24 Pertussis

24.1 Introduction

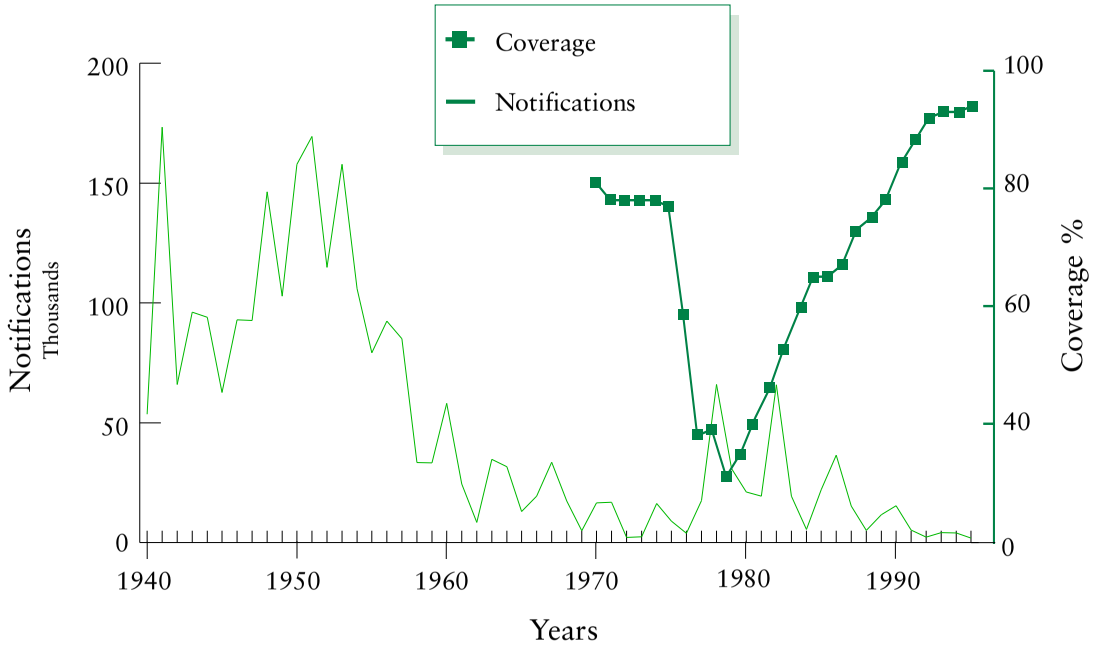
24.1.1 Pertussis is a highly infectious bacterial disease caused by *Bordetella pertussis* and spread by droplet infection; the incubation period is seven to ten days. A case is infectious from seven days after exposure to three weeks after the onset of typical paroxysms. The initial catarrhal stage has an insidious onset and is the most infectious period. An irritating cough gradually becomes paroxysmal, usually within one to two weeks, and often lasts for two to three months. In young infants, the typical 'whoop' may never develop and coughing spasms may be followed by periods of apnoea. Pertussis may be complicated by bronchopneumonia, repeated post-tussive vomiting leading to weight loss, and by cerebral hypoxia with a resulting risk of brain damage. Severe complications and deaths occur most commonly in infants under six months of age.

24.1.2 Before the introduction of pertussis immunisation in the 1950s, the average annual number of notifications in England and Wales (E and W) exceeded 100,000. In 1972, when vaccine acceptance was over 80%, there were only 2069 notifications of pertussis.

24.1.3 Because of public anxiety about the safety and efficacy of the vaccine, acceptance rates fell to about 30% in 1975 and major epidemics with over 100,000 notified cases followed (in E and W) in 1977/79 and 1981/83. However increased vaccine uptake, resulting from the return of professional and public confidence, cut short the next epidemic which died away in 1986, well below the levels of the previous two. In 1992, when uptake had risen to 92%, there were only 2309 notifications, the lowest annual total since 1972. In keeping with the cyclical pattern of pertussis epidemics, notifications rose in 1993, but only reached 4091. By 1995, coverage by the second birthday was 94%; there were 1873 notifications. This is the lowest annual figure ever recorded.

Pertussis notifications to ONS and vaccine coverage figures for children by their 2nd birthday

England and Wales (1940-1995)



■ 24.1.4 Until the mid 1970s, mortality from pertussis was about one per 1000 notified cases with a higher rate for infants under one year. In 1978 however when there were over 65,000 notifications (in E and W), only 12 deaths were notified. The actual number of deaths due to pertussis is undoubtedly higher since not all cases in infants are recognised. In 1990, there were six deaths from pertussis, all in infants under four months of age. The timing of routine pertussis immunisation was accelerated in 1990; from 1991 to 1995 only five deaths attributed to pertussis were reported (in England and Wales), all in infants too young to be immunised.

■ 24.1.5 Since the anxieties in the mid 1970s concerning pertussis vaccine, studies have confirmed that a full course of vaccine confers protection in over 80% of recipients; in those not fully protected the disease is usually less severe. The two large epidemics which followed the reduction in vaccine acceptance are additional evidence of the effectiveness of pertussis vaccine in the prevention of disease. In Regions with particularly low vaccine coverage, pertussis notifications in 1986 were significantly higher than those in Regions with high coverage.

■ 24.2 Vaccine

■ 24.2.1 Pertussis vaccine is a suspension of killed *Bordetella pertussis* organisms with an estimated potency of not less than four International Units in each 0.5ml of vaccine. The vaccine is usually given as a triple vaccine combined with diphtheria and tetanus vaccines (DTP), with an adjuvant such as aluminium hydroxide. The plain vaccine is no longer supplied as it is less immunogenic and causes more systemic reactions, especially fever.

■ 24.2.2 Adsorbed diphtheria/tetanus/pertussis vaccine (DTP): one 0.5ml dose consists of a mixture in isotonic buffer solution of diphtheria toxoid and tetanus toxoid adsorbed on to aluminium hydroxide gel, together with not more than 20,000 million Bordetella pertussis organisms. The potency of the diphtheria component is not less than 30 iu; that of the tetanus component not less than 60 iu and that of the pertussis component not less than an estimated 4 iu. Thiomersal is added as a preservative to a final concentration of 0.01%.

■ 24.2.3 At present, there is no supplier of monovalent **whole cell** pertussis vaccine. As an alternative, an **acellular** monovalent preparation (Acellular Pertussis Vaccine (APV)) is available for use on a 'named patient' basis. This vaccine contains approximately 3 µg of highly purified pertussis toxin (PT), 36 µg of filamentous haemagglutinin (FHA) and small quantities of Pertactin (or 69 kilodalton outer membrane protein) and type 2 fimbriae. The vaccine is adsorbed onto alum hydroxide and phosphate gel and contains thiomersal preservative.

■ 24.2.4 The vaccines should be stored between 2-8°C, but not frozen. If the vaccine is frozen, it should not be used. Vaccine that has been frozen can be identified by the following test: using an ampoule of DTP vaccine that has not been frozen as a control, shake both ampoules, inspect the contents, leave the ampoules to stand for 15 - 30 minutes and inspect again. Frozen vaccine remains cloudy with clumps of flocculated material.

■ 24.2.5 Protect the vaccine from light. Disposal should be by incineration at a temperature not less than 1100°C at a registered waste disposal contractor.

■ 24.3 Route of administration and dosage

The dose of DTP and APV is 0.5ml, given by deep subcutaneous or intramuscular injection.

■ 24.4 Recommendations

■ 24.4.1 Adsorbed pertussis vaccine as a component of the primary course of immunisation against diphtheria, tetanus and pertussis (DTP) is recommended for all infants from two months of age, unless there is a genuine contraindication (see Chapter 7).

■ 24.4.2 The primary course consists of **three doses with an interval of one month between each dose** (see Chapter 11). If the primary course is interrupted it should be resumed but not repeated, allowing appropriate intervals between the remaining doses.

■ 24.4.3 Monovalent acellular pertussis vaccine can be given when the pertussis component has been omitted from earlier immunisations. Children who have received a full course of immunisation against diphtheria and tetanus should be given three doses of monovalent

pertussis vaccine at monthly intervals. APV has been made available solely for this purpose and should not be used in place of the existing DTP for routine primary immunisation.

■ 24.4.4 Where the primary course of diphtheria/tetanus immunisation has been started and the parent wishes pertussis vaccine to be added, DTP vaccine may be used for the subsequent doses, followed by acellular pertussis vaccine at monthly intervals to complete the three doses. Similarly, children presenting for their pre-school diphtheria/tetanus booster who have not previously been immunised against pertussis should be given triple vaccine as the first dose, with two subsequent doses of acellular pertussis vaccine at monthly intervals.

■ 24.4.5 Research from the UK and other countries shows that local reactions and pyrexias occur less often after acellular pertussis vaccine than after whole cell vaccine, especially when the immunisation is given **after** 6 months of age. When the primary immunisation against pertussis was not completed because of a local reaction or pyrexia, it can be completed with acellular pertussis vaccine.

■ 24.4.6 The low uptake of pertussis vaccine from 1975-1985 left a considerable number of unimmunised older children who received DT vaccine only. Such children can be immunised with monovalent acellular pertussis vaccine, both for their own protection and for that of young siblings under the age of immunisation; **there is no upper age limit**.

■ 24.4.7 No reinforcing dose of pertussis vaccine is currently recommended after a course of three injections.

■ 24.4.8 **Children with problem histories:**
When there is a personal or family history of **febrile** convulsions, there is an increased risk of these occurring after pertussis immunisation. In such children, **immunisation is recommended** but advice on the prevention of fever should be given at the time of immunisation.

In a recent British study, children with a family or personal history of **epilepsy** were immunised with pertussis vaccine without any significant adverse events. These childrens' developmental progress has been normal. In children with **a close family history** (first degree relatives) **of idiopathic epilepsy**, there may be a risk of developing a similar condition, irrespective of vaccine. **Immunisation is recommended for these children and for those with a personal history of epilepsy** (see below). Advice on the prevention of pyrexia should be given.

Where there is a still evolving neurological problem, immunisation should be deferred until the condition is stable. **Children whose epilepsy is well controlled may receive pertussis vaccine**. When there has been a documented history of cerebral damage in the neonatal period, immunisation should be carried out unless there is evidence of an evolving neurological abnormality. If immunisation is to be deferred, then this should be stated on the neonatal discharge summary. **Where there is doubt, appropriate advice should be sought from a Consultant Paediatrician, District (Health Board) Immunisation Co-ordinator or Consultant in Communicable Disease Control rather than withholding vaccine.**

■ 24.4.9 HIV positive individuals may receive pertussis vaccine in the absence of contraindications.

■ 24.4.10 If pertussis vaccine is contraindicated, then DT should be offered. There may be an opportunity at a later date to complete pertussis immunisation using APV.

■ 24.5 Adverse reactions

■ 24.5.1 a. Swelling and redness at the injection site are common. A small painless nodule may form at the injection site; this usually disappears and is of no consequence. The incidence of local reactions and pyrexias has been shown to be lower following the accelerated schedule than the previous extended schedule.

b. Crying, screaming and fever may occur after pertussis vaccine in triple vaccine; they may also occur after vaccine which does not contain the pertussis component. Attacks of high pitched screaming, episodes of pallor, cyanosis, limpness, convulsions, as well as local reactions have been reported after both adsorbed DTP and DT vaccines. Both local and systemic reactions were more common after the plain preparations which did not contain adjuvant.

c. More severe neurological conditions, including encephalopathy and prolonged convulsions, resulting in permanent brain damage and death, have been reported after pertussis vaccine. But similar illnesses can develop from a variety of causes in the first year of life in both immunised and unimmunised children and there is no specific test which can identify cases which may be caused by pertussis vaccine. Therefore, no wholly reliable estimate of the risk of such complications due to the vaccine can be made.

d. For these reasons, there has been considerable public and professional anxiety about the safety of pertussis vaccine. In Great Britain, between 1976 and 1979, a total of 1182 children with serious acute neurological illnesses were reported to the National Childhood Encephalopathy Study (NCES). Only 39 of these children had recently had pertussis vaccine and in many of these, the association of the neurological illnesses with immunisation could have occurred by chance.

e. Analysis of the results of the NCES showed that, after taking this into account, the vaccine may very rarely be associated with the development of severe acute neurological illness in children who were previously apparently normal; most of these children suffered no apparent harm. The occurrence of a severe encephalopathy after pertussis immunisation was sometimes associated with long-term residual neurological damage, but the evidence is insufficient to indicate whether or not DTP increases the overall risk of chronic neurological dysfunction. **The number of cases in the NCES, even after three years of intensive case finding, was too small to show conclusively whether or not the vaccine could cause permanent brain damage if such damage occurs at all.**

f. These conclusions have been confirmed by a recent large case control study from the United States that found no significant increased risk of serious acute neurological illness in the seven days after DTP vaccine in children under 2 years of age.

g. In the USA, a group of children who had had convulsions or hypotonic-hyporesponsive episodes within 48 hours of DTP were reviewed six to seven years later; there was no evidence of serious neurological damage or intellectual impairment as a result of these episodes. In another American study, while an association was demonstrated between the first febrile convulsion and the scheduled age of pertussis immunisation, no relationship was demonstrated between immunisation and the age of onset of epilepsy.

h. A major review of studies on adverse events after pertussis vaccine was published by the United States Institute of Medicine in 1991. This concluded that the evidence did not indicate a causal relationship between pertussis vaccine and infantile spasms, hypsarrhythmia, Reye's syndrome and Sudden Infant Death syndrome.

i. Neurological complications after pertussis disease are considerably more common than after vaccine.

j. Cot deaths (Sudden Infant Death Syndrome) occur most commonly during the first year of life and may therefore coincide with the giving of DTP vaccine. However studies have established that this association is temporal rather than causal. The incidence of SIDS appears to be lower in children who have had pertussis vaccine than in those who have not.

■ 24.5.2 Recently available data from linkage of hospital admission records with immunisation details shows that **there is no increase in the likelihood of a febrile convulsion requiring admission to hospital in the week following pertussis containing vaccine, compared with the background risk, if children are immunised before 6 months of age.** Immunisation with pertussis containing vaccine **after** 6 months of age is associated with an increased risk of febrile convulsion, particularly with the third dose. If a febrile convulsion occurs after a dose of triple vaccine, specialist advice should be sought before continuing with any immunisation. Children having such convulsions are at increased risk of further febrile convulsions following subsequent immunisations. However, these risks can be minimised by appropriate measures to prevent fever (eg paracetamol and tepid sponging) and i**mmunisation is recommended.**

■ 24.5.3 It has been suggested that pertussis vaccine is linked with the development of asthma. A recent double-blind study of pertussis vaccines found no significant differences between DTP immunised children and controls for reported wheezing, itchy rash or sneezing. The results suggest that there is no reason to withhold pertussis immunisation because of fear of subsequent asthma or allergy.

■ 24.5.4 When pertussis vaccine is genuinely contraindicated, immunisation against diphtheria and tetanus should still be considered.

■ 24.5.5 Severe or unusual reactions to pertussis vaccine must be reported to the Committee on Safety of Medicines using the yellow card system.

■ 24.6 Contraindications to pertussis immunisation

■ 24.6.1 a. If the child is suffering from any acute illness, immunisation should be postponed until the child has recovered. Minor infections without fever or systemic upset are not reasons to postpone immunisation.

b. Immunisation should not be carried out in children who have a history of a general reaction to a preceding dose. In these children, immunisation should be completed with DT vaccine. Where there has been a local reaction or a pyrexia, acellular pertussis vaccine may be used (see 24.4.5). The following reactions should be regarded as severe:

Local: an extensive area of redness and swelling which becomes indurated and involves most of the antero-lateral surface of the thigh or a major part of the circumference of the upper arm.

General: fever equal to or more than 39.5°F within 48 hours of vaccine; anaphylaxis; bronchospasm; laryngeal oedema; generalised collapse. Prolonged unresponsiveness; prolonged inconsolable or high-pitched screaming for more than 4 hours; convulsions or encephalopathy occurring within 72 hours.

■ 24.6.2 A personal or family history of allergy is **not** a contraindication to immunisation against pertussis, nor are stable neurological conditions such as cerebral palsy or spina bifida. For other 'false contraindications' see 7.6 and 7.7.

Where there is doubt, appropriate advice should be sought from a consultant paediatrician, District (Health Board) Immunisation Co-ordinator or Consultant in Communicable Disease Control, rather than withholding vaccine.

■ 24.7 Management of outbreaks

Since a course of three injections is required to protect against pertussis, vaccine cannot be used to control an outbreak.

24.8 Supplies

DTP vaccines are manufactured by Evans Medical Ltd. (Tel. 0345 451500 or 01372 364000) and
Pasteur Merieux MSD Ltd (Tel. 01628 773200)
Acellular pertussis vaccine is manufactured by Wyeth Lederle Vaccines. (Tel. 01628 414794)
These vaccines are supplied by Farillon (Tel. 01708 379000) as part of the National Childhood Immunisation Programme.

For supplies of single antigen acellular pertussis vaccine in Northern Ireland, contact:
Regional Pharmacist,
Procurement Co-ordinator
Eastern Health and Social Services Board
12-21 Linenhall Street
Belfast
BT2 8BS
Tel. 01232 321313

In Scotland, supplies through Scottish Health Care Services Division of the Common Services Agency (0131-552 6255).

24.9 Bibliography

Infants and children with convulsions and hypotonic/hyporesponsive episodes following DTP immunisation; follow-up evaluation.
Barraff L J, Shields W D et al.
Pediatrics 1988; 81; 789-794.

Relationship of pertussis immunisation to the onset of neurological disorders: a retrospective epidemiological study.
Shields W D, Nielson C et al.
J. Pediatrics 1988: 81; 801-805.

Vaccination and cot deaths in perspective.
Roberts S C.
Arch. Dis. Child. 1987: 12; 754-9.

DHSS Whooping Cough: Reports from the Committee on Safety of Medicines and the Joint Committee on Vaccination and Immunisation. HMSO 1981.

Severity of notified whooping cough.
Miller C L and Fletcher W B.
BMJ 1976, (1), 117-119.

Pertussis immunisation and serious acute neurological illness in children.
Miller D L, Ross E M, Alderslade R, Bellman M H, Rawson N S B.
BMJ 1981: 282; 1595-1599.

Symptoms after primary immunisation with DTP and with DT vaccine.
Pollock T M, Miller E, Mortimer J Y, Smith G.
Lancet 1984: ii; 146-159.

Efficacy of pertussis vaccination in England.
PHLS Epidemiological Research Laboratory and 21 Area Health Authorities.
BMJ 1982: 285; 357-359.

Communicable Disease Report Oct-Dec 1986.
Community Medicine 1987: 9; 176-181

Immunogenicity of combined diphtheria, tetanus and pertussis vaccine given at 2, 3 and 4 months versus 3, 5 and 9 months of age.
Lancet 1991, i, 507-510
Booy R, Aitken SJM, Taylor S, Tudor-Williams G et al.

Risk of serious acute neurological illness after immunisation with diphtheria/tetanus/pertussis vaccine:
JAMA 1994, 271: 37
Gale JL, Thapa PB, Wassilak SGF et al.

Adverse Effects of Pertussis and Rubella Vaccines
National Academy Press, Washington DC, 1991.
Institute of Medicine.

Pertussis immunisation in children with a family or personal history of convulsions: a review of children referred for specialist advice.
Health Trends 1994, 26: 23-4.
Ramsay M, Begg N, Holland B and Dalphinis J.

Sudden Infant Death Syndrome and Diphtheria-Tetanus-Pertussis-Poliomyelitis vaccination status.
Jonville-Bera AP, Autret E, Laugier J.
Fundam. Clin. Pharmacol. 1995; 9: 263-70.

A new method for active surveillance of adverse events from diphtheria/tetanus/pertussis and measles/mumps/rubella vaccines.
Farrington P et al.
Lancet 1995; **345**: 567-69.

Pertussis vaccination and asthma: is there a link?
Odent MR, Culpin EE, Kimmel T.
JAMA, 1994; **272**: 592-293.

Lack of Assosiation between Pertussis Vaccination and Symptoms of Asthma and Allergy
Nillson L et al.
JAMA, 1996; **275**: 760.