

## Pertussis

### PERTUSSIS VACCINES FOR AUSTRALIANS: INFORMATION FOR IMMUNISATION PROVIDERS

#### Disease and epidemiology

- Pertussis, commonly known as ‘whooping cough’, is a highly contagious infection of the respiratory tract caused by the bacterium *Bordetella pertussis*.
- Infants <6 months of age are at the greatest risk of severe disease and death.
- In Australia, pertussis epidemics occur every 3 to 4 years, the most recent between 2008 and 2012. In 2011, 38,732 notified cases were reported nationally. The highest rates of disease were in infants <6 months of age and children 5–9 years of age.

#### Who should be vaccinated

- In Australia, pertussis vaccine is available on the National Immunisation Program (NIP) for children at 2, 4, 6, 18 months and 4 years of age. An adolescent booster dose is available via school-based programs at 12–17 years of age (the age of delivery for school-based immunisation programs varies by state and territory). The additional booster dose at 18 months of age has been funded under the NIP since March 2016.
- Vaccination of pregnant women is recommended during the third trimester of each pregnancy. The vaccine is not funded under the NIP; however, it is currently free under state and territory initiatives.
- The vaccine is recommended for any adults who wish to reduce their likelihood of becoming ill, and is particularly important for those in contact with infants aged <6 months (e.g. family members, healthcare workers, childcare workers). The vaccine is not funded under the NIP for these individuals.

#### Vaccines

- Pertussis vaccine is only available in Australia in combination with diphtheria and tetanus, with or without other antigens such as inactivated poliomyelitis (IPV), hepatitis B (hepB) and *Haemophilus influenzae* type b (Hib).
- The acronym DTPa, using capital letters, signifies child formulations of diphtheria, tetanus and acellular pertussis-containing vaccines. DTPa-containing vaccines are used in children <10 years of age.
- 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.

## The disease

Pertussis (whooping cough) is an acute illness caused by the *Bordetella pertussis* bacterium. It is spread by airborne droplets when an infected person coughs or sneezes, or via direct contact with secretions from the nose or throat. Symptoms usually develop within 7–20 days of exposure. People with pertussis are most infectious in the early stages of illness and remain infectious for up to 21 days after the onset of symptoms.<sup>1</sup>

Pertussis illness begins with an irritating cough that gradually becomes paroxysmal and lasts for 1–2 months or longer. The illness is characteristically known for causing repeated violent bouts of coughing followed by a characteristic high-pitched whooping inspiration. However, the high-pitched whoop may be absent in older children, adults and very young infants.

Immunisation reduces the chance of getting the infection, both in children and adults.<sup>1</sup>

## Epidemiology

Despite the availability of pertussis vaccines for more than 50 years, pertussis remains a challenging disease to control. Control of pertussis is problematic because immunity, whether from immunisation or infection, wanes over time, resulting in renewed susceptibility to infection. Pertussis is always circulating in the community and epidemics occur in Australia every 3–4 years.<sup>2,3</sup>

Between 2008 and 2012, all Australian states and territories experienced their largest pertussis epidemic since national reporting began in 1991. During these epidemics the highest rates of disease were in infants <6 months of age and children 5–9 years of age. Although the high number of cases identified in the recent epidemics was partly due to the increased availability of more sensitive tests,<sup>4</sup> [waning immunity](#) was also a factor.<sup>5,6</sup>

Adults account for half of notified cases each year and are an important source of infection.<sup>7</sup> Evidence from studies of infant pertussis cases indicates that family members, particularly parents, are the source of infection in at least 50% of cases.<sup>8</sup>

Young infants are much more likely to develop severe disease than older age groups. Between 2006 and 2012, infants aged <6 months accounted for 42% (1,832 of 4,408) of pertussis-related hospitalisations.<sup>3</sup> During this period there were 11 deaths attributed to pertussis; 10 of these deaths were in infants <6 months of age.<sup>3</sup>

## Who should be vaccinated

### Children and adolescents

A primary course of 3 doses of the paediatric formulation of diphtheria–tetanus–acellular pertussis (DTPa) vaccine at 2, 4 and 6 months of age is recommended for all infants, unless [contraindicated](#).<sup>9</sup> In view of the high morbidity and mortality associated with pertussis in early infancy, the first dose can be given as early as 6 weeks of age.

Two booster doses of DTPa vaccine are recommended in childhood; the first at 18 months of age and the second (in combination with IPV) at 4 years of age. An additional booster dose, using reduced antigen content formulation diphtheria–tetanus–acellular pertussis (dTpa) vaccine, is given between 12 and 17 years of age. This dose is usually administered via school-based immunisation programs (the age of delivery for school-based immunisation programs varies by state and territory).

### Adults

dTpa vaccine is recommended for any adult who wishes to reduce the likelihood of becoming ill with pertussis, but is particularly important for adults who meet the criteria of a [special risk group](#) (see below).

dTpa vaccine should be used in place of dT vaccine at the age routinely recommended for a diphtheria and tetanus booster (50 years). Adults of all ages who require a booster of dT vaccine should be encouraged to have dTpa vaccine if they haven't received a dose previously. Adults ≥65 years of age should receive a dose of dTpa vaccine if they have not received one in the previous 10 years.

### Special risk groups

#### Pregnant women

dTpa vaccine is recommended during the third trimester of each pregnancy. 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 during pregnancy protects the newborn, especially in the first 6 weeks of life, via antibodies that cross the placenta.

Women who do not receive dTpa vaccine during pregnancy should be vaccinated as soon as possible after delivery (preferably before hospital discharge). This will reduce the likelihood of pertussis occurring in the mother and thus provide some indirect protection to the infant.

#### People in contact with infants

Adult household contacts and carers (e.g. fathers and 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

vaccine is recommended for those who have not received one in the previous 10 years.

Adults working with infants and young children <4 years of age should receive a dose of dTpa vaccine. A booster dose is recommended every 10 years.

### Healthcare workers

All healthcare workers should receive a dose of dTpa vaccine. A booster dose is recommended every 10 years.

## Vaccines

### Formulations available

#### For children (<10 years of age)

The following paediatric formulations of DTPa vaccines are registered in Australia: Infanrix<sup>®</sup> (DTPa), Infanrix<sup>®</sup> hexa (DTPa-hepB-IPV-Hib), Hexaxim<sup>®</sup> (DTPa-hepB-IPV-Hib), Infanrix<sup>®</sup> IPV (DTPa-IPV), Pediacel<sup>®</sup> (DTPa-IPV-Hib), Quadracel<sup>®</sup> (DTPa-IPV) and Tripacel<sup>®</sup> (DTPa).<sup>9</sup>

#### For adolescents and adults (≥10 years of age)

There are four reduced antigen content (dTpa) formulations registered in Australia, including two in combination with IPV: Boostrix<sup>®</sup> (dTpa), Boostrix<sup>®</sup>-IPV (dTpa-IPV), Adacel<sup>®</sup> (dTpa) and Adacel<sup>®</sup> Polio (dTpa-IPV).<sup>9</sup> These vaccines contain less diphtheria and pertussis antigen than paediatric vaccines.

### Vaccine efficacy

#### Paediatric formulation (DTPa)

A 3-dose primary series of immunisation with DTPa vaccine at 2, 4 and 6 months of age results in 84% protective efficacy against severe disease.<sup>10</sup> Observational studies have shown that even a single dose of DTPa has a vaccine effectiveness of 51–55% against hospitalised pertussis.<sup>5,11</sup> However, immunity following DTPa vaccine appears to wane over time. This has been demonstrated in younger children in Australia who had not received an 18 month booster dose, where the effectiveness of 3 doses of vaccine declined progressively from 2 years of age, to less than 50% by 4 years of age.<sup>5</sup> Studies in older children have shown a similar decline in vaccine effectiveness prior to receiving the adolescent booster dose.<sup>6,12</sup>

#### Adolescent or adult formulation (dTpa)

A large clinical trial in adolescents and adults demonstrated overall vaccine efficacy against confirmed pertussis of 92% within 2.5 years of vaccination.<sup>13</sup> 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. Antibody levels then continued to decline steadily, although mean antibody levels remained above baseline 10 years after vaccination.<sup>14</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. Vaccination of mothers in the United Kingdom at least 7 days before delivery reduced pertussis disease by 91% in infants <3 months of age.<sup>15</sup> In comparison, cocoon vaccination (vaccination of household contacts of the infant) against pertussis has been shown to reduce pertussis disease in young infants by approximately 50% when both parents were vaccinated at least 4 weeks before disease onset in the infant.<sup>16</sup>

The exact level of pertussis antibody required in the pregnant woman to achieve this protection is uncertain. However, antibody levels in maternal and umbilical cord blood of mother-and-newborn pairs have shown significant antibody waning over a 2-year interval between pregnancies;<sup>17</sup> hence vaccination is recommended during every pregnancy.

### Vaccine safety

#### DTPa-containing vaccines in children

The current acellular pertussis vaccines are safer than whole-cell pertussis vaccines (DTPw) previously used in Australia. Acellular pertussis vaccines are associated with a much lower incidence of fever (20% vs 45%) and local reactions (10% vs 40%) than DTPw vaccine.<sup>18</sup> Serious side effects are rare.

Extensive limb swelling reactions are a recognised adverse event that occurs rarely following booster doses of DTPa vaccine. Such reactions commence within 48 hours of vaccination, last for 1–7 days and resolve completely.<sup>19</sup> A history of extensive limb swelling after a booster dose of DTPa vaccine is not a contraindication to another booster dose of acellular pertussis-containing vaccine.<sup>20,21</sup> Parents of children about to receive a booster dose of a DTPa-containing vaccine (at 18 months or 4 years of age) 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.

Hypotonic–hyporesponsive episodes (HHE), defined as an episode of pallor, limpness and unresponsiveness, occur rarely following DTPa vaccine, 1 to 48 hours after vaccination. In 2012, 2.2 cases of HHE were reported per 100,000 doses of DTPa-containing vaccine given to children <1 year of age in Australia.<sup>22</sup> Follow-up of children with HHE shows no long-term neurological disorders and these children can receive further doses of DTPa-containing vaccines.<sup>23</sup>

Pertussis vaccines do not cause encephalopathy<sup>24</sup> or sudden infant death syndrome.<sup>25</sup>

**dTpa-containing vaccines in adolescents and adults**  
dTpa vaccines are safe and well tolerated in adults. The incidence of fever is low.<sup>26,27</sup> Booster doses of dTpa vaccine within 10 years are also safe and well tolerated, with no increase in moderate or severe adverse events or fever, and limb swelling reactions are rare.<sup>14,28,29</sup> In adults who report a history of adverse event(s) following DTPw vaccine given in childhood, dTpa vaccine can almost always be given.

#### **dTpa vaccines in pregnant women**

Studies show that there is no increased risk of adverse pregnancy outcomes (such as stillbirth, fetal distress or low birth weight) related to pertussis vaccination during pregnancy.<sup>30-32</sup>

There is a small risk that injection site reactions 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.

#### **Interval between dTpa and other tetanus/diphtheria-containing vaccines**

A single dose of dTpa vaccine can be administered 4 weeks after a dose of a vaccine containing tetanus and diphtheria toxoids. The benefits of protection against pertussis gained from using dTpa vaccine, where recommended, are likely to outweigh the risk of an adverse event.<sup>33</sup>

#### **Contraindications/precautions**

The only contraindications to DTPa and dTpa vaccines are anaphylaxis following a previous dose of an acellular pertussis vaccine-containing, or anaphylaxis following any vaccine component.

#### **Additional resources for primary medical care/vaccination providers**

- *The Australian Immunisation Handbook*, 10th edition – the most up-to-date clinical recommendations are contained in the online version of the *Handbook* [www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home](http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home)
- Immunise Australia website <http://www.immunise.health.gov.au/>
- National Immunisation Program schedule [www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/national-immunisation-program-schedule](http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/national-immunisation-program-schedule)

## **References**

1. Department of Health and Human Services, Centers for Disease Control and Prevention (CDC). Pertussis. In: Atkinson W, Wolfe C, Hamborsky J (editors). *Epidemiology and prevention of vaccine-preventable diseases*. 12th. Washington DC: Public Health Foundation; 2011. p. 215-31.
2. Quinn HE, McIntyre PB. Pertussis epidemiology in Australia over the decade 1995–2005 – trends by region and age group. *Communicable Diseases Intelligence* 2007;31:205-15.
3. Pillsbury A, Quinn HE, McIntyre PB. Australian vaccine preventable disease epidemiological review series: Pertussis, 2006–2012. *Communicable Diseases Intelligence* 2014;38:E179-94.
4. Kaczmarek MC, Valenti L, Kelly HA, et al. Sevenfold rise in likelihood of pertussis test requests in a stable set of Australian general practice encounters, 2000–2011. *Medical Journal of Australia* 2013;198:624-8.
5. Quinn HE, Snelling TL, Macartney KK, McIntyre PB. Duration of protection after first dose of acellular pertussis vaccine in infants. *Pediatrics* 2014;133:e513-9.
6. Misegades LK, Winter K, Harriman K, et al. Association of childhood pertussis with receipt of 5 doses of pertussis vaccine by time since last vaccine dose, California, 2010. *JAMA* 2012;308:2126-32.
7. Australian Government Department of Health and Ageing. National Notifiable Diseases Surveillance System. Available from: [http://www9.health.gov.au/cda/source/rpt\\_5\\_sel.cfm](http://www9.health.gov.au/cda/source/rpt_5_sel.cfm) (Accessed March 2015).
8. Wiley KE, Zuo Y, Macartney KK, McIntyre PB. Sources of pertussis infection in young infants: a review of key evidence informing targeting of the cocoon strategy. *Vaccine* 2013;31:618-25.
9. Australian Technical Advisory Group on Immunisation (ATAGI). *The Australian immunisation handbook*. 10th ed (2015 update). Canberra: Australian Government Department of Health; 2015. Available from: <http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home> (Accessed July 2015).
10. Zhang L, Prietsch SO, Axelsson I, Halperin SA. Acellular vaccines for preventing whooping cough in children. *Cochrane Database of Systematic Reviews* 2012;(3):CD001478. doi:10.1002/14651858.CD001478.pub5.
11. Hviid A, Stellfeld M, Andersen PH, Wohlfahrt J, Melbye M. Impact of routine vaccination with a pertussis toxoid vaccine in Denmark. *Vaccine* 2004;22:3530-4.

12. Sheridan SL, McCall BJ, Davis CA, et al. Acellular pertussis vaccine effectiveness for children during the 2009–2010 pertussis epidemic in Queensland. *Medical Journal of Australia* 2014;200:334-8.
13. Ward JI, Cherry JD, Chang SJ, et al. Efficacy of an acellular pertussis vaccine among adolescents and adults. *New England Journal of Medicine* 2005;353:1555-63.
14. Booy R, Van der Meeren O, Ng SP, et al. A decennial booster dose of reduced antigen content diphtheria, tetanus, acellular pertussis vaccine (Boostrix™) is immunogenic and well tolerated in adults. *Vaccine* 2010;29:45-50.
15. Amirthalingam G, Andrews N, Campbell H, et al. Effectiveness of maternal pertussis vaccination in England: an observational study. *The Lancet* 2014;384:1521-8.
16. Quinn HE, Snelling TL, Habig A, et al. Parental Tdap boosters and infant pertussis: a case-control study. *Pediatrics* 2014;134:713-20.
17. Healy CM, Rench MA, Baker CJ. Importance of timing of maternal combined tetanus, diphtheria, and acellular pertussis (Tdap) immunization and protection of young infants. *Clinical Infectious Diseases* 2013;56:539-44.
18. Decker MD, Edwards KM, Steinhoff MC, et al. Comparison of 13 acellular pertussis vaccines: adverse reactions. *Pediatrics* 1995;96:557-66.
19. Rennels MB. Extensive swelling reactions occurring after booster doses of diphtheria-tetanus-acellular pertussis vaccines. *Seminars in Pediatric Infectious Diseases* 2003;14:196-8.
20. Centers for Disease Control and Prevention (CDC). Use of diphtheria toxoid-tetanus toxoid-acellular pertussis vaccine as a five-dose series. Supplemental recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recommendations and Reports* 2000;49(RR-13):1-8.
21. Centers for Disease Control and Prevention (CDC), Broder KR, Cortese MM, et al. Preventing tetanus, diphtheria, and pertussis among adolescents: use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccines. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recommendations and Reports* 2006;55(RR-3):1-34.
22. Mahajan D, Dey A, Cook J, et al. Surveillance of adverse events following immunisation in Australia, 2012. *Communicable Diseases Intelligence* 2014;38:E232-46.
23. Goodwin H, Nash M, Gold M, Heath TC, Burgess MA. Vaccination of children following a previous hypotonic–hypo-responsive episode. *Journal of Paediatrics and Child Health* 1999;35:549-52.
24. Moore DL, Le Saux N, Scheifele D, Halperin SA, Members of the Canadian Paediatric Society/Health Canada Immunization Monitoring Program Active (IMPACT). Lack of evidence of encephalopathy related to pertussis vaccine: active surveillance by IMPACT, Canada, 1993–2002. *Pediatric Infectious Disease Journal* 2004;23:568-71.
25. Brotherton JM, Hull BP, Hayen A, Gidding HF, Burgess MA. Probability of coincident vaccination in the 24 or 48 hours preceding sudden infant death syndrome death in Australia. *Pediatrics* 2005;115:e643-6.
26. Pichichero ME, Rennels MB, Edwards KM, et al. Combined tetanus, diphtheria, and 5-component pertussis vaccine for use in adolescents and adults. [erratum appears in JAMA. 2005 Dec 28;294(24):3092]. *JAMA* 2005;293:3003-11.
27. Blatter M, Friedland LR, Weston WM, Li P, Howe B. Immunogenicity and safety of a tetanus toxoid, reduced diphtheria toxoid and three-component acellular pertussis vaccine in adults 19–64 years of age. *Vaccine* 2009;27:765-72.
28. Halperin SA, McNeil S, Langley J, et al. Tolerability and antibody response in adolescents and adults revaccinated with tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine adsorbed (Tdap) 4–5 years after a previous dose. *Vaccine* 2011;29:8459-65.
29. Mertsola J, Van Der Meeren O, He Q, et al. Decennial administration of a reduced antigen content diphtheria and tetanus toxoids and acellular pertussis vaccine in young adults. *Clinical Infectious Diseases* 2010;51:656-62.
30. Munoz FM, Bond NH, Maccato M, et al. Safety and immunogenicity of tetanus diphtheria and acellular pertussis (Tdap) immunization during pregnancy in mothers and infants: a randomized clinical trial. *JAMA* 2014;311:1760-9.
31. Donegan K, King B, Bryan P. Safety of pertussis vaccination in pregnant women in UK: observational study. *BMJ* 2014;349:g4219.
32. Kharbanda EO, Vazquez-Benitez G, Lipkind HS, et al. Evaluation of the association of maternal pertussis vaccination with obstetric events and birth outcomes. *JAMA* 2014;312:1897-904.
33. Centers for Disease Control and Prevention (CDC). Updated recommendations for use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) vaccine from the Advisory Committee on Immunization Practices, 2010. *MMWR Morbidity and Mortality Weekly Report* 2011;60:13-5.