Vaccination for vulnerable infants

Immunisation has been an important part of the health care of children in the UK since the introduction of vaccination against smallpox in the early 19th century. Many infectious diseases that were previously the most important causes of death and disability in childhood can now be prevented. In this article, the routine childhood immunisation programme is briefly described, and issues that may be particularly relevant to specific vulnerable groups of infants are highlighted.

Helen E Bedford
BSc, MSc, PhD, RGN, RHV, M(Hon)FPH, FRCPCH
Senior Lecturer in Children's Health
Centre for Paediatric Epidemiology and Biostatistics
Institute of Child Health, London

David A C Elliman
DCH, FRCP, FRCPCH, FFPH
Consultant in Community Child Health
Child Population Health Department
Great Ormond Street Hospital for Children

Keywords

vaccination; immune response; contraindications; risk; MMR vaccine; hepatitis B; pneumococcal vaccines; prematurity; RSV infection

Key points

Bedford, H.E., Elliman, A.C. (2005) Vaccination for vulnerable infants *Infant* 1(5): 144-148.

1. In every instance the benefits of vaccination outweigh any potential adverse reactions.
2. Often vaccination is omitted or delayed from the care of sick infants, yet it is they who need it most.
3. Midwives have a vital role to play in ensuring infants are adequately immunised.

Over the last 60 years a comprehensive programme of vaccination has developed[1]. Although there are some variations in timing and not all countries have the same policies for the use of a few vaccines, there is broad agreement on most of the core programme amongst industrialised nations[2]. The programme is a balance between immunising early to gain protection against diseases such as pertussis, which has its greatest mortality in young infants[3], whilst producing an adequate immune response[4]. **TABLE 1** sets out the current UK schedule.

The change from whole cell to acellular pertussis and from oral live attenuated to injected inactivated polio vaccines took place in the autumn of 2004. Prior to that, the most recent major change to the programme was the introduction of the conjugate meningococcal C vaccine in 1999. As a result, there has been a large reduction in disease caused by this organism from 983 cases in 1999 to 98 in 2003. The introduction of Hib vaccine in 1992 had an even greater effect on Hib disease – in 1998 there were 37 laboratory reports of Hib disease compared with 867 in 1990. This rose to 269 in 2002, but fell to 122 in 2004 after a one-off booster was given to all children under 4 years old. The need for a routine booster is being considered.

Adverse reactions

While most people accept the benefits of vaccination, there is still a lot of confusion about possible side effects and contra-indications. Most vaccines may give rise to mild to moderate local reactions as well as systemic effects such as pyrexia and malaise. Rarely (less than 1 in 100,000 doses), a vaccine may cause anaphylaxis. Some vaccines have more specific side effects, e.g. mild measles after MMR vaccine and encephalitis after yellow fever vaccine. In every instance the benefits of the vaccine outweigh any potential adverse reactions. Unfortunately scares about vaccine safety can develop quickly and that surrounding MMR is the most recent example in the UK.

Contraindications

With increasing experience and research, the number of contraindications has declined considerably. In the UK all vaccines are contraindicated where the recipient has had an anaphylactic reaction to a previous dose of vaccine or one of its constituents. Vaccination should be postponed if the recipient has an acute illness, especially with a fever, or is pregnant (**TABLE 2**).

Live vaccines (e.g. BCG and MMR) may also be contraindicated where the recipient has an abnormality of the immune system. This will depend on the type of vaccine and the nature of the abnormality and there are exceptions, e.g. MMR may be given to people who are HIV positive, but asymptomatic[5].

Measles, mumps and rubella (MMR) vaccine

Although the combined MMR vaccine is not given until the first birthday, parents may ask neonatal practitioners for advice about this vaccine as well as the others, particularly since over the last seven years there has been a lot of publicity around the vaccine, much of it adverse and misleading.

The controversy centres on whether the vaccine might cause autism or inflammatory bowel disease (IBD). In 1998 a paper was published suggesting that autism might be caused by bowel disease in young children[6]. One of the authors suggested MMR vaccine might be the cause of the bowel disease in some children. This caused a fall in the uptake of

Age	Vaccine(s)
Soon after birth	Hepatitis B and BCG to those at risk*
4 weeks	Hepatitis B for those at risk*
8 weeks	Diphtheria/tetanus/acellular pertussis/inactivated polio/Hib vaccine (DTaP/IPV/Hib) and meningococcal C (Men C)
8 weeks	Hepatitis B for those at risk*
12 weeks	DTaP/IPV/Hib and Men C
16 weeks	DTaP/IPV/Hib and Men C
12 months	Measles/mumps/rubella (MMR)
12 months	Hepatitis B for those at risk*
3.5 years	DTaP/IPV 2nd dose of MMR if not given earlier
School leavers	Low dose diptheria/tetanus/IPV (dT/IPV)

* See text

TABLE 1 UK childhood immunisation programme.

the vaccine of over 10%[7]. Since then, a large number of studies have shown no evidence of such a link and uptake rates are beginning to recover[8]. One of the most recent studies was a large case control study looking at children diagnosed with autism in a number of UK General Practices. The researchers found that autism was no commoner in children receiving MMR vaccine than in those not receiving the vaccine[9]. Honda and colleagues found that the ascertained incidence of autism in Japan continued to rise in spite of the withdrawal of the combined MMR vaccine[10]. There is no evidence to support the use of the single measles, mumps or rubella vaccines and they are not licensed for use in UK.

Neonatal vaccination

In the UK, no vaccines are recommended for all neonates, however hepatitis B and BCG vaccines may be indicated for some. Influenza and pneumococcal vaccines may be indicated for some infants who have had a stormy neonatal course or who have chronic conditions.

Hepatitis B

In Europe the commonest source of infection with hepatitis B virus in children is by vertical transmission, i.e. from the mother at or around the time of birth. Babies infected in this way are highly likely to become carriers and, while this is unlikely to cause problems in childhood, about 25% will have potentially fatal liver disease as adults.

Selective screening of pregnant women frequently failed to pick-up those women carrying the virus[11]. From April 2000, all pregnant women should have been offered the opportunity to be tested for hepatitis B infection[12]. If a woman is found to be a carrier, a course of four doses of vaccine (at birth, 1 month, 2 months and 12 months) would be recommended for her baby.

The vaccine is produced from a genetically modified yeast and the contraindications to a killed vaccine apply; it can be given at the same time, or at any interval from, any other vaccine being given. Depending on the results of the mother's tests for e antigen and e antibody some neonates should also be given hepatitis B immunoglobulin The only circumstance in which immunoglobulin should not be given is where e antibody is present in the mother. Blood should be taken at a year or more old, to check that the child has not become infected.

If children receive the full course of vaccine, there is only a very small failure rate (5-10%). A much more common reason for babies failing to become protected is that they do not receive the full course of vaccine. Many of the affected pregnant women are among hard to reach groups such as refugees, asylum seekers and the homeless and they may not speak English. They often move frequently in the first year after giving birth and difficulty in accessing routine services may result in them not being followed up. It is very important that there is a system in place to ensure that this does not happen. Where hepatitis B is relatively common, the appointment of a health visitor or midwife with special responsibility for the programme has ensured that there is a high uptake of the vaccine[13]. No booster

Possible contraindication	Joint Committee on Vaccination and Immunisation Guidance	
	1996[1]	2004[1]
Pregnancy	+	+
Acute infection with fever and/or systemic upset	+	+
Previous severe local or systemic reaction	++	-
Anaphylactic reaction to a previous dose of the vaccine or a constituent	++	++
Static neurological disorder	-	-
Evolving neurological disorder	Consider postponement	Consider postponement
Personal or family history of convulsions	-	-
Immunosuppression	±	±
Prematurity	-	-

Key:
++ absolute contraindication
\+ contraindication, unless risk of infection high
\- not a contraindication
± may be a contraindication for some live vaccines, depending on the nature of the immunosuppression[5]

TABLE 2 Possible contraindications to vaccination.

Age	Maternal serology	
	Maternal e antibody positive or unknown	Maternal e antibody negative
Birth	Hepatitis B vaccine	Hepatitis B vaccine and Hepatitis B immunoglobulin
4 weeks	Hepatitis B vaccine	Hepatitis B vaccine
8 weeks	Hepatitis B vaccine	Hepatitis B vaccine
1 year*	Hepatitis B vaccine	Hepatitis B vaccine

* Serology can be checked at this visit or two-three months later

TABLE 3 Hepatitis B schedule for high risk infants.

doses of vaccine are needed.

Apart from ensuring that the baby is immunised it is also important that the mother is followed up and all her sexual partners and children are tested for infection. Those uninfected should be immunised, whereas those infected should be referred to a specialist as in some cases treatment may be appropriate.

Bacille Calmette-Guérin (BCG) vaccine for tuberculosis

The incidence of TB had been declining in England and Wales for at least 100 years. However, in the late 1980s, reports of TB in England and Wales (plus other European countries and the USA) began to rise. This rise has now slowed, but it continues, particularly in urban areas such as London. A recent report emphasises the increase in children with TB in London[14]. In 2002, the incidence of TB was highest in Black Africans (280/100,000) with people originating from the Indian subcontinent having a rate of 127/100,000 and the white population of 4/100,000. Recent studies have shown that TB continues to be strongly associated with poverty, and some of the current increase in incidence has been attributed to the expansion in the homeless population[15].

As part of a NICE guideline on tuberculosis[16] the efficacy of BCG vaccine given to neonates was reviewed. There was a wide variation in results, but protection against pulmonary disease in the UK was of the order of 74% and higher against disseminated disease.

Until September 2005, BCG vaccination was routinely offered to all children at 12-13 years of age and to neonates at high risk of TB (e.g. those born to parents from countries with a high prevalence of TB; those likely to stay in Africa, Asia, Central or South America for more than one month; and those with a close, recent family history of TB). The universal schools' programme has now ceased and more emphasis is being put on the neonatal programme and children at higher risk[17]. It is recommended that, in areas where the incidence of TB is greater than, or equal to, 40 cases per 100,000 population, all neonates should be offered the vaccine. Children over 12 months old, should have a Mantoux test before receiving the vaccine.

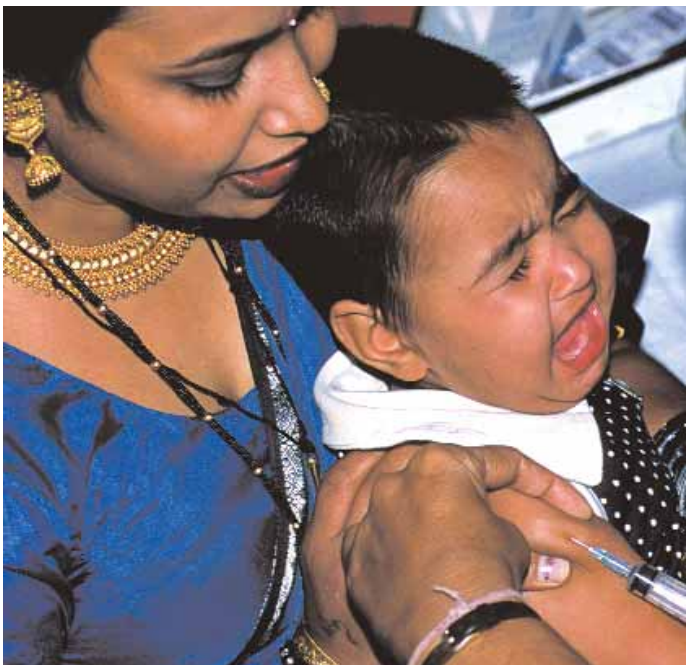

FIGURE 1 A moment of pain may prevent a lifetime of suffering.
Photo: Copyright: WHO/P.Virot.

The vaccine is given intradermally – a difficult procedure that should only be carried out by those who have been appropriately trained and who perform reasonable numbers so as to maintain their skills. The vaccination may be given before the baby leaves hospital or up to several weeks after discharge. In the latter case it is important that the baby is followed up to ensure vaccination is given. It is a common experience that uptake is low[18] and as with the neonatal hepatitis B programme, it may be appropriate for one person, a health visitor or midwife, to take responsibility for delivering the programme.

Influenza and pneumococcal vaccines

Unlike in the USA, currently, neither of these vaccines is given routinely to children in the UK. They are indicated for high risk groups, including those with chronic respiratory, heart, liver or renal disease, diabetes and immunosuppression. In addition, pneumococcal vaccine is indicated in those with splenic dysfunction, chronic liver disease, individuals with cochlear implants and potential or actual CSF leaks, or children under five years old who have previously had invasive pneumococcal disease[1]. Pneumococcal vaccine is given from two months and inflenza vaccine from six months of age.

Prematurity

It has been observed that some premature babies have low levels of antibodies prior to immunisation and so it is very important that immunisations are not delayed[19]. The date of immunisation should be calculated from the child's actual date of birth, not from the expected date of delivery. Therefore some babies will be immunised while they are still in special care or neonatal units. Following immunisation, most premature babies will become immune to the diphtheria, tetanus, pertussis and polio components of vaccines[4]. However there is some evidence that they do not always mount an adequate response to the conjugate vaccines – Hib, meningococcal C and pneumococcal conjugate.

Hib antibodies following the vaccination of premature infants are lower than those in term infants and more preterm infants

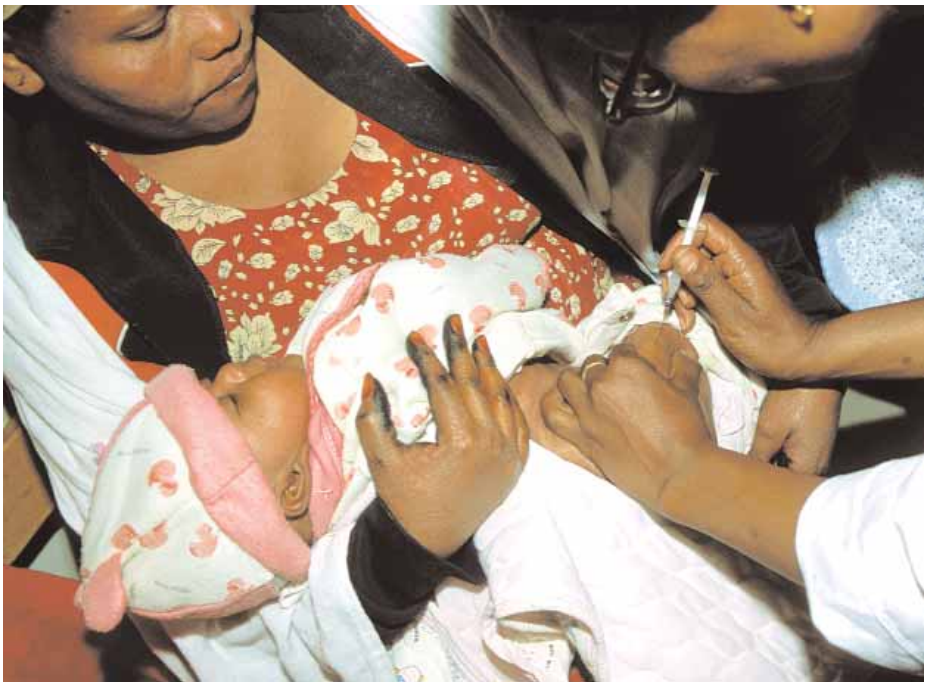

FIGURE 2 Immunisation has dramatically reduced the incidence of many life threatening diseases throughout the world. *Photo: Copyright: WHO/P.Virot.*

fail to develop protective levels of antibody[20]. The initial responses to meningococcal C vaccine are not significantly different from those in term infants[20], but there is some evidence that they wane more quickly[21]. Similarly the initial response to a heptavalent pneumococcal conjugate vaccine was adequate, but waned. The evidence with respect to hepatitis B vaccine is conflicting. A large study[22] suggested that preterm babies gained as much protection as term babies, but there were few very small babies included in the study. Another study found that antibody levels were much lower in some premature babies leaving them unprotected[23]. In view of these findings, it has been suggested that, for babies born at 28 weeks' gestation or earlier, blood samples should be tested after completing their immunisations to check that they do have adequate protection against meningococcal C, Hib, pneumococcal and hepatitis B vaccines. On the other hand, if boosters for the conjugate vaccines become routine, this may not be necessary.

On the whole premature babies do not have an increase in adverse reactions to vaccines, in fact, they tend to have fewer reactions[4]. The exception to this generalisation is where premature infants have a history of apnoea, bradycardia or desaturations[24]. Some of these infants may have an increase in apnoea, bradycardia and/or desaturations in the 48 hours after the first injection of DTaP/IPVHib vaccine. This was found to be commoner in infants still having episodes of instability than in those where they had ceased. Most of these episodes were mild, but a few required brief intervention. This evidence is therefore not a reason to withhold immunisation, but for re-introduction, or continuation, of cardiorespiratory monitoring in high risk infants.

Steroid treatment for chronic lung disease

Some premature babies may be treated with corticosteroids for chronic lung disease. Although immunosuppression is not a contraindication to any of the UK primary course of vaccines as none are live vaccines, steroids may reduce the immunological response to some vaccines, rendering them less effective. Reduced immunogenecity to Hib, has been reported, in such babies[25]. However a fourth dose 6 weeks after the completion of the course, provided no benefit[26]. The same group of researchers, found that responses to a primary course of DTP were adequate[27].

Prophylaxis of respiratory syncytial virus (RSV) infection

RSV infection is an important cause of readmission in premature babies and such infection may result in long term morbidity[28]. It is unlikely that a vaccine will become available in the next five years[29]. However a monoclonal antibody preparation has been shown to provide protection in high risk infants[30]. In the UK it is recommended that its use should be reserved for babies under 2 years of age with severe chronic lung disease, on home oxygen during the RSV season[31].

Conclusion

There are many safe and effective vaccines available for children. Some additional vaccines are given to selected neonates. However special attention is required to ensure that those who would benefit from these vaccines receive them. Often vaccination is omitted, or delayed, from the care of sick infants, yet it is they who need it most. Midwives have an important role to play and are well placed to ensure that the obstacles to delivering some of these vaccines are overcome. Parents should be provided with the Department of Health Immunisation leaflets. Where a parent requires more information, factsheets can be downloaded from the Department of Health website[32]. If parents still require more information, they can be referred to the appropriate paediatrician. Any immunisations given should be notified to the GP and Health Visitor, and recorded in the Personal Child Health Record.

References

1. **Department of Health.** Immunisation against infectious disease. London, HMSO, 1996. http://www.dh.gov.uk/PolicyAndGuidance/HealthAndSocialCareTopics/GreenBook/GreenBookGeneralInformation/GreenBookGeneralArticle/fs/en?CONTENT_ID=4097254&chk=isTfGX. Accessed 9.7.05.
2. **World Health Organisation.** WHO vaccine preventable diseases monitoring system 2004 global summary. WHO, Geneva, 2004. (Available on the world wide web at http://www.who.int/vaccines-documents/GlobalSummary/GlobalSummary.pdf).
3. **Crowcroft, N.S., Booy, R., Harrison, T. et al.** Severe and unrecognised: Pertussis in UK infants. *Arch Dis Child* 2003; **88**(9): 802-06.
4. **Ramsay, M.E., Miller, E., Ashworth, et al.** Adverse events and antibody response to accelerated immunisation in term and preterm infants. *Arch Dis Child* 1995; **72**: 230-32.
5. **RCPCH.** Immunisation of the Immunocompromised Child. Best Practice Statement. February 2002. http://www.rcpch.ac.uk/publications/recent_publications/Immunocomp.pdf.
6. **Wakefield, A.J., Murch, S.H., Anthony, A. et al.** Ileal-lymphoid nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. *Lancet* 1998; **351**: 1327-28.
7. **Health Protection Agency.** COVER (Cover of Vaccination Evaluated Rapidly): a programme for evaluating childhood immunisation. http://www.hpa.org.uk/infections/topics_az/vaccination/vac_cover.htm. Accessed 9.7.05.
8. **Sengupta, N., Bedford, H., Elliman, D., Booy, R.** Does

the MMR triple vaccine cause autism? *Evidence-Based Healthcare & Public Health* 2004; **8**: 239-45.
9. **Smeeth, L., Cook, C., Fombonne, E., et al.** MMR vaccination and pervasive developmental disorders: A case-control study. *Lancet* 2004; **364**(9438): 963-69.
10. **Honda H, Shimizu Y, Rutter M.** No effect of MMR withdrawal on the incidence of autism: A total population study. *J Child Psychol Psychiatry* 2005; **46**(6): 572-79.
11. **Chrystie, I., Sumner, D., Palmer, S., Kenney, A., Banatvala, J.** Screening of pregnant women for evidence of current hepatitis B infection: Selective or universal? *Health Trends* 1992; **24**(1): 13-15.
12. **NHS Executive.** Screening of pregnant women for hepatitis B and immunisation of babies at risk. HSC 1998/127.
13. **Larcher, V.F., Bourne, J., Aitken, C., Jeffries, D., Hodes, D.** Overcoming barriers to hepatitis B immunisation by a dedicated hepatitis B immunisation service. *Arch Dis Child* 2001; **84**: 114-18.
14. **Atkinson, P., Taylor, H., Sharland, M., Maguire, H.** Resurgence of paediatric tuberculosis in London. *Arch Dis Child* 2002; **86**: 264-65.
15. **Communicable Disease Surveillance Centre.** (2002) Disease Facts. http://www.phls.co.uk/facts/TB/TB%20Tables%20and%20figures/TBsurvey1998ethnic.htm. Accessed 9.7.2005.
16. **NICE.** Tuberculosis – full guideline, first consultation. http://www.nice.org.uk/page.aspx?o=263081. Accessed 09.07.05.
17. **Department of Health.** Changes to the BCG Vaccination Programme. PL/CMO/2005/3. http://www.dh.gov.uk/assetRoot/04/11/49/96/04114996.pdf. Accessed 9.7.05.
18. **Tseng, E., Nesbitt, A., O'Sullivan, D.** Audit of the implementation of selective neonatal BCG immunisation in south east London. *Commun Dis Rep CDR Rev* 1997; **7**(11): R165-8.
19. **Ruggeberg, J.U., Collins, C., Clarke, P. et al.** Immunogenicity of the heptavalent pneumococcal conjugate vaccine (PCV7) in preterm UK infants and infection of immunological memory. 23rd Annual Meeting of the European Society for Paediatric Infectious Diseases-ESPID. Valencia, Spain, May 8-20, 2005.
20. **Slack, M.H., Cade, S., Schapira, D. et al.** DT5aP-Hib-IPV and MCC vaccines: Preterm infants' response to accelerated immunisation. *Arch Dis Child* 2005; **90**(4): 338-41.
21. **Collins, C.L., Ruggeberg, J.U., Balfour, G. et al.** Immunogenecity and Immunological Memory of Meningococcal Conjugate Vaccine in Premature Infants. PIDJ. In press.
22. **Belloni, C., Chirico, G., Pistorio, A. et al.** Immunogenicity of hepatitis B vaccine in term and preterm infants. *Acta Paediatr* 1998; **87**(3): 336-38.
23. **da Motta, M.S.F., Mussi-Pinhata, M.M., Jorge, S.M. et al.** Immunogenicity of hepatitis B vaccine in preterm and full term infants vaccinated within the first week of life. *Vaccine* 2002; **20**: 1557-62.
24. **Pfister, R.E., Aeschbach, V., Niksic-Stuber, V., Martin, B.C., Siegrist, C.A.** Safety of DTaP-based combined immunization in very-low-birthweight premature infants: Frequent but mostly benign cardio-respiratory events. *J Pediatr* 2004; **145**(1): 58-66.
25. **Robinson, M.J., Campbell, F., Powell, P., Sims, D., Thornton, C.** Antibody response to accelerated Hib immunisation in preterm infants receiving dexamethasone for chronic lung disease. *Arch Dis Child Fetal Neonatal Ed* 1999; **80**(1): F69-71.
26. **Clarke, P., Powell, P.J., Goldblatt, D., Robinson, M.J.** Effect of a fourth *Haemophilus influenzae* type b immunisation in preterm infants who received dexamethasone for chronic lung disease. *Arch Dis Child Fetal Neonatal Ed* 2003; **88**(1): F58-61.
27. **Clarke, P., Robinson, M.J., Powell, P.J.** DTP immunisation of steroid treated preterm infants. *Arch Dis Child Fetal Neonatal Ed* 2004; **89**(5): F468.
28. **Greenough, A., Alexander, J., Burgess, S., et al.** Health care utilisation of prematurely born, preschool children related to hospitalisation for RSV infection. *Arch Dis Child* 2004; **89**(7): 673-78.
29. **Handforth, J., Sharland, M., Friedland, J.S.** Prevention of respiratory syncytial virus infection in infants. *BMJ* 2004; **328**: 1026-27.
30. **The IMpact-RSV Study Group.** Palivizumab, a humanized respiratory syncytial virus monoclonal antibody, reduces hospitalisation from respiratory syncytial virus infection in high-risk infants. *Pediatrics* 1998; **102**(3 Pt 1): 531-37.
31. **Joint Committee on Vaccination and Immunisation.** Minutes of the Meeting h 2002. http://www.advisorybodies.doh.gov.uk/jcvi/mins01nov02.htm).
32. **Department of Health.** Immunisation Information. http://www.immunisation.net/. Accessed 9.7.05.