4.12 PERTUSSIS

4.12.1 Bacteriology

Pertussis (whooping cough) is caused by *Bordetella pertussis*, a fastidious, Gram-negative, pleomorphic bacillus. There are other organisms (such as *Bordetella parapertussis, Mycoplasma pneumoniae* and *Chlamydia pneumoniae*) that can cause a pertussis-like syndrome.1

4.12.2 Clinical features

Pertussis is a respiratory infection with an incubation period of 7 to 20 days. In unvaccinated persons, *B. pertussis* is highly infectious, spreading by aerosols to 90% of susceptible household contacts.2 Natural infection does not provide long-term protection and repeat infection can occur.2 The characteristic paroxysmal cough with inspiratory whoop seen in unvaccinated children is less common in individuals who have varying degrees of immunity acquired from vaccination or infection.3 It has been estimated that *B. pertussis* accounts for up to 7% of cough illnesses per year in adults and, each year, more than 25% of adults experience a coughing illness of at least 5 days duration.4 Even in adults, pertussis can be associated with significant morbidity, with cough persisting for up to 3 months, and other significant symptoms, such as sleep disturbance or, rarely, rib fracture.5 Identification of pertussis is limited by patient and physician awareness and, in some cases, the limited sensitivity of diagnostic tests; it is generally believed to be significantly under-diagnosed (see 4.12.11 Public health management of pertussis below).

Death due to pertussis is rare in people aged 10–70 years. However, the case-fatality rate in unvaccinated infants <6 months of age is estimated to be 0.8%.6 The most common cause of death in persons with pertussis infection is pertussis pneumonia, sometimes complicated by seizures and hypoxic encephalopathy.3

4.12.3 Epidemiology

Despite a long-standing immunisation program, pertussis remains highly prevalent in Australia and the least well controlled of all vaccine-preventable diseases. Epidemics occur every 3 to 4 years. In unvaccinated populations, these outbreaks can be very large. In vaccinated populations, outbreaks are smaller, with greatly reduced mortality and morbidity, and may continue to occur every 3 to 4 years or be more widely spaced.7 The maximal risk of infection and severe morbidity is before infants are old enough to have received at least 2 vaccine doses.8 In recent years, among highly immunised communities, many cases of pertussis have occurred in adults and adolescents due to waning immunity.8,10 These persons are a significant reservoir of infection. Evidence from several studies of infant pertussis cases indicates that family members, particularly parents, are the source of infection in more than 50% of cases where a primary case can be identified, and the presumed source in a higher proportion.11 There have also been case reports documenting nosocomial infection in young infants acquired from healthcare workers.12-15 Pertussis hospitalisation rates for persons aged ≥60 years are higher than for other adults.16

Between 2000 and 2010, multiple epidemics of pertussis occurred in Australia; however, the timing and frequency of these varied by geographical location. More than 139,000 cases were reported over this 11-year period, with the highest annual incidence of notifications (156 cases per 100,000 population) reported in 2010.17

There have been a number of changes introduced to the NIP schedule over time in an attempt to improve control of pertussis. Introduction of a 5th dose of diphtheria, tetanus and whole-cell pertussis vaccine (DTPw) for 4–5-year-old children in August 1994 was followed by a decrease in notifications consistent with a vaccine effect; first among children aged 5 and 6 years, then by those in the 7–9 years age group.8,11 Subsequently, the average age of pertussis notifications continued to increase. By 2005, the proportion of notifications in adults >20 years of age had reached 83%, compared with 40% in the early 1990s.16

Acellular pertussis vaccine (DTPa) replaced DTPw for booster doses in 1997, and for all doses from 1999. In 2003, the DTPa booster dose at 18 months of age was removed from the NIP, moving the 1st booster dose to 4 years of age. The removal of the 18-month booster dose from the schedule was based on evidence from an Italian longitudinal study of DTPa trial participants. The study found that a primary DTPa course at 2, 4 and 6 months of age provided 76 to 80% protection from prolonged cough disease and this was maintained until 6 years of age.19

In 2009–2010, in contrast to previous epidemics, the highest notification rates in Australia were in children <10 years of age; the proportion of notifications in adults >20 years of age decreased to 57%. The greatest increase in notification rate occurred in 3-year-old children. Although increased and more sensitive diagnostic testing using polymerase chain reaction (PCR) has contributed to this rise, vaccine effectiveness among 3-year olds has been estimated at around 60%,20 consistent with waning of immunity following the primary DTPa course. In contrast to notifications, hospitalisation and death rates from pertussis in the most recent epidemic periods have not increased substantially.21 A high proportion of hospitalisations, and almost all deaths, attributed to pertussis occur in infants too young to have received more than 1 dose of pertussis-containing vaccine.16,22
The prevention of severe pertussis morbidity and deaths, particularly in infants <3 months of age, is a major goal in Australia and similar countries. Two vaccination strategies have been considered to achieve this – indirect protection from immunisation of close adult contacts of newborn infants, known as the ‘cocoon’ strategy23 (see ‘Persons in contact with infants and others at increased risk of pertussis’ in 4.12.7 Recommendations below) and direct protection from immunisation of the mother during the last trimester of pregnancy24 (see ‘Women who are pregnant or post-partum’ in 4.12.7 Recommendations below). Data to evaluate the effectiveness of indirect protection to infants from the cocoon approach are limited.25 However, this approach is expected to reduce infection risk to infants from family members, known to be an important source of pertussis infection, especially for the youngest infants.11

4.12.4 Vaccines

Pertussis vaccine is available in Australia only in combination with diphtheria, tetanus and other antigens. The acronym DTPa, using capital letters, signifies child formulations of diphtheria, tetanus and acellular pertussis-containing vaccines. The acronym dTpa is used for formulations that contain substantially lesser amounts of diphtheria toxoid and pertussis antigens than child (DTPa-containing) formulations; dTpa vaccines are usually used in adolescents and adults.

Acellular pertussis-containing vaccines have been used for both primary and booster vaccination of children in Australia since 1999. Whole-cell pertussis-containing vaccines were used exclusively before 1997. Between 1997 and 1999 acellular vaccines were used for booster doses. There are a number of acellular pertussis-containing vaccines that contain three or more purified components of B. pertussis. In the 3-component vaccines, these components are pertussis toxin (PT), filamentous haemagglutinin (FHA) and pertactin (PRN). In the 5-component vaccines, fimbrial (FIM) antigens are also included.

Pertussis vaccines provide good protection against severe and typical pertussis, but substantially less against milder coughing illness.26,27 Vaccine efficacy of DTPa vaccines with three or more antigens has been reported as 71 to 78% for preventing milder symptoms of pertussis and 84% for preventing typical disease.27 Epidemiological data suggest that receipt of the 1st dose of the primary DTPa course significantly reduces the incidence of severe pertussis disease in young infants, as measured by hospitalisation rates.28-30 Data on the duration of immunity following DTPa vaccine indicate that waning occurs 5 to 6 years after the last dose of vaccine.23,33 However, these studies could not control for levels of circulating pertussis in the population, which may boost the level of immunity and lead to over-estimation of the duration of protection against symptomatic disease.26,27

Reduced antigen content formulation, dTpa, vaccines are immunogenic.32-35 A randomised trial in adults reported a point estimate of 92% efficacy against culture/nucleic acid test-positive disease within 2.5 years of vaccination with a 3-component monovalent pertussis vaccine.4 Data on the duration of immunity to pertussis following a single booster dose of dTpa are limited. Long-term follow-up of adults vaccinated with dTpa has shown a rapid decline in levels of pertussis antibodies within the first 2 years after vaccination, with a continued steady decline out to 10 years after vaccination, although antibody levels remained above baseline.36 A similar long-term follow-up of adolescents demonstrated a more rapid decline, with pertussis antibody levels decreasing to or approaching pre-vaccination levels after 10 years.37 The rate of decline in clinical protection is unknown, but some protection against clinical disease is likely to persist for up to 10 years. Recent studies have indicated that dTpa vaccine is immunogenic in the elderly.35

Vaccination of pregnant women with dTpa has been shown to be effective in preventing pertussis disease in newborn infants via the transfer of maternal antibodies in utero. Vaccination of mothers at least 7 days before delivery reduced pertussis disease by 91% in infants <3 months of age.38 However, the level of pertussis antibody required in the pregnant woman to achieve this level of protection and the impact of waning pertussis immunity in the mother are not known. A study measuring pertussis-specific IgG levels in maternal and umbilical cord serum of mother-and-newborn pairs where the mother had received dTpa vaccine in the previous 2 years showed significant antibody decay in the woman and low antibody levels in the newborn.39 However, another study found detectable antibody levels in the cord blood of infants whose mothers were vaccinated approximately 13 months before delivery.40

Vaccines containing DTPa are available in various combinations with inactivated poliomyelitis, hepatitis B and Haemophilus influenzae type b vaccines.

Formulations for children aged <10 years

- Infanrix hexa – GlaxoSmithKline (DTPa-hepB-IPV-Hib; diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated poliovirus-Haemophilus influenzae type b). The vaccine consists of both a 0.5 mL pre-filled syringe containing ≥30 IU diphtheria toxoid, ≥40 IU tetanus toxoid, 25 µg pertussis toxoid (PT), 25 µg filamentous haemagglutinin (FHA), 8 µg pertactin (PRN), 10 µg recombinant HBsAg, 40 D-antigen units inactivated poliovirus type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett), adsorbed onto aluminium hydroxide/phosphate; traces of formaldehyde, polysorbate 80, polysorbate 20,
polysaccharide (PRP) conjugated to 20–40 µg tetanus toxoid. May contain yeast proteins.

- **Infanrix IPV** – GlaxoSmithKline (DTPa-IPV; diphtheria-tetanus-acellular pertussis-inactivated poliovirus).
  Each 0.5 mL pre-filled syringe contains ≥30 IU diphtheria toxoid, ≥40 IU tetanus toxoid, 25 µg PT, 25 µg FHA, 8 µg PRN, 40 D-antigen units inactivated poliovirus type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett), adsorbed onto aluminium hydroxide; traces of formaldehyde, polysorbate 80, polymyxin and neomycin.

- **Pediacel** – Sanofi Pasteur Pty Ltd (DTPa-IPV-Hib; diphtheria-tetanus-acellular pertussis-inactivated poliovirus-Haemophilus influenzae type b). Each 0.5 mL monodose vial contains ≥30 IU diphtheria toxoid, ≥40 IU tetanus toxoid, 20 µg PT, 20 µg FHA, 3 µg PRN, 5 µg pertussis fimbriae (FIM) 2+3, 40 D-antigen units inactivated poliovirus type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett), 10 µg Hib capsular polysaccharide conjugated to 20 µg tetanus protein; 1.5 mg aluminium phosphate; ≤50 µg bovine serum albumin; phenoxylethanol as preservative; traces of formaldehyde, glutaraldehyde, polysorbate 80, polymyxin, neomycin and streptomycin.

- **Quadracel** – Sanofi Pasteur Pty Ltd (DTPa-IPV; diphtheria-tetanus-acellular pertussis-inactivated poliovirus). Each 0.5 mL monodose vial contains ≥30 IU diphtheria toxoid, ≥40 IU tetanus toxoid, 20 µg PT, 20 µg FHA, 3 µg PRN, 5 µg FIM 2+3, 40 D-antigen units inactivated poliovirus type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett); 1.5 mg aluminium phosphate; ≤50 µg bovine serum albumin; phenoxylethanol as preservative; traces of formaldehyde, glutaraldehyde, polysorbate 80, polymyxin and neomycin.

- **Tripacel** – Sanofi Pasteur Pty Ltd (DTPa; diphtheria-tetanus-acellular pertussis). Each 0.5 mL monodose vial contains ≥30 IU diphtheria toxoid, ≥40 IU tetanus toxoid, 10 µg PT, 5 µg FHA, 3 µg PRN, 5 µg FIM 2+3; 1.5 mg aluminium phosphate; 3.4 mg phenoxylethanol.

### Reduced antigen formulations for adults, adolescents and children aged ≥10 years

- **Adacel** – Sanofi Pasteur Pty Ltd (dTpa; diphtheria-tetanus-acellular pertussis). Each 0.5 mL monodose vial contains ≥2 IU diphtheria toxoid, ≥20 IU tetanus toxoid, 2.5 µg PT, 5 µg FHA, 3 µg PRN, 5 µg FIM 2+3; 0.33 mg aluminium as aluminium phosphate; phenoxylethanol as preservative; traces of formaldehyde and glutaraldehyde.

- **Adacel Polio** – Sanofi Pasteur Pty Ltd (dTPa-IPV; diphtheria-tetanus-acellular pertussis-inactivated poliovirus). Each 0.5 mL monodose vial or pre-filled syringe contains ≥2 IU diphtheria toxoid, ≥20 IU tetanus toxoid, 2.5 µg PT, 5 µg FHA, 3 µg PRN, 5 µg FIM 2+3, 40 D-antigen units inactivated poliovirus type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett); 0.33 mg aluminium as aluminium phosphate; phenoxylethanol as preservative; traces of formaldehyde, glutaraldehyde, polysorbate 80, polymyxin, neomycin and streptomycin.

- **Boostrix** – GlaxoSmithKline (dTpa; diphtheria-tetanus-acellular pertussis). Each 0.5 mL monodose vial or pre-filled syringe contains ≥2 IU diphtheria toxoid, ≥20 IU tetanus toxoid, 8 µg PT, 8 µg FHA, 2.5 µg PRN, adsorbed onto 0.5 mg aluminium as aluminium hydroxide/phosphate; traces of formaldehyde, polysorbate 80 and glycine.

- **Boostrix-IPV** – GlaxoSmithKline (dTpa-IPV; diphtheria-tetanus-acellular pertussis-inactivated poliovirus). Each 0.5 mL pre-filled syringe contains ≥2 IU diphtheria toxoid, ≥20 IU tetanus toxoid, 8 µg PT, 8 µg FHA, 2.5 µg PRN, 40 D-antigen units inactivated poliovirus type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett), adsorbed onto 0.5 mg aluminium as aluminium hydroxide/phosphate; traces of formaldehyde, polysorbate 80, polymyxin and neomycin.

### 4.12.5 Transport, storage and handling

Transport according to National vaccine storage guidelines: Strive for 5°C. Store at +2°C to +8°C. Do not freeze. Protect from light.

Infanrix hexa must be reconstituted by adding the entire contents of the syringe to the vial and shaking until the pellet is completely dissolved. Reconstituted vaccine should be used as soon as practicable. If storage is necessary, hold at room temperature for not more than 8 hours.

### 4.12.6 Dosage and administration

The dose of all pertussis-containing vaccines is 0.5 mL to be given by IM injection.
4.12.7 Recommendations

Infants and children

Pertussis-containing vaccine is recommended in a 3-dose primary schedule for infants at 2, 4 and 6 months of age. Due to the high morbidity and occasional mortality associated with pertussis in the first few months of life, the 1st dose can be given as early as 6 weeks of age (see Table 2.1 Minimum acceptable age for the 1st dose of scheduled vaccines in infants in special circumstances). Giving a 1st dose at 6 weeks of age rather than 2 months of age is estimated to prevent an additional 8% of infant pertussis cases. The next scheduled doses should still be given at 4 months and 6 months of age.28,42

A booster dose of pertussis-containing vaccine, usually provided as DTPa-IPV, is recommended at 4 years of age, but can be given as early as 3.5 years of age. This booster dose is essential as waning of pertussis immunity occurs following receipt of the primary schedule.2,31 For this booster dose, all brands of DTPa-containing vaccines are considered interchangeable.

Where required, DTPa-containing vaccines can be given for catch-up for either the primary doses or booster dose in children aged <10 years (see 2.1.5 Catch-up).

In addition, all household contacts (children and adults) of infants should be age-appropriately immunised to minimise the risk of severe disease occurring in young infants prior to completion of the primary course (see ‘Adolescents’ and ‘Adults’ below).

Parents who wish to minimise the likelihood of their child developing pertussis in the 2nd and 3rd years of life (prior to when the booster dose is due at 4 years of age) should be advised that an additional dose of pertussis-containing vaccine can be given in the 2nd year of life, preferably at 18 months of age. This is particularly recommended for children born to mothers who received a dTpa vaccine during pregnancy (see ‘Women who are pregnant or post-partum’ below). It should be noted that a dose at this age is associated with an increased likelihood of a local adverse event, including extensive limb swelling, in a small percentage of children (see 4.12.10 Adverse events below).32 Any DTPa-containing vaccine may be used for additional dose of a pertussis-containing vaccine at 18 months of age. Under these circumstances, the next dose of a DTPa-containing vaccine should not be given until 4 years of age. The additional dose at 18 months of age is not included on the NIP schedule.

Older children and adolescents

A booster dose is also recommended for adolescents between 10 and 17 years of age, using the reduced antigen content dTpa. The optimal age for administering this dose is 11–13 years, due to waning antibody response following the booster dose recommended at 4 years of age. This adolescent booster dose of pertussis-containing vaccine is essential for maintaining immunity to pertussis (and diphtheria and tetanus) into adulthood.44

For details on the management of children and adolescents who require catch-up vaccination for pertussis, see 2.1.5 Catch-up.

Adults

Vaccination with dTpa is recommended for any adult who wishes to reduce the likelihood of becoming ill with pertussis. Vaccination is particularly important if the adult meets the criteria of a special risk group (see ‘Persons in contact with infants and others at increased risk from pertussis’ below).

dTpa vaccine should be used in place of dT at the age routinely recommended for a tetanus and diphtheria booster (50 years). There is currently insufficient evidence to recommend routine 10-yearly booster doses of dTpa vaccine for all adults (who do not meet the criteria of a special risk group below). However, due to the increased morbidity associated with pertussis in the elderly,46 adults aged ≥65 years should be offered a single dTpa booster if they have not received one in the previous 10 years.46,47 Adults of all ages who require a booster dose of dT vaccine should be encouraged to do so with dTpa vaccine, particularly if they have not received a dTpa dose previously (see 4.19 Tetanus and 4.2 Diphtheria).46

Travellers should receive a booster dose of dT (or dTpa if not given previously) if more than 10 years have elapsed since the last dose of dT-containing vaccine. For persons undertaking high-risk travel, consider giving a booster dose of either dTpa or dT (as appropriate) if more than 5 years have elapsed since the last dose of a dT-containing vaccine (see 4.19 Tetanus and 4.2 Diphtheria).

For those adults requiring additional protection from polio (see 4.14 Poliomyelitis), dTpa-IPV can be used.

For additional information on adults with no history of a primary course of dT or pertussis-containing vaccine requiring catch-up, see 4.19 Tetanus and 2.1.5 Catch-up.
Persons in contact with infants and others at increased risk from pertussis

There is significant morbidity associated with pertussis infection in infants <6 months of age, particularly those <3 months of age,\(^{16}\) and the source of infection in infants is often a household contact\(^{17}\) (see also 4.12.3 Epidemiology above). Pertussis vaccination of the close contacts of young infants is likely to reduce the risk of pertussis occurring in the infant and is recommended for the following groups.

Women who are pregnant or post-partum

dTpa vaccine is recommended as a single dose during the third trimester of each pregnancy. Vaccination during pregnancy has been shown to be more effective in reducing the risk of pertussis in young infants than vaccination of the mother post partum.\(^{25,38}\) This added benefit is due to direct passive protection of the newborn by transplacental transfer of high levels of pertussis antibodies from the vaccinated woman to the fetus. The optimal time for vaccination is between 28 and 32 weeks gestation, but the vaccine can be given at any time during the third trimester up to delivery. Early third trimester vaccination is preferred because pertussis antibody levels do not peak until approximately 2 weeks after vaccination\(^{37}\) and active transport of maternal antibody to the fetus occurs predominantly from 30 weeks gestation onwards.\(^{48}\)

Vaccination is recommended with each pregnancy to provide maximal protection to every infant; this includes pregnancies which are closely spaced (e.g. <2 years). Vaccine-induced pertussis antibodies wane over time and the protective antibody level required in newborn infants is unknown (see 4.12.4 Vaccines above). It is therefore possible that if a mother is not revaccinated during a subsequent pregnancy (even if closely spaced), her newborn will not be adequately protected against severe pertussis illness.

If vaccination during pregnancy is not planned or does not occur, vaccination during the post-partum period, as soon as possible after delivery of the infant (preferably before hospital discharge), will reduce the likelihood of pertussis occurring in the mother and thus provide some indirect protection to the infant.\(^{11}\)

An additional booster dose of a pertussis (dTpa)-containing vaccine at 18 months of age is recommended for children born to mothers who received dTpa vaccine during pregnancy. It is possible that giving dTpa vaccine in the third trimester of pregnancy might interfere with the infant’s immune response to the primary 3-dose DTPa course recommended at 2, 4 and 6 months of age, a phenomenon referred to as ‘blunting’.\(^{24}\) Early studies in children given a booster dose of DTPa-containing vaccine at 12–18 months of age have shown that levels of anti-pertussis antibodies 1 month later are similar irrespective of whether the child’s mother was vaccinated during pregnancy or not.\(^{39,50}\) As correlates of protection are not fully understood, the clinical importance of blunting is uncertain.

Other adult household contacts and carers of infants <6 months of age

Adult household contacts and carers (e.g. fathers, grandparents) of infants <6 months of age should ideally receive a dTpa vaccine at least 2 weeks before beginning close contact with the infant. A booster dose of dTpa is recommended if 10 years have elapsed since a previous dose.\(^{36,37}\)

Healthcare workers

All healthcare workers should receive dTpa vaccine because of the significant risk of nosocomial transmission of pertussis to vulnerable patients.\(^ {12,15}\) (See also 3.3 Groups with special vaccination requirements, Table 3.3.7 Recommended vaccinations for persons at increased risk of certain occupationally acquired vaccine-preventable diseases.) A booster dose of dTpa is recommended if 10 years have elapsed since a previous dose.\(^ {36,37}\) Vaccinated healthcare workers who develop symptoms compatible with pertussis should still be investigated for pertussis. There have been cases of nosocomial transmission of pertussis to infants from healthcare workers who have previously received dTpa vaccine.\(^ {13}\)

Staff working in early childhood education and care

Adults working with infants and young children aged <4 years should receive dTpa vaccine (see 3.3 Groups with special vaccination requirements, Table 3.3.7 Recommended vaccinations for persons at increased risk of certain occupationally acquired vaccine-preventable diseases). A booster dose of dTpa is recommended if 10 years have elapsed since a previous dose.\(^ {36,37,39,40}\)

Interval between dTpa and other tetanus/diphtheria-containing vaccines

A single dose of dTpa can be administered at any time after a dose of a vaccine containing tetanus and diphtheria toxoids. Studies indicate that the adverse reactions to a single dose of dTpa are similar whether administered shortly after (18 months), or at a longer interval after, a previous dose of a vaccine containing tetanus/diphtheria toxoids.\(^ {51-54}\) Where a tetanus- and diphtheria-containing vaccine has been given less than 18 months previously, the benefits of protection against pertussis gained from using dTpa, where recommended, are likely to outweigh the risk of an adverse event.\(^ {55}\)
Persons with a history of pertussis infection

Administration of pertussis vaccine in children, adolescents or adults who have had laboratory-confirmed pertussis infection is safe and is necessary, as natural immunity does not confer life-long protection. In particular, incompletely vaccinated infants <6 months of age who develop pertussis may not mount an adequate immune response following infection and should receive all routinely scheduled pertussis-containing vaccines.

4.12.8 Pregnancy and breastfeeding

dTpa vaccine is recommended for pregnant women (in the third trimester of each pregnancy) (see ‘Women who are pregnant or post-partum’ in 4.12.7 Recommendations above).

dTpa vaccine can be given to breastfeeding women.

Refer to 3.3 Groups with special vaccination requirements, Table 3.3.1 Recommendations for vaccination in pregnancy for more information.

4.12.9 Contraindications

The only absolute contraindications to acellular pertussis-containing vaccines are:

- anaphylaxis following a previous dose of any acellular pertussis-containing vaccine
- anaphylaxis following any vaccine component.

4.12.10 Adverse events

DTPa-containing vaccines in children

Acellular pertussis vaccines are associated with a much lower incidence of fever (approximately 20%) and local adverse events (approximately 10%) than whole-cell pertussis vaccines (approximately 45% and 40%, respectively), which are no longer used in Australia. [Note: text deleted]

Extensive limb swelling, defined as swelling and/or redness involving at least half the circumference of the limb and the joints both above and below the injection site, is a recognised adverse event that occurs rarely following booster doses of DTPa. Such reactions commence within 48 hours of vaccination, last for 1 to 7 days and resolve completely without sequelae. The pathogenesis of extensive limb swelling is poorly understood. In an analysis of 4th and 5th dose follow-up studies that examined 12 different DTPa vaccines, 2% of 1015 children who received consecutive doses of the same DTPa vaccine reported entire thigh swelling, which resolved completely. A history of extensive limb swelling after a booster dose of DTPa is not a contraindication to reduced antigen formulations of dTpa at 11–13 years of age (or older). Parents of children about to receive a booster dose of a DTPa-containing vaccine should be informed of the small but well-defined risk of this adverse event which, even when extensive, is usually not associated with significant pain or limitation of movement.

Febrile convulsions are very infrequently reported following DTPa-containing vaccines, within 48 hours of vaccination. The risk is even lower in infants who complete their primary course at 6 months of age, as febrile convulsions are uncommon in children <6 months of age. Children who experience a febrile convulsion after a dose of DTPa-containing vaccine have a slightly greater risk of a further febrile convolution following a subsequent dose of a DTPa-containing vaccine. This risk can be minimised by appropriate measures to prevent fever, so vaccination is still recommended.

Hypotonic-hyporesponsive episodes (HHE), defined as an episode of pallor, limpness and unresponsiveness, occur rarely following DTPa vaccine, 1 to 48 hours after vaccination. Shallow respiration and cyanosis may also occur in an HHE. An HHE may last from a few minutes to 36 hours. In Australia during 2009, 3.2 cases of HHE were reported per 100 000 doses of DTPa-containing vaccine given to children <1 year of age. Follow-up of children with HHE shows no long-term neurological or other sequelae and they can receive further doses of DTPa-containing vaccines. Children who have an HHE following DTPa-containing vaccines should receive further doses as recommended. Supervision may be required under some circumstances; advice can be obtained from clinics specialising in the management of adverse events following immunisation (see Appendix 1 Contact details for Australian, state and territory government health authorities and communicable disease control).

Pertussis-containing vaccines do not cause infantile spasms or epilepsy. Infants and children known to have active or progressive neurological disease can be safely vaccinated with DTPa-containing vaccines. A large Canadian study found no evidence of encephalopathy following acellular pertussis vaccines. For infants and children with stable neurological disease (including cerebral palsy), or a family history of idiopathic epilepsy or other familial neurological disorder, the risk of adverse events following DTPa-containing vaccines is the same as for other infants of the same age.

Sudden infant death syndrome (SIDS) is not associated with either DTPa or any pertussis-containing vaccine. Some studies suggest a decreased risk of SIDS in children who have been vaccinated.
dTPa-containing vaccines in adolescents and adults

Reduced antigen content dTPa vaccines are safe and well-tolerated in adults.\textsuperscript{32,65,66} The incidence of fever is low, and comparable in vaccine and placebo recipients in clinical trials.\textsuperscript{32,65,66} Studies investigating revaccination within 10 years (and some within 2 years) after a tetanus toxoid-\textsuperscript{1} dT- or dTPa-containing vaccine in non-pregnant adolescents and adults have found no increase in moderate or severe adverse events or subjective fever. However, an increase in mild transient injection site pain is often reported following dTPa-containing booster doses.\textsuperscript{36,37,67} Limb swelling reactions after dTPa-containing booster doses are rare.\textsuperscript{68}

Brachial neuritis (inflammation of a nerve in the arm, causing weakness or numbness) has been described following the administration of tetanus toxoid-containing vaccines, with an estimated excess risk of approximately 0.5–1 in 100 000 doses in adults.\textsuperscript{69}

dTPa vaccines in pregnant women

Studies have found no evidence of an increased risk of adverse pregnancy outcomes (such as stillbirth, pre-eclampsia, fetal distress, low birth weight or neonatal renal failure) related to pertussis vaccination during pregnancy.\textsuperscript{49,70–74}

While dTPa vaccine is generally safe and well-tolerated in adults, there is a small risk that significant injection site reactions following subsequent doses might occur in some women who receive dTPa vaccines during successive closely spaced pregnancies. This low risk is considered to be balanced by the benefit to each infant of protection against pertussis.

4.12.11 Public health management of pertussis

Pertussis (both suspected and confirmed) is a notifiable disease in all states and territories in Australia. Detailed information regarding case definitions and the management of pertussis cases and contacts can be found in the national guidelines for control of pertussis\textsuperscript{5} (www.health.gov.au/cdnasongs).

Further instructions about the public health management of pertussis can also be obtained from state/territory public health authorities (see Appendix 1 Contact details for Australian, state and territory government health authorities and communicable disease control).

Suspected cases of pertussis should be investigated, regardless of vaccination status, as immunisation is not 100% effective and immunity wanes over time. The diagnosis of pertussis can be confirmed by either culture or nucleic acid testing of a per-nasal swab or nasopharyngeal aspirate specimen, or by serology. The appropriate diagnostic test depends on the age, vaccination history and duration of symptoms. PCR is usually the diagnostic method of choice, particularly if pertussis is suspected in someone who has received a pertussis-containing vaccine within the previous 5 years.\textsuperscript{76}

To reduce the risk of transmission of \textit{B. pertussis}, persons with pertussis infection should commence appropriate antibiotic therapy on clinical suspicion, if within 21 days of the onset of coryza. Antibiotic treatment does not shorten the course of the illness, but reduces infectivity if provided early in the illness. Detailed information regarding appropriate macrolide antibiotics and dosing can be found in the national guidelines for control of pertussis.\textsuperscript{77,78}

Management of contacts of cases

Vaccination

Since a primary vaccination course requires three or more injections to protect against pertussis, infant vaccination cannot be effectively used to protect unimmunised infants. Vaccination has not been shown to have a role in controlling outbreaks at any age, even in closed settings. However, unvaccinated or partially vaccinated contacts, up to their 10th birthday, should be offered DTPa-containing vaccines, and older contacts should be offered dTpa (see 2.1.5 Catch-up).

Passive immunisation with normal human immunoglobulin is not effective in the prevention of pertussis.

Chemoprophylaxis

The benefit of chemoprophylaxis in preventing the secondary transmission of pertussis is limited due to multiple factors, including delayed clinical presentation, delayed diagnosis and imperfect compliance.\textsuperscript{78} The use of chemoprophylaxis for prevention of secondary cases should be limited to close contacts of cases in the household setting who are vulnerable to severe complications of pertussis, or who, in settings such as early childhood education and care or healthcare facilities, may transmit pertussis to vulnerable contacts. Further recommendations regarding chemoprophylaxis of close contacts can be found in the national guidelines for control of pertussis.\textsuperscript{75}

4.12.12 Variations from product information

The product information for Infanrix hexa states that this vaccine is indicated for primary immunisation of infants from the age of 6 weeks. The ATAGI recommends that this vaccine may also be used for catch-up of the primary schedule in children <10 years of age.
The product information for Infanrix IPV states that this vaccine is indicated for use in a 3-dose primary schedule for immunisation of infants from the age of 6 weeks and as a single booster dose for children ≤6 years of age who have previously been vaccinated against diphtheria, tetanus, pertussis and poliomyelitis. In addition, the ATAGI recommends that this product may also be used for catch-up of the primary schedule or as a booster in children <10 years of age.

The product information for Quadracel states that this vaccine is indicated for use in a 3-dose primary schedule from the age of 2 months to 12 months and may also be used as a booster dose for children from 15 months to 6 years of age who have previously been vaccinated against diphtheria, tetanus, pertussis and poliomyelitis. The ATAGI recommends that, when appropriate, this product may also be used for either catch-up of the primary schedule or as a booster dose in children aged <10 years. The ATAGI also recommends that the primary schedule may be commenced at 6 weeks of age, if required.

The product information for Tripacel states that this vaccine is indicated for use in a 3-dose primary schedule from the age of 2 months to 12 months and may also be used as a booster dose for children from 15 months to 8 years of age who have previously been vaccinated against diphtheria, tetanus and pertussis. The ATAGI recommends that, when appropriate, this product may also be used for either catch-up of the primary schedule or as a booster dose in children aged <10 years. The ATAGI also recommends that the primary schedule may be commenced at 6 weeks of age, if required.

The product information for Pediaacel states that this vaccine is indicated for primary immunisation of infants from the age of 6 weeks and may also be used as a booster dose for children from 15 to 20 months of age who have previously been vaccinated against diphtheria, tetanus, pertussis, poliomyelitis and Haemophilus influenzae type b. The ATAGI recommends that, when appropriate, this product may also be used for either catch-up of the primary schedule or as a booster dose in children aged <10 years.

The product information for Adacel and Boostrix (reduced antigen content dTpa) states that these vaccines are indicated for booster doses only. The ATAGI recommends instead that, when a 3-dose primary course of diphtheria/tetanus toxoids is given to an adolescent/adult, dTpa should replace the 1st dose of dT, with 2 subsequent doses of dT. If dT is not available, dTpa can be used for all 3 primary doses, but this is not routinely recommended.

The product information for Adacel and Boostrix states that these vaccines should not be used in pregnancy unless there is a high risk of acquiring pertussis. The ATAGI recommends that pregnant or post-partum women receive a dose with every pregnancy.

The product information for Adacel states that there are currently no data upon which to base a recommendation for the optimal interval for administering subsequent booster doses to maintain antibody levels against pertussis; however, the ATAGI recommends that pregnant or post-partum women receive a booster dose with every pregnancy and that other adults in contact with infants and/or at increased risk from pertussis can receive a booster dose every 10 years.

The product information for Boostrix, Boostrix-IPV and Adacel states that dTpa-containing vaccine should not be given within 5 years of a tetanus toxoid-containing vaccine. The product information for Adacel Polio states that dTpa-containing vaccine should not be given within 3 years of a tetanus toxoid-containing vaccine. The ATAGI recommends instead that, if protection against pertussis is required, dTpa-containing vaccines can be administered at any time following receipt of a dT-containing vaccine.

The product information for Adacel, Adacel Polio, Boostrix, Boostrix-IPV, Infanrix hexa, Infanrix IPV, Pediaacel, Quadracel and Tripacel states that these vaccines are contraindicated in children with encephalopathy of unknown aetiology or with neurologic complications occurring within 7 days following a vaccine dose. The ATAGI recommends instead that the only contraindication is a history of anaphylaxis to a previous dose or to any of the vaccine components.

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


RELEVANT TEXT FROM OTHER CHAPTERS OF THE AUSTRALIAN IMMUNISATION HANDBOOK 10TH EDITION

UPDATED TO ALIGN WITH CHANGED RECOMMENDATIONS IN CHAPTER 4.12 PERTUSSIS

3.3 GROUPS WITH SPECIAL VACCINATION REQUIREMENTS

3.3.2 Vaccination of women who are planning pregnancy, pregnant or breastfeeding, and preterm infants

Women planning pregnancy

The need for vaccination, particularly for hepatitis B, measles, mumps, rubella and varicella should be assessed as part of any pre-conception health check. Where previous vaccination history or infection is uncertain, relevant serological testing can be undertaken to ascertain immunity to hepatitis B, measles, mumps and rubella. Routine serological testing for varicella does not provide a reliable measure of vaccine-induced immunity, although can indicate whether previous natural infection has occurred (see 4.22 Varicella). Influenza vaccine is recommended for any person who wishes to be protected against influenza and is recommended for women planning pregnancy. Those with risk factors for pneumococcal disease, including smokers and Aboriginal and Torres Strait Islander women, should be assessed for pneumococcal vaccination. Women who receive live attenuated viral vaccines should be advised against falling pregnant within 28 days of vaccination.

Pregnant women

Table 3.3.1 summarises the recommendations for vaccine use in pregnancy. More detailed information is also provided under the ‘Pregnancy and breastfeeding’ sections of each disease-specific chapter in Part 4 of this Handbook.

Seasonal influenza and dTpa are the only vaccines that are routinely recommended for pregnant women.
Table 3.3.1: Recommendations for vaccination in pregnancy (see also disease-specific chapters in Part 4)

**Vaccines routinely recommended in pregnancy**

<table>
<thead>
<tr>
<th>Inactivated viral vaccines</th>
<th>Recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza vaccine</td>
<td>Recommended for all pregnant women at any stage of pregnancy, particularly those who will be in the second or third trimester during the influenza season.</td>
<td>There is evidence from clinical trial data and observational studies that there is no increased risk of congenital defects or adverse effects in the fetuses of women who are vaccinated against influenza in pregnancy. Influenza immunisation protects the mother, as pregnancy increases her risk of severe influenza, and also protects her newborn baby in the first few months after birth (see 4.7 Influenza).</td>
</tr>
<tr>
<td>Diphtheria-, tetanus-, and pertussis-containing vaccines (dTpa)</td>
<td>dTpa recommended as a single dose during the third trimester of each pregnancy</td>
<td>Pertussis vaccination during the third trimester of pregnancy has been shown to be more effective in reducing the risk of infant pertussis than maternal vaccination post partum. Studies have found no evidence of an increased risk of adverse pregnancy outcomes related to pertussis vaccination during pregnancy. (See 4.12 Pertussis for more details.)</td>
</tr>
</tbody>
</table>

**Vaccines not routinely recommended in pregnancy**

<table>
<thead>
<tr>
<th>Inactivated bacterial vaccines</th>
<th>Recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria-tetanus vaccine (dT)</td>
<td>Not routinely recommended</td>
<td>Tetanus- and diphtheria-containing vaccines have been used extensively in pregnant women, with no increased risk of congenital abnormalities in fetuses of women who were vaccinated during pregnancy.</td>
</tr>
<tr>
<td></td>
<td>Can be given under certain circumstances, such as for management of a tetanus-prone wound.</td>
<td>(See 4.2 Diphtheria and 4.19 Tetanus for more details.)</td>
</tr>
</tbody>
</table>
4.2 DIPHTHERIA

4.2.8 Pregnancy and breastfeeding

Although dT vaccines are not routinely recommended for pregnant women, they can be given under certain circumstances, such as for management of a tetanus-prone wound (see 4.19 Tetanus). dTpa vaccine is recommended for pregnant women (in the third trimester of each pregnancy) to prevent pertussis in pregnant women and their newborns (see 4.12 Pertussis).

4.2.12 Variations from product information

The product information for Adacel and Boostrix states that these vaccines should not be used in pregnancy unless there is a high risk of acquiring pertussis. The ATAGI recommends that pregnant or post-partum women receive a dose with every pregnancy.

The product information for Adacel states that there are currently no data upon which to base a recommendation for the optimal interval for administering subsequent booster doses to maintain antibody levels against pertussis; however, the ATAGI recommends that pregnant or post-partum women receive a booster dose with every pregnancy and that other adults in contact with infants and/or at increased risk from pertussis can receive a booster dose every 10 years.

4.19 TETANUS

4.19.8 Pregnancy and breastfeeding

Although dT vaccines are not routinely recommended for pregnant women, they can be given under certain circumstances, such as for management of a tetanus-prone wound (see 4.19.9 Tetanus-prone wounds below). dTpa vaccine is recommended for pregnant women (in the third trimester of each pregnancy) to prevent pertussis in pregnant women and their newborns (see 4.12 Pertussis).

4.19.14 Variations from product information

The product information for Adacel and Boostrix states that these vaccines should not be used in pregnancy unless there is a high risk of acquiring pertussis. The ATAGI recommends that pregnant or post-partum women receive a dose with every pregnancy.

The product information for Adacel states that there are currently no data upon which to base a recommendation for the optimal interval for administering subsequent booster doses to maintain antibody levels against pertussis; however, the ATAGI recommends that pregnant or post-partum women receive a booster dose with every pregnancy and that other adults in contact with infants and/or at increased risk from pertussis can receive a booster dose every 10 years.