

# 12

## Pneumococcal Infection

NOTIFIABLE

### Introduction

*Streptococcus pneumoniae* (*pneumococcus*) is an important cause of serious infection, especially in young children, older adults and immunocompromised people. Invasive pneumococcal disease (IPD) is defined as the isolation of *S. pneumoniae* from a normally sterile site (e.g. blood, cerebrospinal fluid (CSF), joint, pleural, or pericardial fluid). Non-invasive manifestations of the disease include otitis media, sinusitis and bronchitis. IPD is a disease mainly occurring in children under 5 years and those aged  $\geq 65$  years. Individuals with severe chronic disease or immunodeficiency are also at increased risk of this disease.

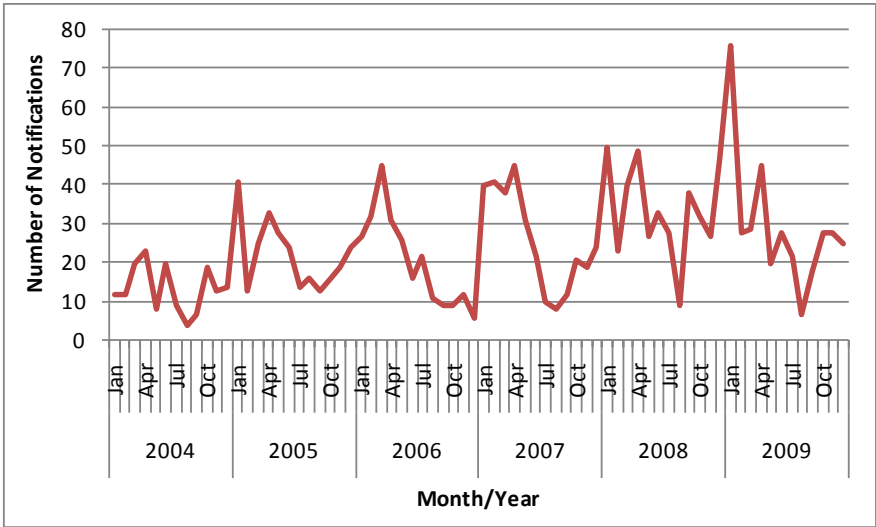
Although more than 90 polysaccharide capsular serotypes of pneumococci are known, most infections are caused by a limited number of serotypes. In higher-income countries the serotypes most commonly implicated are 1, 4, 6B, 7F, 9V, 14, 18C, 19F and 23F. The fact that relatively few serotypes cause most 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 11-16% were reported in Ireland in the years 2004-2009. Transmission is from person to person by droplet infection. The incubation period varies by site 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).

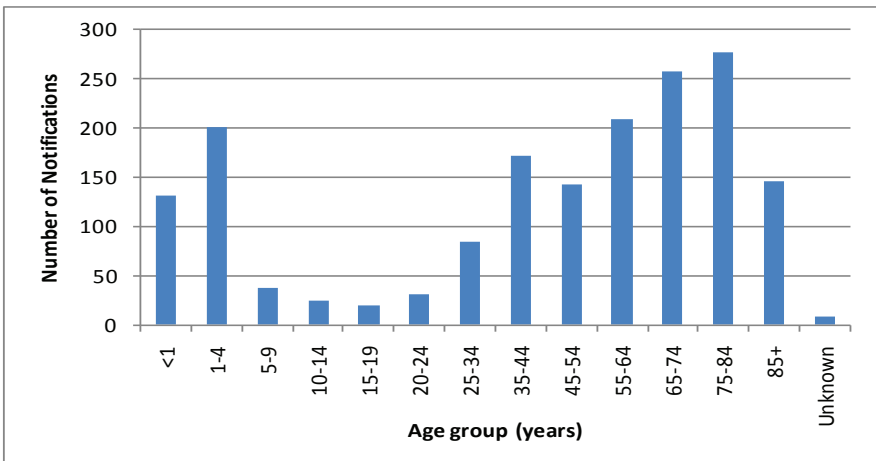
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**Figure 12.1** Invasive pneumococcal disease (IPD) notifications in Ireland by month, 2004-2009. Source: HPSC



From 2004 to 2009 a total of 1741 cases of IPD were reported, 56% male and 44% female. Most cases occurred in older people ( $\geq 65$  years of age, 39%) and in the 0-4 year age group (19%) (Figure 12.2).

**Figure 12.2** Age distribution of invasive pneumococcal disease (IPD) notifications, 2004-2009. Source: HPSC



## Effects of pneumococcal infection

Pneumococcal infection is the most common cause of bacteraemia, septicaemia, bacterial meningitis, pneumonia, sinusitis, and acute 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), and those with other chronic illnesses.

## Pneumococcal vaccines

There are two different types of pneumococcal vaccine:

- 1. Pneumococcal Polysaccharide Vaccine (PPV23).** This incorporates 23 of the most common capsular types\*, which account for up to 90% of all serious pneumococcal infections. The vaccine 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. Pneumococcal Conjugate Vaccines (PCV 7, 10 and 13)** contain polysaccharide antigens from 7, 10 or 13 serotypes\* conjugated to a protein. These vaccines should be kept refrigerated at 2-8°C. They have enhanced immunogenicity compared with the polysaccharide vaccine, and are immunogenic from 6 weeks of age. Conjugate vaccines are active against 75-90% of serotypes causing invasive disease, including a significant number of penicillin-resistant strains. The number of doses required for optimum immunogenicity depends on the age at which immunisation is initiated. There is a lower response to conjugate vaccines in preterm infants, but the response is adequate to confer significant protection.

In Ireland PCV7 was recommended for at risk children in 2002 and was introduced into the routine primary immunisation schedule in September 2008, along with a catch up programme for all children under 2 years of age.

\* The following serotypes are contained in pneumococcal vaccines

PCV 7	4, 6B, 9V, 14, 18C, 19F, 23F
PCV10	1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, 23F
PCV 13	1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F
PPV23	1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, 33F

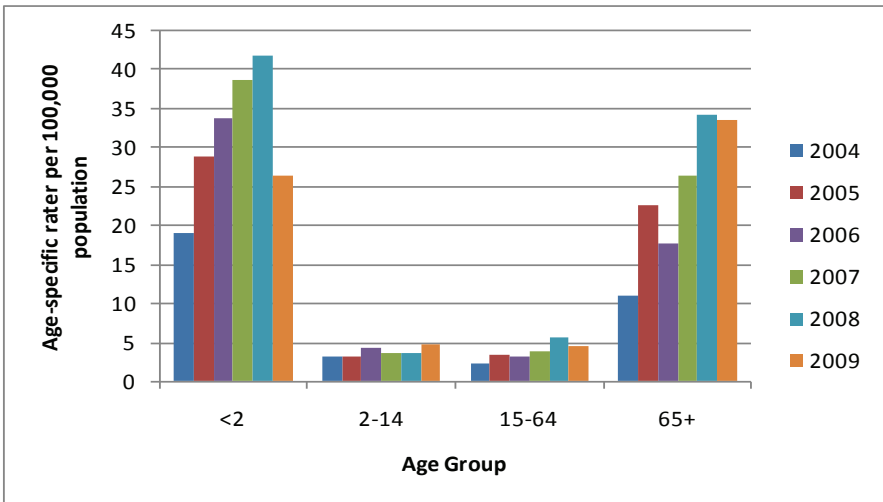
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The incidence of confirmed cases of IPD in Ireland declined by 12% in 2009 compared with the previous year (Figure 12.3), with a 37% reduction in the rates in children younger than 2 years. The introduction of PCV7 into the childhood immunisation schedule in the US in early 2000 resulted in a 69% reduction in the rates of IPD in children under 2 years.

In December 2010 PCV13 vaccine replaced PCV7 in the Irish childhood immunisation programme. PCV13 includes antigens from the seven serotypes contained in PCV7 plus six additional serotypes which cause IPD. The introduction of PCV13 is expected to provide increased protection with coverage of approximately 90% of serotypes responsible for IPD in children under 2 years of age.

Pneumococcal conjugate vaccines reduce the rates of nasopharyngeal colonisation by vaccine serotypes, thus decreasing the potential for transmission from children to other children and to adults. In the US there has been a significant reduction in the incidence of IPD in the adult population since 2001. In Ireland a similar decline is not yet evident (Oct. 2010). In 2008, 160 cases in those aged 65 years and older were notified compared to 157 in 2009; the age specific incidence rates are shown in Figure 12.3.

**Figure 12.3** Age specific incidence rates (ASIR) of invasive pneumococcal disease notifications, 2004-2009. Source: HPSC



### Indications for pneumococcal vaccination.

1. All infants from 2 months of age as part of the routine childhood immunisation schedule (see Chapter 2).
2. All those aged 65 years and older.
3. Individuals at higher risk of IPD, ie those with:
  - a. Asplenia or splenic dysfunction (including splenectomy, sickle cell disease and coeliac disease).
  - b. Chronic renal disease, nephrotic syndrome or renal transplant.
  - 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.  
Note: Individuals with primary immunodeficiency may have a suboptimal response to all vaccines. Pneumococcal vaccines are unlikely to be immunogenic in children with certain primary immune deficiencies involving significant B cell compromise who are receiving regular IVIG replacement therapy. However vaccination should be given as it may have some effect.
  - g. CSF leaks either congenital or complicating skull fracture or neurosurgery.
  - h. Intracranial shunt.
  - i. Candidates for, or recipients of, a cochlear implant.
  - j. Children under 5 years of age following invasive pneumococcal disease, irrespective of vaccine history (See section below Children under 5 years who have had IPD).
  - k. Smokers and alcoholics (see section below for rationale).

For vaccine types and schedule for individuals at risk of IPD see Table 12.2 below.

**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 Vaccines (PCV 7, 10 and 13). 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. Pneumococcal Polysaccharide Vaccine (PPV23). A dose of 0.5 ml should be given by intramuscular injection in the deltoid area.

### Pneumococcal vaccination schedule:

#### 1. **Healthy children under 2 years of age**

Up to 3 doses of PCV are recommended; the number of doses required depends on the age of child as shown in Table 12.1 (see also primary immunisation schedule, Chapter 2).

**Table 12.1** Routine childhood immunisation with Pneumococcal Conjugate Vaccine (PCV13)

Age at first vaccination	Number of doses and intervals between doses
<12 months <b>(3 doses in total)</b>	Doses 1 and 2 at 2 month intervals Dose 3 given at $\geq 12$ months of age, at least 2 months after dose 2 No further dose if any dose given aged $\geq 12$ months

Note:

- (a) Infants who have received 2 doses of PCV7 before PCV13 was introduced can be given PCV13 as the 3<sup>rd</sup> dose.
- (b) Those who have received 1 dose of PCV7 can be given PCV7 as their 2<sup>nd</sup> dose if it is available; if not PCV13 can be used.
- (c) Children aged 12 -< 24 months who have already received one dose of PVC7 at  $\geq 12$  months do not require a dose of PCV13.

#### 2. **Children under 18 years at higher risk of pneumococcal infection** (see a-j above)

Immunisation with PCV13 followed by immunisation with polysaccharide vaccine (PPV23) is recommended to afford broader protection for children up to 5 years of age, as shown in Table 12.2.

Children 5-18 years should be given one dose of PPV23.

PCV13 may be used in those aged 5 -18 years who are at significantly increased risk of IPD\*\*\*see Table 12.2.

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

Age at first vaccination	Pneumococcal vaccine type, number of doses and intervals	
	Pneumococcal conjugate vaccine (PCV13)	Pneumococcal polysaccharide vaccine (PPV23)
6 weeks -<12 months <b>(3 PCV13 +1 PPV23)</b>	Doses 1 & 2 at 2 month intervals Dose 3 given at ≥12 months of age, at least 2 months after dose 2 No further dose if 1 or 2* doses given aged ≥12 months.	One dose given ≥24 months of age at least 2 months after 3rd dose of PCV13
12-<24 months <b>(1 or 2 PCV13 + 1 PPV23)</b>	1 or 2* doses at 2 month intervals	One dose given ≥24 months of age, at least 2 months after final dose of PCV13
24 months to 5 years** <b>(1 or 2* PCV13 + 1 PPV23)</b>	1 or 2* doses at 2 month intervals	One dose (at least 2 months after dose of PCV13)
>5- <18 years*** <b>(0 or 1*** PCV13 + 1 PPV23)</b>	0 or 1*** dose	One dose (at least 2 months after dose of PCV13 if this was given)

\* 2 doses of PCV13 are required when it is anticipated that response may be blunted, e.g. children with asplenia/hyposplenia, IgA-, IgG subclass-, and specific antibody deficiencies. For children with complement deficiency or chronic granulomatous disease one dose of PCV13 followed by one dose of PPV23 is adequate.

\*\*A single dose of PCV13 may be given opportunistically to children under 5 years of age who are in an at risk group and who have completed a course of PCV 7

\*\*\* For children from 5-<18 years with functional or anatomic asplenia, including sickle cell disease, HIV infection or other immunocompromising condition, cochlear implant or CSF leak, consider giving one dose of PCV13 regardless of previous history of PCV7 or PPV23

### 3. Adults aged 65 years and older

One dose of Pneumococcal Polysaccharide Vaccine (PPV23).

### 4. Individuals 18-64 years of age at higher risk of IPD

One dose of Pneumococcal Polysaccharide Vaccine (PPV23).

### 5. Smokers and Alcoholics (added to high-risk group in 2010)

One dose of Pneumococcal Polysaccharide Vaccine (PPV23).

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Cigarette smokers are at increased risk of invasive pneumococcal disease. In a US multi-centre population-based, case-control study, the risk for IPD among immunocompetent cigarette smokers aged 18-64 years was four times the risk for controls who had never smoked (AOR = 4.1; CI = 2.4--7.3). Significant dose-response relationships with risk for IPD also were observed for number of cigarettes smoked and pack-years of smoking.

Subsequent studies confirmed that smoking also increases the risk for IPD among other groups, including immunocompromised persons.

Individuals with a history of alcohol abuse are 1.6- 7.1 times more likely to develop IPD than non-alcoholics. Proposed reasons for the higher risk include increased bacterial colonization, reduced ciliary motility and immune system compromise.

### **Booster doses of PPV23**

Booster doses are not routinely recommended for immunocompetent people as there is a lack of evidence of improved immunity and an increased incidence of local side-effects after repeated doses.

- For individuals whose antibody levels are likely to decline more rapidly, (e.g. those with no spleen, with splenic dysfunction, immunosuppression including that associated with HIV infection, nephrotic syndrome or chronic renal disease), a once only booster PPV23 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 for and benefit of repeated booster doses among other high-risk individuals is unclear, and they are not routinely indicated.

### **Contraindications**

Anaphylactic reaction to a preceding dose of the vaccine or to 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, vaccination 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. Subcutaneous administration may cause a severe local reaction. No increase in localised reactions with repeated doses of PCV has been reported. Reimmunisation with PPV23 has produced severe local reactions especially if less than 5 years has elapsed since the first injection.

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

### Management of cases and contacts, and during 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 the patient's history to establish whether they are in a recognised risk group and have been vaccinated. Patients with risk factors who have not previously been vaccinated should be given vaccination on discharge from hospital; they should continue vaccination as for other at-risk people (see section on recommendations for the use of pneumococcal vaccination).

#### **Children under 5 years of age who had IPD**

All children under 5 years of age who have had IPD, should receive a dose of pneumococcal conjugate vaccine (PCV13) irrespective of vaccine history.

Children under 12 months who are unvaccinated or partially vaccinated should complete the immunisation schedule.

All children under 5 years of age who have had IPD 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 PCV and PPV23 vaccination as for other at-risk children (see section above on Indications for pneumococcal vaccination).

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

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### **Contacts**

Antibiotic prophylaxis is not indicated for close contacts of a case of invasive pneumococcal disease as such contacts are not normally at increased risk of pneumococcal infection. Clusters of invasive pneumococcal disease should be discussed with local health-protection or infection-control teams.

### **Outbreaks**

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

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