15 Pertussis

Vaccine introduced in 1952/53 (DTP) and 1996 (DTaP)

NOTIFIABLE

In some circumstances, advice in these guidelines may differ from that in the product Summary of Product Characteristics (SmPC). When this occurs, NIAC advises that the recommendations in these guidelines, which are based on current expert advice from NIAC, are followed.

Introduction

Pertussis (whooping cough) is a highly infectious bacterial disease caused by *Bordetella pertussis*, a fastidious Gram negative coccobacillus with exclusive affinity for the mucosal layers of the human respiratory tract. The organism survives only a few hours in respiratory secretions and requires special media for culture.

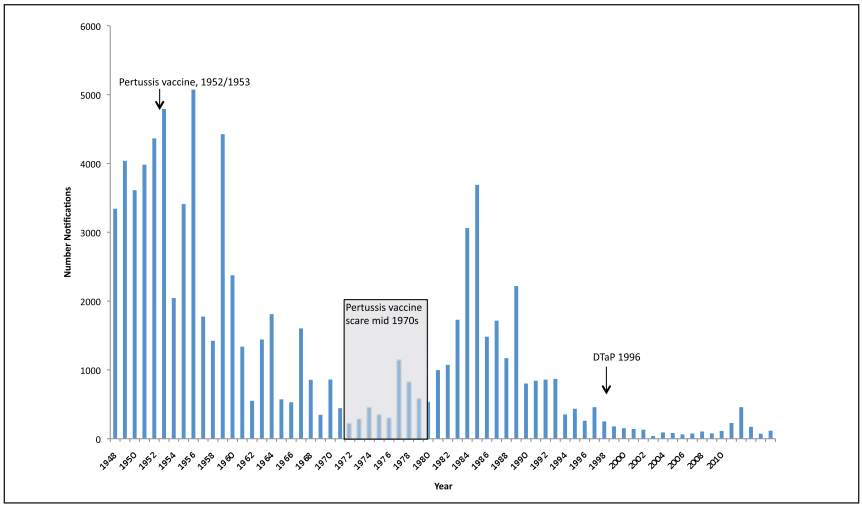
The illness is more severe and mortality rates are highest in infants. Following both infection and vaccination immunity wanes, so that after 10 years, over 50% are susceptible to reinfection. Subsequent disease tends to be subclinical or mild and may not be diagnosed, but is infectious. Up to 16 secondary infections can result from each index case in a fully susceptible population.

Epidemiology

Pertussis occurs endemically with periodic outbreaks. Worldwide, over 45 million cases occur annually, with more than 250,000 deaths. In low resource countries, the case-fatality rate among infants may be as high as 4%. Reported cases of pertussis represent only a fraction of the actual number of symptomatic infections, because under-consultation, under-diagnosis and under-reporting are widespread, particularly in adolescents and adults. Thirty per cent of adults with a cough lasting longer than 2 weeks may have pertussis.

Prior to the introduction of immunisation, epidemics occurred every 4-5 years, most cases occurring in young children. Currently, the highest incidence, morbidity and mortality occur in infants, particularly in those aged <2 months. The source of infection for approximately 80% of infants is a household contact, either a parent or sibling. In recent years there has been an increase in cases among adolescents and adults. This change in the epidemiology of pertussis is due to the waning immunity that occurs after both disease and vaccination, and to a reduction in natural boosting. There may also be a change in the characteristics of the organism, although no vaccine-resistant mutants have been identified.

Figure 15.1 Number of pertussis notifications in Ireland, 1948- 2015
Source: HPSC



The large increase in notifications of pertussis that occurred in the 1980s (see Figure 15.1) followed a scare in the late 1970s regarding a possible association of the vaccine with encephalopathy, which led to low-vaccine uptake. Although vaccine uptake has increased since 2001 the number of notifications increased in 2012 (see Figures 15.2 and 15.3). In 2012 the age group most affected was <12 months of age (infants), particularly those aged <6 months with 143 notifications.

Many of the infants are infected before they have had an opportunity to start their immunisation schedule. It is for this group that maternal vaccination during pregnancy is particularly important, as it is only through maternal-foetal antibody transfer that they can obtain some protection against pertussis infection.

Figure 15.2 Number of pertussis notifications and vaccine uptake in Ireland 1999 - 2015
Source: HPSC

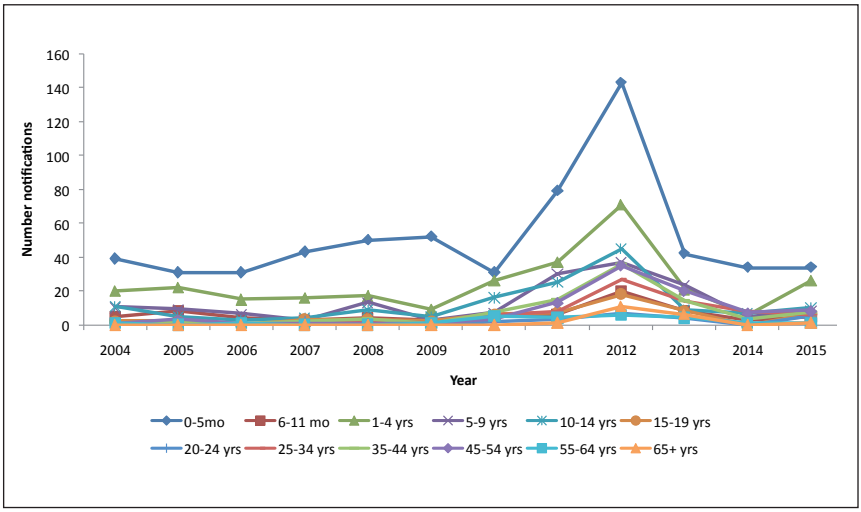
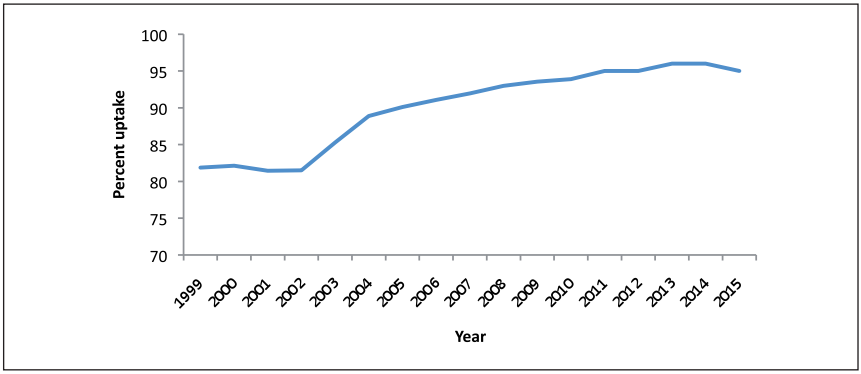


Figure 15.3 National uptake of three doses of pertussis vaccine at 24 months of age 1999-2015
Source: HPSC



Humans are the only known hosts of *B. pertussis*. The incubation period is 7-10 days (range 4-21). Transmission occurs by close contact via droplet infection from the respiratory tract of infected individuals. The basic reproduction rate (Ro) is 12-17, so up to 90% of non-immune contacts may acquire the infection.

Communicability is greatest in the catarrhal stage before the onset of paroxysms of coughing, and may last for up to 3 weeks. Chemoprophylaxis with antibiotics decreases infectivity and reduces duration of cough only

if given to close contacts in the incubation period. They may limit secondary spread if given early in the course of the infection in those aged over 6 months. They have no effect on the course of the illness if given after the cough is established.

Effects of pertussis

Pertussis is primarily a toxin-mediated disease. The bacteria attach to the respiratory cilia and produce toxins which paralyse the cilia. This, and inflammation, interferes with the clearing of secretions. Many factors determine disease severity, including the age of the patient and the length of time since vaccination or previous infection.

Classical pertussis symptoms occur mainly in children. The symptoms are less marked in those who had infection or vaccination within the previous 10 years. The initial catarrhal stage has an insidious onset and is the most infectious period. Cough is absent or mild in the early stages, the main symptom being rhinorrhoea. The cough gradually becomes paroxysmal (>90%), with a characteristic inspiratory whoop (80%) and/or vomiting (>50%). This paroxysmal stage usually occurs within 1-2 weeks, and often lasts for 2- 3 months.

Complications include pneumonia, seizures, encephalopathy, otitis media, dehydration, bladder incontinence, weight-loss, rib fractures, rectal prolapse and loss of consciousness. The case fatality rate ranges from 0.04-4%.

Pertussis in infants

In infants the typical whoop may not develop (30%) and coughing spasms may be followed by periods of apnoea and cyanosis. On occasions, apnoea may occur in the absence of cough. Complications and hospitalisation are significantly more frequent in infants particularly in those <6 months of age.

Of those hospitalised:

- 50% have apnoea
- 20% have pneumonia
- 3% have seizures
- 1-4% may die
- 0.3% develop encephalopathy (as a result of hypoxia from paroxysmal coughing or apnoeic episodes, or possibly due to a direct effect of toxin).

Among infants who die, refractory pulmonary hypertension is a common complication of infection, and encephalopathy will have occurred in approximately 20%. The highest mortality rate is in preterm infants.

Pertussis in adults and adolescents

Up to 30% of adults and adolescents with a cough lasting longer than 2 weeks may have pertussis. The cough is paroxysmal in >80%, but a whoop and post-tussive vomiting are absent in 50-70%. The cough lasts for at least 3 weeks in over 80%, and for up to 3 months in over 25% of cases. Diagnosis on clinical grounds can be difficult and cultures may be negative in previously vaccinated persons.

Diagnosis

Laboratory confirmation is obtained by isolating *B. pertussis* by culture of nasopharyngeal aspirates or per-nasal swabs. There are a variety of media available for the culture of *Bordetella species*. Culture can lack sensitivity as the organism is fastidious, and can be affected by processing delays. The sensitivity of nasopharyngeal culture decreases with time after onset and is highly dependent on specimen quality. The culture for *Bordetella pertussis* is most likely to be successful during the first three weeks of illness. Children, particularly the younger age groups may yield positive cultures for up to 5 to 6 weeks.

Serology may confirm the diagnosis in patients who have been symptomatic for some weeks at which stage culture is likely to be negative. Serology is used for diagnosis of pertussis predominantly in older children and adults. Serological diagnosis amongst infants has limitations e.g. infants less than three months may not develop measurable antibodies. In addition, antibody detection is not a suitable test for patients who have been vaccinated in the previous twelve months and caution is required with interpretation of results for those vaccinated within the previous 24 months. Serology is not recommended for confirmation of immune status.

PCR is a more robust tool than culture for diagnosis in the later stages of illness or when antibiotics have been administered. PCR is also valuable in diagnosing pertussis in young infants in whom serology is not useful and the yield from culture may be low. This is a more sensitive test than culture as the organism does not need to be viable.

Treatment and Chemoprophylaxis

Treatment for pertussis may lessen symptoms if started during the first 1 to 2 weeks before coughing paroxysms occur. If treatment is begun within 3 weeks of onset of symptoms it may limit transmission. If the clinical history is strongly suggestive or the patient is at risk for severe or complicated disease (e.g. infants), treating prior to test results should be strongly considered. Cases should be excluded from child care, school, healthcare and social care

facilities until they have completed 5 days of antibiotic treatment, or for 21 days after the onset of symptoms.

The primary objective of postexposure chemoprophylaxis is to prevent death and serious complications in those at increased risk of severe disease. Postexposure antibiotic use is recommended for those at high risk of developing severe pertussis and for those who will have close contact with persons at high risk. Chemoprophylaxis is recommended for all close contacts when both of the following conditions apply:

- Onset of disease in the index case is within the preceding 21 days **AND**
- There is close contact with a vulnerable person.

Close contacts are defined as those who live in the same house or stayed overnight in the same room as the index case, and adults who work in a healthcare, social care or childcare facility and have contact with vulnerable individuals

Vulnerable close contacts are those who are at increased risk of complications from pertussis and include the following:

- Newborn infants born to mothers with suspected or confirmed pertussis, who are still infectious at delivery (i.e. within twenty one days of onset or <5 days treatment)
- Infants under one year who have received less than three doses of a pertussis containing vaccine
- Children under ten years of age who are not age-appropriately vaccinated
- Pregnant women in in the third trimester (to protect their infant)
- Immunocompromised individuals
- Persons with a chronic illness e.g. pulmonary disease which may predispose them to more severe pertussis infection

For more details see Guidelines for the Public Health Management of Pertussis available at http://www.hpsc.ie/hpsc/A-Z/VaccinePreventable/PertussisWhoopingCough/InformationforHealthcareWorkers/File,13577,en.pdf

Pertussis vaccines

A full course of vaccine confers protection in 75-90% of recipients. Immunity wanes with age, and is usually inadequate 8 -10 years after primary and booster vaccination. High vaccine uptake rates, including booster doses, are therefore very important in order to reduce the incidence of pertussis.

Full dose pertussis vaccines (aP) are recommended for children up to 10 years of age.

Low dose pertussis vaccines (ap) are recommended for children aged 10 years and older.

Acellular pertussis (aP) vaccines contain 1 to 5 pertussis antigens and cause significantly less local and systemic reactions than the previously used whole-cell pertussis (wP) vaccines. Antigen types and amounts differ between vaccines and include pertussis toxin, filamentous haemagglutinin and pertactin. For the primary series, vaccines with 3 or more antigens produce a better immune response. Switching within aP vaccine groups is unlikely significantly to alter the safety profile or immunogenicity.

An up-to-date list of licensed vaccines can be accessed on the HPRA website www.hpra.ie

A list of the vaccines currently available from the National Cold Chain Service can be found at www.immunisation.ie

Pertussis vaccines should be stored between +2 to +8°C. If a vaccine has been frozen, it should not be used.

Dose and route of administration
The dose is 0.5 ml, given by intramuscular injection into the anterolateral thigh or deltoid.

Indications

1. ***Primary vaccination***
   The primary course consists of 3 doses given at 2, 4 and 6 months as 6 in 1 vaccine (DTaP/IPV/Hib/Hep B).

   When 6 in 1 vaccine is given concurrently with PCV, it should be given first as it is less painful.

   If the primary course is interrupted it should be resumed but not repeated, allowing appropriate intervals between the remaining doses (see catch-up schedule in Chapter 2).

   If pertussis vaccine is refused by parents for their children, the only available pertussis-free diphtheria and tetanus vaccines are Td and Td/IPV which contain low dose diphtheria toxoid which is insufficient for primary immunisation in children under 10 years of age. Low-dose pertussis vaccines are not intended for use as part of the primary vaccine schedule and may not give a sufficient immune response if so used.

2. ***Booster vaccination***

Routine

A first booster dose is recommended at 4-5 years of age as 4 in 1 vaccine (DTaP/IPV). In the event of a temporary shortage of this vaccine, Tdap/IPV may be used.

Children who have received four pertussis containing vaccines before their fourth birthday should receive a further further DTaP/IPV or Tdap/IPV booster after their 4th birthday at least 6 months after the 4th dose.

A booster is recommended at 11-14 years as part of a Tdap vaccine which contains low dose acellular pertussis vaccine. No interval is required between this booster and any previous tetanus or diphtheria toxoid containing vaccine.

Health Care Workers

A booster dose of Tdap is recommended for Health Care Workers who are in contact with infants, pregnant women and the immunocompromised. Boosters every 10 years may be considered.

Pregnant Women

Maternal antibodies from women immunised before pregnancy wane quickly and the concentration of pertussis antibodies is unlikely to be high enough to provide passive protection to their infants prior to primary vaccination.

Pregnant women should be offered Tdap as early as possible after 16 weeks and up to 36 weeks gestation in each pregnancy, to protect themselves and their infant.

Tdap can be given at any time in pregnancy after 36 weeks gestation although it may be less effective in providing passive protection to the infant.

Post partum women

Tdap should be offered in the week after delivery to those women who were not vaccinated during their pregnancy.

Adults

Tdap may be considered for adult contacts who have not had a pertussis vaccine in the previous 10 years to decrease the risk of infection to themselves and infants.

3. ***Vaccination of cases***

Unvaccinated or partially vaccinated cases should complete the age appropriate vaccination schedule during convalescence as infection may not confer long term immunity. This includes pregnant women.

4. ***Vaccination of contacts***
   Unvaccinated or partially vaccinated contacts should complete the age appropriate vaccination schedule. Adult contacts, including HCWs, who have not had a pertussis containing vaccine within the previous 10 years should be given Tdap.

5. ***Cocooning***
   Preventing pertussis in infants by immunising their close contacts- parents, siblings, grandparents, child care providers, and health care workers is advised for infants born before 32 weeks gestation as they may not have received protection via maternal antibody transfer.

   Tdap should be offered to all unvaccinated close adult contacts who have not had a pertussis vaccine in the previous 10 years. Ideally, the vaccine should be given at least 2 weeks before beginning close contact with the infant.

   Cocooning of incompletely vaccinated infants should be considered in the event of community outbreaks.

   Children under 10 years should receive full dose pertussis vaccine as DTaP/IPV/Hib/Hep B or DTaP/IPV (or Tdap/IPV in the event of a temporary shortage).

   All aged 10 years and over should receive low dose pertussis vaccine as Tdap or Tdap/IPV depending on other vaccine requirements.

If pertussis vaccine is indicated

for those aged <10 years
There should be an interval of at least 6 months between booster doses of DTaP and the completion of a primary course of DTaP containing vaccines. DTaP containing vaccines can be given at any interval following (an inappropriately administered) Td.

for those aged 10 years and older
Tdap or Tdap/IPV can be given at any interval following a Td containing vaccine.

Contraindications
Anaphylaxis to any of the vaccine constituents.

Precautions
1. Acute severe febrile illness; defer until recovery.
2. Type III (Arthus) hypersensitivity reaction to a previous dose (see Adverse reactions). Persons experiencing these reactions usually have very high serum diphtheria or tetanus antitoxin levels; they should not be given further routine or emergency booster doses of tetanus or diphtheria containing vaccines more frequently than every 10 years.

The following are no longer considered either contraindications or precautions. They have not been shown to cause permanent harm and are significantly less common after acellular than after whole cell pertussis vaccines.

1. Temperature of more than 40.5^{0}C within 48 hours of a previous dose of a pertussis containing vaccine.
2. Hypotonic-hyporesponsive episode within 48 hours of a previous dose of a pertussis containing vaccine.
3. Seizures within 72 hours of a previous dose of a pertussis containing vaccine.
4. Persistent, inconsolable crying lasting more than 3 hours within 48 hours of a previous dose of a pertussis containing vaccine.
5. Active or progressive neurological disease.

Adverse reactions
Local: Pain, palpable lump, swelling and erythema at the injection site occur in up to 20% of recipients. They are more frequent with subsequent doses. Most of these reactions resolve with no treatment. A cold pack or ice wrapped in a cloth applied to the site for 20 minutes per hour as necessary may be required. On occasions paracetamol or ibuprofen may be needed. Antibiotics are very rarely indicated.

Very rarely a Type III hypersensitivity (Arthus) reaction occurs, involving swelling and erythema of most of the diameter of the limb from the shoulder to the elbow or the hip to the knee. This usually begins 2-8 hours after vaccination and is more common in adults. It resolves without sequelae.

General: Malaise, transient fever and headache are uncommon. Temperature >40°C is rare. Dyspnoea, urticaria, angioedema, and neurological reactions are very rare and are not a contraindication to further vaccination.

Anaphylaxis is extremely rare (0.6-3 per million doses).

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