

## Immunise - 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.<sup>1</sup>

### 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.<sup>2</sup> Natural infection does not provide long-term protection and repeat infection can occur.<sup>2</sup> 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.<sup>3</sup> 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.<sup>4</sup> 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.<sup>5</sup> 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 (refer to 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%.<sup>6,7</sup> The most common cause of death in persons with pertussis infection is pertussis pneumonia, sometimes complicated by seizures and hypoxic encephalopathy.<sup>3</sup>

### 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.<sup>8</sup> The maximal risk of infection and severe morbidity is before infants are old enough to have received at least 2 vaccine doses.<sup>9</sup> In recent years, among highly immunised communities, many cases of pertussis have occurred in adults and adolescents due to waning immunity.<sup>8,10</sup> These persons are a significant reservoir of infection. Evidence from studies of infant pertussis cases indicates that household contacts and carers are frequently the source of infection, with parents identified as the source for more than 50% of cases.<sup>11</sup> However, Australian studies have shown that in settings where notification rates in children are high, siblings are a significant source of infant infections.<sup>12,13</sup> There have also been case reports documenting nosocomial infection in young infants acquired from healthcare workers.<sup>14-17</sup> Pertussis hospitalisation rates for persons aged ≥60 years are higher than for other adults.<sup>18</sup>

Between 1995 and 2012, multiple epidemics of pertussis occurred in Australia; however, the timing and frequency of these varied by geographical location. The highest annual incidence of notifications (173 cases per 100 000 population) was reported in 2011, with 38 732 notified cases.<sup>19</sup>

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.<sup>8,20</sup> 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%,<sup>8</sup> compared with 40% in the early 1990s.

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.<sup>21</sup>

In contrast to preceding epidemics, in the 2008–2011 epidemic period the highest notification rates in Australia were in children <15 years of age and the proportion of notifications in older adolescents and adults decreased. Notable increases in pertussis notifications occurred for children between 3 and 9 years of age.<sup>19</sup> Although more accessible and sensitive diagnostic testing with polymerase chain reaction (PCR) contributed to the rise in notified cases,<sup>22</sup> waning of DTPa vaccine-induced immunity has also been demonstrated to be a factor (refer to [4.12.4 Vaccines](#) below).<sup>23–26</sup> Although increased notification rates were observed in the most recent epidemic, hospitalisation and death rates from pertussis did not increase substantially.<sup>27</sup> 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.<sup>18,28</sup>

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 household contacts and carers of newborn infants, known as the ‘cocoon’ strategy,<sup>29</sup> and direct protection from immunisation of the mother<sup>30</sup> during the last trimester of pregnancy<sup>30</sup> (refer to [4.12.4 Vaccines](#) and [4.12.7 Recommendations](#) below).

#### 4.12.4 Vaccines

Pertussis vaccine is only available in Australia in combination with diphtheria and tetanus, with or without other antigens such as inactivated poliomyelitis, hepatitis B and *Haemophilus influenzae* type b. 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 two or more purified components of *B. pertussis*. In the 2-component vaccine these are pertussis toxin (PT) and filamentous haemagglutinin (FHA); in the 3-component vaccines, pertactin (PRN) is also included; and in the 5-component vaccines, two fimbrial (FIM) antigens are also included. In the last decade, 3-component vaccines have been predominantly used in the childhood immunisation schedule in Australia.

Pertussis vaccines provide good protection against severe and typical pertussis, but substantially less against milder coughing illness.<sup>31,32</sup> 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.<sup>32</sup> 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.<sup>33–35</sup> However, there is a growing body of evidence that immunity following DTPa, and in turn vaccine effectiveness, wanes over time. In Australia, the effectiveness of 3 doses of pertussis-containing vaccine declined progressively from 2 years of age, to less than 50% by 4 years of age, in children aged 1–3 years who had not received an 18-month booster dose.<sup>26</sup> Likewise,

studies in older children from both Australia and the United States have shown a reduction in vaccine effectiveness associated with time since the dose of DTPa given prior to starting school.<sup>23-25</sup>

Reduced antigen content formulation, dTpa, vaccines are immunogenic.<sup>36-39</sup> 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.<sup>4</sup> 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.<sup>40</sup> 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.<sup>41</sup> The rate of decline in clinical protection is unknown, but some protection against clinical disease may persist for up to 10 years. Recent studies have indicated that dTpa vaccine is immunogenic in the elderly.<sup>39</sup>

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.<sup>42</sup> 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. On the one hand, pertussis-specific IgG levels in maternal and umbilical cord serum of mother-and-newborn pairs show significant antibody decay over a 2-year interval between pregnancies.<sup>43</sup> On the other hand, pertussis antibody levels in the cord blood of infants whose mothers were vaccinated approximately 13 months previously (following birth of an older sibling) were significantly higher than those in cord blood of the older sibling prior to maternal vaccination.<sup>44</sup>

Studies have shown lower levels of anti-pertussis antibodies at 7 months of age in children born to women vaccinated with dTpa during pregnancy, compared to children of mothers who were not vaccinated. However, when children were given a booster dose of DTPa-containing vaccine at 12–18 months of age, levels of anti-pertussis antibodies 1 month later were similar irrespective of whether the child's mother was vaccinated during pregnancy or not.<sup>45,46</sup>

Cocoon vaccination is an alternative vaccination strategy expected to reduce infection risk to infants, especially the youngest of infants, through the vaccination of household contacts and carers who are known to be an important source of pertussis infection (refer to 4.12.3 *Epidemiology* above).<sup>11</sup> However, the emerging data on the effectiveness of indirect protection to infants from the cocoon approach suggest only a modest benefit.<sup>47</sup>

## Formulations for children aged <10 years

- **Infanrix** – GlaxoSmithKline (DTPa; diphtheria-tetanus-acellular pertussis). Each 0.5 mL monodose vial or pre-filled syringe contains ≥30 IU diphtheria toxoid, ≥40 IU tetanus toxoid, 25 µg pertussis toxoid (PT), 25 µg filamentous haemagglutinin (FHA), 8 µg pertactin (PRN), adsorbed onto 0.5 mg aluminium as aluminium hydroxide.
- **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 PT, 25µg FHA, 8 µg 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, polymyxin and neomycin; *and* a vial containing a lyophilised pellet of 10 µg purified Hib capsular 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 ng bovine serum albumin; phenoxyethanol 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 ng bovine serum albumin; phenoxyethanol 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; 1.5mg aluminium phosphate; 3.4mg phenoxyethanol.

### 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; phenoxyethanol; 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; phenoxyethanol; 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*.<sup>48</sup> 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.

Do not mix DTPa- or dTpa-containing vaccines with any other vaccine in the same syringe, unless specifically registered for use in this way.

## 4.12.7 Recommendations

### Infants and children

#### Primary doses

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 (refer to [Table 2.1.5 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.<sup>33,49</sup>

#### Booster doses

Two booster doses of pertussis-containing vaccine are recommended during childhood to provide ongoing protection against pertussis through to early adolescence (refer to 'Older children and adolescents' below).

The first booster dose of pertussis-containing vaccine (dose 4 in the childhood series), usually provided as DTPa, is recommended at 18 months of age. This booster dose is required due to waning of pertussis immunity following receipt of the primary schedule (refer to [4.12.4 Vaccines](#) above).<sup>26</sup>

The second booster dose of pertussis-containing vaccine (dose 5 in the childhood series), usually provided as DTPa-IPV, is recommended at 4 years of age. This second booster dose is essential to maximise pertussis immunity during childhood as waning occurs progressively with age.<sup>23,24</sup>

For details on the management of children who require catch-up vaccination for pertussis, including minimum acceptable intervals between vaccine doses, refer to [2.1.5 Catch-up](#).

In addition, household contacts and carers 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 (refer to 'Older children and adolescents' and 'Adults' below).

### Older children and adolescents

An additional booster dose of pertussis-containing vaccine (i.e. in addition to those recommended for young children, refer above) is 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 of the antibody response following the booster dose recommended at 4 years of age.<sup>23,24</sup> This adolescent booster dose of pertussis-containing vaccine is essential for maintaining immunity to pertussis (and diphtheria and tetanus) into adulthood.<sup>50</sup>

For details on the management of children and adolescents who require catch-up vaccination for pertussis, refer to [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 (refer to '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,<sup>18</sup> adults aged  $\geq 65$  years should be offered a single dTpa booster if they have not received one in the previous 10 years.<sup>18,51</sup> 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 (refer to [4.19 Tetanus](#) and [4.2 Diphtheria](#)).<sup>52</sup>

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 (refer to [4.19 Tetanus](#) and [4.2 Diphtheria](#)).

For those adults requiring additional protection from polio (refer to [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, refer to [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,<sup>18</sup> and the source of infection in infants is often a household contact<sup>11</sup> (Also refer to [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 (refer to [3.3 Groups with special vaccination requirements](#)). 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.<sup>42,47</sup> 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. As pertussis antibody levels do not peak until approximately 2 weeks after vaccination<sup>53</sup> and active transport of maternal antibody to the fetus occurs predominantly from 30 weeks gestation onwards,<sup>54</sup> the optimal time for vaccination is early in the third trimester (between 28 and 32 weeks). However, the vaccine can be given at any time during the third trimester up to delivery.

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 (refer to [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.

For any pregnancy where antenatal vaccination 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.<sup>47</sup>

### **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.<sup>40,41</sup>

## Healthcare workers

All healthcare workers should receive dTpa vaccine because of the significant risk of nosocomial transmission of pertussis to vulnerable patients.<sup>14-17</sup> (also refer to [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.<sup>40,41</sup> 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.<sup>15</sup>

## Staff working in early childhood education and care

Adults working with infants and young children aged <4 years should receive dTpa vaccine (refer to [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.<sup>40,41</sup>

## 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.<sup>55-58</sup> 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.<sup>59</sup>

## 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) (refer to '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.<sup>31,32,60</sup>

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.<sup>61</sup> 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.<sup>61</sup> 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).<sup>62</sup> 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 convulsion 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.<sup>63</sup> Follow-up of children with HHE shows no long-term neurological or other sequelae and they can receive further doses of DTPa-containing vaccines.<sup>64</sup> 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 (refer to [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.<sup>65</sup> 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.<sup>66</sup> Some studies suggest a decreased risk of SIDS in children who have been vaccinated.<sup>67-69</sup>

## dTpa-containing vaccines in adolescents and adults

Reduced antigen content dTpa vaccines are safe and well-tolerated in adults.<sup>36,70,71</sup> The incidence of fever is low, and comparable in vaccine and placebo recipients in clinical trials.<sup>36,70,71</sup> Studies investigating revaccination within 10 years (and some within 2 years) after a tetanus toxoid-, 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.<sup>40,57,58,72</sup> Limb swelling reactions after dTpa-containing booster doses are rare.<sup>40,41,72</sup> In adults who report a history of adverse event(s) following whole-cell pertussis-containing vaccine given in childhood, dTpa can

almost always be given (refer to [3.3.1 Vaccination of persons who have had an adverse event following immunisation](#)).

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.<sup>73,74</sup>

### **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.<sup>45,75-79</sup>

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](#)<sup>80</sup>.

Further instructions about the public health management of pertussis can also be obtained from state/territory public health authorities (refer to [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.<sup>81</sup>

To reduce the risk of transmission of *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.<sup>80,82</sup>

### **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 (refer to [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.<sup>83</sup> The use of chemoprophylaxis for prevention of secondary cases should be limited to high-risk close contacts of cases. Further recommendations regarding chemoprophylaxis of close contacts can be found in the national guidelines for control of pertussis.<sup>80</sup>

#### 4.12.12 Variations from product information

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

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 Pediacel 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 states that vaccination in pregnancy is not recommended unless there is a definite risk of acquiring pertussis. The product information for Boostrix states that the vaccine should be used during pregnancy only when clearly needed, and the possible advantages outweigh the possible risks for the fetus. The ATAGI recommends that pregnant women receive a dose with every pregnancy.

The product information for Adacel and Boostrix state that there is no recommendation regarding the timing and

frequency of booster doses against pertussis in adults. 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, Infanrix hexa, Infanrix IPV, Pediacel, 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.