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, in untreated cases the communicable stage lasts from the catarrhal stage to 3 weeks after the onset of paroxysmal cough. When treated communicability lasts approximately 2–5 days from the first dose.
Incidence and burden of disease	Widespread outbreaks occur every 3–5 years. Infants aged under 12 months are at highest risk from pertussis, particularly those who have received fewer than two doses of vaccine and if the mother did not receive vaccine in pregnancy.
Funded vaccines	DTaP-IPV-HepB/Hib (Infanrix-hexa). DTaP-IPV (Infanrix-IPV). Tdap (Boostrix).
Dose, presentation, route	0.5 mL per dose. DTaP-IPV-HepB/Hib: pre-filled syringe and glass vial. The vaccine must be reconstituted prior to injection. DTaP-IPV, Tdap: pre-filled syringe. Intramuscular injection.
Funded vaccine indications and schedule	During each pregnancy (recommended from 16 weeks' gestation)	Tdap
	6 weeks, 3 months and 5 months	DTaP-IPV-HepB/Hib
	4 years	DTaP-IPV
	11 years	Tdap
	45 years (catch-up, if individual has not received 4 previous tetanus doses)	Tdap
	65 years	Tdap
	Parents or primary caregivers of infants admitted to neonatal intensive or special care baby units for more than 3 days and whose mothers had not received Tdap at least 14 days prior to birth	Tdap
	For vaccination of previously unimmunised or partially immunised patients	DTaP-IPV-HepB/Hib, DTaP-IPV or Tdap
	For (re)vaccination of eligible patients	

Vaccine effectiveness	Vaccination in pregnancy is over 90 percent effective in preventing pertussis in infants up to age 3 months.
	A 3-dose primary course in infants has 84 percent efficacy against hospitalisation for pertussis.
Contraindications	Contraindicated where anaphylaxis to vaccine or vaccine components is proven.
Potential responses to vaccine	Extensive limb swelling occurs more commonly after increasing number of doses of DTaP. Affecting less than in 2 percent of children, this is typically painless and resolves spontaneously.

14.1 Bacteriology

Pertussis (whooping cough) is a bacterial respiratory infection caused by *Bordetella pertussis*, an exotoxin-producing gram-negative bacillus. The bacillus is fastidious (requires special techniques to grow in culture) and will often have decreased in numbers by the time the typical cough develops, making laboratory confirmation by culture difficult. The availability of sensitive and specific PCR and serological assays has improved laboratory confirmation of suspected *B. pertussis* infection (see section 14.8).

14.2 Clinical features

Pertussis is highly transmissible. It is one of the most infectious vaccine-preventable diseases in humans. The rate of transmission is several-fold greater than most respiratory pathogens, including influenza, such that in a non-immune population, approximately 5–17 secondary pertussis cases are expected from one case (see section 1.2.1).[1] Transmission occurs by aerosolised droplets, and the incubation period is 7–10 days (range 5–21 days).

There are three stages of typical pertussis infection:

1. Catarrhal stage – rhinorrhoea and irritating mild cough (typically lasting 7–10 days).
2. Paroxysmal stage – paroxysms (bursts) of coughing; in children, these may end in vomiting, cyanosis or apnoea and inspiratory gasp or whoop (1–6 weeks). Usually afebrile.
3. Convalescent stage – less persistent cough, gradual recovery (up to 10 weeks).

The communicable period lasts from the onset of symptoms to three weeks after the start of the paroxysmal stage.

Clinical presentation varies with age, immunisation status and previous infection. Pertussis must be considered in infants presenting with apnoea, since apnoea and/or cyanosis may precede paroxysmal cough.[2] In school-aged children, inspiratory whoop, post-tussive vomiting and the absence of wheezing and fever distinguish pertussis from other causes of coughing illnesses.[3, 4] Almost all pertussis infections in adolescents and adults occur in the context of previous infection and/or immunisation. Persistent cough for more than 14 days is the cardinal feature in adults.[4, 5, 6] Coughing is often paroxysmal and worsens at night, with the patient waking with a choking sensation, but post-tussive vomiting and whoop are infrequent.

Studies performed in several countries during both epidemic and non-epidemic periods have shown that between 12 and 37 percent of school-aged children, adolescents and adults with persistent cough (lasting 14 days or more) have evidence of recent *B. pertussis* infection.[3, 5, 7, 8, 9] A primary care-based study in New Zealand performed during the early phase of the 2011–2013 epidemic showed recent *B. pertussis* infection in 17 percent of children aged 5–16 years and 7 percent of adults aged 17–49 years presenting to primary care with a persistent cough of two or more weeks' duration.[10]

The disease is most often severe in infants in the first few months of life. One in six infants with pertussis sufficiently severe to require intensive care admission will either die or be left with brain or lung damage.[11] The most common complications of pertussis are secondary infections, such as otitis media and pneumonia, and the physical sequelae of paroxysmal coughing, (eg, petechiae and other haemorrhages within subconjunctiva, nasopharynx and central nervous system; pneumothorax; hernia; and urinary incontinence). At the peak of the paroxysmal phase, vomiting can lead to weight loss especially in infants and young children.

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. The high prevalence of subclinical infections in household contacts of pertussis cases indicates a significant role in disease transmission to young infants.[13, 14] As observed in Australia, seasonal peaks in incidence in children aged less than 5 years occurred 1–2 months later than for the general population, supporting the theory that older household members are sources of infection to younger children.[15]

14.3.1 Global burden of disease

Pertussis mortality and morbidity rates continue to be highest in the first year of life.[13] In the US during the 1940s pertussis resulted in more infant deaths than measles, diphtheria, poliomyelitis and scarlet fever combined.[16] 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.[17]

Pertussis mortality and morbidity is under-reported.[18, 19] It is estimated that there are three times more deaths due to pertussis than are reported in high-income countries.[18, 20, 21] The burden of pertussis in older adults is underestimated, particularly for those with chronic respiratory conditions, and increases with age.[22, 23] Infants continue to die from pertussis despite advances in intensive care.[11, 24, 25, 26]

Following the introduction of mass immunisation, countries with consistently high immunisation coverage rates have achieved consistently low pertussis incidence rates.[27] The most pronounced decrease in incidence was seen in those aged under 10 years. Although primarily associated with low immunisation coverage, in some instances higher pertussis incidence rates are due to lower or waning vaccine efficacy or less-than-optimal immunisation schedules.[28, 29, 30] The burden of severe disease, particularly since the introduction of acellular vaccines, is highest in infants and unvaccinated young children.[31] However, less severe pertussis cases are also seen in vaccinated children who are further away from the last DTaP and, in some countries, adolescents.[32, 33, 34] Infants too young to have received more than one dose of pertussis vaccine (age 3 months or less) have the highest rate of notification, hospitalisation and death.[35, 36]

Epidemic peaks of pertussis occur every 2–5 years without the consistent seasonal pattern that is typical of most respiratory infections, although evidence from Australia suggests increased incidence (by 15 percent compared with annual average) during spring to summer months.[15] Epidemics are frequently sustained over 18 months or more, during which there are dramatic increases in hospital admission rates. Lack of change in the pertussis epidemic cycle with mass immunisation suggests minimal impact on the circulation of *B. pertussis* in the population, unlike other epidemic vaccine-preventable diseases, such as measles.[12, 19, 37]

14.3.2 New Zealand epidemiology

Pertussis mortality in New Zealand

On average, zero to one deaths are associated with pertussis each year in New Zealand. During the 2011–2013 pertussis epidemic there were three deaths in children: two in infants aged under 6 weeks and one in an unimmunised pre-schooler.[38] No deaths from pertussis (as recorded in EpiSurv) occurred during the latest epidemic from October 2017 to May 2019.[38, 39]

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.

Outbreaks continue to occur throughout New Zealand. For further details refer to the ESR surveillance reports for notifiable diseases (available at **surv.esr.cri.nz/surveillance/surveillance.php**).

Pertussis morbidity in New Zealand as described by notification data

Four epidemics have occurred since pertussis became a notifiable disease, with an epidemic peak annual number of notified cases of 4,140 in 2000, 3,485 in 2004, 5,897 in 2012 and 2956 in 2018 (see Figure 14.1).

The most recent outbreak commenced in October 2017; by the end of May 2019, there were 4,697 cases notified (2,939 laboratory-confirmed).[39] During 2019, 1206 cases were notified, an overall notification rate of 24.5 cases per 100,000 population. Of these cases, 88 (7.3 percent, incidence 148 cases per 100,000) were aged under 1 year and half of these were hospitalised. The youngest infants were at highest risk of hospitalisation with 85 percent of cases age under 2 months, 80 percent age under 3 months and 66 percent aged under 6 months hospitalised (ESR, 8 June 2020). The next highest incidence rate occurred in children aged 1–4 years (68 per 100,000). Pacific and Māori infants had the highest notification rates (300 and 177 per 100,000 respectively), and in children aged 1–4 years, MELAA ethnic group had the highest notification rate (175 per 100,000) followed by European/Other (77 per 100,000).

Figure 14.1: Pertussis notifications and hospitalisations, 1997–2019

Note: Includes confirmed, probable and suspect cases, and notifications still under investigation.
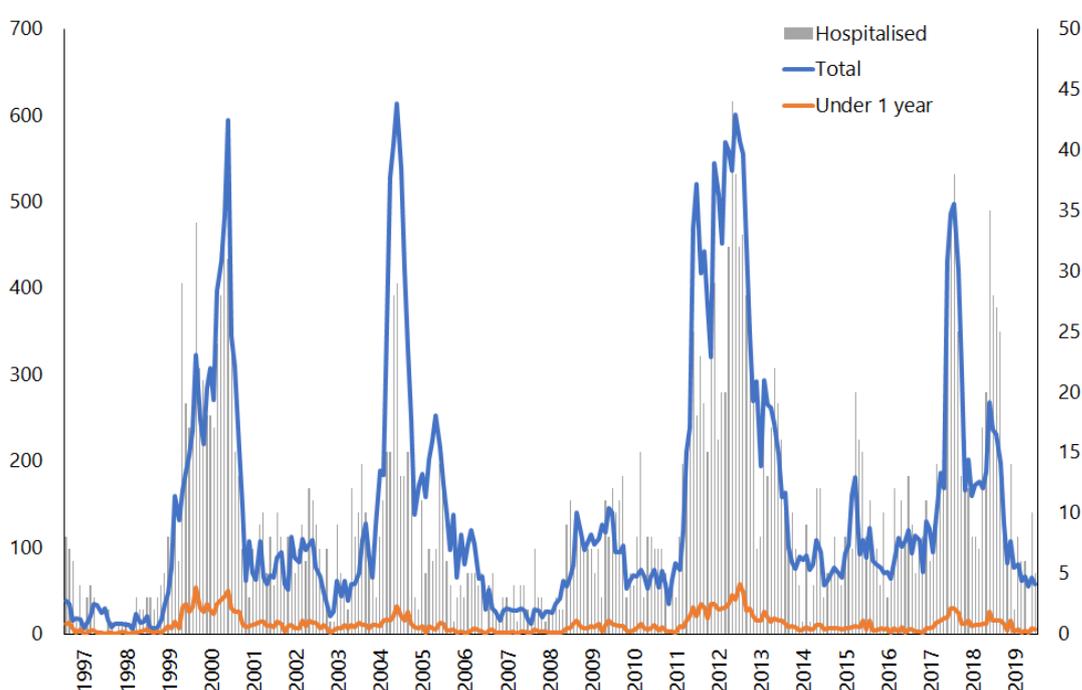
Since pertussis became notifiable, the annual proportion of notified cases aged 30 years or older has increased from 23 percent in 1997 to 48 percent in 2019 (ESR, 8 June 2020).[38] However, the highest proportion of hospitalised cases continues to be in infants. From 2010 to 2019 there were 1,544 notified cases in infants with 769 (53 percent) recorded as hospitalised (Figure 14.2).

Figure 14.2: Age distribution of notified and hospitalised pertussis cases, 2019
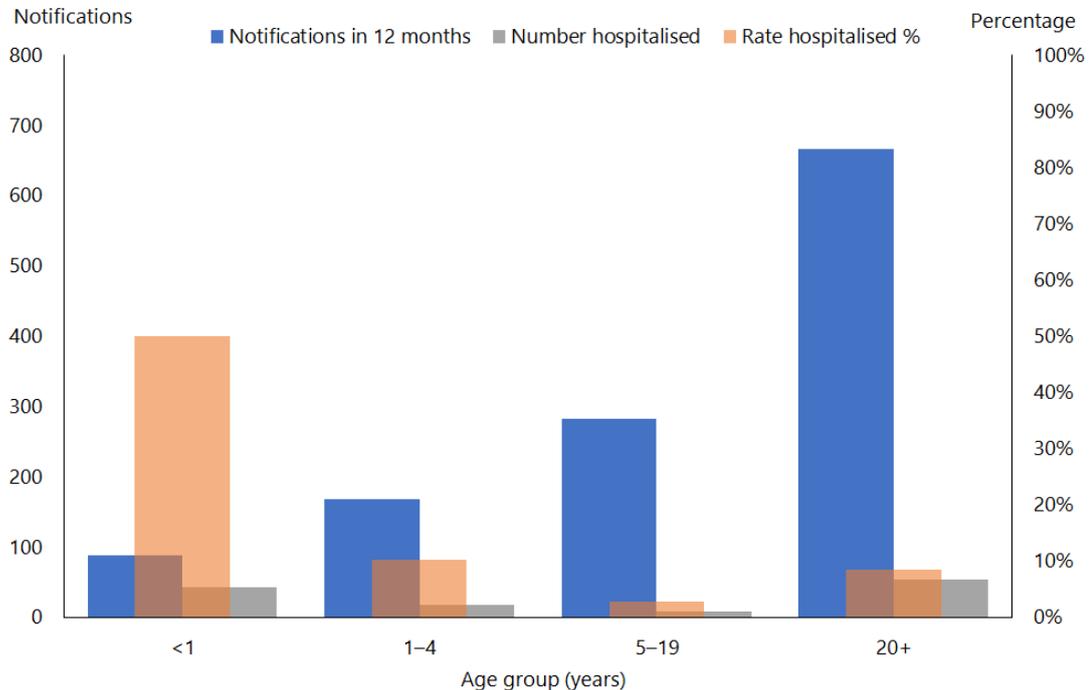
Source: ESR

Pertussis morbidity in New Zealand, as described by hospital discharge data

Infants aged under 1 year with pertussis are more likely (nearly 80 percent) to be admitted to hospital than older children and account for almost all the pertussis cases admitted to the paediatric intensive care unit.[40]

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 it was in the 1990s (2000s versus 1990s, relative risk 0.8 [95% CI: 0.7–0.8]). Despite this decrease, the infant hospitalisation rate for pertussis in New Zealand in the 2000s (at nearly 200 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).[41, 42, 43]

Pertussis hospital admission rates vary with ethnicity and household deprivation. From 2000–2014 the infant (under 1 year old) hospitalisation rates for pertussis fluctuated but were consistently higher for Pacific and Māori than European/Other prioritised ethnicities. Between 2010 and 2014, the hospitalisation rate was over 2.5 times higher for Pacific (4.4 per 1,000) and over 2 times higher for Māori (3.6 per 1,000) than it was for European/Other ethnicities (1.7 per 1,000).[44]

From 2010 to 2014 an infant living in a household in the most deprived quintile was at a five-fold increased risk of being hospitalised with pertussis compared with an infant in the least deprived quintile (4.0 versus 0.8 per 1,000).[44]

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 details.

Other vaccines

Other acellular pertussis-containing vaccines registered (approved for use) and available (marketed) in New Zealand include:

- Tdap: Adacel (Sanofi)

- Tdap-IPV: Adacel Polio (Sanofi).

14.4.2 Efficacy and effectiveness

Immunogenicity

A review of published data on DTaP-IPV-HepB/Hib found it to be highly immunogenic in infants aged under 2 years for primary and booster vaccination.[45] 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.[46]

Efficacy and effectiveness

Vaccination in pregnancy

Maternal vaccination, given more than seven days before delivery, was estimated to be 91 percent (95% CI: 88–94) effective against laboratory-confirmed pertussis in infants younger than 3 months of age[47] Protection of infants is achieved both by passive antibody transfer and reduced exposure to maternal disease.[48] Tdap given in pregnancy was shown to be 85 percent more effective than post-partum vaccination in preventing pertussis in infants younger than 8 weeks of age.[49]

Timing is important because protection is not as good if the mother is vaccinated less than two weeks prior to birth.[50] Vaccinating from 16 weeks' gestation allows time for passive transfer and accumulation of antibody in the fetus, such that by 40 weeks' gestation, infant antibody levels at birth are higher than those in the mother.[51] Giving maternal vaccination during the second trimester rather than later provides more preterm infants with pertussis protection.[52, 53]

See section 14.5.2 for information about maternal pertussis vaccine safety.

Direct protection

The acellular pertussis vaccines approved for use in New Zealand have been shown to provide around 81–85 percent efficacy (95% CI: 51–100) against confirmed pertussis after three infant doses, with follow-up studies suggesting sustained efficacy to age 6 years.[13, 54, 55] In a Swiss study, effectiveness against pertussis hospitalisation increased with each consecutive primary dose in infants from age 2.5 months to 2 years from 42.1 percent (95% CI: 11.3–62.6) after the first dose, 83.9 percent (70.2–92.1) after the second then 98.2 percent (96.1–99.3) to 100 percent (97.9–100) after the third and fourth doses.[56]

While effective, observational data from Australia found that acellular pertussis vaccines may be less effective than the best-performing whole-cell vaccines in preventing whooping cough.[57, 58] However, the quality of the whole cell vaccine varied between countries and a Canadian study found it to be less effective than the acellular vaccine.[59]

Age-appropriate pertussis vaccination in the US was shown to reduce the severity of symptoms and complications of the disease, including 60 percent reduction in the odds of severe disease (seizure, encephalopathy, pneumonia and/or hospitalisation) in children aged 7 months to 6 years, and 30 percent reduction in post-tussive vomiting in those aged 19 months to 64 years.[60]

Duration of protection

Protection against pertussis begins to wane within several years of completion of a three-dose primary and two-dose booster 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.[61] 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.

A decline in effectiveness was seen in children more distant from the last DTaP dose, by 27 percent per year on average.[62] Waning effectiveness is more rapid following the adolescent booster at around 35 percent per year.[63] In children, vaccine was 80 percent (95% CI: 71–86) effective against pertussis from two weeks to a year following vaccination, 84 percent (77–89) after 1–3 years, declining to 62 percent (42–75) after 4–7 years and to 41 percent (0–66) at eight or more years after vaccination.[64] A meta-analysis estimated that only 10 percent of those vaccinated with five doses of DTaP would be immune to pertussis 8.5 years after their last DTaP dose.[65]

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.[66] However, the duration of protection is unknown.

14.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017 (2nd edition)* (available at **www.health.govt.nz/publication/national-standards-vaccine-storage-and-transportation-immunisation-providers-2017**).

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-PRP-T pellet. After adding the vaccine to the pellet, the mixture should be shaken until the pellet is completely dissolved. Use the reconstituted vaccine as soon as possible. If storage is necessary, the reconstituted vaccine may be kept for up to eight hours at 21°C.

14.4.4 Dosage and administration

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

Co-administration with other vaccines

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

14.5 Recommended immunisation schedule

Table 14.1: Immunisation schedule for pertussis-containing vaccines (excluding catch-up)

Age	Vaccine	Comment
Pregnant women: recommended from 16 weeks' gestation of every pregnancy, preferably in the second trimester (funded when given any time in second or third trimester)	Tdap	Booster for mother Passive immunity for infant
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 (individuals who have not received 4 tetanus vaccinations in their lifetime)	Tdap	Booster
65 years	Tdap	Booster

14.5.1 Children

A primary course of pertussis vaccine is given as DTaP-IPV-HepB/Hib (Infanrix-hexa) at ages 6 weeks, 3 months and 5 months, followed by a dose of DTaP-IPV (Infanrix-IPV) at age 4 years (Table 14.1). A further booster is given at age 11 years (school year 7) as Tdap (Boostrix).

It is important to administer all vaccinations on time. Delays in receipt of infant immunisations significantly increase the risk of infants being hospitalised for severe pertussis.[67]

If a course of immunisation is late or interrupted for any reason, it may be resumed without repeating prior doses (see Appendix 2). The minimum interval between doses is four weeks. 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 and boosting of children aged under 10 years.
- Tdap may be used for primary immunisation and boosting of children aged 7 to under 18 years.

Tdap also may be given:

- as a single dose for vaccination of patients aged 65 years old
- as single dose for vaccination of patients aged 45 years old who have not had 4 previous tetanus doses
- for vaccination of previously unimmunised or partially immunised patients
- for vaccination prior to planned or revaccination following immunosuppression (see section 14.5.3)
- for boosting of patients with tetanus-prone wounds (see section 19.5.5).

14.5.2 Pregnancy and breastfeeding

Pregnant women should receive a dose of Tdap in every pregnancy so that antibodies can pass to the fetus to provide protection from birth (funded when given any time in second or third trimester). It is recommended to be given from 16 weeks' gestation of every pregnancy, preferably in the second trimester to protect both the mother and her infant from pertussis.[47, 51] Post-partum maternal vaccination may reduce the risk of a mother infecting her baby but does not have the added benefit of providing the baby with passive antibodies (see section 14.4.2 for details of effectiveness).

Maternal Tdap vaccination has been shown to prevent pertussis disease or reduce severity of the disease and risk of pertussis-related death in very young infants.[68] There is no evidence that Tdap vaccination affects pregnancy outcomes[68, 69, 70] or causes harm to the fetus or neonate.[68, 71]

Tdap vaccines can be given to breastfeeding women, if not given during pregnancy.[72]

14.5.3 (Re)vaccination

Pertussis-containing vaccines are funded for vaccination or re-vaccination of eligible patients who have become immunocompromised, as follows. See also sections 4.2 and 4.3.

DTaP-IPV-HepB/Hib (Infanrix-hexa) and DTaP-IPV (Infanrix-IPV)

An additional four doses (as appropriate) of DTaP-IPV-HepB/Hib (for children aged under 10 years) or DTaP-IPV are funded for (re)vaccination of patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- prior to planned or following other severely immunosuppressive regimens.

Up to five doses of DTaP-IPV-HepB/Hib (for children aged under 10 years) or DTaP-IPV are funded for children requiring solid organ transplantation.

Tdap (Boostrix)

An additional four doses (as appropriate) of Tdap (Boostrix) are funded for patients:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- prior to planned or following other severely immunosuppressive regimens.

A single dose of Tdap is funded for parents or primary caregivers of infants admitted to a neonatal intensive care unit or special care baby unit for more than three days and whose mothers had not received Tdap at least 14 days prior to baby's birth.

14.5.4 Recommended but not funded

Tdap is recommended but not funded, unless given as prophylaxis for a tetanus-prone wound, for:

- lead maternity carers and other health care personnel who work in neonatal units and other clinical settings (such as GPs and practice nurses), and students of these professions where they are in contact with infants (with a booster dose at least at 10-year intervals). Infants with respiratory, cardiac, neurological or other co-morbid conditions are particularly at risk from pertussis.

- household contacts of newborns, including adult household and other close contacts (contacts aged under 18 years who are unimmunised or incompletely immunised for their age can receive funded pertussis vaccine; see Appendix 2 for catch-up schedules)

- regardless of maternal vaccination history, all caregivers of infants born at less than 32 weeks' gestation are recommended to receive a single dose of Tdap (see section 4.2.2)

- early childhood workers and students (with a booster dose at 10-year intervals), although the priority is to ensure all children attending childcare have received age-appropriate vaccination
- adults with a medical condition, not eligible for funded vaccine, who are at increased risk of severe consequences of pertussis (eg, those with chronic respiratory disease).

14.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

14.6.1 Contraindications

The only contraindication is an immediate severe anaphylactic reaction to the vaccine, or any component of the vaccine, following a previous dose.

14.6.2 Precautions

A history of well-controlled seizures in the vaccine recipient or a family history of seizures (febrile or afebrile) or other neurologic disorder is not a contraindication to vaccination against pertussis.[50]

Vaccination for children with an unstable neurological disorder (eg, poorly controlled epilepsy or deteriorating neurological state) has previously been considered a precaution, but as these children may be high risk of severe pertussis complications, vaccination is recommended. Individual cases should be discussed with the specialist.[50]

14.7 Potential responses and AEFIs

Unless the specific contraindications and precautions outlined in section 14.6 above are present, practitioners should have no hesitation in advising the administration of acellular pertussis vaccine. Acellular pertussis vaccine has been used in New Zealand since 2000 and is significantly less reactogenic than the whole-cell pertussis vaccine.

14.7.1 DTaP-containing vaccines

DTaP-containing vaccines (eg, DTaP-IPV-HepB/Hib and DTaP-IPV) are generally well tolerated in children,[73] including preterm (24 to 36 weeks' gestation) and/or low birthweight (820–2,020 g) infants.[74, 75]

Local reactions commonly include pain, redness, swelling and induration at the injection site. Less common reactions include fretfulness, anorexia, vomiting, crying and slight to moderate fever. These local and systemic reactions usually occur within several hours of pertussis immunisation and spontaneously resolve within 48 hours without sequelae.[73]

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.

14.7.2 Tdap vaccine

The adult reduced-concentration Tdap (Boostrix) vaccines have been found to have no safety concerns in those aged 10–64 years and those aged over 65 years.[76, 77, 78, 79] Studies of Tdap in pregnant women have not identified any increased risk of adverse maternal, infant or fetal outcomes.[12, 71, 80, 81, 82]

Local reactions following immunisation of adolescents with Tdap are common but usually mild. They include pain (in 75 percent of recipients), swelling (21 percent) and redness (23 percent) at the injection site.[83] Potential systemic reactions following immunisation of adolescents with Tdap include fever >38°C (5 percent), headache (16 percent), fatigue (14 percent) and gastrointestinal symptoms (10 percent).[83]

14.7.3 Major adverse events associated with pertussis-containing vaccines

The incidence of major adverse events following primary pertussis immunisation is summarised in Table 14.2.

Table 14.2: Incidence of major adverse reactions following acellular pertussis vaccines (based on clinical trial data for DTaP vaccines)

Event following immunisation	Timing post-vaccination	Incidence per 100,000 doses
High fever >38°C	0–2 days	36
Persistent (>3 hours) inconsolable screaming	0–24 hours	44
Seizures	0–2 days	7
Hypotonic-hyporesponsive episode	0–2 days	0–47[a]
Anaphylaxis	0–1 hour	Very rare

a.   Across clinical trials of multiple licensed DTaP formulations

Source: Edwards KM, Decker MD. 2018. Pertussis vaccines. In: Plotkin S, Orenstein W, Offit P, et al (eds) *Plotkin's Vaccines (7th edition)*. Elsevier.

Parents should be alerted to the small but defined risk of extensive limb swelling to the injected thigh or upper arm, particularly following the fourth and fifth DTaP dose. This transient, usually painless and benign swelling occurs in 2–3 percent of children.[73] Resolution occurs without sequelae and it is not a contraindication for further pertussis vaccine doses.[72, 84]

Neither a hypotonic-hyporesponsive episode nor seizures are associated with long-term consequences for the child (see section 2.3.3).[85, 86, 87] Children who have febrile seizures after pertussis immunisation do not have an increased risk of subsequent seizures or neurodevelopmental disability.[88] It is safe to give acellular pertussis vaccine after a hypotonic-hyporesponsive episode has occurred following a previous dose.[89] A significant decrease of 60–67 percent in hypotonic-hyporesponsive episodes was observed in Canada following the switch from whole cell to acellular pertussis vaccines.[90]

14.8 Public health measures

14.8.1 Improving pertussis control

The goal of the pertussis immunisation programme is to protect those most at risk of developing severe disease; that is, infants in the first year of life. Two key strategies for reducing the burden of disease in infants are the administration of Tdap vaccination during pregnancy and on-time infant immunisation. Vaccination during pregnancy is recommended and funded for women from the second trimester, preferably from 16 weeks' gestation (see section 14.5.2). This is the most effective way to protect young infants. More complete and timely delivery of the current infant immunisation schedule would reduce the infant pertussis disease burden in older infants.[67] It is important that all children attending early childhood services are fully vaccinated for their age.

Data on the protective effects of indirect strategies is currently incomplete. 'Cocoon strategy' is the term used to describe the protection of infants by immunising those who are potential sources of *B. pertussis*.[91] Three identified target groups who have the most contact with young and vulnerable infants are (1) new mothers who have not had recent immunisation, family and close contacts of newborns; (2) health care workers; and (3) early childhood workers. Some protection may be provided to infants by cocoon immunisation of parents and other potential household contacts post-partum, may be pertinent in some circumstances where maternal vaccination did not occur, such as preterm birth, and infants in neonatal intensive care.[92]

Health care workers in particular are at increased risk of pertussis and can transmit pertussis to other health care workers and to patients.[93] Outbreaks in maternity wards, neonatal units and outpatient settings have been described.[94] Fatalities occur as a result of such nosocomial spread.[95]

Mass immunisation cannot be used to control an established community outbreak, although action to update age-appropriate vaccination in institutional settings (schools and early childhood services for staff and students) is appropriate. When an outbreak occurs, individual immunisation status should be checked, and any missing doses given. Vaccination in pregnancy is particularly important to protect the most vulnerable, young infants.

14.8.2 Notification

It is a legal requirement that all cases of pertussis be notified immediately on suspicion to the local medical officer of health.

A suspected pertussis case can be confirmed if a clinically compatible illness is laboratory-confirmed or is epidemiologically linked to a confirmed case. Because transmission is by aerosolised droplets, health care personnel looking after pertussis cases should be vaccinated and 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 should only be done in consultation with the medical officer of health and the local microbiologist for public health purposes.

A negative test does not necessarily rule out pertussis: consider exposure, clinical compatibility, the test used and the timing of the test.

For further information about laboratory testing, refer to the *Pertussis* chapter of the *Communicable Disease Control Manual* (available at **www.health.govt.nz/our-work/diseases-and-conditions/communicable-disease-control-manual**).

14.8.4 Antimicrobial treatment of case

A range of antibiotics are available for the treatment and prophylaxis of pertussis. Prompt treatment with macrolide antibiotics may reduce the severity and duration of clinical disease 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.[73, 96, 97] Antibiotics are of limited value if started after 21 days of illness, but should be considered where there are high-risk contacts (eg, young infants and pregnant women). Refer to the *Pertussis* chapter of the *Communicable Disease Control Manual*[98] (available at **www.health.govt.nz/publication/communicable-disease-control-manual-2012**).

To minimise transmission to newborn infants, it is recommended that pregnant women diagnosed with pertussis in the third trimester be treated with appropriate antibiotics (see Table 14.3), if within six weeks of cough onset.[99]

Macrolide use during pregnancy, lactation and in the neonatal period has been associated with 2–3 times increased risk of infantile pyloric stenosis (which affects 1–3 in 1,000 infants).[100, 101] The risk is lower when given during pregnancy and breastfeeding than when given to the infant during the neonatal period.[102] With erythromycin, the risk is highest when given within the first two weeks of life (relative risk 10.7; 95% CI: 5.2–21.9), and increased duration of treatment.[102, 103, 104] The risk is presumed to be lower with azithromycin, although there are case reports of infantile pyloric stenosis occurring when azithromycin has been used during pregnancy.

Parents should be informed of the risks of this complication and of the symptoms and signs of infantile hypertrophic pyloric stenosis. The infant should be monitored for this complication for four weeks after completion of treatment.[73, 105, 106]

Table 14.3: Recommended antimicrobial therapy and post-exposure prophylaxis for pertussis in infants, children, adolescents and adults

| | Azithromycin[a] | | Trimethoprim-sulfamethoxazole[b] | |
Age	Recommended	Age	Recommended
Younger than 4 weeks	Day 1: 10 mg/kg per day in a single daily dose Days 2–5: 5 mg/kg per day in a single daily dose	Under 2 months	Contraindicated (risk for kernicterus)
From age 1 month older, and children	Day 1: 10 mg/kg per day in a single daily dose (maximum 500 mg per day) Days 2–5: 5 mg/kg per day in a single daily dose (maximum 250 mg per day)	Aged 2 months or older	TMP, 8 mg/kg per 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	Adolescents and adults	TMP, 320 mg per day; SMX, 1,600 mg/day in 2 divided doses for 14 days

a. Preferred macrolide during pregnancy, lactation and in infants aged <1 month because of risk of idiopathic hypertrophic pyloric stenosis associated with erythromycin.

b. TMP = trimethoprim; SMX = sulfamethoxazole. TMP-SMX can be used as an alternative agent to macrolides in patients aged ≥2 months who are allergic to macrolides, who cannot tolerate macrolides or who are infected with a rare macrolide-resistant strain of *Bordetella pertussis*.

Adapted from: Centers for Disease Control and Prevention. 2005. Recommended antimicrobial agents for treatment and post exposure prophylaxis of pertussis. *Morbidity and Mortality Weekly Report* 54(RR14): 1–16.

Exclusion

Exclude the case from school, early childhood services, other institutions or work until they have received at least two days of azithromycin (this lengthens to five days if other antibiotics, are used), or exclude them for three weeks from the date of onset of typical paroxysms of cough or until the end of the cough, whichever comes first.[98]

Children who have laboratory-confirmed pertussis should complete their immunisation series with all 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, see the latest version of the 'Pertussis' chapter of the *Communicable Disease Control Manual*.[98]

A contact can be defined as someone who has been in close proximity (within one metre)[105] 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.[98]

Those most at risk from pertussis and high-priority contacts for public health follow-up are:

- children aged under 12 months; particularly those whose mothers did not received Tdap in pregnancy or who have received fewer than two pertussis-containing vaccine doses by 14 days prior to exposure
- children and adults who live with, or spend time around a child including in health care and education settings
- unvaccinated pregnant women, especially in the last month of pregnancy
- individuals at risk of severe illness or complications (eg, with chronic respiratory conditions, congenital heart disease or immune deficiency).

As the evidence for the effectiveness of chemoprophylaxis of contacts is limited, antibiotics are currently only recommended for household or household-like settings where high-priority contacts as listed above reside – if prophylaxis is given, all members of the contact group should receive it. 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.

Refer to the *Pertussis* chapter of the *Communicable Disease Control Manual* (available at **www.health.govt.nz/our-work/diseases-and-conditions/communicable-disease-control-manual/pertussis**).

Restriction

Any contacts, high priority or otherwise, should be advised to avoid attending early childhood services, school, work or community gatherings if they become symptomatic. It is important to clearly explain that symptoms in the early stages of pertussis are indistinguishable from minor respiratory tract infections, and pertussis is highly contagious.[98]

Refer to the *Pertussis* chapter of the *Communicable Disease Control Manual* (available at **www.health.govt.nz/our-work/diseases-and-conditions/communicable-disease-control-manual/pertussis**).

14.9 Variations from the vaccine data sheets

The DTaP-IPV-HepB/Hib (Infanrix-hexa) and DTaP-IPV (Infanrix-IPV) data sheets state that these vaccines are indicated for primary immunisation of infants and as a booster dose for children. The Ministry of Health recommends that DTaP-IPV-HepB/Hib and DTaP-IPV vaccines may also be used for catch-up of the primary schedule in children aged under 10 years (see Appendix 2).

The data sheets for DTaP-IPV-HepB/Hib, DTaP-IPV and Tdap (Boostrix) state that these vaccines are contraindicated in children with encephalopathy of unknown aetiology or with neurologic complications occurring within seven days following a vaccine dose. The Ministry of Health recommends that the only contraindication is a history of anaphylaxis to a previous dose or to any of the vaccine components (see section 14.6.1). The risks and benefits of withholding vaccination until the clinical situation has stabilised should be considered on an individual basis (see section 14.6.2).

Tdap is not approved for use (registered) for primary immunisation. However, the Ministry of Health recommends that children aged from 7 years and adults may receive Tdap for catch-up of the primary schedule (see Appendix 2).

The Tdap data sheet states that the vaccine may be used during pregnancy when the possible advantages outweigh the possible risks for the fetus. However, the Ministry of Health recommends Tdap vaccine for all pregnant women from 16 weeks' gestation of every pregnancy, preferably in the second trimester, but at least two weeks before birth. It is funded when given any time in second or third trimester (see section 14.5.2).

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