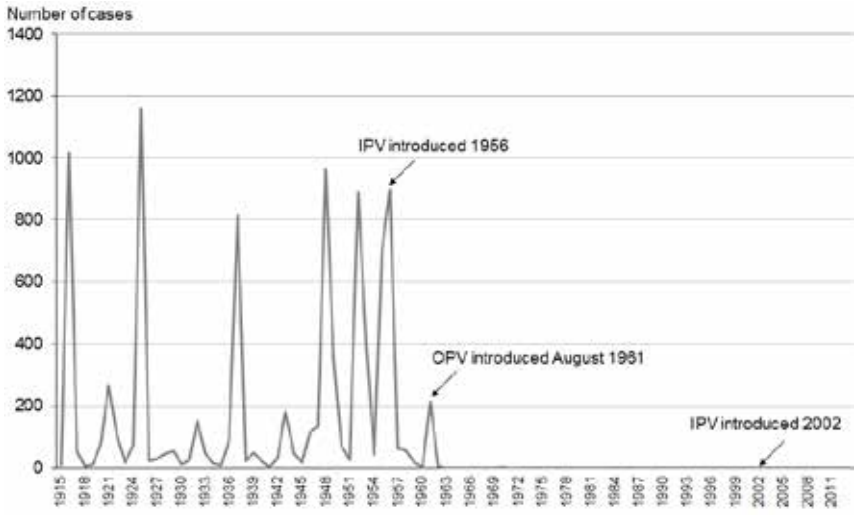
In 2012 the World Health Assembly declared the persistence of polio 'a programmatic emergency for global public health' and called on the WHO to develop a comprehensive polio end game strategy. The *Polio Eradication & Endgame Strategic Plan 2013–2018*[1] was developed by the Global Polio Eradication 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.

16.3.3 New Zealand epidemiology

New Zealand has been free of wild-type polio for about 50 years (see Figure 16.1). Since 1962 only six polio cases have been reported.[5] Four of these cases were laboratory confirmed as VAPP and two were classified as probable VAPP. There were no polio notifications in 2013.

Figure 16.1: Numbers of cases of poliomyelitis, 1915–2013



Key: IPV – inactivated polio vaccine; OPV – oral polio vaccine.

Source: Ministry of Health and the Institute of Environmental Science and Research

The New Zealand Paediatric Surveillance Unit carries out active surveillance of AFP. In 2012 there were eight cases of AFP notified to the Unit. All cases have been reviewed by the New Zealand National Certification Committee for the Eradication of Polio (NCCEP) and all have been classified as non-polio.[5]

16.4 Vaccines

New Zealand switched from oral polio vaccine (OPV) to inactivated polio vaccine (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-aventis NZ Ltd): contains three strains of poliovirus (40D antigen units of the Mahoney, 8D 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 vaccines

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

- DTaP-IPV: Quadracel (Sanofi-aventis NZ Ltd)
- Tdap-IPV: Boostrix-IPV (GSK) and Adacel Polio (Sanofi-aventis NZ Ltd).

Oral poliomyelitis vaccine (OPV)

OPV is no longer used in New Zealand. OPV continues to be used in many countries because it remains the vaccine for the WHO Expanded Programme on Immunization, but the WHO plans to withdraw this vaccine worldwide by 2019/20[1] (see section 16.3.2).

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 will seroconvert after three doses of IPV vaccine, and more than 85 percent will seroconvert after two doses. The efficacy of IPV is greater than 90 percent.[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.[6]

Duration of protection

Available data indicates the persistence of antibodies up to school age, following two or three doses of IPV-containing vaccine in the first year of life and a booster in the second year. There is no data beyond this because a preschool booster is given at this time. There is a strong anamnestic response to this preschool booster and it is expected to confer long-term protection, possibly lifelong.[6]

16.4.3 Transport, storage and handling

Transport according to the *National Guidelines for Vaccine Storage and Distribution*.[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, it may be kept at room temperature for up to eight hours but discarded after that time.

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 2.3).

The dose of monovalent IPV (IPOL) is 0.5 mL, administered by subcutaneous injection (see section 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

16.5.1 Usual childhood schedule

A primary course of poliomyelitis 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 Preterm infants

Preterm infants who are still in hospital at age 6 weeks should receive IPV as DTaP-IPV-HepB/Hib, as per the Schedule, at the usual chronological age.

16.5.3 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 four weeks between the first two doses, followed by the third dose approximately six months later (see Appendix 2). However, if necessary they may be given with a minimum of four weeks between doses.

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. It is not necessary in this situation to start the full IPV series, and it is acceptable to continue the series using IPV for the final doses.

Note: all immunosuppressed individuals and their household contacts may receive IPV. OPV was contraindicated in the immunosuppressed because of the risk of VAPP (see section 16.3.1). There is no risk of VAPP with IPV.

16.5.4 (Re-)vaccination

Polio-containing vaccine is funded for (re-)vaccination following immunosuppression. See also sections 4.2 and 4.3.

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 14.6 for information about DTaP-IPV-HepB/Hib vaccine.

16.6.1 Contraindications

See section 1.4 for general contraindications for all vaccines. 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.

16.6.2 Precautions

Pregnancy

No adverse effects on the fetus have been reported following administration of polio vaccine 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, then two doses should be administered four weeks apart prior to departure. If departure cannot be delayed to allow a four-week gap, then two doses should be given 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.

16.7 Expected responses and adverse events following immunisation (AEFI)

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.[6] There is no poliovirus excretion following IPV.

16.7.2 Adverse events following immunisation

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. IPV-containing vaccines are licensed in more than 100 countries, and approximately 25 to 30 million newborn infants and approximately 15 million children, adolescents and adults receive them every year.[6] There has been no association found with subsequent polio, Guillain-Barré syndrome, anaphylaxis or other serious reaction.

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 the Institute of Environmental Science and Research (ESR). Contact the polio reference laboratory for specific advice on the specimens required, and on packing and transporting the specimens (see also www.esr.cri.nz/SiteCollectionDocuments/ESR/PDF/Health/ESR%20Request%20Form%20Human.pdf).

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 (NZPSU). 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.[8] The NZPSU 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 (PHEIC), and the Director of Public Health at the Ministry of Health should be contacted urgently. The *National Poliomyelitis Response Plan for New Zealand* 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).

For more details on control measures, refer to the *Communicable Disease Control Manual 2012*[9] or the *Control of Communicable Diseases Manual*.[10]

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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	Immediately before, and up to 1–2 weeks after, the onset of symptoms.
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	RV5 (RotaTeq), a live attenuated, orally administered, pentavalent vaccine.
Funded immunisation schedule	At ages 6 weeks, 3 and 5 months. For catch-up schedules, the first dose should be given before age 15 weeks and the third dose should be given by age 8 months and 0 days.
Vaccine efficacy/ effectiveness	High effectiveness against severe rotavirus diarrhoea; some evidence for efficacy against all-cause diarrhoea and for herd protection.
Contraindications	Acute or moderate gastroenteritis. With conditions that predispose the infant to intussusception. Severe combined immune deficiency.
Adverse events to vaccine	Potentially a very small risk for intussusception; the benefits of immunisation outweigh this potential risk.

17.1 Virology

The rotaviruses are segmented, double-stranded RNA viruses of the family Reoviridae.[1] They possess two independent neutralising antigens on the outer capsid, VP4 protease cleaved haemagglutinin (P) and VP7 glycoprotein (G), which allows for a binary classification system. While more than 60 G-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.[2]

17.2 Clinical features

Rotavirus infects almost all children during infancy or early childhood. Transmission occurs through the faecal–oral route both 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, 3] Up to one-third of children will develop a fever of >39°C.[4, 5] The illness lasts from three to eight days. Children with rotavirus are infectious immediately before, and up to one to two weeks after, the onset of symptoms. Large quantities of rotavirus are shed in the stool, and few virions are required to cause infection in a susceptible host.[6]

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, 7]

Severe dehydrating gastroenteritis caused by rotavirus occurs predominantly in infants and children aged 3 months to 2 years.[2] 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 developed and developing 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[8, 9] and results in 2.4 million paediatric hospital admissions.[10] Virtually all of the deaths occur in developing countries. Prior to the introduction of licensed rotavirus vaccines in developed countries, more than 220,000 children were hospitalised with rotavirus gastroenteritis every year.[11, 12]

Rates of rotavirus illness in children in developed and developing countries are similar, 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, 13, 14, 15, 16] Rotavirus gastroenteritis is not, however, more severe in HIV-infected children, although viral shedding may be longer.[2]

Rotavirus is an important cause of hospital-acquired infection[17] and can also cause disease in adults, especially those caring for children[18] 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.[19] 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, and more than three-quarters are protected against subsequent rotavirus gastroenteritis and 85–90 percent against severe rotavirus gastroenteritis.[20] The proportion with protection against both infection and symptomatic rotavirus gastroenteritis increases with successive episodes.[20]

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 and gastroenteritis are incompletely understood, it is likely that both mucosal and serum antibodies are associated with protection against rotavirus infection and disease.[21]

17.3.2 New Zealand epidemiology

At present rotavirus is not a notifiable disease, so there is no national surveillance data available. Data estimates of the burden of disease predict that by the age of 5 years, 1 in 5 children will have sought medical advice for rotavirus gastroenteritis and 1 in 43 children will be hospitalised.[11]

Data was collected prospectively on children aged under 3 years with acute diarrhoea who were admitted to eight hospitals in New Zealand from 1 May 1998 to 30 April 2000. The estimated national hospitalisation rate for rotavirus diarrhoea in children aged under 3 years, standardised for age and season, was 634 per 100,000 (95% CI: 597–672).[22]

Of the 2019 hospitalised children enrolled in the study, 1138 had stools available for testing, of which 485 (42.5 percent) tested rotavirus positive. Rotavirus detection in stool samples varied significantly by age (27 percent of stool samples from infants aged 0 to 5 months, 43 percent from children aged 6 to 11 months, and 52 percent from children aged 12 to 35 months; $p < 0.001$). A winter peak was apparent, with rotavirus detected in 51 percent of the samples collected during winter/spring compared with 25 percent during summer/autumn ($p < 0.001$).[22]

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. There are two vaccines registered (approved for use) and available (marketed) in New Zealand. Both are orally administered, live attenuated vaccines. The live attenuated vaccine viruses replicate in the intestinal mucosa and are shed in the stools of vaccine recipients.[23, 24, 25]

Funded vaccine

RV5 (RotaTeq, MSD) is a pentavalent bovine–human reassortant vaccine representing the common viral protein types G1–4 and P[8]. Each dose contains at least 2.0 x 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.

Other vaccine

The other rotavirus vaccine registered and available in New Zealand is:

- RV1 (Rotarix, GSK), which is a monovalent human G1 rotavirus vaccine; each dose contains at least 10^6 $CCID_{50}$ (cell culture infective dose 50 percent) after reconstitution; other components and residuals include sucrose, disodium adipate and culture medium.

17.4.2 Efficacy and effectiveness

Prevention of disease

A 2012 Cochrane review[26] 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 probably have an effect on severe all-cause diarrhoea (moderate to low quality of evidence).

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)	2344 (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)	3190 (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)	1029 (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)	5916 (1)	Low

Source: 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).

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.[27]

Cross-protection

Rotavirus vaccine strains vary considerably, and multiple strains can occur at the same time. In developed countries, both vaccines appear to provide some cross-protection against non-vaccine serotypes.[28, 29]

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.[30] 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 developing countries.[31, 32]

Effectiveness

Post-licensure surveillance studies have demonstrated large reductions in rotavirus-positive stool isolates from children with gastroenteritis (US)[2] and in diarrhoea-related deaths (Mexico).[33, 34] 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.[35]

Following vaccination, vaccine viruses are shed in the stool and they may be transmitted from vaccinated to unvaccinated children. This may contribute to providing herd immunity.[36] Post-market surveillance studies in the US[2, 37] and Australia[38] have shown significant declines in rotavirus gastroenteritis among unvaccinated populations, suggesting indirect benefits from reduced transmission in the community. Herd immunity effects have also been noted after routine vaccination in El Salvador, Panama, Mexico and Austria.[39]

17.4.3 Transport, storage and handling

Transport according to the *National Guidelines for Vaccine Storage and Distribution*.[40] Store in the dark at +2°C to +8°C. Do not freeze.

17.4.4 Dosage and administration

The dose of RV5 (RotaTeq) is 2.0 mL, administered orally (see the package insert for administration instructions).

The three-dose course should be started before age 15 weeks (ie, 14 weeks and 6 days) and completed by age 8 months and 0 days. If a partially vaccinated infant reaches age 8 months before the third dose is given, the first or second doses already given will offer them some protection against disease.

Co-administration with other vaccines

Rotavirus vaccines can be administered at the same time as other scheduled vaccines.

Interchangeability

Some infants may have commenced their immunisation course with RV1. There is no data on the interchangeability of RV1 and RV5. 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 defined in section 17.5.2 below, are met.

17.5 Recommended immunisation schedule

RV5 is recommended (and funded) for all infants. (See section 17.5.2 for RV5 age limit information.)

Immunisation is especially encouraged for those who will be attending early childhood education services or where there is an immune-compromised 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, 20]

17.5.1 Routine schedule

Three RV5 doses are given orally, at ages 6 weeks, 3 and 5 months.

17.5.2 Catch-up schedules

The first dose of RV5 should be given before age 15 weeks (ie, 14 weeks and 6 days), with subsequent doses administered at a minimum dose interval of four weeks. 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 remainder of the series should be completed, but all three doses should be given by age 8 months and 0 days.[1] 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.

17.5.3 Preterm infants

It is best to vaccinate preterm infants as they leave hospital. However, if discharge is not anticipated before age 15 weeks, then giving rotavirus vaccine in hospital is acceptable. If the standard universal precautions are maintained, administration of rotavirus vaccine to hospitalised infants, including hospitalised preterm infants, would be expected to carry a low risk for transmission of vaccine viruses.[41]

17.6 Contraindications and precautions

17.6.1 Contraindications

- Rotavirus vaccine should not be given to infants with acute moderate or severe gastroenteritis until the condition improves.
- If a dose of rotavirus vaccine is regurgitated or vomited, a repeat dose *should not be given*. Remaining doses should be administered as recommended.

- Rotavirus vaccine should not be given to infants with a history of a severe allergic reaction after a previous dose or to a vaccine component. RV5 is preferred over RV1 in infants with or at risk of latex allergy (eg, with spina bifida or bladder extrophy) as the RV1 applicator contains latex.
- Rotavirus vaccines should not be given to infants with a history of an uncorrected congenital malformation of the gastrointestinal tract that would predispose the infant to intussusceptions[2] (see section 17.7.1).
- Rotavirus vaccine should not be given to infants with severe combined immune-deficiency syndrome.[42]

17.6.2 Precautions

Rotavirus vaccine can be administered to infants with a mild illness, including gastroenteritis and upper respiratory tract infections.

Because both rotavirus vaccines are live attenuated, the safety of immune-compromised patients and their contacts is an important consideration. Shedding of vaccine virus in the stool is possible, and is more likely with RV1[43] and in immune-compromised 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.

So far there are no safety concerns, but there is also no data to confirm the safety of these vaccines for immune-compromised patients. The potential risk of transmission of vaccine virus should be weighed against the risk of acquiring and transmitting natural rotavirus. Contacts of vaccinees should observe careful hygiene measures when changing infants' nappies.[44]

17.7 Expected responses and adverse events following immunisation (AEFI)

The 2012 Cochrane review[26] described above 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.[44]

17.7.1 Intussusception

Intussusception is a cause of an acute abdomen when one part of the intestine slides into another part of the intestine. 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 5000–10,000 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. New evidence from Australia[45] indicates that after the first dose, RV5 had a relative incidence (relative risk) of 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 periods of 1 to 7 days and 8 to 21 days after vaccination, respectively. For RV1, the relative incidence was 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 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 RV5 was 2.8 (95% CI: 1.2–6.8, p = 0.02) and for RV1 it was 2.8 (95% CI: 1.1–7.3, p = 0.03). There was no evidence of increased risk of intussusception following a third dose of RV5.[45]

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.[45]

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.[46] 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.[47] Both the World Health Organization[48] and the Australian Technical Advisory Group on Immunisation (ATAGI)[46] continue to recommend the use of rotavirus vaccine for infants.

17.8 Public health measures

Rotavirus cannot be diagnosed solely on clinical presentation; stool antigen testing is required. However, often testing is not performed because treatment is for symptoms and for dehydration. Treatment is supportive, and oral rehydration is preferred. (For further details on management, see *Starship Clinical Guidelines: Gastroenteritis,* at www.adhb.govt.nz/starshipclinicalguidelines/Gastroenteritis.htm) Pedialyte is the preferred oral rehydration solution in New Zealand. Early initiation of re-feeding is also important.[49]

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 soap and water. Disinfectants (eg, 70 percent ethanol) inactivate rotavirus and may help to prevent disease transmission resulting from contact with environmental surfaces.[44]

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18 Rubella

Key information

Mode of transmission	By direct or droplet 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	A live attenuated vaccine (MMR II), containing measles, mumps and rubella viruses.
Funded immunisation schedule	Children at ages 15 months and 4 years. Adults who are susceptible to 1 or more of measles, mumps and rubella.
Serological testing	Rubella is rare in New Zealand, and so: · routine serological testing of children after vaccination is not indicated · women planning to get pregnant should know their rubella immunity status – serological testing for rubella immunity is part of routine antenatal care · pregnant women with a rubella antibody level <10 IU/mL should avoid contact with known cases of rubella, and should receive MMR after delivery (if they have not already received 2 doses of a rubella-containing vaccine).
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*.[1]

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 6000 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. A history of rubella should never be accepted as proof of immunity without laboratory confirmation.

Transmission of rubella is through direct or droplet contact with infected nasopharyngeal secretions. 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 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.

Maternal rubella 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 the congenital rubella syndrome (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 below and Table 11.1).

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	8055 (40%)
Deaf–blind children	3580 (18%)
Intellectually handicapped children	1790 (9%)

Source: Adapted from Reef S, Plotkin SA. 2013. Rubella vaccine. In: Plotkin SA, Orenstein WA, Offit PA (eds). *Vaccines* (6th edition). 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. Asymptomatic infection is common. In the pre-vaccine era the highest incidence of clinical cases occurred in the spring among 5- to 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 significant reduction, especially where there is extensive use of the rubella vaccine.

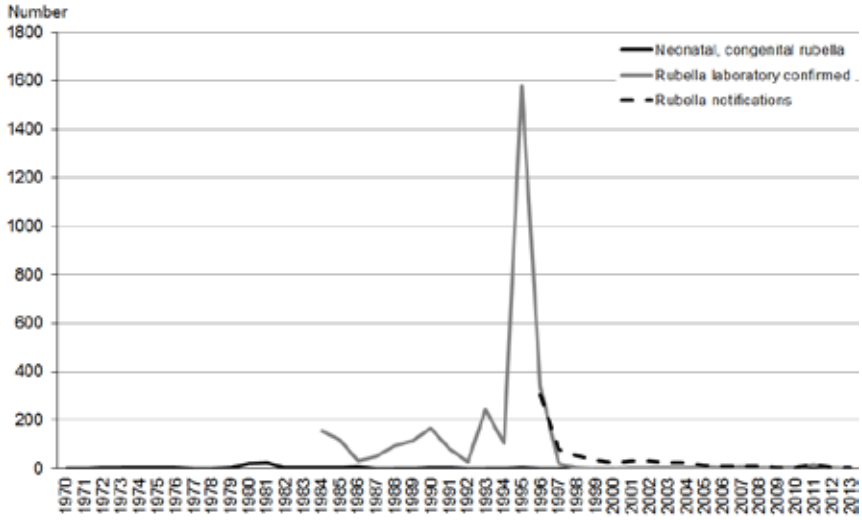
18.3.2 New Zealand epidemiology

Rubella immunisation was introduced in 1970 (see Appendix 1) and rubella has been a notifiable disease since 1996. The last 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.

In 2013 there was one notified case of rubella and no laboratory-confirmed cases. Four cases of rubella were notified in 2012, of which three were laboratory confirmed.[2] Since the last rubella outbreak there has been a steady decrease in the number of cases notified each year, except for an increase in notifications in 2011 (22 cases) during the measles outbreak (Figure 18.1). All cases in 2012 were in males: two from the 1–4 years age group, and one each from the 20–29 years and 40–49 years age groups. Of the two cases for which risk factor information was recorded, one reported overseas travel during the incubation period for this disease. One hospitalisation and no deaths due to rubella were reported.

There have been no reported cases of CRS in New Zealand since 1998.

Figure 18.1: Notifications of congenital rubella, 1970–2012, notifications of rubella 1996–2013, and laboratory-confirmed cases, 1984–2013



Source: Ministry of Health and the Institute of Environmental Science and Research

18.4 Vaccines

18.4.1 Available vaccines

Rubella vaccine is one of the components of the live attenuated measles-mumps-rubella (MMR) and measles-mumps-rubella-varicella (MMRV) vaccines, considered in sections 11.4.1 and 21.4.1. Single-antigen rubella vaccine is no longer available in New Zealand.

Funded vaccine

MMR vaccine funded as part of the Schedule is MMR II (MSD), which contains further attenuated Enders' Edmonston (Moraten) strain measles, RA 27/3 rubella, and Jeryl Lynn mumps. (See section 11.4.1 for more information.)

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, 3] 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 Guidelines for Vaccine Storage and Distribution*.[4] Store in the dark 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 in the dark 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 in the deltoid area to all age groups (see section 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.

18.5 Recommended immunisation schedule

As in other developed countries, New Zealand's primary strategy for preventing and eventually eliminating rubella is to vaccinate both boys and girls with two doses of MMR. This strategy is backed up by checking the immune status of pregnant, or about to become pregnant, women and some health care and child care workers. Non-immune women can then be offered up to two more doses of vaccine.

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 should prevent the circulation of rubella (which is less infectious than measles) and therefore lead to the elimination of both rubella and CRS.

18.5.1 Children

Two doses of rubella vaccine as MMR are recommended at age 15 months and age 4 years. 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 Women planning pregnancy and pregnant women

It is recommended that women be screened for rubella immunoglobulin G (IgG) antibody when pregnancy is planned (not funded) or in the antenatal period of every pregnancy (funded); see section 18.5.4. This is to provide a baseline level of information in the very rare event of them being exposed during the early part of pregnancy, when the risks and consequences of CRS are greatest. It also indicates a need for vaccination, if non-immune, with two doses of MMR (funded) when not pregnant.

The following groups of women are more likely to be seronegative 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
- non-English-speaking women
- women over the age of 35 years.

CRS is less likely after reinfection with rubella in pregnancy compared with a primary infection. It is estimated that the prevalence of CRS is 85 percent after primary infection of the mother, and 5 percent after reinfection with rubella in the first trimester. The risk of CRS is negligible after 16 weeks of pregnancy.[6]

Pregnant women with a rubella antibody level below 10 IU/mL (see section 18.5.4) should be advised to avoid situations in early pregnancy where contact with rubella is more likely, such as with overseas travel to countries with endemic disease or known outbreaks. If the antibody level is below 10 IU/mL, the woman should be offered MMR after delivery if she has not already received two doses of a rubella-containing vaccine as an adult (funded).

If MMR vaccine and anti-D immunoglobulin are required after delivery, both the vaccine and anti-D immunoglobulin 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 immunoglobulin 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. Rubella serology should be checked in women six to eight weeks after MMR vaccination to ensure that seroconversion has occurred; give a single further dose of MMR if it has not. There is no risk to the mother or child in giving MMR to breastfeeding women.[1]

18.5.3 Other adults

If an individual has no documented history of immunisation with MMR, they should be given two doses of MMR four weeks apart (funded) rather than performing serology. There are no significant adverse effects from 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

Over 95 percent of individuals will become immune to rubella after two doses of a rubella-containing vaccine. While most developed countries have for many years included rubella vaccination on their immunisation schedules, this has not been the case for low- and middle-income countries such as those in the Pacific Islands, although these countries may have had single-antigen measles vaccine. Surveys of susceptibility to rubella in women of childbearing age have found rates greater than 25 percent in India, Israel, Malaysia, Nigeria, Singapore, Sri Lanka and Thailand, and rates of 10–25 percent in many African, Middle Eastern and South American countries.

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 1 year, should be offered either one or two doses (four weeks apart) to bring them up to two doses (funded if eligible). 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.

Health care workers and students

Health care workers and students without a documented history of two doses of MMR vaccine or documented rubella antibody IgG (see section 18.5.4) are recommended (and funded) to receive two doses of MMR vaccine (four weeks apart), which are needed to provide protection against the three diseases.

18.5.4 Immunity testing and interpretation

A person is considered to be immune to rubella if he or she has received two documented doses of MMR, or their immunity is proven through serological testing as an adult. (Routine serological testing of children after vaccination is not indicated.)

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.

Serological testing is not usually performed except as part of routine antenatal care (funded) or for women who are planning pregnancy (not funded). Where serological testing has been performed, the following guidelines apply.

The WHO cut-off for immunity is rubella IgG antibody levels above 10 IU/mL.[7] However, licensed assays do not always give consistent results between 5 and 10 IU/mL, the equivocal range. They can reliably detect immunity from past infection, but post-vaccination immunity is harder to measure reliably.[8] The previous edition of the *Handbook* recommended 15 IU/mL as providing a margin of error for the determination of protection, but in line with Australian and other recommendations we now recommend following the testing laboratory's interpretative comments.

If a person is found to be rubella IgG seronegative, vaccination should be offered according to the recommendations above. Those with equivocal results should be reassured that they are probably protected, but it would be wise to offer revaccination with up to two doses to obtain IgG levels above 10, preferably 20, IU/mL.

18.6 Contraindications and precautions

18.6.1 Contraindications

The general contraindications that apply to all immunisations are relevant to MMR (see sections 1.4 and 11.6.1).

Anaphylaxis to a previous dose of MMR, MMRV or any of the vaccine components (including neomycin and gelatin) is a contraindication to a further dose of MMR or MMRV.

MMR vaccine should not be given to women who are pregnant, and pregnancy should be avoided for four weeks after immunisation.[9] 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 adverse events following immunisation (AEFI)

See also section 11.7.

18.7.1 Expected responses

Mild reactions after immunisation with MMR vaccine include fever, sore throat, lymphadenopathy, rash, arthralgia and arthritis (see section 11.7.1). The prevalence of these side-effects is age related. Joint symptoms may be reported in 0–3 percent of children and 12–20 percent of adult women. 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.

It was previously thought that the rubella vaccine might lead to long-term arthritis. However, two large controlled studies found no supporting evidence of this.[10, 11] Another study did find a slight increase in risk from rubella vaccine, but this was of borderline statistical significance.[12] 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.[13]

18.7.2 Adverse events following immunisation

Immune thrombocytopenic purpura (ITP) and, rarely, neurological disturbances have been reported (see section 11.7.2).

18.8 Public health measures

Rubella (including congenital rubella syndrome) is a notifiable disease, and suspected cases should be notified by the clinician on suspicion to the local medical officer of health. Every effort should be made to make an accurate diagnosis in that person.

The preferred method of diagnosis is by PCR or culture (see Appendix 8), which can be performed in LabPlus (Auckland) and Canterbury Health Laboratories (Christchurch). 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 congenital rubella 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

Exclusion should be considered for unimmunised contacts from early childhood services, school or work. MMR should be given. Female staff should ensure they are immune to rubella.

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. Normal human immunoglobulin (NHIG) does not prevent rubella infection after exposure and should not be used for that purpose.[9]

The local medical officer of health will advise on contact management.

18.8.3 Management of pregnant contacts

Testing

It is critical to accurately document the rubella status of all people who may have rubella and potentially exposed a pregnant woman (see above). 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.

All women should have been routinely tested for the presence of rubella antibodies before or early in every pregnancy (see sections 18.5.2 and 18.5.4). If this result is available and the woman is known to be immune, she may be reassured.

An exposed pregnant woman with low anti-rubella antibody levels should have her serology repeated if she comes into contact with a probable or confirmed case of rubella; almost always this is someone who has recently arrived or returned from overseas.

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 that all requests to laboratories 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.

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.

Coordination of management

Coordinated care and management are essential (Table 18.2). Ideally this will be done by the woman's GP, who will liaise with the medical officer of health, an obstetrician and/or infectious diseases (ID) specialist and the LMC.

The routine use of immunoglobulin (IG) for post-exposure prophylaxis of rubella in early pregnancy is not recommended. It 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 *Communicable Disease Control Manual 2012*[14] or the *Control of Communicable Diseases Manual*.[15]

Table 18.2: Suggested roles of health professionals

	LMC	Medical officer of health	GP	Obstetrician/ ID specialist/ maternal fetal medicine specialist
Check rubella status in every pregnancy and vaccinate any woman who is not immune **AFTER delivery**	ü			
Investigate initial suspected rubella case and trace contacts		ü		
Coordinate care of exposed non-immune pregnant woman and arrange serology testing			ü	
Review clinical and laboratory results, and discuss options with the pregnant woman if rubella is confirmed				ü

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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).
Funded immunisation 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 pregnancy (from 28 to 38 weeks' gestation): Tdap.
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 developing countries.

19.3 Epidemiology

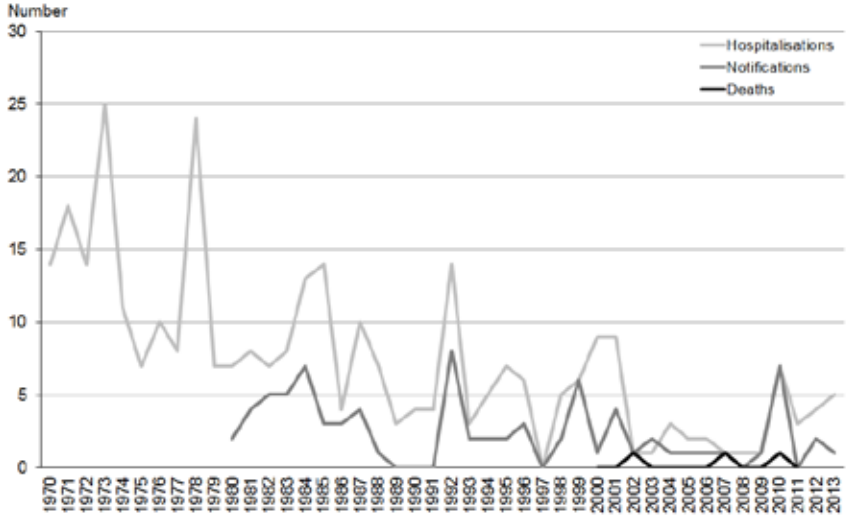
The incidence of tetanus reflects the effectiveness of the local immunisation programme, with low incidence in regions with high immunisation coverage. A person with tetanus is not infectious to others, and vaccination provides individual protection only, with no herd immunity. Suffering tetanus does not confer immunity. See section 19.5.2.

19.3.1 New Zealand epidemiology

One case of tetanus was notified in New Zealand in 2013 and two cases were notified in 2012. This is similar to the number of cases notified each year since 2002 (between zero and two cases each year), except in 2010, when seven cases were notified (Figure 19.1).[1] In 2012 one case was in the 5–9 years age group and the other in the 70 years and over age group. The child was not vaccinated and the adult was vaccinated over 20 years ago.

Ministry of Health data for 2013 recorded five hospitalisations (four females aged 60 years or older and one male in the 5–9 years age group) with tetanus as the primary reason for admission. This indicates that not all cases are notified, as illustrated in Figure 19.1 below.

Figure 19.1: Tetanus hospitalisations 1970–2013, tetanus notifications 1980–2013 and tetanus deaths 2000–2011



Source: Ministry of Health (hospitalisations and deaths) and the Institute of Environmental Science and Research (notifications)

Older adults without a primary course

Universal tetanus vaccine was introduced in 1960 (see Appendix 1). Of the 21 tetanus cases between 2001 and 2012, 17 were in adults. Of these, two were vaccinated (15 to 20 years previously), five were unvaccinated, and 10 had an unknown vaccination status. Nine of the individuals with an unknown vaccination status were born before 1960 and are therefore less likely to have received a primary series of tetanus vaccine.

Children

Between 2001 and 2012 there were four cases of tetanus in children aged between 1 and 9 years. None of the children were vaccinated.

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, bioCSL): 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:

- DTaP-IPV: Quadracel (Sanofi-aventis NZ Ltd)
- Tdap: Adacel (Sanofi-aventis NZ Ltd)
- Tdap-IPV: Boostrix-IPV (GSK) and Adacel Polio (Sanofi-aventis NZ Ltd).

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).[2]

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).[2] 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.[3]

(See also sections 5.4.2 and 14.4.2.)

19.4.3 Transport, storage and handling

Transport according to the *National Guidelines for Vaccine Storage and Distribution*.[4] 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, hold at room temperature for up to eight hours.

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 2.3).

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 immunoglobulins.

(See also section 14.4.4.)

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	Booster
65 years	Td	Booster

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. 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).

Dose intervals between Td and Tdap

No minimum interval between Td and Tdap is required,[5, 6, 7] unless Tdap is being given as part of a primary immunisation course.

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.

19.5.2 Adults and children from age 10 years

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). 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.

For children given a primary course as infants and a booster at age 4 years, a further booster of tetanus toxoid-containing vaccine is given at age 11 years as Tdap vaccine.

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.

People born before 1960 are less likely to have had a primary series of tetanus vaccine. GP visits at or around ages 45 and 65 years should be used to check on the immunisation history. If there is no reliable history of the patient having received a primary series, the vaccine at that episode should be considered the first of a funded primary series (both the vaccine and the administration are funded). The next two doses in the primary series should be given at four-week intervals, and a booster dose is recommended at least six months after the third dose (note that the vaccine is funded for the booster but not the administration).

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.[8]

Tdap boosters are also funded for pregnant women, from 28 to 38 weeks' gestation (see section 14.5.2).

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).

Dose intervals between Td and Tdap

No minimum interval between Td and Tdap is required,[5, 6, 7] unless Tdap is being given as part of a primary immunisation course.

19.5.3 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.

Table 19.2: Guide to tetanus prophylaxis in wound management

History of tetanus vaccination	Time since last dose	Type of wound	Td or Tdap as appropriate[a,b]	TIG[e]
≥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[c]	No
≥3 doses	>10 years	Tetanus-prone wounds	Booster dose[c]	No
<3 doses or uncertain		Clean minor wounds	Complete the course[d]	No
<3 doses or uncertain		Tetanus-prone wounds	Complete the course[d]	Yes

a See Appendix 2 for catch-up schedules for previously unimmunised children. DTaP-containing vaccine may be used in children aged under 10 years.

b Td is funded; Tdap may be given to, but is not funded for, individuals aged 18 years and older.

c If appropriate, this may count as the age 45 or 65 years booster dose.

d To complete the 3-dose primary immunisation course, give 1 to 3 doses at not less than 4-weekly intervals.

e 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.

Tetanus immunoglobulin (TIG) availability and storage

TIG is issued in ampoules, each containing 250 IU. (Ampoules of 2000 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.

19.5.4 (Re-)vaccination

Tetanus toxoid-containing vaccine is funded for (re-)vaccination following immunosuppression. (See also sections 4.2 and 4.3.)

19.6 Contraindications and precautions

(See also sections 5.6 and 14.6.)

19.6.1 Contraindications

See section 1.4 for general contraindications for all vaccines.

Immunisation with Td, Tdap or another tetanus toxoid-containing vaccine should not be repeated in individuals who have had previous severe hypersensitivity reactions. 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.

See section 14.6.2 for precautions to pertussis-containing vaccines, including DTaP-IPV-HepB/Hib.

19.7 Expected responses and adverse events following immunisation (AEFI)

See also sections 5.7 and 14.7 for expected responses and adverse events following immunisation 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.[9]

Tdap has a safety profile similar to Td and both vaccines are generally well tolerated.[10, 11]

19.7.2 Adverse events following immunisation

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.[12] A large population-based study did not find a link with Guillain-Barré syndrome in an estimated 730,000 children who were of eligible age to receive DTwP in a population of 2.2 million children aged under 15 years, nor in adults who received tetanus toxoid-containing vaccines.[13]

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 the discussion on preventing tetanus following injury in section 19.5.3.

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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 immunosuppressed, particularly HIV-infected individuals, are more at risk of disease and complications. The New Zealand burden is seen in foreign-born residents and those in low socioeconomic groups.
Vaccine	Can only be administered by a gazetted vaccinator. Live attenuated vaccine, which must be reconstituted.
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 (see www.health.govt.nz/immunisation for a list of high-incidence countries) · during their first 5 years will be living for 3 months or longer in a country with a TB rate ≥40 per 100,000.

Continued overleaf

Contraindications	Immunosuppression for any reason, or suspected of being immunocompromised. HIV-positive or potentially HIV-positive individuals. Infants of mothers taking anti-tumour necrosis factor (anti-TNF) therapies (eg, infliximab) during pregnancy. Positive tuberculin skin test or interferon gamma release assay (IGRA). Generalised infected skin conditions.
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, particularly the lymph nodes.

The initial infection with *M. tuberculosis* usually goes unnoticed, and most of those infected enter a latent phase (LTBI). The lifetime risk for infected people progressing from this latent phase to active TB disease is as high as 20 percent, but this risk is strongly affected by the age of the person, the presence of healed lesions on chest X-ray and immunosuppression.[2, 3]

When TB disease does occur, clinical manifestations most often appear one to six months after infection. The most common site of infection is the lung (pulmonary TB), where TB infection classically causes an asymmetrical pulmonary infiltrate, which undergoes caseation, cavity formation and fibrosis if it progresses. Young children with active TB disease may be asymptomatic or present with symptoms of fever, lassitude and cough. 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.

20.3 Epidemiology

20.3.1 Global burden of disease

Worldwide the incidence rate of TB is slowly falling by about 2 percent per year, but tuberculosis remains a major global health problem.[4] The WHO estimates there were 8.6 million new TB cases in 2012 and 1.3 million deaths; 320,000 of these deaths were in HIV-positive individuals.[4] The majority of the TB burden exists in 22 high-burden countries.[4]

The peak age for TB infection in most Western countries is adults over 50 years. However, among ethnic and racial minorities, rates are higher and often more common in young adults and children. Certain environments tend to make TB incidence much higher: poverty, poor nutrition, poor access to health care and crowded conditions.

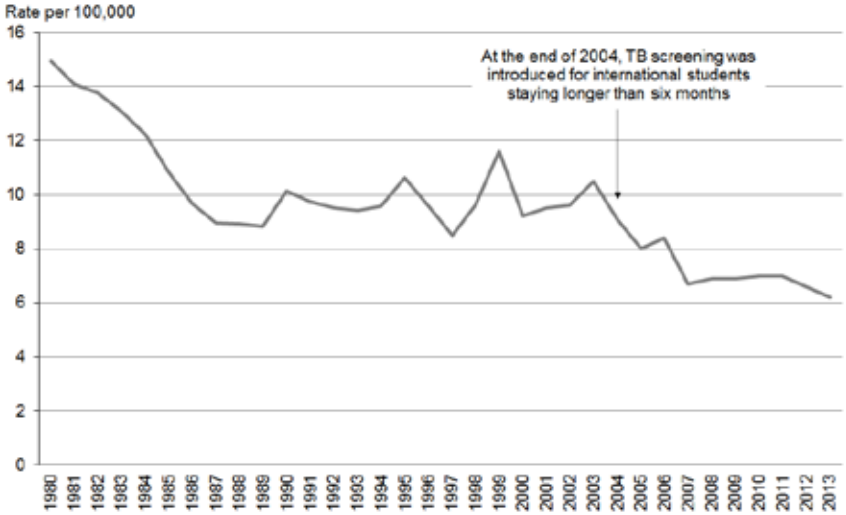
20.3.2 New Zealand epidemiology

The overall rate of active TB in New Zealand is low compared with many countries, although TB remains one of the most common notifiable infectious diseases. Cases of TB in New Zealand declined substantially between 1980 and 2007, but they have remained relatively stable since then (Figure 20.1).[5] In 2013 there were 278 notifications (6.2 per 100,000 population), compared to 294 notifications in 2012 (6.6 per 100,000).

Most cases in 2012 were associated with people born in Asia, Africa and the Pacific Islands, particularly recent immigrants from these areas. Risk factors for being diagnosed with TB include being born overseas in

a high-prevalence country, recent immigrant, prior or recent contact with TB, and identified as living in an area of higher deprivation.[5]

Figure 20.1: Notification rate of tuberculosis disease, 1980–2013



Source: Institute of Environmental Science and Research

Bovine infection with *M. bovis* has spread to feral possums, placing cattle and deer herds at risk. At present, because of herd testing and the widespread pasteurisation of milk, this causes very few cases of human *M. bovis* disease (fewer than 10 cases were reported each year between 2008 and 2012).

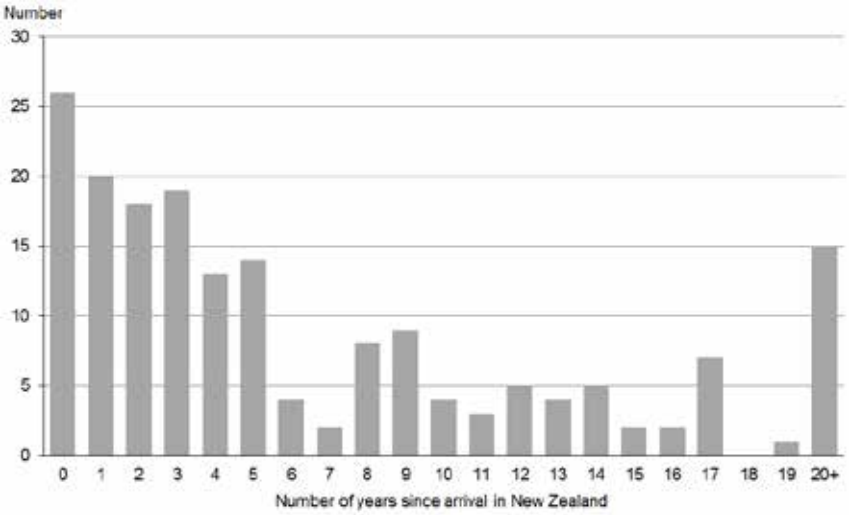
In 2012 there were 294 TB notifications, including 279 new cases and 15 relapses/reactivations. The 2012 notification rate was 6.6 cases per 100,000 population, a slight decrease from the 2011 rate (7.0 per 100,000). Ethnic-specific notification rates were higher in the Asian (41.4 per 100,000) and Middle Eastern/Latin American/African (31.8 per 100,000) ethnic groups, lower for Pacific peoples (12.4 per 100,000) and even lower for Māori (5.4 per 100,000) and European/Other (0.9 per 100,000) groups. Over 60 percent of new cases resided in the four most deprived deciles (NZDep 7–10). There is significant regional variation in rates.[5]

Of the 279 new TB disease cases in 2012, 65 were born in New Zealand and 214 were born overseas. The highest disease rate was among those born in Southern and Central Asia (152.5 per 100,000), followed by those born in South-East Asia (89.2 per 100,000), then the Pacific Islands (21.3 per 100,000) and Sub-Saharan Africa (20.3 per 100,000).[5]

The most commonly reported risk factor was being born overseas (76 percent of all cases) and current or recent residence with a person born outside of New Zealand (68.8 percent of cases). Prior contact with a confirmed case of TB was recorded in 21.6 percent of cases.[5]

The date of arrival was recorded for 181 of the 214 new TB cases born outside of New Zealand. The interval between the date of arrival and the TB notification date ranged from two days to 64 years, with a mean interval of 7.7 years and median interval of 4 years (Figure 20.2).[5]

Figure 20.2: Tuberculosis notifications (new cases) born outside of New Zealand, by number of years since arrival in New Zealand, 2012



Note: The date of arrival was not recorded for 38 cases.

Source: Institute of Environmental Science and Research

20.4 Vaccine

Bacillus Calmette-Guérin (BCG) vaccine types vary widely, with different strains. The incidence of side-effects with BCG vaccination differs between strains that are considered 'strong' (ie, those that elicit stronger immune responses in animal models) and strains that are considered 'weak'.[6] The strong strains have also been associated with a higher rate of lymphadenitis and osteitis, especially among neonates. Reducing the vaccination dosage for the strong strains also reduces the incidence of lymphadenitis.

20.4.1 Available vaccine

BCG vaccine (bioCSL) is a live attenuated vaccine. The adult dose contains 2–8 x 10^5 colony-forming units (cfu) of the Danish 1331 strain of *M. bovis*, and the infant dose contains 1–4 x 10^5 cfu. 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*.[6] While it is unlikely that any single, simple measure of cellular immune function will be useful as a direct correlate of protection, new breakthroughs in technology that could improve the diagnostic tools available are on the horizon.

The principal role of BCG is to protect young children who are at greatest risk from severe disease, particularly miliary and meningeal disease.[6] The vaccines provide protection against meningitis and disseminated TB in children, particularly in newborns and young infants. However, BCG vaccines do not prevent primary infection, are only partially effective against severe infection in children, are unreliable against adult pulmonary TB, and are not effective against reactivation of latent pulmonary infection. In persons infected with TB, subsequent vaccination with BCG does not augment the immune response.[6]

The efficacy of BCG vaccines ranges from 0 to 80 percent.[6] There are significant differences in efficacy across populations and geographical areas. Maternal factors, genetic factors, nutritional factors and environmental factors all appear to influence efficacy. Efficacy and immunogenicity responses vary considerably across vaccine strains, but the data to date cannot differentiate which strains are overall more effective.[7] In developing countries, a birth dose of BCG significantly reduces overall infant mortality.[8] One possible aspect of this effect may be that BCG appears to enhance the production of vitamin D.[9] HIV-exposed uninfected infants show a blunting of the immune response to BCG given in early infancy.[10]

BCG has had little effect in reducing the population rate and transmission of TB,[11] 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.[6]

There have been a number of different approaches to using BCG in the control of TB in developed countries.[12] 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.[13] 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 9000 children from countries with rates greater than 50 per 100,000 population would have to be given BCG to prevent a severe case.[14]

The current recommendation to use neonatal BCG vaccination in populations with high rates of active TB is just part of a comprehensive control and treatment programme for TB in New Zealand, which includes active contact tracing and treatment of LTBI.

There are large international efforts working to enhance TB control by improving BCG vaccine and by developing new, more effective vaccines.[15]

20.4.3 Transport, storage and handling

Transport according to the *National Guidelines for Vaccine Storage and Distribution*.[16] Store in the dark at +2°C to +8°C. Do not freeze.

BCG vaccine is presented as freeze-dried material with a diluent in a separate ampoule. Reconstituted vaccine should be stored at 4°C and used within four hours.

20.4.4 Dosage and administration

Under the Tuberculosis Regulations 1951, BCG immunisation in New Zealand may legally be performed only by gazetted BCG vaccinators.

After reconstitution, the dose for infants aged under 12 months is 0.05 mL, and the dose for adults and children aged over 12 months is 0.1 mL.

The vaccine is administered by intradermal injection over the point of insertion of the left deltoid muscle. This is not much higher than the mid-point of the upper arm. For full details about administration, refer to the *Technical Guidelines for Tuberculin Testing and BCG Vaccination 1996*[17] (or the current edition).

No follow-up tuberculin skin testing is required.

BCG immunisation given in other countries

Care must be taken when assessing for previous vaccination. 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[18] 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.[13]

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 varicella vaccines.

Hepatitis B immunoglobulin (given at birth to babies of mothers with chronic hepatitis B infection) or 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 non-Māori and non-European people in New Zealand. However, all pregnant women should have a discussion with their lead maternity carer about the risk of TB for their baby.

A list of high-incidence countries and their TB rates is available on the immunisation pages of the Ministry of Health website (www.health.govt.nz/immunisation) and in the Ministry of Health resource *HE2204: BCG Vaccine: Information for Health Professionals,* available at www.healthed.govt.nz or the local authorised health education resource provider or public health unit.

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.

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; Taiwan
- South East Asia (except Singapore)
- some parts of the Pacific (Kiribati and Papua New Guinea have consistently high rates; see the sources listed above for the specific high-incidence countries).

Neonates at risk should be identified antenatally by lead maternity care providers and antenatal referral made to the neonatal BCG service. Midwives, GPs, practice nurses and obstetricians 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.

Infants born before 34 weeks' gestation should have their BCG vaccination delayed until 34 weeks' post-conceptual age.[19] Babies born after this or with low birthweight appear to produce an adequate response, based on tuberculin skin test responses.[20, 21, 22]

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 will 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 National Immunisation Register (NIR) collects information on neonatal BCG immunisation, unless the individual or their parent/guardian has opted off the NIR (see section 2.8). The BCG vaccinator usually enters the immunisation data onto a form, which is sent to the DHB NIR Administrator to enter onto the NIR.

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 (IGRA)-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.

The local medical officer of health may recommend vaccination programmes for specific populations with a high risk of TB, depending on local epidemiology. Staff and residents of rest homes, prisons and other closed populations may be recommended for vaccination from time to time, depending on local epidemiology and in consultation with the medical officer of health.

Vaccination for overseas travel (even prolonged travel in areas with a TB rate ≥40 per 100,000) should be discouraged. An exception to this is a child aged under five years travelling for prolonged residence in an area with a TB rate ≥40 per 100,000. In these circumstances vaccination should be considered.

20.6 Contraindications and precautions

20.6.1 Contraindications

See section 1.4 for general contraindications for all vaccines.

BCG vaccine should not be given to individuals:

- receiving corticosteroids or other immunosuppressive treatment, including radiotherapy (see section 4.3)
- suffering from malignant conditions such as lymphoma, leukaemia, Hodgkin's disease or other tumours of the reticulo-endothelial system
- in whom an immune-compromising disease 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 took anti-tumour necrosis factor (anti-TNF) therapies (eg, infliximab) during pregnancy – BCG vaccination should be delayed until the infant is at least 8–9 months old;[23] these drugs may cross the placenta and cause immunosuppression in the infant
- with a positive tuberculin skin test reaction or who have a positive IGRA
- 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 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.[19]
- Avoid or defer immunisation in a child born with a condition that may require immunosuppressive therapy in future.

20.7 Expected responses and adverse events following immunisation (AEFI)

20.7.1 Expected responses

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 take months to resolve; usually no treatment is required.

20.7.2 Adverse events following immunisation

Adverse events following immunisation with BCG vary with age and vaccine strain and are summarised in Table 20.1.

Table 20.1: 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

Source: Lotte A, Wasz-Hockert O, Poisson N, et al. 1988. Second IUATLD study on complications induced by intradermal BCG-vaccination. *Bulletin of the International Union against Tuberculosis and Lung Disease* 63: 47–59.

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 immune-compromised 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.[24] 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 the local medical officer of health in the interests of quality control of the BCG vaccination technique, and to the Centre for Adverse Reactions Monitoring (CARM) (see 'AEFI reporting process – notifying CARM' in section 2.5). Information about adverse reactions to BCG vaccine 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).

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 Tuberculosis Act 1948, the medical officer of health is given wide powers to investigate and control all TB cases and their contacts, while district health boards are required to make provision for the treatment and supervision of patients and their contacts.

BCG is a relatively minor component of TB control programmes, which rely primarily on case finding of active disease, contact tracing and selective screening, and treatment of active disease and LTBI (using directly observed therapy, if necessary). The local medical officer of health can advise on local TB control programmes, including BCG immunisation policies.

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.

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 (IGRA) has the advantage of greater specificity and convenience, but it is more expensive.[25] These tests, their use and interpretation are discussed fully in the Ministry of Health publications *Guidelines for Tuberculosis Control in New Zealand 2010*[1] and *Technical Guidelines for Tuberculin Testing and BCG Vaccination 1996*.[17] For further information, refer to these Ministry of Health publications (or the most recent editions), the *Communicable Disease Control Manual 2012*[26] or the *Control of Communicable Diseases Manual*.[27]

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21 Varicella (chickenpox)

Key information

Mode of transmission	Airborne droplets, or contact with infected respiratory tract secretions or vesicular lesions.
Incubation period	Usually 14–16 days (range 10–21 days).
Period of communicability	From 1 to 2 days before onset of the rash until all lesions have crusted.
Burden of disease	Without immunisation, most people who reside in temperate climates have infection during childhood. Groups at risk of severe complications include pregnant women and their unborn babies, and immune-compromised individuals.
Vaccines	Varicella vaccines (Varilrix; Varivax) and MMRV vaccine (ProQuad) are live attenuated vaccines.
Recommended immunisation schedule	Recommended and funded (Varilrix) for certain high-risk groups and their contacts. Recommended but not funded for all susceptible children, adolescents and adults.
Vaccine efficacy/ effectiveness	High after 1 dose, but 2 doses prevent outbreaks.
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	Small increased risk of febrile seizures when MMRV is used for the first dose in toddlers.
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. Varicella vaccine may be used for post-exposure prophylaxis 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, or contact with infected respiratory tract secretions or vesicular lesions. The incubation period is usually 14 to 16 days (range 10 to 21 days), and cases are infectious from 1 to 2 days before the onset of the rash until all the lesions have crusted. A maculopapular rash, which becomes vesicular, appears first on the face and scalp, later spreading to the trunk and abdomen and eventually to the limbs. The vesicles dry and crust after three to four days, but may be followed by further lesions.

A wide variation in the number of lesions is possible, ranging from a few to many hundred. The hallmark of the disease is the presence of lesions in varying stages of development. Lesions 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 and self-limiting disease, but complications requiring hospitalisation and fatalities do occur. Secondary bacterial infections and VZV encephalitis are the most common morbidities. Serious complications include central nervous system involvement (encephalitis, cerebellar ataxia, stroke), pneumonia, secondary invasive bacterial infections, and even death. Primary infection in adults is rare but has a higher rate of complications, with pneumonia being the most common. VZV pneumonia often requires mechanical ventilation and carries an overall mortality rate of 10–30 percent despite appropriate antiviral therapy. Adults with VZV are 25 times more likely to develop severe disease than children.

Pregnant women and their unborn babies are particularly vulnerable to VZV (see section 21.8.6). Maternal varicella occurring in the first half of pregnancy can cause the rare but devastating congenital varicella syndrome (see Table 21.2), whereas disease very late in pregnancy (from five days before to two days after delivery) may cause severe neonatal varicella infection. Women who contract varicella while pregnant have an estimated 10–20 percent risk of developing VZV pneumonia, which is a higher rate than observed in non-pregnant women.

Others vulnerable to both VZV and HZ are those who are immune compromised, such as people taking immunosuppressive medications (eg, cancer treatment or organ transplant patients) and those with human immunodeficiency virus (HIV) infection. Varicella can be a fatal disease in the immune compromised.

VZV infection is followed by the production of VZV-specific antibody and VZV-specific T-cell mediated immunity. The latter is necessary to maintain the latency of VZV in the ganglia and therefore prevent HZ. The immune response is boosted by subclinical reactivation of latent virus or exposure to wild-type virus (contact with a case of chickenpox or shingles). 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

The epidemiology of this infection appears to be similar in all developed countries with temperate climates. Epidemics occur each winter/spring, with some variability from year to year. Approximately 3 percent of each birth cohort are infected during infancy. Thereafter, 8–9 percent of the birth cohort are infected each year throughout childhood, so that by age 10 years fewer than 15 percent, and by age 14 years fewer than 10 percent, remain susceptible. The infection rate drops rapidly in adolescence and young adulthood to about 1 percent per year. By age 40 years almost the entire birth cohort (over 97 percent) have been infected, so that only a few adults remain susceptible.

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 characteristics of infection appear to conspire at times to maximise the disruption to families. If a child is exposed outside the home, by the time the rash occurs the child will have been infectious for two days. This means that any susceptible household contacts will become unwell just as the first child is starting to recover. This results not only in morbidity but also in financial consequences for parents missing work.

Varicella vaccine 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.[1, 2, 3] Following the introduction of varicella vaccine onto the childhood schedule, exposure to wild-type virus decreases, and therefore adults are less likely to boost immunity to latent HZ. It is hypothesised that lack of boosting may lead to an increase in HZ in older adults.

However, a study in the US[4] from 1992 to 2002 has shown that although the incidence of varicella decreased in children (from 2.63 cases per 1000 person-years in 1992 to 0.92 cases per 1000 person-years in 2002), there was no increase in HZ in adults of any age: the age-adjusted rate of HZ was 4.05 cases per 1000 person-years in 1992 and 3.7 cases per 1000 person-years in 2002. Studies from the UK and Canada have 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.[5, 6] It is inevitable that HZ rates will rise in New Zealand as the population ages.

It remains unclear whether the introduction of childhood mass VZV vaccination does significantly alter the epidemiology of HZ. Studies that have investigated this issue have been unable to attribute any increase in incidence of HZ to the childhood VZV vaccine programme.[7, 8]

21.3.2 New Zealand epidemiology

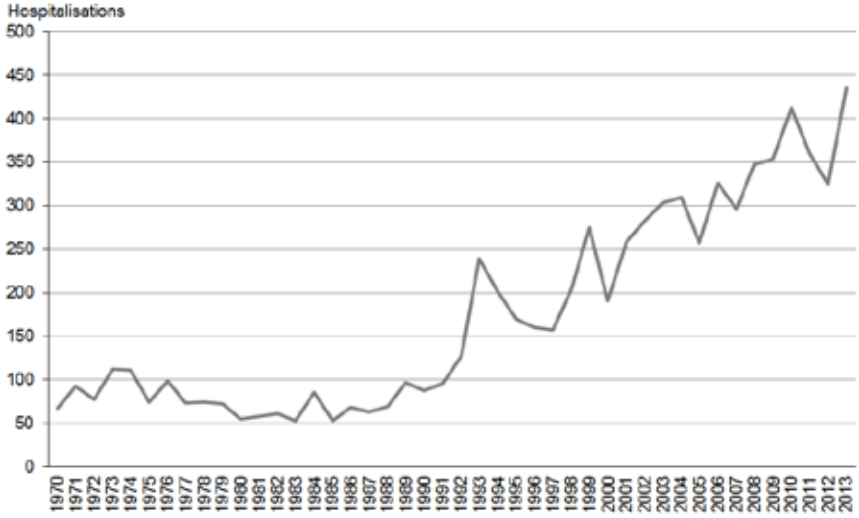
In New Zealand it is expected that 90 percent of children will have had varicella infection before adolescence, with peak incidence in the 5–9 years age group. With higher participation in early childhood services, a greater proportion of infections may now be occurring in preschool-aged children.

As varicella is not a notifiable disease, accurate data collection is limited for uncomplicated varicella, and hospital discharge data depends on accurate coding. This may result in under-reporting of complications secondary to varicella infection.

Hospitalisation

Hospital discharge information for varicella between 1970 and 2013 is shown in Figure 21.1. The rate of hospital discharges for the 0–4 and 5–9 years age groups was higher compared with older age groups because the disease is most common in childhood. However, adults, adolescents and infants are more likely to suffer severe illness or the complications of chickenpox.[9]

Figure 21.1: Hospitalisations for varicella, 1970–2013



Source: Ministry of Health

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.

Mortality

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.[10] 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 immune compromised. A further eight children (31 percent) had ongoing disability at discharge, most having had no prior medical condition.

In summary, in a typical year New Zealand is estimated to experience approximately 50,000 chickenpox infections, of which several hundred result in hospitalisation, one to two cases result in residual long-term disability or death, and 0.5–1 cases result in severe congenital varicella syndrome. About two-thirds of this burden is borne by otherwise healthy children, and less than one-tenth by children with a disease associated with immunosuppression. Approximately one person per year dies from VZV, and most of the VZV-associated deaths occur in adults.

21.4 Vaccines

21.4.1 Available vaccines

There are two live attenuated monovalent varicella vaccines (VV) and one quadrivalent live attenuated measles-mumps-rubella-varicella (MMRV) vaccine registered (approved for use) and available (marketed) in New Zealand. Varicella-containing vaccines are not on the Schedule, but VV is recommended and funded for certain high-risk groups (see section 21.5.1).

Funded vaccine

Monovalent varicella vaccine (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, human albumin, lactose, neomycin sulphate and polyalcohols.

Other vaccines

- Monovalent varicella vaccine (Varivax, MSD) contains not less than 1350 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.
- The MMRV vaccine (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. See also section 11.4.1 for more information about MMR vaccines.

21.4.2 Efficacy and effectiveness

Single-dose varicella vaccination programmes have had a dramatic impact on the incidence of VZV infections,[11, 12, 13] hospitalisations[1, 2, 14] and serious outcomes,[3] particularly when high coverage rates are achieved. Indirect effects are also apparent. However, single-dose programmes are associated with outbreaks even among highly vaccinated groups.[9] 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.[15, 16] 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.[9, 15]

The antigenic components of MMRV vaccines are non-inferior compared with simultaneous administration of MMR and varicella vaccines,[17, 18] for both the first and second doses.

Duration of immunity

Varicella vaccination provides long-term but probably not lifelong immunity against VZV, in contrast to VZV natural infection. Long-term studies are needed in countries with universal vaccine programmes to assess the duration of the immune response and protection from varicella in the absence of external boosting from exposure to wild-type virus.[17]

21.4.3 Transport, storage and handling

Transport according to the *National Guidelines for Vaccine Storage and Distribution*.[19]

> Monovalent VV and MMRV vaccines require 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. Reconstituted vaccine should be used immediately. However, if this is not possible, it may be kept for up to 90 minutes at room temperature (25°C) and up to eight hours in the refrigerator (+2°C to +8°C).
- Varivax is presented as a lyophilised powder for reconstitution with the supplied diluent. The vaccine should be stored in its original packaging in the refrigerator at +2°C to +8°C. Reconstituted vaccine must be used immediately or discarded if it has not been used within 30 minutes.
- ProQuad is supplied in vials as a sterile lyophilised preparation together with vials of diluents (containing sterile water). The lyophilised preparation should be stored at +2°C to +8°C and the diluent at room temperature. Reconstituted vaccine must be used immediately or discarded if it has not been used within 30 minutes.

21.4.4 Dosage and administration

The dose of monovalent VV and MMRV vaccine is 0.5 mL, administered by subcutaneous injection in the deltoid area (see section 2.3).

Co-administration with other vaccines

Monovalent VV or MMRV vaccine 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

- VV (Varilrix): until 2011 the manufacturer had recommended one dose for children aged 9 months to 12 years inclusive and two doses six weeks apart for those aged 13 years and older. The manufacturer now recommends two doses six weeks apart for all individuals from age 9 months, for the benefit of an enhanced immune response to the varicella virus.
- VV (Varivax): until 2013 the manufacturer had recommended one dose for children aged 12 months to 12 years inclusive and two doses four to eight weeks apart for those aged 13 years and older. The manufacturer now recommends two doses for all individuals from age 12 months, to ensure optimal protection against varicella. For children aged 12 months to 12 years inclusive, the second dose is given at least three months after the first.
- MMRV (ProQuad): a single dose is sufficient for children aged 12 months to 12 years, inclusive. ProQuad can be used if a second dose of varicella-containing vaccine is recommended, given at least one month after the first dose.

Varicella vaccine can be administered at age 15 months with MMR, Hib and PCV13 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 varicella vaccine. (This requires four injections at the 15-month visit.) For a second dose of varicella vaccine, or first doses after age 4 years, either VV or MMRV can be used.

Because New Zealand does not have a universal vaccination programme, chickenpox continues to circulate liberally in the community, providing boosting. For healthy children who have received varicella vaccine, a second dose is not essential if they were aged over 12 months but under 13 years when first vaccinated. Data from Japan indicates that when chickenpox continues to circulate at high levels, giving many opportunities for regular boosting of vaccine-induced immunity, protection lasts for at least 20 years.[20] Varicella vaccine is voluntary in Japan and immunisation coverage was estimated to be around 20 percent. Antibody levels were higher at 20 years post-vaccination

than at 10 years post-vaccination, confirming that boosting of immunity had occurred.[20]

21.5.1 Funded vaccine for high-risk groups

Two doses of varicella vaccine (Varilrix) are recommended and funded for the following groups (see also sections 4.2 and 4.3).

Table 21.1: High-risk groups eligible for funded varicella immunisation

Note: See the Pharmaceutical Schedule (www.pharmac.health.nz) for the number of funded doses and any changes to the funding decisions.

High-risk groups funded for immunisation are:
· 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*
· 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
· individuals with inborn errors of metabolism at risk of major metabolic decompensation, with no clinical history of varicella
· household contacts of paediatric patients who are immune compromised or undergoing a procedure leading to immune compromise, 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 immune compromised or undergoing a procedure leading to immune compromise, where the household contact has no clinical history of varicella.

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

21.5.2 Healthy infants and children

Varicella vaccine is not yet on the Schedule. One dose is, however, recommended for children from age 12 months to 12 years, inclusive.

21.5.3 Adolescents and adults

Varicella vaccine 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)[9]
- 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)[9]
- 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)[9]
- susceptible non-pregnant women of childbearing age[9]
- susceptible international travellers[9]
- health care workers (see below)
- susceptible individuals who have been exposed to varicella.

See section 21.8.1 for information about assessing susceptibility.

21.5.4 Immunosuppressed individuals

The vaccine should not be given to immunosuppressed individuals except under the direction and care of a specialist, following a suitable protocol[9] (see sections 4.2 and 4.3). Immunosuppressed individuals are at highest risk of severe varicella and zoster infections. The original vaccine formulations, in particular Varivax, have been studied in immunosuppressed 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.[21, 22] The combination MMRV vaccine should not be used in immunosuppressed individuals.

Where immunosuppressed 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). Immunisation of children with congenital T-cell immune deficiency syndromes is generally contraindicated, but those with impaired humoral immunity may be immunised (see below for further contraindications).

Health care workers

All health care workers on obstetric, paediatric and neonatal units, and those caring for immunosuppressed children and adults, should be immunised with varicella vaccine if they are susceptible to varicella. When a health care worker has a good history of prior varicella infection,[23] 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 below).

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 immunosuppressed or other at-risk patients and allocated other duties, or excluded from their place of work, for the duration of the rash. As varicella vaccine-induced immunity is less complete than following natural infection, when exposure to wild chickenpox occurs, previously vaccinated health care workers should examine themselves daily for a rash from days 10 to 21 after exposure. If a rash appears, they should seek advice from their occupational health service.

21.6 Contraindications and precautions

21.6.1 Contraindications

See section 1.4 for general contraindications for all vaccines.

Monovalent VV and MMRV vaccine are contraindicated for the following people:

- individuals with primary or acquired T-cell immune deficiency states – consult the child's paediatrician for advice[24]
- children 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 known systemic hypersensitivity to neomycin
- individuals with active untreated tuberculosis
- women during pregnancy – women should be advised to avoid pregnancy for four weeks after vaccination[24] (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 mother 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).

There is also a relative contraindication for children on salicylates: 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 varicella vaccine is given. There has been no reported association between the vaccine and Reye syndrome, but avoidance of salicylates is recommended as a precaution,[24] 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.

See also section 11.6.1 for contraindications to MMR vaccines.

21.6.2 Precautions

On the advice of their specialist, varicella vaccine 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 varicella vaccine, see Table 1.3.

See also section 11.6.2 for precautions to MMR vaccines.

21.7 Expected responses and adverse events following immunisation (AEFI)

In general, side-effects from varicella-containing vaccines are mild and self-limiting, and include local reactions, fever and mild papulo-vesicular rash in normal healthy individuals. 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. 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.[24]

In healthy vaccinees, transmission of vaccine virus has been exceedingly rare, with only 10 documented occurrences from nine vaccinees (one vaccinee transmitted virus to two other people), most commonly after household exposures.[17] Err on the side of caution and isolate the vaccinee if a post-immunisation rash occurs, particularly if they are household contacts of immunosuppressed individuals. If an immunosuppressed individual inadvertently comes in contact with a vaccinee who has a varicella-like rash, the administration of zoster immunoglobulin (ZIG, for use after exposure to varicella or zoster) and/or acyclovir should be considered (see below).[24] Intravenous acyclovir may be required for the immunosuppressed individual if symptoms develop.[24]

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.[21] No cases of HZ in vaccinated adults caused by the Oka strain have been recorded.[17]

Compared with the use of MMR vaccine and varicella vaccine at the same visit, use of MMRV vaccine results in 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 2300–2600 MMRV vaccine doses).[25] 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 varicella vaccine.

This is why MMRV vaccine is not recommended 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.

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. Maternal 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.[24] Consult with the local laboratory about the availability and interpretation of tests.

21.8.2 Post-exposure prophylaxis with zoster immunoglobulin (ZIG)

ZIG is a high-titre immunoglobulin (IG) 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.[26, 27] Intravenous IG (IVIG) can be given when ZIG is unavailable.

The decision whether to offer ZIG depends on:

- 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:

- household contact – individuals living in the same house are very likely to be infected if susceptible
- playmate contact – this can be defined as more than one hour of play indoors with an infected individual
- newborn infant contact – this occurs when the mother of a newborn infant develops chickenpox (but not zoster) from seven days before to seven days after delivery.

Provided exposure has occurred and susceptibility is likely**, ZIG is recommended for**:

- pregnant non-immune women (see section 21.8.6 below)
- newborn infants whose mother had onset of chickenpox (but not zoster) 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 who are 1000 g in weight, irrespective of maternal history
- immune-compromised individuals.

Dosage of ZIG

The ZIG prepared by CSL Behring in Melbourne, from New Zealand donors, contains 100 IU/mL (ie, 200 IU per 2 mL vial) (see section 1.5). The recommended dose is 6 mL for adults, 4 mL for children aged 6–12 years and 2 mL for children aged 0–5 years. ZIG should be given intramuscularly, not intravenously. 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 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 zoster in an immune-compromised 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; those who are not immune should be offered vaccination.

21.8.4 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
- high-risk children should be excluded from early childhood education services or school until three weeks after the last documented case.

21.8.5 Post-exposure vaccination and outbreak control

Varicella vaccine may be used for post-exposure prophylaxis. Data from the US and Japan from household, hospital and community settings indicates that the varicella vaccine is effective in preventing illness or modifying varicella severity if used within three days, and possibly up to five days, of exposure. The US Advisory Committee on Immunization Practices (ACIP) recommends the vaccine for use in susceptible individuals following exposure to varicella.[9]

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 the varicella vaccine during the pre-symptomatic or prodromal stage of illness increases the risk for adverse events following immunisation. Note that although this method of immunisation may be successful, it is not necessarily reliable.[28] Immunisation before exposure is therefore recommended as the preferred method of preventing outbreaks.

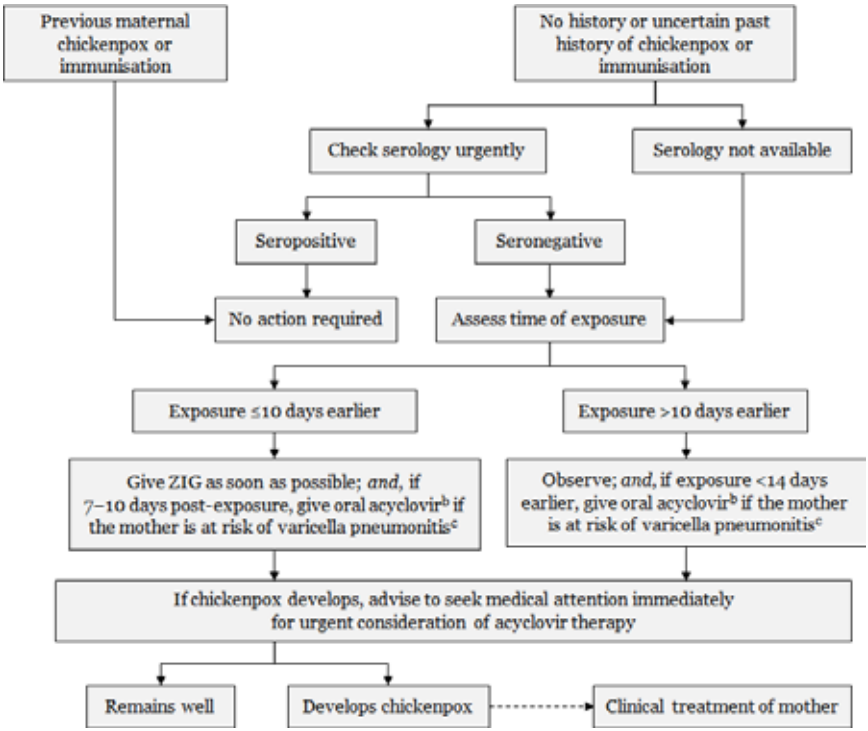
21.8.6 Care of pregnant women after exposure

Pregnant women are at higher risk of severe complications from varicella. If an immune-competent pregnant woman is exposed to varicella, it is recommended, where possible, that her varicella antibodies be assessed if she has no history of varicella (Figure 21.2). 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 21.3).

Figure 21.2: 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 immune compromised; is a smoker.

Source: adapted from Palasanthiran P, Starr M, Jones C (eds). 2002. *Management of Perinatal Infections*. Sydney: Australian Society for Infectious Diseases. (Under review.)

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 21.2). 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.

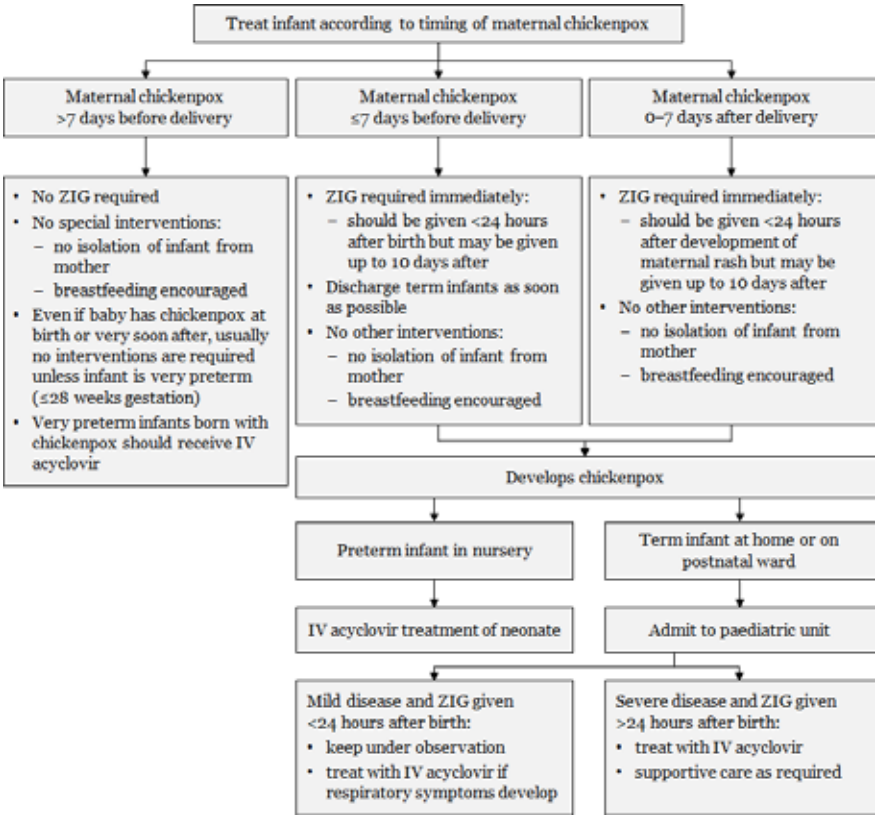
There is no single diagnostic test available for CVS. Regular fetal ultrasound for developing anomalies is recommended. VZV fetal serology is unhelpful but amniocentesis may be considered; negative VZV PCR may be reassuring.

Table 21.2: 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%

Source: adapted from Palasanthiran P, Starr M, Jones C (eds). 2002. *Management of Perinatal Infections*. Sydney: Australian Society for Infectious Diseases. (Under review.)

Figure 21.3: 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.

Source: adapted from Palasanthiran P, Starr M, Jones C (eds). 2002. *Management of Perinatal Infections*. Sydney: Australian Society for Infectious Diseases. (Under review.)

For more details on control measures, refer to the *Control of Communicable Diseases Manual*.[29]

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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 immune-compromised patients.
Period of communicability	Until lesions have crusted.
Burden of disease	Increasing incidence with age; lifetime risk about 1 in 3.
Vaccine	Zoster vaccine (Zostavax), a higher titre formulation of the live attenuated varicella vaccine. **Do not give to children.**
Recommended immunisation schedule	One dose for adults aged 50 years and older.
Vaccine efficacy/ effectiveness	Reduces the burden of zoster illness: by 61 percent in all adults aged over 60 years, by 65.5 percent in those aged 60–69 years and by 55.4 percent in those aged 70 years and older.
Contraindications	Certain immune deficiency states – consult the individual's specialist for advice. High-dose steroids. Known systemic hypersensitivity to neomycin. Active untreated tuberculosis. 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

Herpes zoster (shingles) results from an inadequate cell-mediated immune response to 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. Herpes zoster 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. The risk for post-herpetic neuralgia in patients with zoster is 10–18 percent, although it is uncommon in healthy children and young people and the risk rises with age. Another complication of zoster is eye involvement, which occurs in 10–15 percent of zoster episodes and can result in prolonged or permanent pain, facial scarring and loss of vision.

Herpes zoster occurs more commonly in immunosuppressed individuals (eg, cancer treatment or organ transplant patients) and those with human immunodeficiency virus (HIV). Up to 10 percent of children treated for a malignant neoplasm may develop herpes zoster. In immunosuppressed patients, 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]

22.3 Epidemiology

22.3.1 Global burden of disease

Herpes zoster 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.[3] The annual risk for adults aged over 60 years is 1.1 per 100 persons.[2]

Recurrence is greater in females than males (about 7 percent after eight years compared with 4 percent for males). Third episodes are rare.

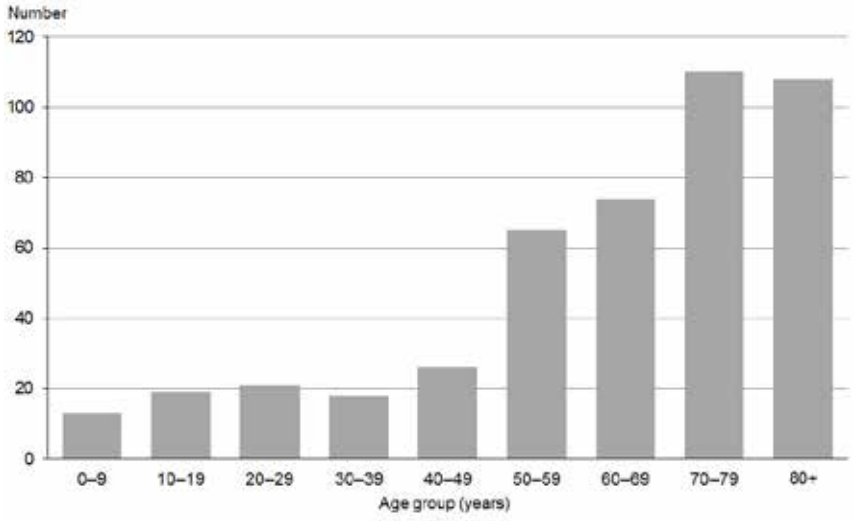
VZV is present in lesions of herpes zoster and is transmissible via contact with the vesicles to other susceptible individuals (causing chickenpox). Airborne transmission can occur from immune-compromised individuals with disseminated HZ. Episodes of HZ in older individuals provide a constant mechanism for reintroducing the virus, causing varicella in non-immune individuals who are in close contact, who then spread the virus to other susceptible individuals.

Several countries have published mathematical models of the potential impact of the VZV childhood vaccination programme on the incidence of HZ. These models predict a possible increase in HZ over the next few decades following the institution of a childhood programme, followed by a rapid decline, based on the absence of circulating VZV to boost immunity. However, it is still not known whether circulating VZV does contribute to reducing varicella zoster disease, and therefore whether the introduction of childhood mass VZV vaccination does significantly alter the epidemiology of HZ. Studies that have investigated this issue have been unable to attribute any increase in incidence of HZ to the childhood VZV vaccine programme.[4, 5, 6, 7, 8] (See also section 21.3.1.)

22.3.2 New Zealand epidemiology

Zoster hospitalisations by age group during 2013 are shown in Figure 22.1 below, with more than 60 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.

Figure 22.1: Herpes zoster hospitalisations by age group, 2013



Source: Ministry of Health

22.4 Vaccine

Herpes zoster vaccine (HZV) is not on the Schedule.

22.4.1 Available vaccine

HZV (Zostavax, Merck) 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 herpes zoster.[9] 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.

Each HZV dose contains a minimum of 19,400 plaque-forming units (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 in all age groups, by 65.5 percent in the age group 60–69 years, and by 55.4 percent in those aged 70 years and older. There was also a 66.5 percent reduction in post-herpetic neuralgia in all age groups.[9] A cohort study of individuals in the US aged 65 years and older found zoster vaccine was associated with a 48 percent reduction in incident zoster, including a 37 percent reduction in those with immunosuppression.[10]

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 seven years using a subgroup of individuals from the Shingles Prevention Study discussed above. Vaccine efficacy was statistically significant for the incidence of HZ and the HZ burden of illness through year five after vaccination.[11] How long protection will last is not known and further doses may be required.

22.4.3 Transport, storage and handling

Transport according to the *National Guidelines for Vaccine Storage and Distribution*.[12] Store in the dark at +2°C to +8°C. The supplied diluent can be stored separately at room temperature (+20°C to +25°C), or in the refrigerator 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.

The dose of reconstituted HZV is 0.65 mL, to be administered subcutaneously in the deltoid muscle (see section 2.3).

Co-administration with other vaccines

HZV can be concurrently administered with influenza vaccine using separate syringes and sites. Recent evidence[13] 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.[14] The US Centers for Disease Control 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.[14]

22.5 Recommended immunisation schedule

HZV is not on the Schedule. It is recommended but not funded for adults aged 50 years and older.

22.6 Contraindications and precautions

Do not give to children.

Contraindications to HZV include:

- a history of hypersensitivity to any component of the vaccine, including gelatin and neomycin
- primary and acquired 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, cellular immune deficiencies
- immunosuppressive therapy (including high-dose corticosteroids), although HZV is not contraindicated for use in individuals who are receiving topical/inhaled corticosteroids or low-dose systemic corticosteroids, or who are receiving corticosteroids as replacement therapy (eg, for adrenal insufficiency)
- active untreated tuberculosis
- pregnancy.

22.7 Expected responses and adverse events following immunisation

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 varicella zoster virus than to the vaccine virus.[2]

22.7.2 Adverse events following immunisation

A large safety review of HZV in 193,083 individuals aged 50 years and older supports the pre-licensure clinical trial data. 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.[15]

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.[16]

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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	Becomes 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 becomes 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 becomes available, although usage is 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 is discontinued in the South Island. Phased out in the North Island by 1990.
	1976	Neonatal BCG is introduced initially in high-risk districts, and then variably implemented throughout New Zealand.
	1990	Neonatal BCG is given for high-risk groups only. This continues in 2014.
Salk poliomyelitis (IPV)	1956	Becomes available; initially 8–9-year-olds are targeted, then 5–10-year-olds, then 11–15-year-olds.
	1960	Offered to all those aged 6 months to 21 years.
	2002	IPV replaces OPV on the Schedule, either as IPV or combined with the DTaP vaccine. See Hib for more information.
DTwP (diphtheria, tetanus, whole-cell pertussis)	1958	DTwP becomes available and the first Schedule commences.
	1960	DTwP is 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 receive 2 doses; in September it is offered to all adults and adolescents (administered by the Department of Health).
	1967	From April GPs are able to administer OPV along with DTwP at ages 3, 4, 5 and 18 months.
	2002	Sabin OPV is replaced by Salk-derived IPV on the Schedule, as DTaP-IPV, at ages 6 weeks, 3, 5 and 15 months, and 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 is suspended in late 1969 until the Edmonston B strain vaccine becomes available in February 1970.
	1974	The recommended age changes to age 12 months.
	1981	The recommended age changes to age 12–15 months.
	1990	Measles, mumps, rubella (MMR) vaccine is 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, spurs a change to a vaccination for girls at age 11 years (year 7/form 1).
	1990	MMR is introduced to the Schedule for all infants at age 12–15 months. See MMR for more information.
Hepatitis B	1985	Plasma-derived vaccine is 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 is introduced to the Schedule for all infants (catch-up programmes for preschoolers are implemented during 1988).
	1989	In December 1989 recombinant hepatitis B vaccine replaces the plasma-derived vaccine.
	1990	Funded hepatitis B immunisation is extended to all children aged under 16 years (catch-up school programmes are also implemented).
	1996	The third Hep B dose is brought forward from 12–15 months to age 5 months. See Hib for more information.

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 is introduced for 11-year-old (school year 7/form 1) boys and girls.
	2001	The second dose of MMR is changed from age 11 years to age 4 years. A school-based catch-up programme is offered for all 5–10 year-olds.
		The 2-dose schedule at ages 15 months and 4 years continues in 2014.
Haemophilus influenzae type b (Hib)	1994	Hib vaccine is 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 are 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.
	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 2014.
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 2014.
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 become 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 become eligible to receive the funded vaccine.

Continued overleaf

Vaccine	Year the vaccine was introduced, plus comments	
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 is introduced for all infants to replace whole cell pertussis vaccine at ages 6 weeks, 3 and 5 months (see also Hib).
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 2014.
	2013	Pregnant women from 28 to 38 weeks' gestation become eligible for the funded vaccine. This continues in 2014.
Pneumo-coccal conjugate vaccine	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 replaces PCV7 on the Schedule. PCV13 replaces PCV7 for high-risk children.
	2014	PCV13 replaces PCV10 on the Schedule.
Human papilloma-virus vaccine (HPV)	2008	HPV4 is introduced to the Schedule at age 12 years, for females only. There is a catch-up programme for females born from 1990.
	2013	HPV4 is 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 continues for girls aged 12 years, plus a targeted programme for high-risk individuals.
		Women aged under 26 years with HIV infection become eligible for HPV4.
Rotavirus	2014	RV5 vaccine is introduced to the Schedule at ages 6 weeks, 3 and 5 months.

A1.2 Previous national immunisation schedules

Table A1.2: 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)							● x 3 doses		
45 years								●	
65 years								●	●

Table A1.3: 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)							● x 3 doses		
45 years								●	
65 years								●	●

Table A1.4: 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 A1.5: 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 age 45 and 65 years, 10-yearly boosters were no longer recommended.

Table A1.6: January 2001 immunisation schedule

	DTaP	Hib-HepB	Hep B	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 A1.7: August 2000 immunisation schedule

	DTaP	Hib-HepB	Hep B	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 A1.8: 1996 immunisation schedule

	DTwPH	Hep B	Polio (OPV)	MMR	Td
6 weeks	●	●	●		
3 months	●	●	●		
5 months	●	●	●		
15 months	●			●	
11 years			●	●	●

Table A1.9: 1994 immunisation schedule

	DTwPH	Hep B[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 A1.10: 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 A1.11: 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 A1.12: 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 A1.13: 1967 immunisation schedule

	DTwP	Polio[a]	DT
3 months	●	●	
4 months	●	●	
5 months	●	●	
18 months		●	●[b]
5 years			●

a Between 1961 and 1967 polio was administered by the Department of Health.

b The DT booster at age 18 months was introduced in 1964.

Table A1.14: 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 and varicella) 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 A1.3.12: '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 invasive pneumococcal disease 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.

A1.3.3 Hepatitis B-containing vaccines

Hepatitis B vaccine 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 hepatitis B-specific immunoglobulin (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 hepatitis B vaccine was brought forward from 15 to 5 months of age to give early protection to infants and to complete the hepatitis B vaccine schedule in the first year of life, in the expectation that this would improve vaccine uptake. This schedule continues in 2014, 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 hepatitis B vaccine (HBvaxPRO, 5 µg) plus HBIG is given at birth.

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.

Since 2011 the HPV immunisation has only been offered in participating schools to females in school year 8. HPV immunisation is also available through family doctors, local health centres and most Family Planning clinics for females who do not attend a participating school or who do 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.

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.

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-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.

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-*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.

A1.3.9 Pneumococcal vaccines

The 7-valent pneumococcal conjugate vaccine (PCV7, Prevenar 7) became part of the Schedule in June 2008, with four doses recommended at ages 6 weeks, 3 months, 5 months and 15 months. It was available at age-appropriate doses for all children born from 1 January 2008 and for some high-risk children since 2006. 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.

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 four-month OPV dose 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-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.

A1.3.11 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 abolishing congenital rubella syndrome (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.

In 2014 the rubella schedule continues as two doses of MMR vaccine offered at ages 15 months and 4 years.

A1.3.12 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 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 (TT) 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 adult tetanus diphtheria vaccine (Td), which had been changed from TT 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 age 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 primary schedule for tetanus has been given in combination vaccines at age 6 weeks, 3 months, 5 months (DTaP-IPV-HepB/Hib), 4 years (DTaP-IPV) and 11 years (Tdap).

The adult tetanus diphtheria vaccine (Td) replaced the tetanus toxoid (TT) 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.

A1.3.13 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 tuberculosis.

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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 A2.1 discusses catch-up requirements for children aged under 18 years, and section A2.2 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.

> Vaccinators should always check the manufacturer's recommendations for age-appropriate vaccine recommendations and the interval(s) required between dose(s). It is important to give all the required doses of each antigen, even if this necessitates an extra dose of another antigen.

For assistance with planning catch-up schedules, contact your immunisation coordinator, the Immunisation Advisory Centre freephone line on 0800 466 863, or discuss with an experienced colleague.

A2.1 For children 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.

In the past, catch-up tables were provided, but infants/children seldom fitted these unless they were completely unvaccinated, or there was no documented history and they were assumed to be unvaccinated. Trying to fit an infant's/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 requires.

A2.1.1 Principles of catch-up for 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, vaccines may be given simultaneously and the catch-up schedule shortened to four-weekly intervals (unless otherwise stated by the manufacturer) 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 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 for primary immunisation of children aged 7 to under 18 years (note that Tdap is not registered for children aged under 10 years or for primary immunisation, but there are not expected to be any safety concerns).

7. The first dose of rotavirus vaccine (RV5, RotaTeq) should be given before age 15 weeks (ie, 14 weeks and 6 days), with subsequent doses administered at a minimum dose interval of four weeks. All three doses must be given by age 8 months and 0 days. Where the first dose is inadvertently given at age 15 weeks or older, the remainder of the series should be completed, but all three doses must be given by age 8 months and 0 days.

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. For infants commencing PCV13 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 least four months after the completion of the primary course. Unimmunised children aged 12–23 months require two PCV13 doses, eight weeks apart. Unimmunised children aged 2 to under 5 years require one dose of PCV13.

11. Remember to check whether the infant/child has any specific health conditions that may make them eligible for additional vaccines (see chapter 4: 'Immunisation of special groups' and the relevant disease chapters).

12. 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 children aged under 10 years

<12 months	12 months to <5 years	5 years to <10 years
3 DTaP[a]	3 or 4 DTaP[e, f]	4 DTaP[f]
3 Polio (IPV)[a]	3 or 4 Polio (IPV)[e, f, g]	3 or 4 Polio (IPV)[g]
3 Hep B[b]	3 Hep B[b]	3 Hep B[b]
3 Hib	1 Hib[h]	2 MMR
3 PCV[c]	1 or 2 PCV[i, j]	
3 RV[d]	1 or 2 MMR[k]	

a Use DTaP-IPV-HepB/Hib or DTaP-IPV for the 3-dose primary series (at a minimum of 4-weekly intervals). They then continue on the usual childhood Schedule with a booster dose of DTaP-IPV given at age 4 years, and at least 6 months after the 3rd dose of the primary series.

b If the child received Hep B at birth, they will require a total of 4 Hep B doses.

c 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 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 least 4 months after the completion of the primary course.

d The 1st dose of rotavirus vaccine should be given before age 15 weeks (ie, 14 weeks and 6 days), with subsequent doses administered at a minimum dose interval of 4 weeks. All 3 doses must be given by age 8 months and 0 days. Where the 1st dose is inadvertently given at age 15 weeks or older, the remainder of the series should be completed but all 3 doses must be given by age 8 months and 0 days.

e Children commencing immunisation at age 12 months to under 4 years require 3 doses of DTaP- and IPV-containing vaccines – use DTaP-IPV-HepB/Hib or DTaP-IPV (at a minimum of 4-weekly intervals). They then continue on the usual childhood Schedule with a booster dose of DTaP-IPV given at age 4 years, and at least 6 months after the 3rd dose.

f Children commencing immunisation from age 4 years require 4 doses of DTaP. Use DTaP-IPV-HepB/Hib or DTaP-IPV for the 3-dose primary series (at a minimum of 4-weekly intervals). The 4th DTaP-containing dose is given at least 6 months after the 3rd dose.

g A minimum of 3 polio doses are required for the primary series 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). The minimum recommended interval between IPV doses 1 and 2 is 4 weeks; the 3rd IPV dose should be given at least 6 months after dose 2. If the 3rd dose is given in a shorter time interval than this (eg, if used with a DTaP catch-up) then a 4th IPV dose should be given at least 6 months after the 3rd dose.

h 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.

i For children commencing immunisation at age 12–23 months, 2 PCV doses are required, a minimum of 8 weeks apart. If vaccination commences at age 24 months (2 years) or older, only 1 PCV dose is required.

j If a full primary course (ie, 3 doses) of PCV7 or PCV10 has been given, only 1 further PCV13 dose is required if the age at presentation is 12 months to under 5 years. A minimum interval of 4 months is required between the primary course and this booster dose. If the child has completed all 4 doses of PCV10 (the primary series and the 15-month booster), no further dose of PCV13 is required.

k Children commencing immunisation at age 12 months to under 4 years require 1 dose of MMR. They then continue on the usual childhood Schedule with a 2nd dose of MMR given at age 4 years, and four weeks after the 1st dose. Children commencing immunisation at age 4 years require 2 doses of MMR 4 weeks apart.

A2.1.2 Principles of catch-up for children 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. Vaccines may be given simultaneously and the catch-up schedule shortened to four-weekly intervals (unless otherwise stated by the manufacturer) to ensure the required number of doses are administered to offer the best protection in the shortest time possible.

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 a child is uncertain or unknown, plan the catch-up schedule assuming the vaccine has 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 children from age 10 years to under 18, Tdap is recommended and funded for primary and booster immunisation. While Tdap is not approved for use (registered) as a primary course, there are expected to be no safety concerns in using Tdap for primary immunisation in children aged 10 to under 18 years. Therefore, using Tdap should be considered for all catch-up schedules for primary and booster immunisations.

7. For children aged 11–15 years, an alternative two-dose hepatitis B catch-up schedule may be considered using the monovalent hepatitis B vaccine (HBvaxPRO 10 µg), with the second dose given four to six months after the first.

8. Remember to also check whether the child has any specific health conditions that may make them eligible for additional vaccines (see chapter 4: 'Immunisation of special groups' and the relevant disease chapters).

9. Once the child 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 children aged 10 to under 18 years at the time of presentation

10 years to <18 years
4 Tdap[a]
3 Polio (IPV)[b]
3 Hep B (5 µg) for children aged 10 to <18 years; or 2 Hep B doses (10 µg) for children aged 11–15 years[c]
2 MMR
3 HPV (≥12 years, girls only)

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 The minimum recommended interval between IPV doses 1 and 2 is 4 weeks; the 3rd IPV dose should be given at least 6 months after dose 2. If the 3rd dose is given in a shorter time interval than this, a 4th IPV dose should be given at least 6 months after the 3rd dose.

c If aged 10 years to under 18 years, 3 doses of Hep B (5 µg) are required. An alternative 2-dose schedule of Hep B (10 µg; HBvaxPRO) may be used for children aged 11–15 years, with the 2nd dose given 4–6 months after the 1st.

A2.1.3 National Immunisation Schedule catch-up guides for infants and children aged up to 18 years

Note, these are a guide only. 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	RV*
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 3rd dose must be given before age 8 months and 0 days.

Table A2.4: 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 child has received the appropriate vaccines for their age, continue on the Schedule as usual.		

* 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 also receive 2 further doses of PCV to complete the primary course.

Table A2.5: Age at presentation: 12–23 months

Note: subtract previous doses given.

Dose	Vaccines		
First dose	DTaP-IPV-HepB/Hib[a]	PCV[b, c]	MMR[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, c]	
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 A child commencing PCV vaccination at age 12–23 months requires 2 doses with a minimum interval of 8 weeks between doses.

c If the child has had a primary course of PCV in their 1st year, they only require 1 dose in their 2nd year. A minimum interval of 8 weeks is required between the primary course in the 1st year and the booster dose in the 2nd year.

d 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.

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 Hep B vaccines as 2 separate injections instead of the combination DTaP-IPV-HepB/Hib vaccine.

Table A2.6: Age at presentation: 2 years to under 5 years

Note: subtract previous doses given.

Dose	Vaccines		
First dose	DTaP-IPV-HepB/Hib[a]	PCV	MMR
4 weeks later	DTaP-IPV-HepB/Hib[b]		MMR[c]
4 weeks later	DTaP-IPV-HepB/Hib[b]		
6 months later	DTaP-IPV[d]		
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 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 Hep B vaccines as 2 separate injections instead of the combination DTaP-IPV-HepB/Hib vaccine.

c Administer the 2nd MMR dose at age 4 years. If the child is older than age 4 years, administer the 2nd MMR dose a minimum of 4 weeks after the 1st dose.

d Administer DTaP-IPV at age 4 years, but note the ideal interval is 6 months after the final DTaP-IPV-HepB/Hib dose. If the child is older than age 4 years, administer DTaP-IPV a minimum of 6 months after the final DTaP-IPV-HepB/Hib dose.

Table A2.7: Age at presentation: 5 years to under 10 years

Note: subtract previous doses given.

Dose	Vaccines		
First dose	DTaP-IPV-HepB/Hib[a] or DTaP-IPV[b]	Hep B[c]	MMR
4 weeks later	DTaP-IPV-HepB/Hib[a,d] or DTaP-IPV[b,d]	Hep B[c]	MMR
4 weeks later	DTaP-IPV-HepB/Hib[a,d] or DTaP-IPV[b,d]	Hep B[c]	
6 months later	DTaP-IPV[d]		
Once the child has received the appropriate vaccines for their age, continue on the Schedule as usual.			

a 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 the DTaP-IPV and Hep B vaccines as 2 separate injections instead of the combination DTaP-IPV-HepB/Hib vaccine.

c Hep B is not required if DTaP-IPV-HepB/Hib is given.

d If a child turns 10 years before completing their catch-up programme, they should continue on the 10 to under 18 years catch-up schedule (refer to Table A2.8).

Table A2.8: Age at presentation: 10 years to under 18 years

Note: subtract previous doses given.

Dose	Vaccines			
First dose	Tdap[a]	IPV	Hep B[b]	MMR
4 weeks later	Tdap[a]	IPV	Hep B	MMR
4 weeks later	Tdap[a]		Hep B	
6 months later, or at age 11 years	Tdap	IPV		
At age ≥12 years				HPV[c] (girls only)

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 two-dose hepatitis B catch-up may be considered for children aged 11–15 years (use HBvaxPRO 10 µg), with the 2nd dose given 4–6 months after the 1st.

c A 3-dose HPV course is given at 0, 2 and 6-months. If a shortened schedule is required, the 2nd dose should be administered at least 1 month after the 1st dose and the 3rd dose should be administered at least 3 months after the 2nd dose.

A2.2 Immunisation catch-up for 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 A2.9 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, vaccines may be given simultaneously and the catch-up schedule shortened to four-weekly intervals (unless otherwise stated by the manufacturer) 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 vaccination (Tdap) is currently recommended and funded between 28 and 38 weeks' gestation in every pregnancy. A single dose of unfunded Tdap may be considered for adults requesting pertussis 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 proof of immunity or 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). Refer to chapter 18: 'Rubella'. If they have received one documented dose of MMR, a second dose should be administered.

6. Women who were under age 20 years when they commenced HPV vaccination are currently funded to complete the three-dose course, even if they are older than 20 years when they complete it.

7. Check whether the individual has any additional immunisation requirements, such as certain medical conditions or occupational risk (see chapter 4: 'Immunisation of special groups').

Table A2.9: Primary immunisation requirements for adults aged 18 years and older

Antigens and number of doses required
3 Td[a]
3 Polio (IPV)[b]
2 MMR[c]
3 HPV[d] (women only)

a A primary course of 3 doses of adult Td vaccine 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 doses of IPV is recommended and funded for unimmunised or partially-immunised adults. The minimum recommended interval between IPV doses 1 and 2 is 4 weeks; the 3rd IPV dose should be given at least 6 months after dose 2. If necessary, the interval may be shortened to 4 weeks between doses, but this is not the preferred schedule.

c Two doses of MMR (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 due to circulating wild disease at that time.

d Women who were under age 20 years when they commenced HPV vaccination are currently funded to complete the 3-dose course, even if they are older than 20 years 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 offering immunisation services' (see section A3.4) apply to the delivery of all National Immunisation Schedule vaccines and any other vaccines authorised by a medical officer of health or the Director-General of Health.

It is recommended that all vaccinators and immunisation providers offering privately purchased vaccines adhere to the 'Immunisation standards' and 'Guidelines for organisations offering immunisation services'.

The Schedule aims to protect children and adults against 13 serious vaccine-preventable diseases and offers publicly funded immunisation to individuals at risk of hepatitis A, influenza, varicella, tuberculosis, meningococcal and/or pneumococcal disease.

Note: the term 'vaccinator' used throughout these standards applies to both registered nurse vaccinators and pharmacist vaccinators.

A3.2 HDC Code of Health and Disability Services Consumers' Rights Regulation 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 they should have a current authorisation certificate from a medical officer of health or the Director-General of Health.

1.2 An approved pharmacist vaccinator completes a vaccinator training programme approved by the Ministry of Health and a clinical assessment, and vaccinates in accordance with the specific vaccine's gazetted medicines classification.[1]

1.3 The authorised vaccinator provides a summary of their immunisation practice over the preceding 12 months. Pharmacist vaccinators need to maintain a summary[2] of their immunisation practice over the preceding 12 months.

1.4 The vaccinator remains current with developments in immunisation theory, practice and policy. Every two years the vaccinator undertakes specific Ministry of Health-approved education updates (minimum of four hours), either by attending an education course or by completing an online course.

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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).

1.5 The vaccinator understands the importance of effective vaccine cold chain management and contributes to the practice/clinic achieving and maintaining Cold Chain Accreditation (CCA).[3]

1.6 The vaccinator ensures all the vaccines they administer have been stored at the recommended temperature range of +2°C to +8°C at all times.

1.7 The vaccinator is able to respond to and manage vaccine reactions, including anaphylaxis, and can perform resuscitation if necessary. The vaccinator is familiar with the adverse events reporting process to the Centre for Adverse Reactions Monitoring (CARM), and is aware of the process to submit an adverse event report.

1.8 The vaccinator is able to deal with spillages (blood or vaccine), and the safe disposal of needles, syringes and vaccines.[4]

1.9 The vaccinator effectively communicates immunisation information to families and individuals in a culturally competent way and provides evidence-based balanced information to enable informed decision-making.

1.10 The vaccinator has had specific National Immunisation Register (NIR) education and training to enable them to check a child's immunisation records (or request this information if they do not have access to the NIR), administer the correct vaccines and provide follow-up services.

1.11 The vaccinator has had training in the correct use of their practice management system or school-based immunisation system or the NIR manual forms to enable them to correctly enter an individual's information on the NIR (if applicable).

1.12 The vaccinator maintains linkages with other providers associated with immunisation delivery; for example, immunisation coordinators, outreach immunisation providers and their local DHB NIR team.

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[3] Refer to Appendix 6.

[4] Refer to Appendix 7.

Standard 2: The vaccinator obtains informed consent to immunise

Required characteristics of the vaccinator

2.1 Evidence-based information about the disease and vaccines must be given to individuals/parents/guardians to enable them 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 education material.

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 National NIR (if applicable) unless the individual/parent/guardian chooses to opt off the NIR. (Note: some school-based immunisation programmes will collect an individual's information on the NIR; if this is the case, information about the NIR will be contained on the consent form.)

2.5 Consent does not need to be given in writing (except for school-based immunisation programmes and BCG vaccination), but the vaccinator should keep a written summary of the discussion as well as a record that verbal consent was obtained.

2.6 The vaccinator obtains consent for each immunisation episode and records 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] (Note: for school immunisation programmes, written consent must be given when the parent/guardian will not be present at the immunisation.)

[5] Refer to chapter 2.

2.7 If the individual/parent/guardian chooses to opt off the collection of their or their child's information on the NIR, the vaccinator informs them that they/their child can still be immunised but the information will not be sent to the NIR. The vaccinator also must inform the individual/parent/guardian what they need to do to opt off, what information will be retained by the NIR, why this information is retained, and that they can reconsider their decision at any time in the future.

2.8 If the individual/parent/guardian declines to be immunised/to immunise their child, the vaccinator provides information about keeping themselves and others healthy. The vaccinator should advise the individual/parent/guardian that they can reconsider their decision at any time in the future.

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 should be present for vaccination; at least one must be an authorised vaccinator and both must be trained in basic emergency techniques, including resuscitation and anaphylaxis.

3.3 The vaccinator holds a current CPR certificate[7] consistent with their practice, education and assessed competence as a vaccinator.

[6] Refer chapter 2.

[7] Refer to Appendix 4.

3.4 The vaccinator can treat adverse events following immunisation (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 follows the practice/clinic cold chain management policy. The vaccinator ensures the practice/clinic achieves Cold Chain Accreditation.[8]

3.7 Before vaccinating, the vaccinator:

- determines the current health of the vaccinee and the possible immunosuppression status of contacts[9]
- ascertains the date of the last immunisation to ensure doses are spaced correctly (if applicable)
- enquires about any reactions following previous vaccine doses
- checks for true contraindications.[10]

3.8 The vaccinator uses clean techniques in the preparation and administration of all vaccines,[11] visually checks the vaccine, checks expiry date, reconstitutes vaccines with the diluent supplied (as appropriate) and uses vaccines within the recommended period after reconstitution.

3.9 The vaccinator provides verbal and written information that is evidence based and follows best practice principles about care after immunisation, including management of expected vaccine responses and accessing advice and medical attention, if required, during office and after office hours.[12]

3.10 The vaccinator is recommended to carry indemnity insurance for their personal/professional protection.

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8 Refer to Appendix 6.

9 Refer to the pre-vaccination checklist in chapter 2.

10 Refer to chapter 1 and the specific disease chapters.

11 Refer to chapter 2 and Appendix 7.

12 Refer to chapter 2.

Standard 4: The vaccinator documents information on the vaccine(s) administered, and maintains patient confidentiality

Required characteristics of the vaccinator

4.1 The vaccinator documents the individual's personal details, including: National Health Index number (NHI), name, date of birth, ethnicity, address, contact telephone number, next of kin details and general practitioner (if the vaccinator is not the usual primary care provider).

4.2 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
- 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 well documented)
- the immunisation event in the child's *Well Child Tamariki Ora Health Book* (if applicable)
- the date for the next immunisation in the child's *Well Child Tamariki Ora Health Book* (if applicable)
- advice and resources given.

4.3 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.

4.4 The vaccinator ensures the Immunisation Certificate is accurately completed following the 15-month and 4-year immunisation events.

4.5 When an individual is registered on the NIR, all associated providers are notified that an immunisation event has occurred. If the practice/clinic is not the usual primary care provider, and if the individual/parent/guardian consents, then the individual's general practitioner or other primary care provider is informed by the vaccinator within five working days of giving the vaccine.

4.6 The vaccinator ensures the Immunisation Benefit Claim is accurately completed and submitted, including the correct NHI number (if applicable).

4.7 All clinical documentation is appropriately managed and stored to maintain confidentiality, and is made available to the individual/parent/guardian on request.

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 If informed consent is obtained, 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 well documented.[13]

[13] Refer to chapter 1 and the specific disease chapters.

Standard 6: The vaccinator reports adverse events following immunisation promptly, accurately and completely

Required characteristics of the vaccinator

6.1 All serious or unexpected adverse events following immunisation are reported by the vaccinator to the Medical Assessor, Centre for Adverse Reactions Monitoring (CARM),[14] and to the individual's general practitioner (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, the vaccinator informs the DHB NIR Administrator (completes an NIR4 form) so that the adverse event code can be recorded on the NIR.

6.4 The vaccinator seeks specialist (eg, general practitioner, 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 Health Book* (if applicable) and in the patient records and appropriate follow-up is carried out.

[14] Refer to chapter 2 for the adverse event reporting process.

A3.4 Guidelines for organisations storing and/or offering immunisation services

These guidelines apply to all organisations who store and/or offer vaccines, including (but not limited to) general practices, public health units, pharmacies, travel clinics, emergency medical services, hospital wards and departments/pharmacies and occupational health clinics.

The organisation that employs vaccinators to offer immunisation services has links to primary health care and to Well Child Tamariki Ora providers

Required characteristics

- Childhood immunisation is delivered, not in isolation, but as an integrated part of Well Child Tamariki Ora activities through primary health care.
- 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 appropriately and routinely 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, kaiawhina, community health workers) for vaccinators working in the community.

[15] See the Cold Chain pages on the Ministry of Health website (www.health.govt.nz/coldchain).

- 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 ongoing training and support specific to the NIR, practice management systems and/or the school-based vaccination system (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.
- Non-resident children are eligible to receive funded Schedule vaccines, and providers may claim the immunisation benefit for these children. Further information on eligibility can be found on the Ministry of Health website.
- Immunisations are provided at all times when the organisation or service is open.
- Immunisations are provided without the need for an appointment.
- 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[16] in different languages).

[16] 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.

A3.5 Recommended resources

Ministry of Health (available at www.health.govt.nz)

- The current *Immunisation Handbook*
- National Immunisation Register Privacy Policy
- The current *National Guidelines for Vaccine Storage and Distribution*
- Cold Chain Management Policy Template
- Cold Chain Accreditation Practice Provider Self-Assessment Form
- Cold Chain Accreditation Provider Reviewer Form
- *Kōrero Mārama: Health Literacy and Māori*, February 2010, available from www.maorihealth.govt.nz (search under publications)

Immunisation Advisory Centre (www.immune.org.nz)

- *Standards for Delivery of Vaccinator Training Courses for Non-Medical Vaccinators*
- *Standards for Delivery of Updates for Trained Non-Medical Vaccinators*

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/cornerstone-general-practice-accreditation
- Pharmacy Council of New Zealand. 2013. *Statement on Pharmacist* Vaccinators. URL: www.pharmacycouncil.org.nz/standards_guidelines

A3.6 Relevant legislation and regulations[17]

- 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[18]
- Health Practitioners Competence Assurance Act 2003
- Privacy Act 1993
- Care of Children Act 2004
- Accident Compensation Act 2001
- Health and Safety in Employment Act 1992
- Resource Management Act 1991
- Primary Maternity Services Notice 2007,[19] pursuant to section 88 of the New Zealand Public Health and Disability Act 2000

[17] See www.legislation.govt.nz

[18] See www.hdc.org.nz

[19] See www.health.govt.nz

Appendix 4: Authorisation of vaccinators and criteria for pharmacist vaccinators administering vaccines

A4.1 Protocol for authorisation of vaccinators in New Zealand – 2014

See section A4.2 for pharmacist vaccinators.

A4.1.1 Authority

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.

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

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 training) 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[1] and any other vaccine as authorised by a medical officer of health. This would not normally include travel vaccines.

Authorisation for vaccinating other populations (eg, hepatitis B or influenza vaccination of workplace staff as part of a locally approved programme) will be subject to whatever conditions are stipulated by the medical officer of health.

The authorised vaccinator will have to apply to the local medical officer of health for the approval of a local vaccination programme (eg, a non-funded influenza immunisation programme provided by a medical centre) (see section A4.4).

A4.1.2 Process for initial vaccinator authorisation

Applicants applying to become an authorised vaccinator must complete the following.

1. Demonstrate that within the preceding 12 months they have attended, completed and passed a vaccinator training course that meets the current *Standards for Delivery of Vaccinator Training Courses* published by the Immunisation Advisory Centre (IMAC). Specifically, the course should consist of:
   - a minimum of 16 hours' educational input
   - a written test (minimum one-hour duration consisting of a combination of multiple choice and short answers, which may be oral at the facilitator's discretion).

[1] See the Introduction or www.health.govt.nz/immunisation for more information about the National Immunisation Schedule.

2. Following successful completion of the course, the applicant will 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 this assessment.

3. Provide evidence that they hold a current practising certificate. The *Competencies for Registered Nurses* (Nursing Council 2007) state 'Registered nurses are accountable for ensuring all health services they provide are consistent with their education and assessed competence, meet legislative requirements and are supported by appropriate standards'.[2]

Note: see section A4.3 for resuscitation requirements for vaccinators.

A4.1.3 Process for vaccinator re-authorisation

Authorisation is for a period of two years from the date of the initial training but it can be renewed subject to meeting certain requirements (refer to Appendix 3: Immunisation standards for vaccinators, Standards 1.3 and 1.4).

Applicants for re-authorisation will be required to:

1. provide evidence that they have attended specific vaccination education sessions of a minimum of four hours' duration during the last two years

2. provide evidence of holding a current practising certificate

3. provide a summary[3] of their immunisation practice over the past 12 months.

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[2] Nursing Council of New Zealand. 2007. *Competencies for Registered Nurses*. Wellington: Nursing Council of New Zealand [reprint 2012]. URL: http://nursingcouncil.org.nz/Nurses/Continuing-competence (accessed 17 November 2013).

[3] 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).

A4.1.4 Process when authorisation has not been maintained (ie, where the authorisation expired more than six months previously)

More than five years since vaccinator training

If it is more than five years since the applicant completed their initial vaccinator training, they will be required to attend, complete and pass a vaccinator training course. This is because there will have been significant developments in vaccination delivery in the intervening interval. The course must comply with the current edition of the IMAC *Standards for Delivery of Vaccinator Training Courses*.

Following successful completion of the course, applicants would need to complete the following and submit the documentation to the medical officer of health.

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. Provide evidence that they hold a current practising certificate. The *Competencies for Registered Nurses* (Nursing Council 2007) state 'Registered nurses are accountable for ensuring all health services they provide are consistent with their education and assessed competence, meet legislative requirements and are supported by appropriate standards'.[4]

3. Provide a summary of their immunisation practice over the past 12 months.

Note: see section A4.3 for resuscitation requirements for vaccinators.

[4] Nursing Council of New Zealand. 2007. *Competencies for Registered Nurses*. Wellington: Nursing Council of New Zealand [reprint 2012]. URL: http://nursingcouncil.org.nz/Nurses/Continuing-competence (accessed 17 November 2013).

Less than five years since vaccinator training but never requested authorisation

If the applicant has completed a vaccinator training course within the past five years, they must:

1. have had a clinical assessment by an immunisation coordinator or approved assessor (as approved by the medical officer of health) within the past three months
2. provide evidence of successfully attending a Ministry of Health-approved vaccinator training course within the last five years
3. provide evidence that they have attended specific Ministry of Health-approved vaccination education sessions, of a minimum of four hours' duration, during each two-year period since they completed the vaccinator training course
4. provide a summary of their immunisation practice over the past 12 months
5. provide evidence of holding a current practising certificate.

The applicant must submit the documentation described above to the medical officer of health. The applicant will be assessed on a case-by-case basis.

More than six months but less than five years since last re-authorised, and have attended vaccinator update training every two years

When an authorised vaccinator has failed to re-authorise within six months of their authorisation expiring they must:

1. have had a clinical assessment by an immunisation coordinator or approved assessor (as approved by the medical officer of health) within the past three months
2. provide evidence that they have attended specific Ministry of Health-approved vaccination education sessions, of a minimum of four hours' duration, during each two-year period since they were last re-authorised

3. provide a summary of their immunisation practice over the past 12 months
4. provide evidence of holding a current practising certificate.

The applicant must submit the documentation described above to the medical officer of health. The applicant will be assessed on a case-by-case basis.

A4.1.5 Process when the applicant 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 independently. The applicant will be required to provide:

1. evidence of current authorisation in another health district
2. evidence of holding a current practising certificate
3. details of their proposed work in the district.

A4.2 Process for pharmacist vaccinators administering vaccines – 2014

A4.2.1 Authority

In 2012, following an application to the Medicines Classification Committee (MCC), the influenza vaccine was reclassified as a 'prescription medicine except when administered to a person 18 years of age or over by a pharmacist who has successfully completed a vaccinator training course approved by the Ministry of Health New Zealand and is complying with the immunisation standards of the Ministry of Health'. The reclassification means that pharmacists will need to complete a defined vaccinator training course to become vaccinators. However, unlike most vaccinations, the vaccination programme administered within their pharmacy practice does not need medical officer of health's approval or oversight because the vaccine is not a prescription medicine when administered by a pharmacist.

At the time of writing, influenza, meningococcal, Tdap and zoster vaccines to adults have been reclassified and gazetted. It is anticipated that future reclassification of other vaccines will widen the range of vaccines that a pharmacist vaccinator is able to administer. It is the vaccine's medicine classification which gives a pharmacist (who meets the conditions of the classification) the authority to administer the vaccine.

A4.2.2 Process for pharmacist vaccinators – vaccine classification requirements

A pharmacist seeking to administer vaccines under the vaccine medicines classification must complete the following.

1. Demonstrate that within the preceding 12 months they have attended, completed and passed a Ministry of Health-approved vaccinator training course that meets the current *Standards for Delivery of Vaccinator Training Courses* published by the Immunisation Advisory Centre (IMAC). Specifically, the course should consist of:
   - a minimum of 16 hours' educational input
   - a written test (minimum one-hour duration consisting of a combination of multiple choice and short answers, which may be oral at the facilitator's discretion).
2. Following successful completion of the course, the applicant must undergo an independent clinical assessment by an immunisation coordinator or an approved assessor (as approved by the medical officer of health). The immunisation coordinator will need to sight the phamacist's evidence that they hold a current Pharmacy Council of New Zealand (PCNZ) practising certificate and a Vaccinator Training Certificate (VTC). Information about the practice environment and Cold Chain Accreditation (CCA) will be collected at the time of this assessment.

   Pharmacists will not be able to vaccinate until they have completed the vaccinator course and forwarded confirmation they have completed an independent clinical assessment to the PCNZ. A list of approved pharmacist vaccinators is available on the PCNZ's website. (www.pharmacycouncil.org.nz/standards_guidelines).

This website is updated quarterly by the PCNZ when they have received confirmation from:

- the VTC provider that the pharmacist has completed their VTC, and
- the pharmacist has confirmed with PCNZ they have passed the clinical assessment

Note: see section A4.3 for resuscitation requirements for vaccinators.

A4.2.3 Process for pharmacist vaccinators to meet the two-yearly update requirements

The vaccine classification requirements for a pharmacist vaccinator require the pharmacist to complete a Ministry of Health-approved education update course every two years (refer Appendix 3: Immunisation standards for vaccinators, Standards 1.3 and 1.4).

Pharmacist vaccinators will be required to:

1. provide evidence that they have attended specific vaccination education sessions of a minimum of four hours' duration during the last two years
2. maintain a summary[5] of their immunisation practice over the past 12 months.

Prior to the expiry of their previous course, pharmacists will need to complete an approved update course to be able to continue vaccinating. The pharmacist will need to notify PCNZ when they have completed their update course. A list of pharmacist vaccinators is available on the PCNZ's website (www.pharmacycouncil.org.nz/standards_guidelines).

Note: see section A4.3 for resuscitation requirements for vaccinators.

[5] 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).

A4.2.4 Process when approval criteria have not been maintained by the pharmacist vaccinator (ie, where the approval expired more than six months previously)

More than five years since vaccinator training

If it is more than five years since the applicant completed their initial vaccinator training, they will be required to attend, complete and pass a vaccinator training course. This is because there will have been significant developments in vaccination delivery in the intervening interval. The course must comply with the current edition of the IMAC *Standards for Delivery of Vaccinator Training Courses*.

Following successful completion of the course, the applicant must complete the following.

1. Undergo a clinical assessment by an immunisation coordinator or an approved assessor. The immunisation coordinator/approved assessor will need to sight the pharmacist's evidence that they hold a current PCNZ practising certificate and a Vaccinator Training Certificate (VTC). Information about the practice environment and Cold Chain Accreditation (CCA) will be collected at the time of this assessment.
2. Send confirmation to PCNZ that they have completed an independent clinical assessment. A list of pharmacist vaccinators is available on the PCNZ's website (www.pharmacycouncil.org.nz/standards_guidelines).

Note: see section A4.3 for resuscitation requirements for vaccinators.

Less than five years since vaccinator training but never requested pharmacist vaccinator approval

If the applicant has completed a vaccinator training course within the past five years, they must:

1. undergo a clinical assessment by an immunisation coordinator or approved assessor (within the past three months)
2. provide evidence of successfully attending a Ministry of Health-approved vaccinator training course within the last five years

3. provide evidence that they have attended specific Ministry of Health-approved vaccination education sessions of a minimum of four hours' duration during each two-year period since they completed the vaccinator training course

4. maintain a summary of their immunisation practice over the past 12 months.

The applicant must submit the documentation described above to the PCNZ.

More than six months but less than five years since last re-approved and have attended vaccinator update training every two years

When an approved pharmacist vaccinator has failed to seek re-approval within six months of their vaccinator approval expiring they must:

1. have had an independent clinical assessment by an immunisation coordinator or approved assessor (as approved by the medical officer of health) within the past three months

2. provide evidence that they have attended specific Ministry of Health-approved vaccination education sessions of a minimum of four hours' duration during each two-year period since they were last re-authorised

3. maintain a summary of their immunisation practice over the past 12 months.

The applicant must submit the documentation described above to the PCNZ.

A4.3 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:

- infant, child and adult Cardiac Pulmonary Resuscitation (CPR) including mouth-to-mouth, mouth-to-mask and the management of choking
- use of airway adjuncts, including the sizing and insertion of oropharyngeal and laryngeal mask airways
- use of an Automated External Defibrillator
- one- and two-person bag valve mask ventilation and mouth-to-mask technique
- use of supplemental oxygen.

New Zealand Resuscitation Council (NZRC) classifies rescuer levels and identifies Level 4 as the first health professional level. This group might include occupation groups such as nursing graduates, anaesthesic technicians, radiographers and other hospital and community health-trained support staff.

Resuscitation training for all vaccinators should be at a standard equivalent to that set for NZRC Rescuer Level 4. The 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 2.4).

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 sections 2.4.4 and 2.4.5.

A4.4 Authorised vaccinators delivering an immunisation service

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.

		Office use only
1.	**Location/s** (specify)	Yes / No
2.	**Staff** There should be two people present for outreach or non-clinical immunisation, one of whom must be an authorised vaccinator; the other must be a competent adult able to call for emergency support.	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: · 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)* · Current certificate in basic life support* (for the second person if they are not an authorised vaccinator) · Indemnity insurance*	Yes / No
5.	**Legal** You should have knowledge of the provisions contained in the following legislation: · The Code of Health and Disability Consumers' Rights Regulation 1996 · Privacy Act 1993 (in relation to the storage and transfer of information) · The 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. a. 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?* b. 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 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 · minimum-maximum thermometer or temperature monitoring/recording device[#] · gloves · 0.5% hypochlorite · approved biohazard bag.	Yes / No
9.	**Optional additional emergency equipment** Intravenous cannula and administration sets: · intravenous fluids · hydrocortisone for injection · antihistamine for injection · sodium bicarbonate solution · saline flush	Yes / No

Note: Please ensure that you have included the documentation marked with an asterisk (*).

See the *National Guidelines for Vaccine Storage and Distribution* (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 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 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 general practitioner, practice nurse or public health nurse can help them to get an immunisation certificate if they do not have one.

Appendix 6: The cold chain: vaccine storage, transportation and destruction

A6.1 The cold chain

The 'cold chain' is the system of transporting and storing vaccine at +2°C to +8°C from the place of manufacture to the point of vaccine administration (the individual).

The success of an immunisation programme depends on the cold chain to maintain vaccine potency. To achieve this, the recommended temperature of +2°C to +8°C must be maintained during storage and distribution at all times to avoid irreversible loss of potency from thermal insult (heat or freezing). All immunisation providers who store or transport vaccines should maintain their vaccine refrigerators as close as possible to +5°C, which gives a safety margin of plus or minus 3°C.

The integrity of the cold chain is dependent not only on the equipment used, but also on the people involved and the practices they undertake.

The distribution of the funded vaccines throughout New Zealand is through a direct delivery system, which reduces the potential for vaccine damage to occur (see section A6.5 for information about the National Cold Chain Audit). Vaccines are distributed by courier, in appropriate insulation, and delivery and unpacking must occur within the predetermined 'window' period (see section A6.2.4).

In the event of any sudden variations in refrigerator temperature, or recordings outside the recommended +2°C to +8°C range, or equipment failure, the immunisation coordinator, medical officer of health, public health service or the regional immunisation advisor should be contacted for advice and support.

Key points for cold chain management

- All immunisation providers who offer immunisation services must achieve cold chain accreditation, including public health units, pharmacies, travel clinics, hospital wards, clinics and departments, and pharmacies.
- Each immunisation provider must have a written cold chain management policy in place and ensure their policy is reviewed and updated annually.
- 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 temperatures must be monitored and recorded at the same time on a daily basis.
- All immunisation providers must have an electronic temperature recording device (eg, data logger) that records and downloads data from the previous month.

A6.1.1 Vaccine reference information

All immunisation providers should have easy access to the current *Immunisation Handbook*, and to the *National Guidelines for Vaccine Storage and Distribution* and the *Annual Cold Chain Management Guide and Record* (available at www.health.govt.nz/coldchain). These are essential documents to ensure the vaccines delivered within New Zealand have been stored correctly to maximise their effectiveness.

A6.1.2 Cold chain accreditation programme

Cold chain accreditation (CCA) is a tool to support an immunisation provider's cold chain management practices. Immunisation providers demonstrate their cold chain management through self-assessment, followed by a review by an approved CCA reviewer (eg, immunisation coordinator or approved assessor) to confirm all requirements have been achieved.

CCA is valid for up to three years, based on the reviewer's findings. All immunisation providers who store vaccines must achieve CCA, including general practices, public health units, pharmacies, travel clinics, occupational health clinics, emergency medical services, and hospital wards, departments and pharmacies.

Completing this process will enable immunisation providers to meet the cold chain Aiming for Excellence indicator 17 of the Royal New Zealand College of General Practitioners (RNZCGP) Cornerstone Programme.

CCA is based on the following five assessment sections:

1. practice policies
2. vaccine reference information
3. vaccine stock management
4. temperature monitoring and performance
5. refrigerator details.

A CCA review measures performance against the criteria as follows:

- **met:** fully meets the CCA requirements in this area, as per the *National Guidelines for Vaccine Storage and Distribution*
- **not met:** fails to meet the CCA requirements.

If the CCA requirements are not met, a remedial plan is put in place while the provider meets the CCA requirements. The provider is still able to administer vaccines while this remedial plan is being achieved if the recommended temperature range can be maintained at all times. Failure to take remedial action to meet the requirements by the time of the repeat review/assessment may lead to the vaccine supply being temporarily suspended.

For a practice to achieve CCA, it must meet all the requirements for cold chain management. Refer to the CCA Provider Self-Assessment and CCA Immunisation Provider Review forms available on the Cold Chain pages of the Ministry of Health website (www.health.govt.nz/coldchain).

Cold chain management policy

Each immunisation provider should have an individualised and documented cold chain management policy. This should include details of the designated cold chain management staff member, vaccine stock requirements, vaccine ordering and storage processes, vaccine disposal, refrigerator operation, and maintenance and management processes, along with an emergency procedure for dealing with equipment and power failures.

The cold chain management policy should be dated and signed by the relevant staff and reviewed on an annual basis. A cold chain management policy template, which covers all the areas of cold chain management required to achieve CCA, is available on the cold chain pages of the Ministry of Health website (www.health.govt.nz/coldchain).

A6.2 Vaccine storage

Key points for vaccine storage

- All immunisation providers must use a pharmaceutical refrigerator to store vaccines. Food is not to be stored in the vaccine refrigerator.
- All vaccines must be stored between +2°C and +8°C.
- The refrigerator temperature needs to be monitored and documented at the same time each working day (ideally by the same person) and entered in the temperature log/register or *Annual Cold Chain Management Guide and Record*.
- All immunisation providers must have an electronic temperature recording device (eg, data logger) that records and downloads data from the previous month.
- Vaccines should be left in their original packaging. This acts as insulation and promotes good stock management.
- Vaccines should be refrigerated immediately on arrival from the distributor. MMR diluent may be stored at room temperature.

- Air should be able to circulate in the refrigerator (ie, do not store vaccines against the walls, to the top of each shelf, or in the bottom of the refrigerator). There should be 25–30 mm between the vaccines and the back of the refrigerator and the shelf above.
- Stock with the shortest expiry date should be used first. Vaccines should be stored with the batch number and expiry date label showing. Record this in the vaccine stock log/register.
- To avoid overcrowding and to ensure stock rotation, order vaccines at appropriate frequencies to maintain sufficient vaccine stock levels for two to six weeks' supply.
- Opening of the refrigerator door should be minimised in order to reduce temperature fluctuations.
- All persons using vaccines have a responsibility to report and correct any problems relating to cold chain storage to their employer/manager and immunisation coordinator.

A6.2.1 Medicines Act, Section 47

All vaccines must be stored at the recommended temperature range, but there are other specific requirements in the Medicines Act 1981 and Regulations for the storage and handling of vaccines.

Part 5 of the Medicines Regulations 1984 sets out legal requirements in relation to the packaging, storage and handling of medicines in general. Section 47 of the Medicines Act 1981 sets out some specific requirements relating to the storage and delivery of prescription and restricted medicines, including vaccines.

The Medicines Act 1981, section 47, Storage and delivery of medicines states:

1. No person who is in possession or charge of any prescription medicine or restricted medicine shall put it:
    a. in any cupboard, box, shelf, or other place of storage in which articles of food or drink are stored or kept for ready use; or
    b. in any place to which young children or unauthorised persons have ready access.

2. No person shall pack any medicine, or prepare it for use in any room or on any bench that is used for the purpose of packing, preparing or consuming any food or drink.

3. Except as otherwise provided in any regulations made under this Act, no person who is in possession, for the purposes of any business, of a prescription medicine or a restricted medicine that is kept for the time being within any building or vehicle shall leave that building or vehicle unattended, unless he has taken all reasonable steps to secure that building or vehicle, or the part of it in which the medicine is kept, against unlawful entry.

4. No person shall deliver on retail sale, or in circumstances corresponding to retail sale, any medicine otherwise than through the post or by handing it or causing it to be handed to the person, or another person reasonably believed to be acting on that person's behalf, to whom it is addressed or for whose use it is intended.

5. Every person commits an offence against this Act who, without reasonable excuse, contravenes any of the provisions of this section.

A6.2.2 Vaccine refrigerator

Refrigerator details

The refrigerator should be of sufficient size to accommodate vaccine storage requirements without exceeding the manufacturer's recommendations for maximum storage capacity. Contact the local immunisation coordinator for advice before purchasing new cold chain equipment.

Refrigerator placement

The refrigerator should have an independent power point and a plug-in surge protection unit. The plug should be taped over (with a written warning against unplugging) to overcome the risk of disconnection. An alternative may be to permanently wire the refrigerator into the outlet.

The refrigerator must be in a reasonably sized, well-ventilated room and not in direct sunlight or against a heat source/external wall, because the efficiency of refrigeration equipment declines with high ambient temperatures. There should be sufficient ventilation around the condenser of the refrigerator (the recommendations are at 7.5 cm from the refrigerator's back and sides) to allow air to circulate, because this will help to reduce cyclical fluctuations. Contact the manufacturer of a pharmaceutical refrigerator before moving the refrigerator.

Refrigerator maintenance

The following actions should be taken to ensure the efficient refrigeration of vaccines.

Table A6.1: Actions (and their frequency) to ensure safe vaccine handling and storage

Daily
Record the refrigerator temperature in the temperature log/register.
Ensure the top of the refrigerator remains clear (except for the temperature log/register).
Monthly
Review the temperature log/register for any cyclical fluctuations and climatic changes.
Check the back plate inside the refrigerator for any visible ice.
Six-monthly
Check that the door seal grips the door all around the frame; that there are no large air gaps that will affect the efficiency of the fridge; that there are no large splits or cuts in the seal that will affect hygiene; and that the seal is clean and free from mould and debris.
Leave the door open to perform the self-closing door check. The door should close automatically. To ensure this, alter the height adjusters underneath the refrigerator so that the door hinge side of the refrigerator is set slightly higher than the non-hinge side.
All interior and exterior surfaces of the refrigerator should be cleaned at least every six months with a solution of 0.03 percent hypochlorite solution (1 part domestic bleach to 99 parts water).

Continued overleaf

Annually

Annual independent validation of the refrigerator's temperature is undertaken by the local immunisation coordinator. Contact the immunisation coordinator for more information.

Service the refrigerator annually, according to the manufacturer's instructions or if the temperature fluctuates.

During power failures

During a power failure the refrigerator door should be left closed.

If the power fails for more than four hours, vaccines should be transferred to an appropriately sized insulated vaccine container with the correct number and size of ice packs to ensure the vaccines will remain at +2°C to +8°C. A minimum/maximum thermometer will assist with temperature monitoring.

If the power is not restored, the vaccines will need to be transferred to an alternative refrigerator that has a power supply, as outlined in your cold chain policy (see the information on vaccine transportation in section A6.3).

A6.2.3 Temperature monitoring and performance

Each refrigerator storing vaccines must have an electronic temperature-recording device (eg, a data logger) that measures the current temperature and the minimum and maximum temperatures reached since the device was last reset. The device should be able to record and download data from the previous month.

The temperature should be read and recorded daily, preferably at the same time each day. These recordings should be reviewed every four weeks and compared with monthly data logger recordings to identify cyclical fluctuations and climatic changes. The immunisation coordinator may be able to assist with further information on refrigerator temperature recording devices.

Once CCA has been achieved, six-monthly/annual electronic monitoring can also be undertaken by the PHO or the practice's refrigerator temperature recording device. Temperature records need to be retained for a minimum of 10 years.

A6.2.4 Vaccine stock management

Stock management plan

All immunisation providers should have a system for recording vaccine stock levels (ie, a stock management plan). The plan should include vaccine requirements, ordering, stock rotation, and the use of a log/register to document the date, name and batch numbers of vaccines arriving from the supplier, vaccine expiry dates and date of receipt.

Vaccine deliveries

When a vaccine delivery arrives, the vaccinator or workplace should check the cardboard box or chilly bin contents against the order form. Check that the vaccine delivery is within the stated delivery window. Once satisfied with the vaccine order, the vaccinator or receptionist should sign for the vaccines. If the cardboard box or chilly bin has a yellow sticker, see section A6.5 for information about the National Cold Chain Audit.

If the vaccinator has reason to believe the vaccines have not been kept at the required temperature, they should notify the supplier and contact their local immunisation coordinator for advice and, if necessary, return the vaccines.

A6.2.5 Managing cold chain failures

Key steps if the vaccine refrigerator temperature recordings go outside the recommended +2°C to +8°C temperature range at any time

- Refer to the *Annual Cold Chain Management Guide and Record*.
- Label the vaccines 'not for use' and leave them in the refrigerator – do not re-open the refrigerator door.
- Download the electronic temperature monitoring device (eg, data logger) and check for inconsistencies or temperature fluctuation.
- Contact your local immunisation coordinator for advice and actions to be taken before continuing to vaccinate or discarding vaccines.
- Document the steps and actions you have taken.
- If you need to recall or re-immunise any individuals, please inform the Ministry of Health's National Immunisation Programme by emailing immunisation@moh.govt.nz or by contacting the Manager Immunisation directly.

Immunisation providers also need to consider whether there may have been multiple breaches of the cold chain. This means that all breaches should be managed on an event and/or batch-by-batch basis. There may also be situations where a breach is not identified until some time later (ie, retrospectively). It is important to note that thermal damage to vaccines is cumulative.

Table A6.2 below provides general guidelines to help guide action in specific situations. The immunisation coordinator will consult with the vaccine manufacturer because they may have additional information on the thermostability of the vaccine. The manufacturer will advise the coordinator on a batch-by-batch basis whether the vaccine can be used and within what timeframe.

Table A6.2: Recommendations for the use of vaccines exposed to temperatures outside +2°C to +8°C

Vaccine	Protect from light	Exposed to temperatures below 0°C	Exposed to temperatures between 8°C and 25°C
BCG Diluent	Yes No	Use Do not use*	Contact the immunisation coordinator with details of vaccine batch number, maximum temperature reached and duration of exposure to determine if the vaccine is suitable for use.
DTaP-IPV-HepB/Hib Hib pellet in the above	Yes No	Do not use* Use	Contact the immunisation coordinator with details of vaccine batch number, maximum temperature reached and duration of exposure to determine if the vaccine is suitable for use.
DTaP-IPV, Tdap	No	Do not use*	Contact the immunisation coordinator with details of vaccine batch number, maximum temperature reached and duration of exposure to determine if the vaccine is suitable for use.
Hib	No	Use	Contact the immunisation coordinator with details of vaccine batch number, maximum temperature reached and duration of exposure to determine if the vaccine is suitable for use.
Diluent	No	Do not use*	Use.
Hepatitis A	No	Do not use*	Contact the immunisation coordinator with details of vaccine batch number, maximum temperature reached and duration of exposure details to determine if the vaccine is suitable for use.
Hepatitis B	No	Do not use*	<5 days: Use. ≥5 days: Do not use.*
HPV4	Yes	Do not use*	<72 hours: Use. ≥72 hours: Do not use.*

Continued overleaf

Vaccine	Protect from light	Exposed to temperatures below 0°C	Exposed to temperatures between 8°C and 25°C
Influenza: Fluarix Influvac	 No Yes	Do not use*	Contact the immunisation coordinator with details of vaccine batch number, maximum temperature reached and duration of exposure details to determine if the vaccine is suitable for use.
IPV	No	Do not use*	Contact the immunisation coordinator with details of vaccine batch number, maximum temperature reached and duration of exposure details to determine if the vaccine is suitable for use.
MCV4-D	Yes	Do not use*	Contact the immunisation coordinator with details of vaccine batch number, maximum temperature reached and duration of exposure details to determine if the vaccine is suitable for use.
MenCCV	No	Do not use*	Contact the immunisation coordinator with details of vaccine batch number, maximum temperature reached and duration of exposure details to determine if the vaccine is suitable for use.
MMR	Yes	Use	Contact the immunisation coordinator with details of vaccine batch number, maximum temperature reached and duration of exposure details to determine if the vaccine is suitable for use.
Diluent	No	Do not use*	Use.
PCV10	Yes	Do not use*	Contact the immunisation coordinator with details of vaccine batch number, maximum temperature reached and duration of exposure details to determine if the vaccine is suitable for use.

Continued overleaf

Vaccine	Protect from light	Exposed to temperatures below 0°C	Exposed to temperatures between 8°C and 25°C
PCV13	No	Do not use*	Contact the immunisation coordinator with details of vaccine batch number, maximum temperature reached and duration of exposure details to determine if the vaccine is suitable for use.
23PPV	No	Do not use*	Contact the immunisation coordinator with details of vaccine batch number, maximum temperature reached and duration of exposure details to determine if the vaccine is suitable for use.
RV5	Yes	Do not use*	Contact the immunisation coordinator with details of vaccine batch number, maximum temperature reached and duration of exposure details to determine if the vaccine is suitable for use.
Td	Yes	Do not use*	<5 days: Use. ≥5 days: Do not use.*
Varicella Diluent	Yes Yes	Do not use* Do not use*	Contact the immunisation coordinator with details of vaccine batch number, maximum temperature reached and duration of exposure details to determine if the vaccine is suitable for use.

* Send the vaccine for destruction (see section A6.4).

A6.3 Vaccine transportation

When transporting vaccines the temperature must be maintained between +2°C and +8°C at all times. Therefore, immunisation providers must use insulated containers (designated transport containers or polystyrene containers) when transporting vaccines (eg, for a school immunisation programme) or if there is a power or equipment failure. A temperature monitoring device (eg, data logger) should be placed with the vaccines during this time.

Ice packs must be frozen at least two days before being used for transporting vaccines. When placing ice packs in the freezer, set them on their edge and allow space between them to ensure even freezing. Table A6.3 below describes the process for preparing vaccines for transport.

Table A6.3: Preparing for vaccine transportation

Use only proven methods for transporting vaccines, such as an insulated vaccine container* (solid-wall transport containers, double-walled transport containers and polystyrene containers) with a clip-on lid.
Use a vaccine container of a size suitable for the amount of vaccine to be transported.
Use the appropriate number and size of ice packs for the vaccine container size, to ensure the vaccines will remain at +2°C to +8°C throughout their journey.
Monitor the vaccine container with an electronic temperature-monitoring device at all times (eg, a data logger).
Before placing the ice packs in the vaccine container, warm them until frost no longer forms on their surface.
Place approved* insulation material in the bottom of the vaccine container, then place the vaccines so that the most heat sensitive are nearest the ice packs and the most freeze sensitive are furthest away from the ice packs.
Separate the ice packs from the vaccine with the approved insulation material. This will prevent contact with the ice packs and thus ensure they will not freeze the vaccines.
Secure the lid in place using the clips, or, if not present, adhesive tape.

* Contact the immunisation coordinator for information regarding approved vaccine containers and materials.

Following these recommendations will keep the temperature within +2°C to +8°C for up to five hours and allows for the vaccine container to be opened briefly, up to four times.

In a school-based immunisation programme, when vaccines are likely to be stored in containers for longer periods and more frequent opening will occur, extra care must be taken with cold chain maintenance. To keep the temperature between +2°C and +8°C, an extra insulated container of frozen slicker pads or Environfreeze should be carried and added to the vaccine container as needed for temperature control.

When multiple vaccine containers are required, use one at a time – use all of the vaccines from one container before opening and using the next container.

A6.4 Vaccine destruction

Vaccines for destruction must be correctly disposed of, as required under the Resource Management Act 1991.

Immunisation providers should contact the local immunisation coordinator before disposing of vaccines. Unwanted, discontinued or expired vaccines and/or those subject to a cold chain failure should be prepared as follows and returned to the supplier.

- Pack the vaccines in a cardboard box with all the needles removed.
- Include the reason for destruction in the box.
- Clearly label the box 'Vaccines for Destruction', along with the supplier details, address and phone number.

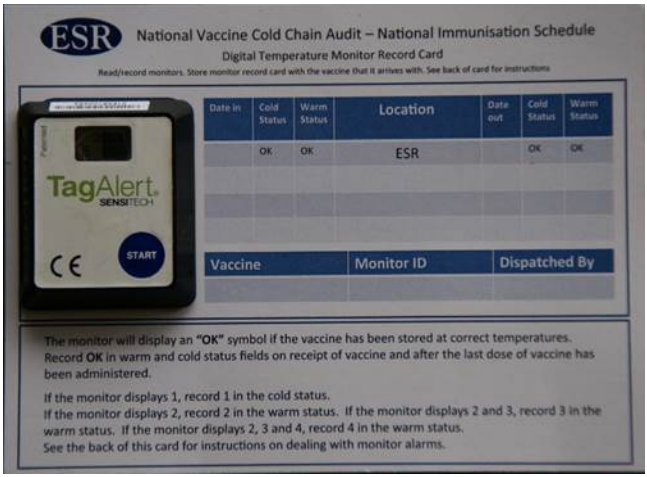
For advice on the return of non-Schedule vaccines, contact the supplier directly.

A6.5 National Cold Chain Audit

PHARMAC and the Ministry of Health commission the National Cold Chain Audit to monitor Schedule vaccines. The audit monitors the cold chain of vaccines from their origin at the National Vaccine Store until immunisation providers have administered all doses in the vaccine pack/box.

Follow the guidelines below when a digital monitor and record card are included with a vaccine pack/box.

Figure A6.1: Photo of the digital monitor and record card



1. When a digital monitor and record card are included with the vaccines, a yellow sticker will be attached to the vaccine pack/box.

2. Record the following information in the appropriate spaces on the record card before you place the vaccine in the refrigerator.

    a. 'Date in'.

    b. Cold and warm status from the digital monitor display. The monitor displays an 'OK' symbol if the temperature the vaccines have been stored in has been between +2°C to +8°C. If the display shows any of the alert numbers (1, 2, 3, or 4) contact the immunisation coordinator.

    c. 'Location' – enter your clinic's/organisation's name and location.

3. Keep the digital monitor and record card with the vaccines it arrived with – secure the card to the pack/box and ensure it remains with the vaccines in the refrigerator. If vaccines are transported to a clinic off-site, the record card must accompany the vaccines and the change of location, current temperature, etc needs to be entered on the record card.

4. Check the monitor's display every time a vaccine is used from the pack/box. A visible alarm will display on the monitor if the refrigerator/storage container temperature has gone outside the recommended range. Do not use the vaccines and contact the immunisation coordinator for advice.

5. When the last vaccine in the pack/box is being prepared for administration, record the following information in the appropriate spaces on the record card:

    a. 'Date out'

    b. Cold and warm status from the digital monitor display. If the display shows any of the alert numbers (1, 2, 3, or 4) contact the immunisation coordinator.

6. Return the completed monitor card to ESR in the envelope provided.

More information on the National Cold Chain Audit can be found in the current *National Guidelines for Vaccine Storage and Distribution* and the *Annual Cold Chain Management Guide and Record* (available at www.health.govt.nz/coldchain).

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 plastic dosing tube, and the BCG vaccine, which is supplied as a multi-dose vial.

A vial is a glass container with a rubber[1] 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 information 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 2.3).

[1] 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 (see Appendix 6).
- 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 a National Immunisation Register 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.

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.
- 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.
- 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. Note: keeping firm pressure on the needle during insertion prevents cutting the rubber core from the seal.

- 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 patient management system).

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. Keeping firm pressure on the needle during insertion prevents cutting the rubber core from the seal.
- 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 package insert 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 patient management system).

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. Keeping firm pressure on the needle during insertion prevents cutting the rubber core from the seal.
- 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 package insert 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 patient management system).

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.
- 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.
- Administer the vaccine.
- Dispose of the used syringe and needle into the sharps container.
- Complete the required documentation (eg, in the patient management system).

A7.2.4 Preparing the rotavirus vaccine

The rotavirus vaccine is administered orally. It is available as a single, prefilled dose in a plastic dosing tube with a twist-off cap. The dosing tube is contained in a pouch. The container and delivery system are latex-free.

- Where applicable, remove the detachable portion of the label 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.

- Tear open the pouch and remove the dosing tube.
- Clear the fluid from the dispensing tip by holding the tube vertically and tapping the cap.
- Open the dosing tube and:
  - puncture the dispensing tip by screwing the cap **clockwise** until it becomes tight
  - remove the cap by turning it ***counter*clockwise**.
- Administer the dose by gently squeezing the liquid into the infant's mouth, towards the inner cheek, until the dosing tube is empty. (A residual drop may remain in the tip of the tube.)
- Discard the empty tube and cap into the sharps container.

A7.2.5 Preparing vaccines supplied as multi-dose vials[2]

- 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 dose-sparing 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).

[2] Sources: World Health Organization. *Policy Statement: The use of opened multi-dose vials of vaccine in subsequent immunization sessions*. http://whqlibdoc.who.int/hq/2000/WHO_V&B_00.09.pdf; the Australian Technical Advisory Group on Immunisation (ATAGI) and the National Centre for Immunisation Research and Surveillance (NCIRS).

- 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 six hours after first opening (or, follow the manufacturer's instructions), even if the vaccine has not been used.

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 failure), see Appendix 6.

- 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 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 hepatitis B immunoglobulin 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 8.5.3 for the management of blood and body fluid exposures (hepatitis B), the *Starship Clinical Guidelines for Needle-stick Injuries*[3] or your local DHB guidelines (if available).

[3] Available at www.adhb.govt.nz/starshipclinicalguidelines/Needlestick%20Injuries.htm

Appendix 8: Notifiable disease case definitions and laboratory tests

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

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.

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 Tables A8.1 and A8.2 in this appendix. The source of the information is the *Communicable Disease Control Manual 2012*.[1] For the most up-to-date information, refer to the online version (available on the Ministry of Health website, www.health.govt.nz).

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

Table A8.1: Case definitions for notifiable vaccine-preventable diseases

Disease	Clinical description	Under investigation	Suspected case	Probable case	Confirmed case	Not a case
Diphtheria[1]	Respiratory diphtheria is characterised by infection primarily involving the tonsil(s), pharynx and/or larynx, low-grade fever, with or without an asymmetrical greyish-white adherent membrane of the tonsil(s), pharynx and/or nose. In moderate to severe cases there can be marked neck swelling, resulting in a 'bull neck' appearance. Toxic effects can arise, including cardiac and neurological symptoms (eg, myocarditis and neuropathies). Cutaneous diphtheria is characterised by secondary infection of other skin conditions or chronic ulcers with a grey membrane. Cutaneous diphtheria can act as a reservoir of bacteria capable of causing pharyngeal disease.	A case that has been notified, but information is not yet available to classify it as probable or confirmed.		A clinically compatible illness that is not laboratory confirmed.	A clinically compatible illness that is laboratory confirmed or is epidemiologically linked to a laboratory-confirmed case.	A case that has been investigated and subsequently found not to meet the case definition.

[1] All isolates of *C. diphtheriae* and *C. ulcerans* are notifiable until toxigenicity is determined, including cutaneous isolates. If the isolate is determined to be non-toxigenic, the case should be denotified.

Disease	Clinical description	Under investigation	Suspected case	Probable case	Confirmed case	Not a case
Diphtheria (continued)	Toxic sequelae in cutaneous cases are rare. Other extra-respiratory presentations have also been described, including septic arthritis, conjunctivitis, and vaginal and external auditory canal infections.					
Haemophilus influenzae type b (Hib) invasive disease	Invasive disease due to Hib may manifest as bacteraemia, meningitis, epiglottitis, cellulitis, septic arthritis, pneumonia, empyema, pericarditis or osteomyelitis.	A case that has been notified, but information is not yet available to classify it as probable or confirmed.		A clinically compatible illness with detection of a positive antigen test in cerebrospinal fluid (CSF), or a confident diagnosis of epiglottitis by direct vision, X-ray, or laryngoscope.	A clinically compatible illness that is laboratory confirmed.	A case that has been investigated and subsequently found not to meet the case definition.
Hepatitis B (acute)	The clinical manifestations of acute hepatitis B infection in adults range in severity from minimal symptoms to fulminant hepatitis (in less than 1% of cases). Adults may experience the insidious onset of fever, malaise, abdominal discomfort and anorexia with jaundice and/or elevated serum aminotransferase levels.	A case that has been notified, but information is not yet available to classify it as probable or confirmed.		A clinically compatible illness with a positive HBsAg test (aged 12 months and older).	A clinically compatible illness that is laboratory confirmed, including a positive HBsAg test in infants aged under 12 months.	A case that has been investigated and subsequently found not to meet the case definition.

Disease	Clinical description	Under investigation	Suspected case	Probable case	Confirmed case	Not a case
Hepatitis B (acute) (continued)	Acute hepatitis B infection in the first few months of life seldom causes clinical disease, and symptoms or signs are less common in children than adults. The acute illness, but not the carrier state, is to be notified.					
Measles[2]	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.	A case that has been notified, but information is not yet available to classify it as probable or confirmed.		A clinically compatible illness.	A clinically compatible illness that is laboratory confirmed or epidemiologically linked to a confirmed case.	A case that has been investigated and subsequently found not to meet the case definition.

[2] WHO is moving towards world eradication of measles, and this places a greater emphasis on laboratory confirmation of the disease. When cases of measles are clinically diagnosed, practitioners *must directly notify on suspicion*.

Disease	Clinical description	Under investigation	Suspected case	Probable case	Confirmed case	Not a case
Meningococcal invasive disease (sepsis and/or meningitis)	Meningococcal disease (caused by *Neisseria meningitidis*) is a serious invasive disease with an acute onset. It may start as a mild flu-like illness and rapidly progress to fulminant septicaemia and death. Cases typically experience acute fever, malaise, nausea, myalgia, arthralgia and prostration. A rash occurs in about two-thirds of cases – this may be ill-defined and macular, petechial or purpuric. More severe infection leads to shock, disseminated intra-vascular coagulation (DIC), acrocyanosis and multi-organ failure.	A case that has been notified, but information is not yet available to classify it as probable or confirmed.		A clinically compatible illness.	A clinically compatible illness that is laboratory confirmed.	A case that has been investigated and subsequently found not to meet the case definition.
Mumps	An illness with acute onset of fever and unilateral or bilateral tenderness and swelling of the parotid or other salivary gland(s), lasting more than two days, and without other apparent cause.	A case that has been notified, but information is not yet available to classify it as probable or confirmed.		A clinically compatible illness.	A clinically compatible illness that is laboratory confirmed or epidemiologically linked to a confirmed case.	A case that has been investigated and subsequently found not to meet the case definition.

Disease	Clinical description	Under investigation	Suspected case	Probable case	Confirmed case	Not a case
Pertussis	A disease characterised by a cough lasting longer than two weeks, and including one or more of the following: · paroxysms of cough · cough ending in vomiting or apnoea · inspiratory whoop.	A case that has been notified, but information is not yet available to classify it as suspect, probable or confirmed.	In children aged under 5 years: any paroxysmal cough with whoop, vomit or apnoea for which there is no other known cause.	A clinically compatible illness with a high *B. pertussis* IgA test or a significant increase[3] in antibody levels between paired sera at the same laboratory *OR* a cough lasting longer than two weeks and one or more of the following, for which there is no other known cause: · paroxysmal cough · cough ending in vomiting or apnoea · inspiratory whoop.	A clinically compatible illness that is laboratory confirmed or epidemiologically linked to a confirmed case.	A case that has been investigated and subsequently found not to meet the case definition.
Pneumococcal invasive disease[4]	Depending on the site of infection, the main presenting conditions are meningitis, pneumonia or septicaemia.				A clinically compatible illness that is laboratory confirmed.	A case that has been investigated and subsequently found not to meet the case definition.

[3] A significant increase is generally taken as a 4-fold rise in titre. However, interpretation of serology results should be discussed with the testing laboratory or ESR.

[4] In the absence of invasive disease, isolation of *S. pneumoniae* from a non-sterile site (such as sputum, nasal aspirates and ear discharge) is not notifiable. A positive urine antigen test is also not notifiable.

Disease	Clinical description	Under investigation	Suspected case	Probable case	Confirmed case	Not a case
Poliomyelitis	A disease with no other apparent cause, characterised by: · acute flaccid paralysis of one or more limbs with decreased or absent deep tendon reflexes in affected limbs · no sensory or cognitive loss · a possible effect on bulbar muscles.	A case that has been notified, but information is not yet available to classify it as probable or confirmed.		A clinically compatible illness with epidemiological link.[5]	A clinically compatible illness that is laboratory confirmed.	A case that has been investigated and subsequently found not to meet the case definition, including cases aged under 15 years who have been deemed to have a non-polio paralytic illness by the National Certification Committee for the Eradication of Polio.
Rubella	An illness with a generalised maculopapular rash and fever and one or more of the following: · arthralgia/arthritis · lymphadenopathy · conjunctivitis.	A case that has been notified, but information is not yet available to classify it as probable or confirmed.		A clinically compatible illness.	A clinically compatible illness that is laboratory confirmed or epidemiologically linked to a confirmed case.	A case that has been investigated and subsequently found not to meet the case definition.

[5] An epidemiological link for polio is defined in the National Poliomyelitis Response Plan: www.health.govt.nz/publication/national-poliomyelitis-response-plan-new-zealand

Disease	Clinical description	Under investigation	Suspected case	Probable case	Confirmed case	Not a case
Rubella (continued)	Rubella often presents atypically and is difficult to diagnose clinically with certainty. Up to 50% of rubella infections are subclinical. If accurate diagnosis is important, it must be laboratory confirmed.					
Rubella (congenital)	In general, the younger the fetus when infected, the more severe the illness. Severe cases may spontaneously abort, or have multiple manifestations in infancy; mild cases may have only a single manifestation. The most common anomalies are deafness, cataract or glaucoma, congenital heart disease, and mental retardation. In addition, infants with congenital rubella syndrome are often growth retarded and may have radiolucent bone disease, hepatosplenomegaly, thrombocytopenia and purpuric skin lesions.	A case that has been notified, but information is not yet available to classify it as probable or confirmed.		A clinically compatible illness.	A clinically compatible illness that is laboratory confirmed.	A case that has been investigated and subsequently found not to meet the case definition.

Disease	Clinical description	Under investigation	Suspected case	Probable case	Confirmed case	Not a case
Tetanus	Most commonly presents with gradual onset of muscular rigidity and painful spasms, starting in the jaw (lockjaw, trismus) then spreading to the neck, trunk and extremities. Tetanus may cause laryngeal spasms, respiratory failure and autonomic dysfunction (fluctuations in pulse and blood pressure), leading to death – even with modern intensive care. In less than 20% of cases, muscle rigidity and spasms are limited to a confined area close to the site of injury.	A case that has been notified, but information is not yet available to classify it as confirmed.		Not applicable.	A clinically compatible case, as diagnosed by a medical practitioner.	A case that has been investigated and subsequently found not to meet the case definition.

Table A8.2: Confirmatory laboratory tests for vaccine-preventable diseases[6]

Disease	Laboratory basis for confirmation	Specimen	When to take specimens
Diphtheria	Isolation of toxigenic *Corynebacterium diphtheriae* or *Corynebacterium ulcerans* from a clinical specimen.	Swab from area of the lesion (eg, nose, throat, or skin in case of ulcer).	At presentation of illness. Laboratories must be informed that the sample is from a suspected case of diphtheria as selective media are required.
Haemophilus influenzae type b (Hib)	Isolation of *H. influenzae* type b, or detection of *H. influenzae* type b nucleic acid from a normally sterile site.	CSF and/or blood culture or aspirate from a normally sterile site.	At presentation of illness.
Hepatitis B (acute)	At least **one** of the following: · HBsAg positive in an infant aged under 12 months · change from HBsAg negative to HBsAg positive within a 12-month period (if testing is performed at the same laboratory and the cumulative history is readily available within the laboratory information systems) · anti-HB core IgM reactive (unless HBsAg positive more than 6 months ago and the history is readily available in laboratory information systems) · detection of hepatitis B virus (HBV) nucleic acid.	Blood.	At presentation of illness.

[6] See www.esr.cri.nz/SiteCollectionDocuments/ESR/PDF/Health/ESR%20Request%20Form%20Human.pdf for a copy of the ESR lab test form.

Disease	Laboratory basis for confirmation	Specimen	When to take specimens
Measles[7]	If the case **received a vaccine** containing the measles virus in the 6 weeks prior to symptom onset, the laboratory confirmation requires:[8]		
	· evidence of infection with a wild-type virus strain obtained through genetic characterisation.	Urine; nasopharyngeal swab/saliva swab for virus.	At initial presentation of illness (note: culture of virus takes up to 35 days and viral transport medium is required).
	If the case **did not receive a vaccine** containing the measles virus in the 6 weeks prior to symptom onset, then laboratory confirmation requires at least **one** of the following:		
	· detection of IgM antibody specific to the virus	Blood.	Single specimen taken 3–4 days after onset of rash.
	· IgG seroconversion or a significant rise (4-fold or greater) in antibody level for the virus between paired sera tested in parallel where the convalescent serum was collected 10–14 days after the acute serum	Blood.	One specimen taken at onset of illness and a second taken at least 10–14 days later. Most useful in the first few days of illness when serology may be negative and in immune-compromised people when serology may be unreliable.

7 For instructions on measles specimen collection and transport, see the National Measles Laboratory (www.measles.co.nz).

8 Laboratory evidence of proven measles infection in an individual who was vaccinated with a measles-containing vaccine in the 6 weeks before symptom onset requires evidence of infection with a wild-type measles strain obtained through genetic characterisation. It is strongly recommended that, for any sporadic cases of suspected measles, 2 or more samples be taken: preferably blood for serology and nasopharyngeal swab and urine sample for PCR testing. PCR testing is not normally used in an established outbreak. Genetic characterisation should be carried out on any wild-type measles strain.

Disease	Laboratory basis for confirmation	Specimen	When to take specimens
Measles (continued)	· isolation of measles virus by culture	Urine; nasopharyngeal swab/saliva swab for virus.	At presentation. Note: viral transport medium is required.
	· detection of measles virus nucleic acid.	Urine; nasopharyngeal swab/saliva swab for virus.	At presentation.
Meningococcal invasive disease	At least **one** of the following: · isolation of *Neisseria meningitidis* bacteria or detection of *N. meningitidis* from blood, CSF or other normally sterile site · detection of gram-negative intracellular diplococci in blood or CSF or skin petechiae · detection of meningococcal antigen in CSF.	Blood, CSF, other sterile site.	At presentation of illness.
Mumps	If the case **received a vaccine** containing the mumps virus in the 6 weeks prior to symptom onset, the laboratory confirmation requires:		
	· evidence of infection with a wild-type virus strain obtained through genetic characterisation.[9]	Urine; nasopharyngeal swab/saliva swab for virus.	At initial presentation of illness.
	If the case **did not receive a vaccine** containing the mumps virus in the 6 weeks prior to symptom onset, then laboratory confirmation requires at least **one** of the following:		
	· detection of IgM antibody specific to virus	Blood.	Single specimen taken 3–4 days after onset of symptoms.
	· IgG seroconversion or a significant rise (4-fold or greater) in antibody level for the virus between paired sera tested in parallel where the convalescent serum was collected 10–14 days after the acute serum	Blood.	One specimen taken at onset of illness and a second taken at least 10–14 days later.

[9] In New Zealand, genetic characterisation is generally only performed for measles virus.

Disease	Laboratory basis for confirmation	Specimen	When to take specimens
Mumps (continued)	· isolation of mumps virus by culture	Saliva or viral swab taken from mouth or throat, CSF or urine.	At presentation. Note: viral transport medium is required.
	· detection of mumps virus nucleic acid.	Saliva or viral swab taken from mouth or throat, CSF or urine.	At presentation.
Pertussis	Isolation of *Bordetella pertussis* or detection of *B. pertussis* nucleic acid, preferably from a nasopharyngeal swab.[10]	Nasopharyngeal swab; for PCR, ensure the correct swab is used.	At initial presentation of clinically compatible illness.
Invasive pneumococcal disease	At least **one** of the following:	Blood, CSF or other normally sterile site.	On presentation to health service.
	· isolation of *S. pneumoniae* from blood, CSF or other normally sterile site[11]		
	· detection of *S. pneumoniae* nucleic acid from blood, CSF or other normally sterile site	Blood, CSF or other normally sterile site.	
	· a positive newer generation *S. pneumoniae* antigen test on CSF in individuals from whom samples were obtained after antibiotic treatment.[12]	CSF.	

[10] When testing for pertussis, alternative serological tests may be available. Serology is not accepted as a confirmatory test for surveillance in the *Communicable Disease Control Manual 2012*. A case diagnosed from clinical findings and positive serology would be classified as 'probable' and not 'confirmed'. Blood should be taken at the initial clinical presentation and a second specimen taken at least 4 days later. A positive serological test for pertussis IgA and/or IgM or rising titres would be indicative of recent infection; while serology is sometimes used, it is not a confirmatory test.

[11] Isolation of *S. pneumoniae* from a non-sterile site (such as sputum, nasal aspirates and ear discharge) is not notifiable. Note: a positive urine antigen test does not fit the definition for a positive laboratory test for the above case definition being used; a decision was made by the working group to take a pragmatic approach and only include those with a positive culture to enable serotyping and/or to include a positive CSF antigen test, as it was thought that cases of pneumococcal meningitis, especially in children, were possibly being missed.

[12] Occasionally, antigen test results are positive when culture results are negative.

Disease	Laboratory basis for confirmation	Specimen	When to take specimens
Invasive pneumococcal disease (continued)	Note: detection of *S. pneumoniae* from CSF by microscopy (ie, detection of gram-positive diplococci and/or a positive pneumococcal immunochromatographic test (PICT)) can be a useful diagnostic test, but is not sufficient for case confirmation.		
Poliomyelitis	Isolation of poliovirus or detection of poliovirus nucleic acid from a clinical specimen. CSF, NPS/TS, EDTA blood can be used for enterovirus PCR test. Stools are suitable for poliovirus isolation. Serum is suitable for detecting polio neutralising antibodies. Depending on the type of polio suspected, different types of poliovirus will need to be tested for (eg, wild poliomyelitis or vaccine-associated strains). All specimens are sent to the national poliovirus reference laboratory at ESR.[13]		
		Faeces.	At initial presentation of illness (0–14 days after the onset of paralysis) and a second specimen collected at least 24 hours later.
		Throat swab and CSF samples may also be collected if clinically indicated.	As soon as possible.
	Acute poliomyelitis titres may assist diagnosis, but viral isolation and identification are required to confirm a case of poliomyelitis.	Blood.	At initial presentation and 14 days later.

[13] Address: WHO National Poliovirus Reference Laboratory, Institute of Environmental Science and Research, National Centre for Biosecurity and Infectious Disease, Wallaceville Science Centre, 66 Ward Street, Wallaceville, Upper Hutt.

Disease	Laboratory basis for confirmation	Specimen	When to take specimens
Rubella	If the case **received a vaccine** containing the rubella virus in the 6 weeks prior to symptom onset, then laboratory confirmation requires:		
	· evidence of infection with a wild-type virus strain obtained through genetic characterisation.[14]		
	If the case **did not receive a vaccine** containing the rubella virus in the 6 weeks prior to symptom onset, the laboratory confirmation requires at least **one** of the following:		
	· detection of IgM antibody specific to the virus	Blood.	Four days after onset of illness.
	· IgG seroconversion or a significant rise (4-fold or greater) in antibody level for the virus between paired sera tested in parallel where the convalescent serum was collected 10–14 days after the acute serum	Blood.	One specimen taken at onset of illness and a second taken at least 10–14 days later.
	· isolation of rubella virus by culture	Blood, CSF, nasopharyngeal swab.	Taken within 3 days of initial presentation of illness.
	· detection of rubella virus nucleic acid.	Blood, CSF, nasopharyngeal swab.	Taken within 3 days of initial presentation of illness. (Note: rubella virus isolation rate is poor and takes 4 weeks. Viral transport medium is required. Serology and PCR are preferred.)

[14] In New Zealand, genetic characterisation is generally only performed for measles virus.

Disease	Laboratory basis for confirmation	Specimen	When to take specimens
Rubella (congenital)	At least **one** of the following:		
	· demonstration of rubella-specific IgM antibody	Blood.	Cord or infant blood specimen.
	· infant rubella antibody level that persists at a higher level and for a longer period than expected from passive transfer of maternal antibody (ie, rubella titre that does not drop at the expected rate of a 2-fold dilution per month)	Blood.	One specimen at birth and second 14–21 days later.
	· isolation of rubella virus by culture	Throat swab.	At birth. (Note: rubella virus isolation rate is poor and takes 4 weeks. Viral transport medium is required. PCR and serology are the preferred tests.)
	· detection of rubella virus nucleic acid.	Blood, CSF, placenta.	At birth.
Tetanus	None. Isolation of *Clostridium tetani* from culture of the wound site supports the diagnosis, but yield is poor, and a negative culture does not rule out tetanus. In general, laboratories have a reduced role in the diagnosis of tetanus.	None.	

Appendix 9: Websites

New Zealand-based websites

Ministry of Health

www.health.govt.nz or www.health.govt.nz/immunisation

The official site for the Ministry of Health, which includes information on vaccination laws and practices in New Zealand, and provides information for parents/guardians 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 published on the Ministry of Health website.

Pharmaceutical Management Agency (PHARMAC)

www.pharmac.health.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.

Don't Assume You're Immune

www.getimmunised.org.nz

Immunisation information for young adults.

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.

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.

Well Child Tamariki Ora

www.wellchild.org.nz

Information for parents, guardians and whānau about babies, infants, toddlers and preschoolers aged under 5 years, in relation to keeping them well, growing and developing to their fullest potential.

Kidshealth

www.kidshealth.org.nz

A joint initiative between the Paediatric Society of New Zealand Inc (PSNZ) 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.

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.

www.who.int/ith/en/

Immunisation information for travellers.

Centers for Disease Control and Prevention (CDC)

www.cdc.gov/vaccines

This site includes sections on 'Vaccines and preventable diseases' and 'For specific groups', and also includes safety fact sheets 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.

American Academy of Pediatrics

www.healthychildren.org

Information for parents and clinicians, which includes colourful (and graphic) pictures. Excellent articles include 'Why immunize your child?' and 'Vaccine safety: the facts'.

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.

Institute of Medicine (IOM)

www.iom.edu

An independent, non-profit organisation that works outside of government to provide unbiased and authoritative advice to decision-makers and the public. IOM has released reports on vaccine safety and adverse events.

Influenza-related websites

National Influenza Specialist Group

www.influenza.org.nz

A not-for-profit group of doctors and nurses who aim to promote the benefits of immunisation for those most at risk. Its aims are to increase public awareness of influenza, its seriousness and the importance of immunisation to prevent the disease.

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

www.esr.cri.nz/competencies/shivers/Pages/default.aspx

The SHIVERS study (Southern Hemisphere Influenza, Vaccine Effectiveness, Research and Surveillance) is collecting New Zealand data to help better understand the burden of disease and how to prevent its

spread. Includes weekly community and hospital surveillance reports for severe acute respiratory infections and influenza-like illness.

https://surv.esr.cri.nz/virology/virology.php

Weekly influenza surveillance reports from sentinel general practices throughout New Zealand.

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.

Centers for Disease Control and Prevention (CDC)

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.

Funded vaccines for special groups

Vaccine	Individuals eligible for funded vaccine
Hep A	Transplant patients. Children with chronic liver disease. Close contacts of hepatitis A cases.
Hep B and HBIG	Babies of mothers with chronic hepatitis B infection need both Hep B vaccine and HBIG at birth and then continue with usual schedule. Hep B vaccine for HIV- or hepatitis C-positive individuals; for household and sexual contacts of those with chronic hepatitis B infection; following immunosuppression;* for transplant or dialysis patients.
Hib	Individuals pre- or post-splenectomy. Children <18 years with functional asplenia.
HPV4	Individuals <26 years with HIV infection. Transplant patients.
Influenza	Individuals ≥65 years. Individuals <65 years with certain medical conditions (including infants and children ≥6 months). Pregnant women.
MenCCV and MCV4-D	For individuals: pre- or post-splenectomy or with functional asplenia; with HIV, complement deficiency (acquired or inherited) or pre- or post-solid organ transplant; close contacts of meningococcal cases; bone marrow transplant patients; following immunosuppression.*
Tdap	Pregnant women, from 28 to 38 weeks' gestation.
PCV13 and 23PPV	PCV13 for high-risk children who have previously received 4 doses of PCV10. PCV13 for children aged 5 to <18 years who are eligible for (re-) vaccination. 23PPV for individuals pre- or post-splenectomy or with functional asplenia; for high-risk children aged under 18 years.
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 solid organ transplant; prior to elective immunosuppression.* 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 individuals with mild or moderate immunosuppression who are non-immune to varicella, on advice of their specialist. Individuals with inborn errors of metabolism at risk of major metabolic decompensation, with no clinical history of varicella. Household contacts of paediatric patients who are immune compromised, or undergoing a procedure leading to immune compromise, 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 immune compromised or undergoing a procedure leading to immune compromise, where the household contact has no clinical history of varicella.

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