

# 12

## Pneumococcal Infection

NOTIFIABLE

### Introduction

*Streptococcus pneumoniae* (*pneumococcus*) is an important cause of serious infection, especially in young children, older adults and immunocompromised individuals. Invasive pneumococcal disease (IPD) is defined as the isolation of *S. pneumoniae* from a normally sterile site (e.g. blood, cerebrospinal fluid, or less commonly, joint, pleural, or pericardial fluid). Non-invasive manifestations of the disease include otitis media, sinusitis and bronchitis. IPD is a disease mainly of young children and older adults. Individuals with severe chronic conditions or immunodeficiencies are also at increased risk of this disease.

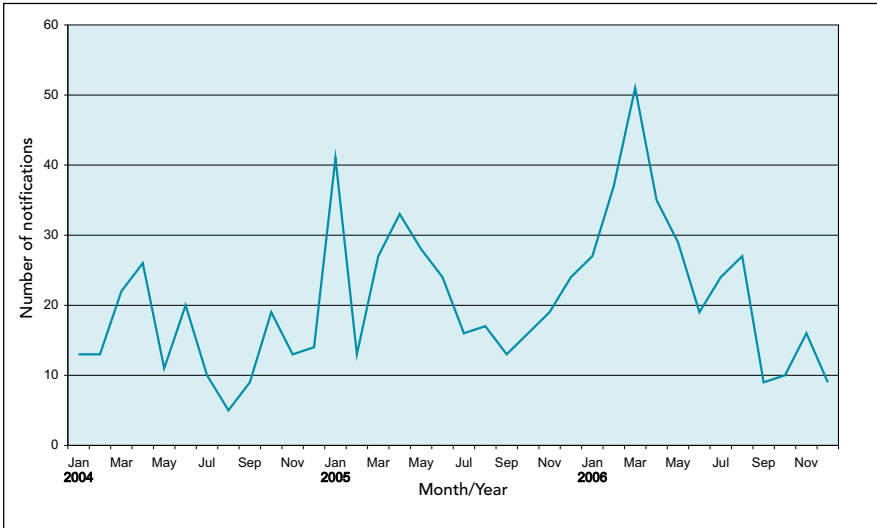
Although more than 90 polysaccharide capsular types, or serotypes of pneumococci are known, most infections are caused by a limited number of serotypes. In high-income countries the serotypes most commonly implicated are 1, 4, 6B, 7F, 9V, 14, 18C, 19F and 23F. The fact that relatively few serotypes cause most invasive disease has allowed for the development of effective vaccines.

### Epidemiology

Pneumococcal infection is a leading cause of death worldwide. Mortality is highest in patients who develop sepsis or meningitis. Pneumococcal meningitis case fatality rates of 7-16% were reported in Ireland over the years 2000-2006. Transmission is from person to person by droplet infection. The incubation period varies by type of infection, and can be as short as 1-3 days. Infection can occur at any time throughout the year but rates peak during the winter months (Figure 12.1).

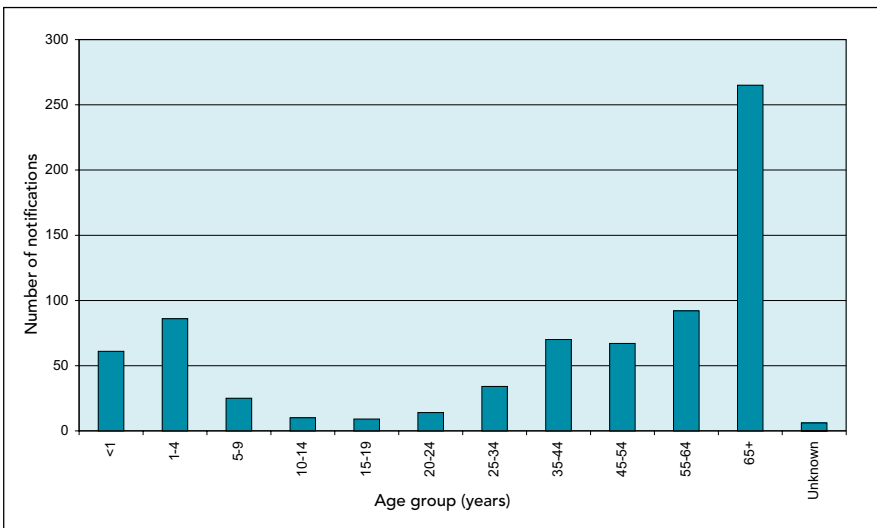
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**Figure 12.1** Invasive pneumococcal disease (IPD) notifications in Ireland by month, 2004-2006. Source: HPSC



During 2004-2006 a total of 739 cases of IPD were reported, 56% male and 44% female. Most cases were reported among the elderly ( $\geq 65$  years of age) (36%) and in young children in the 0-4 year age group (20%) (Figure 12.2).

**Figure 12.2** Age distribution of invasive pneumococcal disease notifications, 2004-2006. Source: HPSC



### Effects of pneumococcal infection

Pneumococcal infection is the most common cause of bacteraemia, sepsis, meningitis, pneumonia, sinusitis, and acute bacterial otitis media in children. It can also cause periorbital cellulitis, endocarditis, pericarditis, peritonitis, and soft tissue, bone and joint infection. Individuals who are more susceptible to pneumococcal infection include those with hyposplenism or asplenia (including those with sickle cell and coeliac disease), those immunocompromised by disease or its treatment (e.g. leukaemia), or with other chronic illnesses.

### Pneumococcal vaccines

There are two different types of pneumococcal vaccine:

1. Polysaccharide Pneumococcal Vaccine (PPV23). This incorporates 23 of the most common capsular types which together account for up to 90% of serious pneumococcal infections. It should be kept refrigerated at 2-8°C. It is only suitable for use in those  $\geq 2$  years of age. An adequate antibody response does not develop in those under 2 years of age.
2. A conjugate 7 valent vaccine (PCV7) containing polysaccharide antigens from the 7 most common serotypes conjugated to a protein (CRM 197) has enhanced immunogenicity compared with the polysaccharide vaccine. It is immunogenic even in infancy. It is active against approximately 70% of isolates causing invasive disease, and against a significant number of penicillin-resistant strains.

There is a lower response to PCV7 in preterm infants, but the response is probably adequate to confer protection.

PCV7 can be given as early as 6 weeks of age. The number of doses required for optimum immunogenicity depends on the age at which immunisation is initiated.

The introduction of PCV7 into the routine childhood immunisation schedule in the US in early 2000 has resulted in dramatic declines in the rates of invasive pneumococcal disease (IPD). In 2001 the rate of IPD in children under 2 years of age was 69% lower than 1998 and 1999. An additional unanticipated benefit following introduction of childhood vaccination has been the simultaneous reduction in the incidence of IPD in the adult population. This has been attributed to a decrease in transmission of pneumococci from children to adults. Conjugate vaccines reduce the rates of nasopharyngeal colonisation by vaccine serotypes,

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thus decreasing the potential for transmission from children to adults. This rapid induction of 'herd immunity' is an additional benefit of childhood immunisation with PCV7.

Based on a recent study of IPD in children in the Greater Dublin Area, it is anticipated that the introduction of routine pneumococcal vaccination in infancy using a conjugate 7 valent vaccine (PCV7) could protect against 81% of all IPD and against 82% and 90% of meningitis and sepsis respectively.

### Indications

#### Recommendations for pneumococcal vaccination:

1. All infants should be offered pneumococcal vaccination as part of the routine childhood immunisation schedule (see Chapter 2).
2. Those aged 65 years and older should be offered vaccination.
3. Individuals with the following conditions are at increased risk of pneumococcal infection, and should be vaccinated. (For vaccination schedule for individuals at risk of IPD see Table 12.2 below):
  - a. Asplenia or splenic dysfunction including surgical splenectomy, sickle cell disease and coeliac syndrome
  - b. Chronic renal disease or nephrotic syndrome
  - c. Chronic heart, lung, or liver disease, including cirrhosis
  - d. Diabetes mellitus
  - e. Complement deficiency (particularly early component deficiencies C1, C2, C3, C4)
  - f. Immunosuppressive conditions (e.g. some B- and T-cell disorders, HIV infection, leukaemia, lymphoma, Hodgkin's disease) and those receiving immunosuppressive therapies  
[Individuals with primary immunodeficiency may have a suboptimal response to vaccine. Immunisation may be omitted in children with certain primary immune deficiencies involving significant B cell compromise and who are receiving regular IVIG replacement therapy. Immunisation is unlikely to be immunogenic in these children.]
  - g. CSF leaks either congenital or complicating skull fracture or neurosurgery
  - h. Intracranial shunt
  - i. Candidate for, or recipient of, a cochlear implant
  - j. Children under 5 years of age with a history of invasive pneumococcal disease, irrespective of vaccine history.

**Pneumococcal vaccination should ideally be completed at least 2 weeks prior to elective splenectomy or cochlear implant.**

### Dose and route of administration

1. Pneumococcal Conjugate Vaccine (PCV7). A dose of 0.5 ml should be given by intramuscular injection in the deltoid area or the antero-lateral aspect of the thigh.
2. Polysaccharide Pneumococcal Vaccine (PPV23). A single dose of 0.5 ml should be given intramuscularly in the deltoid area or the antero-lateral aspect of the thigh.

### Pneumococcal vaccination schedule

1. **For normal newborns and healthy children less than 2 years of age:**  
Up to 3 doses of conjugate vaccine are recommended. The number of doses required depends on the age at time of initiation, (see Table 12.1 and also Primary immunisation schedule, Chapter 2).

**Table 12.1** Routine childhood immunisation with Pneumococcal Conjugate Vaccine (PCV7)

Age at first vaccination	Number of doses and intervals between doses
<12 months (3 doses in total)	Doses 1 and 2 two months apart Dose 3 given at >12 months of age, at least 2 months after dose 2
12-23 months (1 dose in total)	One single dose

2. **For individuals at higher risk of pneumococcal infection** (see a-j above)

Immunisation with conjugate vaccine (PCV7) followed by immunisation with the polysaccharide vaccine (PPV23) is recommended for children to afford a greater breath of protection. For adults a single dose of PPV23 is generally sufficient, see Table 12.2.

**Table 12.2** Pneumococcal immunisation for individuals at increased risk of IPD

Age at first vaccination	Pneumococcal vaccine type Number of doses and intervals between doses	
	<b>7 valent conjugate vaccine (PCV7)</b>	<b>23 valent polysaccharide vaccine (PPV23)</b>
<12 months (Minimum age for initiation 6 weeks) <b>(4 doses in total (3PCV7 + 1PPV))</b>	Doses 1 & 2 given 2 months apart Dose 3 given at >12 months of age, at least 2 months after dose 2	Single dose given $\geq 24$ months of age at least 2 months after Dose 3 PCV7
12-23 months <b>(2-3 doses in total (1 or 2 PCV7 + 1PPV))</b>	1 or 2* doses at least 2 months apart	Single dose given $\geq 24$ months of age at least 2 months after previous dose of PCV7
24 months to 5 years <b>(2 or 3 doses in total (1 or 2 PCV7 + 1PPV))</b>	1 or 2* doses with minimum interval of 2 months	Single dose as least 2 months after previous dose of PCV7
At risk children aged over 5 years and at risk adults	PCV is not recommended	Single dose of PPV23

\* 2 doses of PCV7 required where it is anticipated that response may be blunted, e.g. children with asplenia/hyposplenia, IgA-, IgG subclass-, and specific antibody deficiencies, whereas for children with complement deficiency or chronic granulomatous disease a single dose of PCV7 followed by PPV23 is adequate.

### 3. For adults aged 65 and older

A single dose of Pneumococcal Polysaccharide Vaccine (PPV23).

#### Reinforcing doses of PPV23

Booster doses are not routinely recommended

- Once children and adults have completed the appropriate vaccination schedule, additional booster doses are not currently recommended, unless these individuals have antibody levels likely to decline more rapidly, e.g. those with no spleen, with splenic

dysfunction, immunosuppression including HIV infection, nephrotic syndrome or chronic renal disease. In these circumstances re-immunisation with 23-valent polysaccharide vaccine should be given 5 years after the first dose.

- Adults 65 years or older should receive a second dose of PPV23 if they received vaccine more than 5 years before and were less than 65 years of age at the time of the first dose.
- The need and benefit for repeated booster doses among high-risk individuals is unclear and is not routinely indicated.

### Contraindications

Anaphylactic reaction to a preceding dose or any of the constituents.

### Precautions

1. Revaccination within 5 years of a previous dose of Polysaccharide Pneumococcal Vaccine. However, if the vaccine has been given during chemotherapy or radiotherapy, revaccination 3 months after treatment is recommended.
2. Acute severe febrile illness, defer until recovery.
3. Pregnancy. As a general principle, unnecessary interventions in pregnancy should be avoided. Pneumococcal vaccination can however be given in pregnancy if there is an urgent need for protection.

### Adverse reactions

**Local:** Localised tenderness and erythema at the injection site may occur. Intradermal administration may cause a severe local reaction. No increase in localised reactions with repeated doses of PCV7 has been reported. Reimmunisation with the PPV23 has produced severe local reactions especially if less than 5 years have elapsed since the first injection.

**General:** Occasional low-grade fever lasting less than 24 hours.

### Management of cases, contacts and outbreaks

#### **Cases of invasive pneumococcal disease (IPD)**

Any case of invasive pneumococcal infection or lobar pneumonia believed to be due to *S. pneumoniae* should prompt a review of patients' medical history to establish whether they are in a recognised risk group and whether they have been vaccinated. Patients with risk factors who have not previously been vaccinated should be given vaccination on discharge from hospital.

### ***Children under 5 years of age***

All children under 5 years of age who have had IPD, e.g. pneumococcal meningitis or pneumococcal bacteraemia or lobar pneumonia attributed to pneumococcus, should be given a dose of PCV7 irrespective of previous vaccination history. Children under 13 months who are unvaccinated or partially vaccinated should complete the immunisation schedule.

### ***Vaccine failure***

These children should be evaluated for risk factors predisposing them to pneumococcal infection. If they are found to fall into one of the risk groups, they should continue vaccination as for other at-risk children (see section on recommendations for the use of pneumococcal vaccination).

All new cases of IPD in children eligible for routine PCV will require follow-up as part of the surveillance of this new vaccination programme.

### ***Contacts***

Close contacts of pneumococcal meningitis or other invasive pneumococcal disease are not normally at an increased risk of pneumococcal infection and therefore antibiotic prophylaxis is not indicated. Clusters of invasive pneumococcal disease should be discussed with local health protection teams.

### ***Outbreaks***

Outbreaks of pneumococcal respiratory disease in hospitals and residential care homes need prompt investigation. Control measures including vaccination may be appropriate; these should be agreed in discussion with local health protection or infection control teams.

### Bibliography

Black S et al (1998). Efficacy of hepatavalent conjugate pneumococcal vaccine (Wyeth Lederle) in 37,000 infants and children: results of the northern California Kaiser Permanente efficacy trial, abstr. LB-9, 38th Interscience Conference on Antimicrobial Agents and Chemotherapy, San Diego, CA. American Society of Microbiology.

Black SB, Cimino CO, Hansen J, Lewis E, et al (2006). Immunogenicity and safety of measles-mumps-rubella, varicella and Haemophilus influenzae type b vaccines administered concurrently with a fourth dose of heptavalent pneumococcal conjugate vaccine compared with the vaccines administered without heptavalent pneumococcal conjugate vaccine. *Pediatr Infect Dis J*; 25(4):306-11.

CDC (2005). Direct and indirect effects of routine vaccination of children with 7-valent pneumococcal conjugate vaccine on incidence of invasive pneumococcal disease – United States, 1998-2003. *MMWR*: 54(36):893-7.

Clarke SC, Jefferies JM, Smith AJ, et al (2006). Potential impact of conjugate vaccine on the incidence of invasive pneumococcal disease among children in Scotland. *J Clin Microbiol*; 44 (4):1224-8.

Cotter S (2006). Epidemiology of invasive pneumococcal disease in Ireland. HPSC Report for the National Immunisation Advisory Committee.

Fitzsimons J, Lee Chong A, Cafferkey M, Butler K (2008). Epidemiology of invasive pneumococcal disease in children in a region of Ireland – the potential for conjugate pneumococcal vaccination. *Ir J Med Sci* (in press).

Hammit LL, Bruden DL, Butler JC, et al (2006). Indirect Effect of conjugate vaccine on adult carriage of *Streptococcus pneumoniae*: an explanation of trends in invasive pneumococcal disease. *J Infect Dis*; 193(11):1487-94. Epub 2006 Apr 27.

Hausdorf WP, Bryant J, Paradiso PR, Siber GR (2000). Which pneumococcal serogroups cause the most invasive disease: implications for conjugate vaccine formulation and use, part 1. *Clin Infect Dis*; 30(1):100-21.

Ispahani P, Slack RC, Donald FE, Weston VC, Rutter N (2004). Twenty year surveillance of invasive pneumococcal disease in Nottingham: serogroups responsible and implications for immunisation. *Arch Dis Child*; 89(8):757-62.

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Jackson LA, Benson P, Sneller V, et al (1999). Safety of revaccination with pneumococcal polysaccharide vaccine. *JAMA*; 281:243-8.

Knuf M, Habermehl P, Cimino C, Petersen G, et al (2006). Immunogenicity, reactogenicity and safety of a 7-valent pneumococcal conjugate vaccine (PCV7) concurrently administered with a DTPa-HBV-IPV/Hib combination vaccine in healthy infants. *Vaccine*; 24(22):4727-36. Epub 2006 Mar 24.

Kyaw MH, Lynfield R, Schaffner W, Craig AS, et al (2006). Effect of introduction of the pneumococcal conjugate vaccine on drug-resistant *Streptococcus pneumoniae*. *NEJM*; 14(354):1455-63.

McBean AM, Park YT, Caldwell D, Yu X (2005). Declining invasive pneumococcal disease in the U.S. elderly. *vaccine*: 23(48-49):5641-5.

Miller E, Waight P, Efstratiou A, Brisson M et al (2000). Epidemiology of invasive and other pneumococcal disease in children in England and Wales 1996 – 1998. *ACTA Paediatr Suppl*; 435:11-16.

Poehling KA, Talbot TR, Griffin MR, Craig AS, et al (2006). Invasive pneumococcal disease among infants before and after introduction of pneumococcal conjugate vaccine. *JAMA*; 295(14):1668-74.

Royal College of Paediatrics and Child Health (2002). Best Practice Statement Immunisation of the Immunocompromised Child. [www.rcpch.ac.uk/Publications/Publications-list-by-title](http://www.rcpch.ac.uk/Publications/Publications-list-by-title)

Shinefield HR, Black S, Ray P et al (1999). Safety and immunogenicity of heptavalent pneumococcal CRM 197 conjugate vaccine in infants and toddlers. *Pediatr Infect Dis J*; 18:757-63.

Whitney CG, Farley MM, Hadler J, et al (2003). Decline in Invasive Pneumococcal Disease after the Introduction of Protein–Polysaccharide Conjugate Vaccine *NEJM* 348; 18:1737-46.