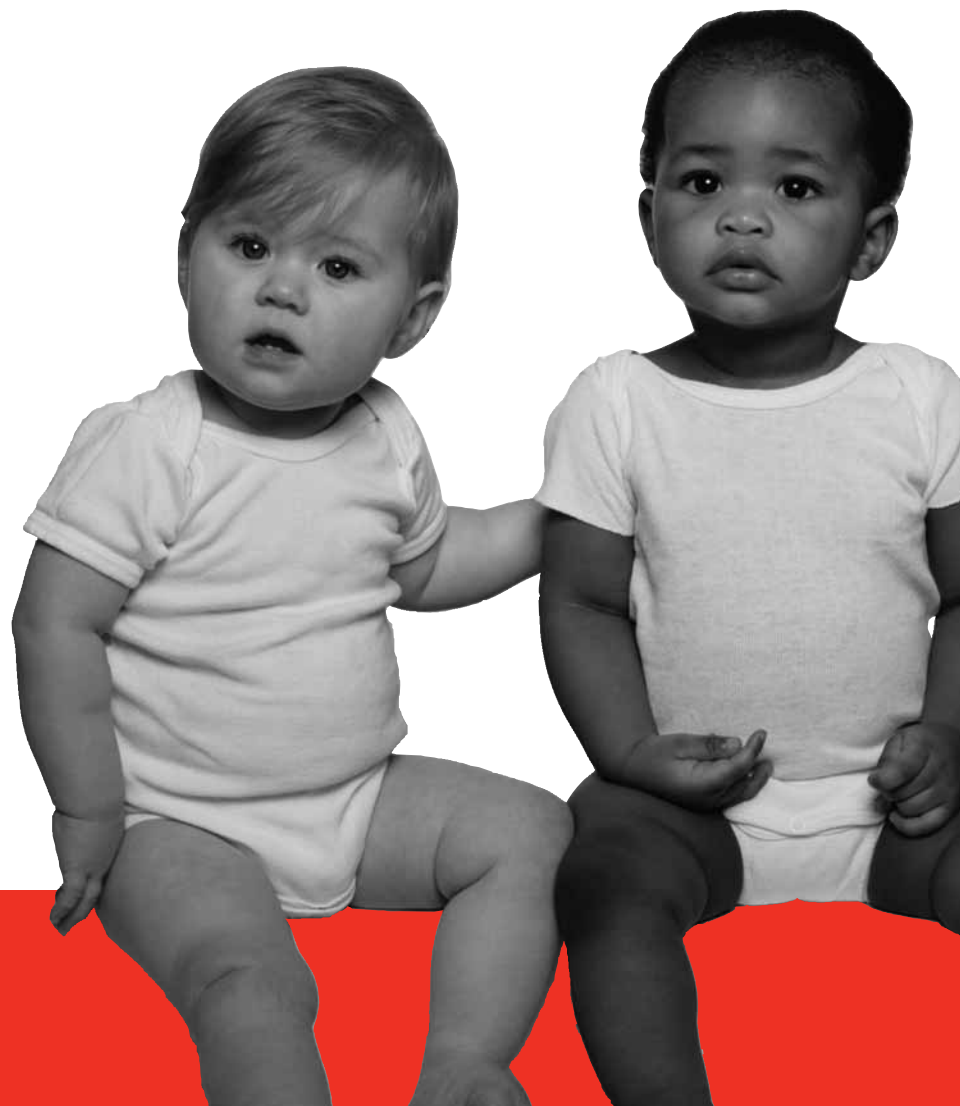


# Factsheet

## Pneumococcal conjugate vaccine (PCV) for children



This factsheet describes pneumococcal disease and the very serious illnesses that it causes such as meningitis and septicaemia. It also describes the vaccine that helps protect against these diseases.

Pneumococcal conjugate vaccine (PCV) was introduced into the routine childhood immunisation programme in 2006. This included a catch-up programme to offer the vaccine to all children under two years of age.

This factsheet explains this change to the programme and why it was made. It also provides background information on the vaccine and describes the diseases against which it protects.

For information on the other vaccines used in the routine childhood immunisation programme, please refer to the NHS Immunisation Information website [www.immunisation.nhs.uk](http://www.immunisation.nhs.uk) or [www.dhsspsni.gov.uk/phealth](http://www.dhsspsni.gov.uk/phealth)

## The disease

### What is pneumococcal disease?

Pneumococcal disease is the term used to describe infections caused by the bacterium *Streptococcus pneumoniae*.

Pneumococcal infection causes a range of illnesses depending on which part of the body is affected (Table 1, page 4). It is a major cause of life-threatening illnesses, such as meningitis, septicaemia and severe pneumonia. It also causes less serious but common illnesses such as ear infections (otitis media), mild pneumonia (where infection is restricted to the lungs) and bronchitis. The more severe types of illnesses (e.g. meningitis, septicaemia and pneumonia) are caused when the pneumococcal bacteria infect the bloodstream. This type of illness is called invasive pneumococcal disease (IPD) and is more likely to lead to death than non-invasive infections.

Over 90 different serotypes (strains) of *Streptococcus pneumoniae* have been identified so far. Most pneumococcal disease in the world is caused by 20-30 of the most common serotypes.

*Streptococcus pneumoniae* is becoming increasingly resistant to antibiotics in the UK and worldwide. As pneumococcal disease becomes harder to treat because of this resistance, its prevention by immunisation becomes more important.

The common signs and symptoms of meningitis and septicaemia in babies, older children and adults are listed in Table 2, page 5.

### Who is at risk from pneumococcal disease?

Pneumococcal infection is most common in young children and the elderly (see Figure 1, page 4).

Following the successful introduction of *Haemophilus influenzae* type b (Hib) and meningitis C (MenC) vaccines into the UK's

childhood immunisation programme, pneumococcal infection is now one of the most common causes of invasive bacterial infection in children. Along with Group B meningococcal disease, it is one of the two most common causes of bacterial meningitis.

### How many children does pneumococcal disease affect?

Each year, around 530 cases of invasive pneumococcal disease in children under two years are reported in England and Wales (Health Protection Agency website). Of these, up to a third are cases of pneumococcal meningitis (Health Protection Agency; Ispahani P *et al.*, 2004). Pneumococcal infection is also the most common bacterial cause of mild pneumonia and otitis media (ear infections) in children.

Pneumococcal pneumonia is the cause of over 4500 hospital admissions each year in children under five years of age (Melegaro *et al.*, 2006).

Although less severe than IPD, ear infections are a common complaint and cause of distress for young children. Ear infections affect one in three children each year and up to a third of these are caused by pneumococcal infection (Health Protection Agency).

### How serious is pneumococcal disease?

Estimates vary but at least 16 and as many as 53 children under two years of age die from invasive pneumococcal disease in England and Wales each year (Health Protection Agency; Ispahani P *et al.*, 2004).

The most severe and potentially fatal form of IPD is meningitis. Between 10% and 20% of pneumococcal meningitis cases result in death (Health Protection Agency; Ispahani P *et al.*, 2004).

Of those young children who survive pneumococcal meningitis, about 50% or so are left with permanent disability, including deafness, intellectual impairment, speech and language problems, paralysis, cerebral palsy, epilepsy and blindness (Bedford *et al.*, 2001).

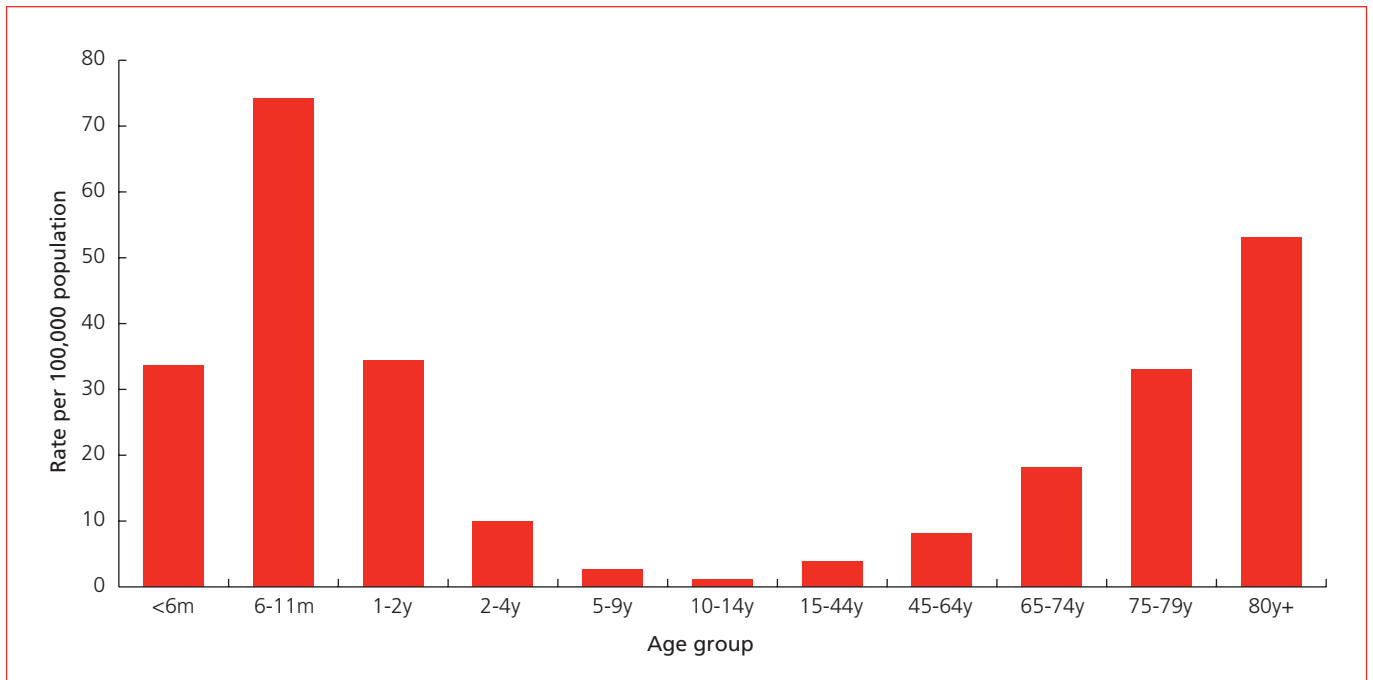


Figure 1 Invasive pneumococcal disease (IPD) rates by age per 100,000 population (Data from epidemiological year 1 July 2003 to 30 June 2004)  
Source: Health Protection Agency

Table 1 The diseases caused by pneumococcal infections

Disease caused by pneumococcal infection	Symptoms	Serious complications
Pneumonia	Cough, breathing difficulties, chest pains, fever, headache, confusion	Can lead to septicaemia (bacteria in the bloodstream) where the infection can spread to the lining of the heart (pericarditis) or brain (meningitis)
Septicaemia (blood poisoning)	Fever, confusion, low blood pressure (shock)	Can cause death
Meningitis (inflammation around the brain)	Confusion, fever, headache	Can cause death. Five out of ten cases of meningitis result in permanent damage including deafness, intellectual impairment, speech and language problems, paralysis, cerebral palsy, epilepsy and blindness.
Bronchitis	Coughing, mucus secretion	
Peritonitis (inflammation of the lining of the abdomen)	Abdominal pain, fever	Can cause death
Otitis media (inflammation of the middle ear)		'Glue ear' requiring insertion of grommets. Perforation of the eardrum. Both of these can lead to hearing loss which may result in speech and language delays. Children with pneumococcal acute otitis media can also go on to develop invasive disease.

Table 2 Signs and symptoms of meningitis and septicaemia

The first symptoms of both meningitis and septicaemia may be non-specific and can be mistaken for a cold or flu (i.e. fever, vomiting, irritability and restlessness). However, individuals can become seriously ill within hours.

If the presentation is predominantly one of septicaemia (blood poisoning), symptoms may include:

**in babies:**

- rapid or unusual patterns of breathing
- skin that is pale, blotchy or turning blue
- fever with cold hands and feet
- shivering
- vomiting, refusing to feed
- red or purple spots that do not fade under pressure (do the glass test explained below)
- pain or irritability from muscle aches or severe limb or joint pain
- floppiness
- severe sleepiness

**in older children, adolescents and adults:**

- being sleepy, less responsive, vacant, or confused (a late sign in septicaemia)
- severe pains and aches in arms, legs and joints
- very cold hands and feet
- shivering
- rapid breathing
- red or purple spots that do not fade under pressure (do the glass test explained below)
- vomiting
- fever
- diarrhoea and stomach cramps

If the presentation is predominantly one of meningitis, symptoms may include:

**in babies:**

- a high-pitched, moaning cry
- being irritable when picked up
- a bulging fontanelle
- being drowsy and less responsive or difficult to wake
- being floppy and listless or stiff with jerky movements
- refusing feeds, vomiting
- skin that is pale, blotchy or turning blue
- fever

**in older children, adolescents and adults:**

- a stiff neck (check that they can kiss their knees or touch their forehead with their knees)
- a very bad headache (this alone is not a reason to get medical help)
- a dislike of bright lights
- vomiting
- fever
- being drowsy, less responsive or confused
- a rash<sup>†</sup>

### Important information

Not everyone will develop all the symptoms listed above and symptoms can appear in any order. If an individual develops some of the symptoms listed above, especially red or purple spots (resembling bruises) that do not fade under pressure is indicative of septicaemia.



Press the side of a clear drinking glass firmly against the rash so you can see if the rash fades and loses colour under pressure.

<sup>†</sup>This type of rash is more likely in meningococcal infection and is very uncommon in pneumococcal infection. This condition must be treated immediately with antibiotics. If you cannot get in touch with your doctor, or are still worried after getting advice, trust your instincts and take your child to the emergency department of your nearest hospital. As the disease progresses, photophobia (dislike of light), disorientation and reduced awareness, possibly leading to coma, may develop.

## How is pneumococcal infection spread?

The pneumococcal bacteria are spread mainly by respiratory droplets in the air expelled during coughing or sneezing. It can also be spread indirectly, for example, by coming into contact with the respiratory droplets on another person or object and passing these to one's own mouth or nose.

Pneumococcal bacteria are common inhabitants of the respiratory tract (ear, nose and throat). Around half of all young children (and around eight in every 100 adults) carry these bacteria at any one time in their nose or throat without any symptoms (Hussain *et al.*, 2005). Because it is common to carry the bacteria in the nose or throat, people can spontaneously develop serious infection without catching it from others.

During the winter months, there is an increase in the number of people with upper respiratory tract infections (such as colds). As a consequence, more people cough and sneeze, leading to an increase in the amount of circulating pneumococcal bacteria. This in turn leads to an increase in pneumococcal disease. People who have had influenza are at an increased risk of developing pneumococcal pneumonia as a secondary infection.

## The vaccine

### What can we do to protect ourselves from pneumococcal infection?

Two pneumococcal vaccines are available that help to protect against pneumococcal disease.

### Pneumococcal conjugate vaccine (7-valent) – 'PCV'

Children can be protected against some of the most common serotypes of pneumococcal bacteria using pneumococcal conjugate vaccine. It contains parts of the polysaccharide (sugar) coat from seven serotypes of pneumococcal bacteria (a 7-valent vaccine) that have been joined to protein to make it more effective.

PCV was licensed in the UK in 2001. Since 2002, it has been recommended for children at an increased risk of pneumococcal disease because of a medical condition (CMO letter, 2002). It is now recommended for all infants as part of the routine childhood immunisation programme (CMO letter, 2006).

### **PCV cannot cause pneumococcal infection.**

The PCV currently used for primary immunisation is Prevenar®.

## Polysaccharide pneumococcal vaccine (23-valent) – ‘Pneumo’ or ‘PPV’

A 23-valent polysaccharide vaccine has been available for a number of years and is recommended for adults aged 65 years and over, and for people aged two years and over in certain medical risk groups (CMO letter, 2005). Polysaccharide vaccines do not stimulate a long-lasting antibody response in young children and so are not suitable for children under two years of age.

### PPV cannot cause pneumococcal infection.

The PPV currently used for immunisation in high risk individuals aged two years and over is Pneumovax.

## When are children routinely given the pneumococcal conjugate vaccine?

Because babies can catch these diseases from birth, it is important to protect them as soon as possible. PCV is given at two and four months of age. A booster dose is given at about 15 months of age to provide longer-term protection. It is given at the same time as other childhood vaccines (see table below).

Age	Vaccine
Two months	DTaP/IPV/Hib + pneumococcal (PCV)
Three months	DTaP/IPV/Hib + MenC
Four months	DTaP/IPV/Hib + MenC and PCV
12 months	Hib/MenC
15 months	MMR + PCV

## How effective is PCV?

The vaccine provides protection against seven common pneumococcal serotypes that are responsible for 82% of invasive disease in children under five years in the UK (CDR Weekly, 2003).

The vaccine has been shown to be 96% effective at preventing IPD caused by these seven serotypes when given as a two-dose schedule in the first year of life (Whitney, 2005). This level of protection is equivalent to the three-dose vaccination schedule (given at two, four and six months of age) used in the United States (US).

PCV also provides protection against pneumonia and otitis media (ear infections). Studies have shown that it reduces the incidence of confirmed cases of pneumococcal pneumonia in children under five years of age by 18% (Black *et al.*, 2002). The number of episodes of otitis media caused by the serotypes contained in the vaccine fell by 57% in vaccinated children who were followed up to two years of age (Eskola *et al.*, 2001).

## How long does the protection from PCV last?

The pneumococcal vaccine has been used in the US since 2000 and so far has provided good long-term protection against pneumococcal disease.

## How safe is this vaccine?

Before being licensed, all medicines (including vaccines) are thoroughly tested to ensure that they are of high quality, and to assess their safety and immunogenicity. Once licensed and in use, vaccines are carefully monitored. Experience of using PCV in other countries has shown this vaccine to have an excellent safety record. However, as with other medicines, vaccines can have side effects. These are outlined below.

## What side effects may be seen?

Swelling and redness at the injection site and low grade fever are among the most commonly reported adverse reactions (between ten and 20 children in every 100 immunised) (Black *et al.*, 2000). Other mild side effects such as a slightly raised temperature, irritability, sickness, diarrhoea and loss of appetite may also occur. No serious side effects have been reported that are specific to PCV.

As with all vaccines, there is a very rare possibility (approximately one in a million doses) of this vaccine causing a severe allergic reaction called anaphylaxis. All health professionals responsible for immunisation are trained to deal with the recognition and treatment of anaphylaxis.

## Are there any reasons why a baby should not receive this vaccine?

There are very few medical reasons why a baby cannot be immunised. The only situations in which immunisation is contraindicated are where a baby has had:

- a confirmed anaphylactic reaction to a previous dose, or
- a confirmed anaphylactic reaction to any component of the vaccine

If a baby is ill, with a fever, immunisation should be postponed until the child has recovered. This is to avoid wrongly associating any cause of fever, or its progression, with the vaccine and to avoid increasing any pre-existing fever. Babies with a minor illness without a fever, e.g. a cold, should be offered immunisation.

## Experience from other countries

### Is PCV vaccine recommended in other countries?

In the US, PCV has been part of the universal childhood immunisation programme since 2000. Canada, Australia, Austria, Italy, Greece, Spain, Norway, Luxembourg, Qatar, Switzerland and the Netherlands have also introduced PCV into their routine immunisation schedule. Other countries have introduced selective immunisation programmes for children in whom pneumococcal infection would be particularly serious.

Over 90 million doses of PCV have now been used worldwide.

### What has been the impact of introducing this vaccination programme in the US?

Since its introduction, the incidence of IPD caused by the seven serotypes in the vaccine has fallen by 94% in children under five years of age, and by 62% in individuals aged five and over (CDC, 2005). The significant decline in IPD in individuals who have not been vaccinated points to a more widespread population effect, similar to the UK experience after the introduction of meningococcal C vaccination.

## Questions about the UK schedule

### What evidence do we have that two doses of PCV in the first year of life followed by a booster dose are as good as the immunisation schedule used in the US (three doses and a booster)?

Clinical trials carried out in infants and toddlers examined the efficacy of PCV when given alongside the other vaccines in the UK immunisation schedule. They found that a two-dose primary vaccination schedule, when given with an interval of two months between doses, provides the same protective levels of antibody as a three-dose primary immunisation course (Goldblatt *et al.*, 2005).

### Can three separate vaccines be given at the same time at four months of age?

Three separate vaccines can be given at the same time with no additional adverse effects from such a procedure.

In fact, there have already been occasions when three injections have been necessary as part of the UK routine programme. For example, when MenC was introduced in 2000, pre-school-age children had three injections – MenC, a pre-school booster (DT) and a second dose of MMR. A similar situation occurred for the same age group as part of the Hib booster campaign in 2003. In addition, UK trials of the new schedule have found that three injections at one appointment were acceptable to the nurses doing the immunisations and to the parents. In the US, the routine programme requires three and sometimes four different injections at the same time.

Although some parents and health professionals may feel anxious about giving three injections at the same time, this will not harm the baby and is recommended in order to protect babies at the earliest age possible.

For children under one year of age, where three immunisations are required, it is recommended that two of the injections should be given in one thigh and the third in the other thigh. This is because the anterolateral aspect of the thigh provides a larger area for the administration of two injections. Where the two injections are given in the same limb, they should be administered at least 2.5cm apart. (American Academy of Pediatrics, 2003).

It is not recommended that immunisations be administered in the arm of infants under one year of age.

### Is it possible to give one of these three injections at a later date?

Vaccinations should be completed according to the recommended schedule because it ensures that children are fully protected from serious disease as early as possible. The Department of Health, Social Services and Public Safety recommends that the three vaccines are given at the same time.

## What evidence do we have that PCV can be given safely at the same time as MMR vaccine at 15 months of age?

MMR vaccine and PCV have been given together routinely as part of the US childhood immunisation programme since 2000.

Following its introduction, reports of adverse reactions submitted to the Vaccine Adverse Event Reporting System (VAERS) were closely monitored. The majority of reports identified expected minor adverse events (see section on recognised side effects above). No serious adverse reactions were identified that were caused by the vaccine (Wise *et al.*, 2004).

It is not currently recommended that PCV is given at the same time as the conjugate Hib/MenC booster. This is a precautionary measure until more data accumulates as to whether these two particular conjugate vaccines can be given at the same time without any interference between them.

## Can PCV be given at the same time as non-routine vaccines, e.g. for travel?

PCV can be given at the same time as other vaccines such as flu and hepatitis B vaccines. Each vaccine should be given in separate sites at least 2.5cm apart (American Academy of Pediatrics, 2003a) or in different limbs.

## Is it possible to overload the immune system by giving too many vaccines to children?

From birth, babies' immune systems protect them from the germs that surround them. Without this protection, babies would not be able to cope with the tens of thousands of bacteria and viruses that cover their skin, nose, throat and intestines.

There is no evidence that any vaccine programme overloads a child's immune system. If a baby's immune system was 'overloaded', you would expect to see more infections in vaccinated children compared to unvaccinated children. This has been shown not to be the case in a study that looked at the risk of serious bacterial infections in the first three months after MMR vaccination. Rather than vaccination increasing the rate of bacterial infections, the study found that vaccinated children suffered from fewer bacterial infections than unvaccinated children (Miller *et al.*, 2003).

In theory, a baby could respond safely and effectively to around 10,000 vaccines at any one time (Offit *et al.*, 2002). So the baby can and does easily cope with the additional doses of vaccine in the immunisation programme.

## What about older children who have missed the jab – are they at risk, and will they get the vaccine?

Children under two years of age are at an increased risk of pneumococcal disease compared to older children (Figure 1). All children under two years of age will be offered PCV as part of a catch-up programme.

Older children are at much lower risk from pneumococcal infection so will only be offered the vaccine if they fall into a high-risk group. As more young children are vaccinated, the circulation of pneumococcal bacteria in the population will decline. So, older children and adults will also benefit from the addition of PCV to the infant immunisation programme because of the reduced circulation of pneumococcal bacteria among vaccinated children (herd immunity).

## What vaccination course should children follow if they are identified as being at an increased risk from pneumococcal infection because of a medical condition?

Children at an increased risk from pneumococcal infection include those who have a heart condition, chronic lung disease, chronic liver disease, diabetes mellitus, a weakened immune system, cochlear implants, a damaged spleen or no spleen (see the pneumococcal chapter in *Immunisation against infectious disease*, [www.dh.gov.uk/greenbook](http://www.dh.gov.uk/greenbook)).

Infants under one year of age identified as being at increased risk of pneumococcal infection should have PCV vaccine as routinely recommended at two and four months of age with a booster dose at around 15 months of age.

Children aged over 12 months and under five years of age (who have not previously had PCV vaccine) should receive a single dose of PCV either at the time of their routine appointment at around 15 months, or as soon as possible any time after this up to their fifth birthday.

At-risk children under five years of age who have already received 23-valent pneumococcal polysaccharide vaccine (PPV) should receive one dose of PCV, at least two months after the polysaccharide vaccine.

Children in this age group who have a damaged spleen or no spleen, or who have a weakened immune system, need a second dose of PCV (two months after the first dose) as they may have a reduced immune response to the first dose of the vaccine.

All at-risk children should receive one dose of PPV after their second birthday, and at least two months after the final dose of PCV.

At-risk children aged five years and over are not recommended PCV.

## Glossary of terms

### **Acellular vaccine**

An acellular vaccine contains only parts of cells which can produce immunity in the person receiving the vaccine.

### **Adverse reaction**

A side effect of any medicine, including vaccines.

### **Allergic reactions**

Sensitivity to certain substances that can lead to conditions such as asthma, eczema, hay fever and headache.

### **Anaphylaxis**

An immediate and severe allergic reaction.

### **Antibodies**

Proteins produced by the body to neutralise or destroy toxins and disease-carrying organisms.

### **Bacterium/bacteria**

Single cell micro-organisms, some of which cause disease. Others are essential for our bodies to work properly.

### **Carrier**

A person who is infected but does not show symptoms of a disease.

### **Cellulitis**

A bacterial skin infection.

### **Chronic bronchitis**

Inflammation of the air passages in the lung, characterised by the coughing up of excessive mucus.

### **Commission on Human Medicines (CHM)**

Statutory independent body responsible for advising on the licensing and safety of human medicines.

### **Community (herd) immunity**

The protection conferred on individuals who have not been immunised because sufficient numbers of the rest of the population have been immunised.

### **Conjugate vaccine**

Vaccines made with part of the sugar (polysaccharide) coating of a bacterium being combined (conjugated) with a protein (e.g. tetanus or diphtheria) which makes it work better and gives better protection over a long period of time.

The conjugate vaccines in the childhood immunisation schedule are Hib, MenC and PCV.

### **Contraindication**

A reason why a vaccine should not be given.

### **DTaP/IPV/Hib**

Combined vaccine that protects against five different diseases – diphtheria, tetanus, pertussis (or whooping cough), polio and *Haemophilus influenzae* type b (Hib).

### **Diphtheria**

Diphtheria is a disease that usually begins with a sore throat and can quickly cause problems with breathing. It can damage the heart and nervous system and, in severe cases, it can kill.

### **Efficacy**

The measure of a vaccine's effectiveness. It is measured by the proportion of those immunised who don't get a disease when exposed to it, or by the number of antibodies produced by the immune system.

### **Encapsulated**

Bacterium surrounded by a sugar coat.

### **Epidemiology**

The study of patterns of diseases, including their occurrence, severity and distribution.

### **Epiglottitis**

Inflammation or swelling of the epiglottis that can cause a blockage of the airway, which can be fatal.

### ***Haemophilus influenzae***

The family of bacteria that cause Hib disease. They occur in two forms – those with capsules (encapsulated) and those without (non-encapsulated). Serious disease is usually caused by the encapsulated organism, of which there are six types (a-f). Type b caused the majority of invasive disease before the introduction of Hib vaccine in 1992. Non-encapsulated strains are mainly associated with ear and chest infections.

**Hib**

Hib is an infection that can cause a number of major illnesses such as meningitis, blood poisoning and pneumonia. All of these illnesses can kill if they are not treated quickly.

**Immune response**

The body's response to an immunisation or infection.

**Immunisation**

The priming of the body's immune system with a vaccine.

**Induration**

The hardening of an area around an injection site.

**Invasive disease**

Serious forms of infections where bacteria such as *Pneumococcus*, Hib and *Meningococcus* have entered the bloodstream, leading to septicaemia, or other parts of the body such as the brain, causing meningitis.

**Meningitis**

Meningitis is an infection of the lining of the brain. It is very rare but very serious, although if it's picked up early enough, most people make a full recovery.

***Meningococcus***

*Meningococcus* is a type of bacteria of which there are over 13 serogroups, of which B and C are the most common in the UK although the number of cases of both has dropped greatly in the last few years. Other serogroups such as A, Y, W135, 29E and Z occur much less frequently.

**Mortality rate**

The chances of dying from a particular condition.

**Nephrotic syndrome**

A kidney condition leading to loss of protein.

**Otitis media**

Inflammation of the middle ear, usually due to viral or bacterial infection.

**Pericarditis**

Inflammation of the lining of the heart.

**Pertussis (whooping cough)**

Whooping cough is a disease that can cause long bouts of coughing and choking, which can make it hard to breathe. It can last for up to ten weeks. It is not usually serious in older children, but it can be very serious in babies under one year old.

**Pneumococcal pneumonia**

Pneumonia caused by the *Streptococcus pneumoniae* bacterium.

**Pneumonia**

Inflammation of the lung from a variety of causes, such as viruses and bacteria, particularly *Streptococcus pneumoniae*.

**Poliomyelitis/polio**

A disease caused by a virus that attacks the nervous system, leading to paralysis of the muscles. If it affects the chest muscles, it can kill.

**Polysaccharide vaccines**

Polysaccharide vaccines are manufactured from parts of the sugar (polysaccharide) coat of a bacterium, e.g. *Pneumococcus*, Hib and *Meningococcus*.

**Red Book**

Personal Child Health Record (PCHR).

**Septic arthritis**

Serious infection in a joint.

**Septicaemia**

A serious form of blood poisoning (infection of the blood) due to the bacteria.

**Serotypes**

Different types of the same bacteria.

***Streptococcus pneumoniae***

*Streptococcus pneumoniae* is a type of bacterium, of which there are over 90 different serotypes.

**Surveillance**

The routine monitoring of disease levels, how many people are being immunised against the disease and the impact of immunisation programmes.

## Tetanus

Tetanus is a painful disease that affects the muscles and can cause breathing problems. It is caused by bacteria that are found in soil and manure and can get into the body through open cuts or burns. Tetanus affects the nervous system and, if it is not treated, it can kill.

## Vaccines

Vaccines are manufactured in different ways using part of the germ or virus which causes the disease. Since live, attenuated oral polio vaccine was withdrawn in 2004, they cannot cause the disease for which they give protection.

## Yellow Card reporting scheme

The Yellow Card Scheme is for voluntary reporting of suspected adverse drug reactions (ADRs), including those following vaccination, for routine post-marketing surveillance of medicines. These cards may be completed by parents, carers, doctors, dentists, pharmacists, coroners and nurses, and by pharmaceutical companies under statutory obligations. They are submitted to the Commission on Human Medicines (CHM), Medicines and Healthcare products Regulatory Agency (MHRA).

## References

Anon. (2003) Invasive pneumococcal infection. England and Wales: 2000 *CDR Weekly* 3-9.

American Academy of Pediatrics (2003) Active immunization. In Pickering LK (ed.) *Red Book: 2003 Report of the Committee on Infectious Diseases*. 26th edition. Elk Grove Village, IL: American Academy of Pediatrics, p 33.

Bedford H, de Louvois J, Halket S *et al.* (2001) Meningitis in infancy in England and Wales: follow-up at age 5 years. *BMJ* 323: 533-6.

Black SB, Shinefield HR, Ling S *et al.* (2002) Effectiveness of heptavalent pneumococcal conjugate vaccine in children younger than five years of age for prevention of pneumonia. *Pediatr Infect Dis J.* 9: 810-5.

Centers for Disease Control and Prevention (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 Morb Mortal Wkly Rep.* 54: 893-7.

Eskola J, Kilpi T, Palmu A *et al.* (2001) Finnish Otitis Media Study Group. Efficacy of a pneumococcal conjugate vaccine against acute otitis media. *N Engl J Med.* 344: 403-9.

Goldblatt D, Southern J, Ashton L *et al.* (2006) Immunogenicity and boosting after a reduced number of doses of a pneumococcal conjugate vaccine in infants and toddlers. *Pediatr Infect Dis J.* 25: 312-9.

Health Protection Agency.  
[www.hpa.org.uk/infections/topics\\_az/pneumococcal/menu.htm](http://www.hpa.org.uk/infections/topics_az/pneumococcal/menu.htm)

Hussain M, Melegaro A, Pebody RG *et al.* (2005) A longitudinal household study of *Streptococcus pneumoniae* nasopharyngeal carriage in a UK setting. *Epidemiol Infect.* 133: 891-8.

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

Melegaro A, Edmunds WJ, Pebody R *et al.* The current burden of pneumococcal disease in England and Wales (2006). *J Infect.* 52: 37-48.

Miller E, Andrews N, Waight P *et al.* (2003) Bacterial infections, immune overload, and MMR vaccine. Measles, mumps, and rubella. *Arch Dis Child.* 88: 222-3.

Offit PA, Quarles J, Gerber MA, *et al.* (2002) Addressing parents' concerns: do multiple vaccines overwhelm or weaken the infant's immune system? *Pediatrics.* 109: 124-9.

Whitney CG (2005). Impact of conjugate pneumococcal vaccines. *Pediatr Infect Dis J.* 24: 729-30. Review.

Wise RP, Iskander J, Pratt RD *et al.* (2004) Postlicensure safety surveillance for 7-valent pneumococcal conjugate vaccine. *JAMA.* 292: 1702-10.



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