

Child health policy

# The National Service Framework for Children

A Craft

“Children are the living message we send to a time we will not see”<sup>1</sup>

There is an increasing recognition that the wellbeing of the pregnant mother, foetus, and growing child are important determinants of health in later life. However, the effects may not become apparent until at least the age of 50. Although Churchill said that one of the best investments a government can make is to put milk into the stomachs of children, it would be a brave and farsighted political party that would invest in something which was not going to show any real benefits within a parliamentary time scale or two—that is, a maximum of 10 years.

We have seen over the last few years that children are a high priority for the government of the UK across a broad spectrum. The recognition that the future of our nation depends on the education of children was highlighted by the Prime Minister’s assertion of his priorities: “Education, education, education”. The Chancellor of the Exchequer has been trying hard to end child poverty and to reduce the gap between rich and poor. Youth offending and behaviour have been the target of much action. But what of health?

The long awaited National Service Framework (NSF) for Children for England was recently published.<sup>2</sup> A separate NSF for Children for Wales has also appeared.<sup>3</sup> The messages in both are similar but the Welsh version comes with more of an action plan. The NSFs were part of the NHS Modernisation Plan, and several have already been published. For example, the NSF for cancer has been particularly effective in improving services, and the falling death rate across all ages is a tribute to it. Of course, the UK is only just catching up with much of Europe, which has long had better access to services which are much better funded. Cardiovascular, diabetes, mental health, and renal disease are some of the other NSFs. The children’s NSF is different. It covers a complete age group rather than a disease and, unlike the first NSFs much more importantly, it comes without any hypothecated money. The early NSFs had clear targets but these have

been replaced by standards with suggestions as to how to measure whether local services meet these standards.

The publication of the children’s NSF has coincided with announcements of several other government initiatives aspiring to improve the lives of children—for example, Every Child Matters and the Children Act 2004. There is a risk that its impact and implementation strategy will be confused during the range of multi-agency work needed to achieve such an ambitious programme, so that health and healthcare services for children may not receive the attention they deserve. Much targeted work within the health service ought to take place during implementation while forwarding the cross agency work given so much attention in the NSF reports.

There is much to welcome in the NSF. The importance of health to all of the other initiatives for children is recognised. Educational achievements will be greater if children are healthy. Many patterns of health are established in childhood, and lifelong health depends on a good early start. Parents are the most important people in children’s lives, and stable relationships, safe homes, and economic opportunities are vital for health. Public services are there to help parents with their vital responsibilities.

There are a few new ideas. By one year of age, there will be a comprehensive assessment of physical, social, and emotional development along with family needs. Therapy services will be readily available to all who need them. School diets will be improved, and there should be 60 minutes of exercise each day. All disabled children will have a key worker, and methods will be put in place to reduce stress levels in carers. There are clear recommendations around improving the safety and efficacy of medicines for children.

The NSF is made up of 11 modules and each contains important messages. They cover the whole spectrum of childhood from the maternity module through to adolescence and the transition to adulthood. One of the most

important is that on Medicines for Children. At present the majority of medicines prescribed for children are not licensed for that purpose. There is a clear need to undertake work to improve this state of affairs and to move towards a situation where we have the right medicine, for the right illness, tailored to the child’s individual needs, in the most appropriate formulation, and all backed up by evidence. The new clinical trial networks, recently announced by the Secretary of State, including one for children, will go a long way to achieving this important aim. The networks are modelled on those for cancer which have resulted in an increase of all patients with cancer going into trials from 2% to 7%.

The Maternity Services module gives clear guidance on how to build neonatal networks for which some money has been made available. The mental health section is also important given the increasing recognition of morbidity in this area.

Little attention has been given in the NSF to the extensive existing Department of Health guidance on the care of children in hospital and community settings or to why local implementation of these reports has not made greater progress—not through a lack of local advocacy by dedicated healthcare professionals but largely resulting from the limited priority given to children’s healthcare services. From this experience, for the NSF to succeed there is a need for central and regional direction and either dedicated funding or robust performance management to support the enthusiasm and involvement of local healthcare providers.

There is a programme of children’s topics in the work programmes of the National Institute for Health and Clinical Excellence (NICE) and the Healthcare Commission to assist in implementation, including national audits and the Confidential Enquiry into Maternal and Child Health (CEMACH) deaths enquiries.

Recognising that children are sick is perhaps more difficult than it might at first appear. The decreasing numbers of babies and children who are really sick means that new ways have to be found to educate and update all professionals. Dr Ffion Davies has produced a DVD entitled “Spotting the Sick Child”,<sup>4</sup> 11 000 copies of which have been distributed to a wide range of professionals.

Children and parents should expect accessible services that are clearly understandable, with user friendly information about conditions. Both should be involved in decision making in partnership with health professionals

and services should be effective, well coordinated, and achieve the desired outcome. Motherhood and apple pie? Perhaps so, but the present services often do not adhere to these principles.

The NSF is not prescriptive, and in line with NHS policy it will be left to local initiative to ensure that the standards are met. There will be no central direction. There are messages for clinicians: use evidence based initiatives, consider the child's "illness journey", maintain competence, value teamwork, make clinical decisions with parents, and where possible develop flexible services.

There is much here that is good, but is it likely to be implemented and make a difference? Is the government really taking children seriously? As I mentioned earlier, there is no money dedicated to it. Health policy needs to recognise children as a priority. There are no long trolley waits, and very few children die for lack of care, and so children are often forgotten when priorities are set. There is a huge initiative on chronic disease management in adults, but children and their families suffer too. Children and young people want choice, yet a serious shortage of trained professionals makes this impossible in the near future. Choice—which is a key issue in health policy—is therefore not an option for children.

In spite of the policy of decentralisation of power, a clear message must come from the centre that strategic health authorities and primary care trusts must take children's health seriously. They particularly need to focus on those children with complex health needs and serious disability. The quality of life of the whole family is affected by a lack of coordinated services. They bear the brunt, children are excluded from school, and they do not achieve their full potential.

More and more can be done, and is expected, for children thanks to medical advances. However, local services are not able to meet their needs when they are discharged from hospital. Will this initiative work and make a real difference to the health of

children and the lives of them and their families?

In the commissioning of services it needs to be recognised that planning cannot succeed at a very local level, and the entire spectrum of care needs must be considered. Managed networks of care covering the whole of the patient's illness journey need to be developed. The importance of multi-agency working is stressed. Although implementation is not compulsory, the inspection agencies (the HealthCare Commission in conjunction with OFSTED) will have a key role to play in ensuring that standards are met.

But what can central government do to help? They can continue to reduce inequalities in opportunity for children and families—this means reducing and ending child poverty. Indeed, reduction in poverty has the potential to improve health much more than health service interventions. The importance of child poverty is recognised but measures aimed at its reduction may increase inequalities unless there is targeted action; there is limited emphasis given to how this might be achieved.

Children's interests cross government department boundaries, and the development of information systems that cross boundaries is paramount. Health, social services, and education would be a start, but others could be usefully included. There are moves to have a single individual record number for all of these services and, if the confidentiality problems can be overcome, a single electronic patient record as proposed by the National Programme for Information Technology (NPFIT) could make a real difference.

In December 2004 the National Director for Mental Health produced his five year report following the publication of the mental health NSF. He reported suicide rates at their lowest recorded level, most users of services having a positive experience, staff numbers increasing, and much more. The Health Minister welcomed the report and announced a further £30 million in investment for general psychiatric intensive care. Similar improvements

have been seen in cancer services, cardiovascular disease, and diabetes. Unfortunately there are no such clear outcome measures that can be identified in the children's NSF.

There has been a large investment in child and adolescent mental health services and money made available to develop neonatal intensive care. However, it will take substantial investment in all healthcare services for children to ensure that in five years' time the National Director of Children's Services can write a similarly glowing report.

It is almost 30 years since the last comprehensive review of children's services by the late Donald Court. It took many years for its important recommendations to be implemented. The National Director of Children's Services, Professor Al Aynsley Green, has put enormous energy and enthusiasm into the NSF. He has managed to persuade all government departments to think about children. He should be congratulated on the birth of an NSF weighing in at 2.4 kg. It is an excellent blueprint, and could be implemented over the next 5–10 years. However, it will need real and committed priority given to children across government departments, a clear implementation plan, and deserves to have targeted funding.

*Arch Dis Child* 2005;**90**:665–666.  
doi: 10.1136/adc.2004.066225

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Accepted 4 April 2005

Competing interests: none declared

## REFERENCES

- 1 Postman N. *The disappearance of childhood*. US: Vintage Books, 1994.
- 2 National Service Framework for Children, Young People and Maternity Services. London: Department of Health 2004.
- 3 A National Service Framework for Children in Wales. Cardiff: Department of Health 2004.
- 4 Davies F. Spotting the sick child—an educational tool for health care practitioners. DVD. London: Department of Health, 2004.

# Conjugate vaccines

A Finn, P Heath

## Time for more of them or less of them?

It all used to seem so simple with conjugate vaccines. You added them to your infant schedule and, faster than anyone had dared to hope, the disease more or less vanished.<sup>1,2</sup> Not only did immunisation protect against invasive disease but it reduced upper respiratory carriage rates too,<sup>3</sup> so there was herd immunity. Even when odd, unexpected mixing problems cropped up out of the blue—like acellular pertussis and *Haemophilus influenzae* type b (Hib) combinations<sup>4,5</sup>—it didn't really seem to matter.<sup>6</sup> In 1999 we watched as meningococcus group C (MenC) set off down the path to oblivion<sup>7,8</sup> previously trod by Hib in 1992.<sup>9</sup>

Then, suddenly, with the arrival of the new millennium, it began to get more complicated. With the MMR vaccine scare still buzzing in people's heads and the schedule busier with the addition of MenC, the 7-valent pneumococcal conjugate vaccine turned up in 2001 with a central European licence and unassailable evidence showing that it prevents invasive pneumococcal disease<sup>10</sup> leading to its general introduction in the USA in 2000. The way this vaccine arrived was in stark contrast to MenC—which was a programme driven by strategic thinking from within the UK Dept of Health<sup>11</sup> in which three manufacturer's had responded to the call and an enthusiastic public waited impatiently for a partial solution to the problem of meningococcal disease which they knew of and dreaded. Here was a vaccine specifically developed by one manufacturer, who had, by a combination of luck and shrewd judgement, stolen the march on all other contenders, with the US market as their primary target. (The luck was that the conjugates in their vaccine turned out to be very immunogenic: the US Food and Drug Administration takes the very inflexible view that new vaccines admitted to the marketplace must be at least as "good", as judged by immunogenicity, as any already there. As a result, development of several subsequent vaccines by other manufacturers, all of which would almost certainly have been highly effective,<sup>12</sup> has been dropped as it became apparent they would not reach the lucrative US

market). Anyway, the British public had never heard of pneumococcus—the name suggested pneumonia not meningitis, and people thought pneumonia was an illness of the elderly. So a new vaccine was suddenly available, which few people, if any, realised they wanted or needed and the purchase of which would cost more, by some distance, than all the existing routine childhood vaccines put together. On the face of it, this was hardly a five star political opportunity.

Just as the prolonged period of head scratching about this got underway, it was noticed that more cases of Hib disease were occurring.<sup>13</sup> For a decade the UK had been using three priming doses of Hib vaccine in early infancy and, unlike most anyone else, no boosting dose in the second year, and apparently getting away with it.<sup>14,15</sup> But not any more. The lower primary antibody responses to Hib when combined with acellular pertussis vaccines first noted in the mid-1990s<sup>4,5</sup> turned out to matter after all.<sup>16</sup> In addition, the cohort of older children immunised in the first catch up programme in 1992–93 had now grown up so that all children aged up to 10 years had received Hib vaccine only in infancy. The catch-up campaign's contribution to herd immunity had been more important than previously appreciated. In 2003 a repeat catch-up programme was implemented to plug the gap.<sup>17</sup> But seeds of doubt concerning unboosted priming schedules had been sown. Sure enough, data on MenC effectiveness has duly confirmed that long term protection of those immunised with three doses as infants is poor, but is much better in those immunised with only one dose aged 1 year or older.<sup>18</sup>

So policy makers are now confronted not only with the question of whether and how to introduce universal conjugate pneumococcal immunisation<sup>19</sup> but also questions about the best future schedules for Hib and MenC. It would make sense to make changes to the schedules for these three vaccines all at once rather than piecemeal, given the need to keep everyone involved properly and clearly informed and considering that even the introduction of simpler

and less reactogenic vaccines in September 2004 induced a flurry of anxious media reports.<sup>20</sup> A quirk of history (the decision to undertake initial Hib conjugate immunogenicity studies in Finland using their three dose DTP schedule<sup>21</sup>) determined the design of initial efficacy studies<sup>22,23</sup> and precipitated the common licensure and use of three priming Hib vaccine doses in infancy. This in turn seems to have set the standard for subsequent thinking about all conjugate vaccines, even though the Finns themselves went on to show that two priming doses were fine<sup>24</sup> and use a schedule of two doses in early infancy and a booster early in the second year to this day.<sup>25</sup> They even showed good priming, despite somewhat lower antibody responses, after only one dose of Hib–OMP and –tetanus conjugate vaccines,<sup>26</sup> the immunological basis for which has been the subject of subsequent study.<sup>27</sup> Phase two studies with MenC CRM197 conjugates also suggested that the majority of antibody is generated after two doses<sup>28</sup> and the decision to use three priming doses in the UK may have had more to do with "keeping things simple" (see below) than any real need for that many doses. The MenC tetanus conjugate appears to be highly immunogenic after two or even just one priming dose<sup>29</sup> and fewer priming doses also appear to induce larger memory responses to subsequent boosters.<sup>29</sup> A recent UK study commissioned by the Department of Health to explore alternative regimens for the conjugate pneumococcal vaccine likewise suggests that two priming doses may be enough,<sup>30</sup> and a recent study from the Philippines showed similar antibody concentrations at age 9 months, after one or three doses of an 11-valent pneumococcal diphtheria/tetanus conjugated vaccine given in infancy.<sup>31</sup>

The Americans seem to take a different approach towards the design and logistics of their infant and early childhood schedule. A new vaccine is shown to be safe and efficacious, the cost-benefit argument is rehearsed, and the change is made. More injections, more visits, that's just the way it is. In the USA, by the age of 5 a fully immunised child has received up to 24 injections (not including flu) given over about seven visits. Over this side of the Atlantic the issues of what is acceptable to and practical for parents (we can easily guess what the children might say, if asked!) and the primary care staff delivering the vaccines seems to have more influence on decisions. Giving exactly the same vaccines at all infant visits is a lot simpler and less error prone than having different ones each time



and has been the rule for the first three UK immunisation visits to date. Giving a smaller number of injections or a single combination vaccine, rather than multiple injections at any single visit is much less distressing to all concerned and the latter approach becomes downright impossible with some pre-school children, necessitating additional appointments. Add to this the observation that not only can combining conjugate vaccines in the same syringe result in changes in their immunogenicity<sup>32</sup> but so can giving them at different sites at the same time,<sup>33</sup> and deciding how to deliver, say, two priming doses each of Hib, MenC, and pneumo conjugates alongside three doses each of DTP and polio vaccines—ignoring, for the moment, hepatitis B—becomes quite a puzzle. Literally dozens of possible options are conceivable and, so far, no other country has really pointed the way.

But the European Union is bigger now than it was before and includes countries that are not yet systematically using Hib vaccine.<sup>34</sup> This is at least in part because of the purchase costs of the vaccines.<sup>34</sup> That being the case, general European use of conjugate pneumococcal vaccine, which is much more expensive than Hib vaccines, by the schedule used in the USA and under which it is licensed in Europe (three doses in infancy followed by one in the second year of life) or even a “reduced” two dose priming course followed by booster, seems a long way off. Indeed, since manufactured supplies of pneumococcal conjugate vaccine have at times been insufficient to meet demand in the USA, it seems more likely to be logistically feasible to provide fewer than four doses to every European child, if this proves to be acceptable and effective. The latest data from the USA, now four years into general use of 7-valent conjugate vaccine, in addition to continuing to show impressive overall effectiveness in vaccine recipients, also shows remarkable levels of herd immunity among unimmunised age groups.<sup>35–36</sup> Imagine that a country decided it wished to reduce the burden of invasive pneumococcal disease but that it could afford or obtain only one dose of the conjugate vaccine per child: it might choose to administer it at around a year of age, at a time when a single dose might reasonably be expected to induce substantial antibody responses and immunological memory and reasonable long term protection in recipients. This is certainly now the experience with single doses of Hib and MenC administered as one dose only in older children.<sup>18–37</sup> Indeed some countries (for example, the Netherlands and Australia) newly introducing MenC

have adopted this one dose schedule. Of course this approach would deliver vaccine too late for many, if disease patterns in infants remained the same. But what if significant herd immunity effects were observed? In the case of pneumococcal disease perhaps immunised toddlers would introduce fewer vaccine-type strains into their households<sup>38</sup> so that invasive disease rates would drop in their infant siblings too?

Given slightly larger but still limited budgets, if money were saved by withholding infant doses and was instead used to purchase vaccine to immunise older children in a catch-up programme at the outset, would the resulting additional extra public health benefits of broader paediatric herd immunity outweigh those of more conventional infant immunisation? Mathematical modelling may help address this. A programme of this kind in a single small European country with an efficient delivery machinery for paediatric vaccines and a well organised clinical and microbiological surveillance system to pick up cases of invasive disease could not fail to deliver significant public health benefit locally and might teach us much about the potential power of herd immunity in the use of pneumococcal conjugate vaccines.

As we look back at the first decade and a half of use of conjugate vaccines in young children, in our excitement at the discovery of a tool that works in infants who are the most common victims of invasive community acquired bacterial infections, perhaps we have paid too little attention to the capacity of these vaccines to induce herd immunity. Instead of seeing this simply as an added bonus, perhaps we should put it at the centre of future strategic planning. Although fears about “immunological overload” are unfounded, no one would argue that today’s childhood vaccine schedules are busy and set to get busier. Furthermore, many licensed vaccines of known efficacy are not yet in general use in many places, at least in part because of competing priorities on the public purse. Examples in the UK include hepatitis B and varicella vaccines and broader use of flu vaccine in healthy children, as well as the conjugate pneumococcal vaccine discussed above. In this setting, an international collaborative approach to vaccine studies designed to optimise and rationalise (and, who knows, maybe even “harmonise”) current schedules, which are based as much on tradition as science, may be timely. Even if individual countries remain too stubborn to consider adopting “foreign practices”, it certainly appears that, in some cases,

the numbers of doses of conjugate vaccines used might safely be reduced.

*Arch Dis Child* 2005;**90**:667–669.

doi: 10.1136/adc.2005.072173

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Competing interests: The University of Bristol and St George's Hospital Medical School have received funding for research projects and consultancy on behalf of Adam Finn and Paul Heath respectively from Wyeth who manufacture 7-valent pneumococcal vaccine and also from other manufacturers of conjugate vaccines

#### REFERENCES

- 1 **Peltola H**, Kilpi T, Anttila M. Rapid disappearance of *Haemophilus influenzae* type b meningitis after routine childhood immunisation with conjugate vaccines. *Lancet* 1992;**340**:592–4.
- 2 **Teare EL**, Fairley CK, White J, *et al*. Efficacy of Hib vaccine. *Lancet* 1994;**344**:828–9.
- 3 **Takala AK**, Eskola J, Leinonen M, *et al*. Reduction of oropharyngeal carriage of *Haemophilus influenzae* type b (Hib) in children immunized with an Hib conjugate vaccine. *J Infect Dis* 1991;**164**:982–6.
- 4 **Bell F**, Heath P, Shackley F, *et al*. Effect of combination with an acellular pertussis, diphtheria, tetanus vaccine on antibody response to Hib vaccine (PRP-T). *Vaccine* 1998;**16**:637–42.
- 5 **Eskola J**, Olander R-M, Hovi T, *et al*. Randomised trial of the effect of co-administration with acellular pertussis DTP vaccine on immunogenicity of *Haemophilus influenzae* type b conjugate vaccine. *Lancet* 1996;**348**:1688–92.
- 6 **Eskola J**, Ward J, Dagan R, *et al*. Combined vaccination of *Haemophilus influenzae* type b conjugate and diphtheria-tetanus-pertussis containing acellular pertussis. *Lancet* 1999;**354**:2063–8.
- 7 **Chief Medical Officer**. *Start of the new meningococcal C conjugate vaccine immunisation programme*, CMO's letter. Department of Health, October, 1999.
- 8 **Ramsay ME**, Andrews NJ, Trotter CL, *et al*. Herd immunity from meningococcal serogroup C conjugate vaccination in England: database analysis. *BMJ* 2003;**326**:365–6.
- 9 **Department of Health**. *Immunisation against infectious disease*. London: HMSO, 1992.
- 10 **Black S**, Shinefield H, Fireman B, *et al*. Efficacy, safety and immunogenicity of heptavalent pneumococcal conjugate vaccine in children. Northern California Kaiser Permanente Vaccine Study Center Group. *Pediatr Infect Dis J* 2000;**19**:187–95.
- 11 **Miller E**, Salisbury D, Ramsay M. Planning, registration, and implementation of an immunisation campaign against meningococcal serogroup C disease in the UK: a success story. *Vaccine* 2001;**20**:S58–67.
- 12 **Kilpi T**, Ahman H, Jokinen J, *et al*. Protective efficacy of a second pneumococcal conjugate vaccine against pneumococcal acute otitis media in infants and children: randomized, controlled trial of a 7-valent pneumococcal polysaccharide-meningococcal outer membrane protein complex

- conjugate vaccine in 1666 children. *Clin Infect Dis* 2003;**37**:1155–64.
- 13 **Heath PT**, McVernon J. The UK Hib vaccine experience. *Arch Dis Child* 2003;**86**:396–9.
  - 14 **Booy R**, Heath PT, Slack MPE, *et al.* Vaccine failures after primary immunisation with Haemophilus influenzae type-b conjugate vaccine without booster. *Lancet* 1997;**349**:1197–202.
  - 15 **Heath PT**, Booy R, Azzopardi HJ, *et al.* Antibody concentration and clinical protection after Hib conjugate vaccination in the United Kingdom. *JAMA* 2000;**284**:2334–40.
  - 16 **McVernon J**, Andrews N, Slack MP, *et al.* Risk of vaccine failure after Haemophilus influenzae type b (Hib) combination vaccines with acellular pertussis. *Lancet* 2003;**361**:1521–3.
  - 17 **Chief Medical Officer.** *Planned Hib vaccination catch-up campaign*, CMO's update, 2003.
  - 18 **Trotter CL**, Andrews NJ, Kaczmarek EB, *et al.* Effectiveness of meningococcal serogroup C conjugate vaccine 4 years after introduction. *Lancet* 2004;**364**:365–7.
  - 19 **Anon.** Officials fear parent revolt over new baby vaccine. *Guardian* 5 January, 2005.
  - 20 **Anon.** Chaos over 5-in-1 baby jab. *Daily Mail* 9 August, 2004.
  - 21 **Eskola J**, Kayhty H, Peltola H, *et al.* Antibody levels achieved in infants by course of Haemophilus influenzae type B polysaccharide/diphtheria toxoid conjugate vaccine. *Lancet* 1985;**1**:1184–6.
  - 22 **Eskola J**, Peltola H, Takala AK, *et al.* Efficacy of Haemophilus influenzae type b polysaccharide-diphtheria toxoid conjugate vaccine in infancy. *N Engl J Med* 1987;**317**:717–22.
  - 23 **Eskola J**, Kayhty H, Takala AK, *et al.* A randomized, prospective field trial of a conjugate vaccine in the protection of infants and young children against invasive Haemophilus influenzae type b disease. *N Engl J Med* 1990;**323**:1381–7.
  - 24 **Peltola H**, Eskola J, Kayhty H, *et al.* Clinical comparison of the Haemophilus influenzae type B polysaccharide-diphtheria toxoid and the oligosaccharide-CRM197 protein vaccines in infancy. *Arch Pediatr Adolesc Med* 1994;**148**:620–5.
  - 25 **Peltola H**, Salo E, Saxen H. Incidence of Haemophilus influenzae type b meningitis during 18 years of vaccine use: observational study using routine hospital data. *BMJ* 2005;**330**:18–19.
  - 26 **Kurikka S**, Kayhty H, Saarinen L, *et al.* Immunologic priming by one dose of Haemophilus influenzae type b conjugate vaccine in infancy. *J Infect Dis* 1995;**172**:1268–72.
  - 27 **Perez-Melgosa M**, Ochs HD, Linsley PS, *et al.* Carrier-mediated enhancement of cognate T cell help: the basis for enhanced immunogenicity of meningococcal outer membrane protein polysaccharide conjugate vaccine. *Eur J Immunol* 2001;**31**:2373–81.
  - 28 **MacLennan JM**, Shackley F, Heath PT, *et al.* Safety, immunogenicity, and induction of immunologic memory by a serogroup C meningococcal conjugate vaccine in infants: a randomized controlled trial. *JAMA* 2000;**283**:2795–801.
  - 29 **Borrow R**, Goldblatt D, Finn A, *et al.* Immunogenicity of, and immunologic memory to, a reduced primary schedule of meningococcal C-tetanus toxoid conjugate vaccine in infants in the United Kingdom. *Infect Immun* 2003;**71**:5549–55.
  - 30 **Goldblatt D**, Ashton L, Southern J, *et al.* Immunogenicity and boosting following a reduced number of doses of a pneumococcal conjugate vaccine in infants and toddlers. Helsinki, Finland: 4th International Symposium on Pneumococci and Pneumococcal Diseases, 2004.
  - 31 **Lucero MG**, Puumalainen T, Ugbo JM, *et al.* Similar antibody concentrations in Filipino infants at age 9 months, after 1 or 3 doses of an adjuvanted, 11-valent pneumococcal diphtheria/tetanus-conjugated vaccine: a randomized controlled trial. *J Infect Dis* 2004;**189**:2077–84.
  - 32 **Choo S**, Seymour L, Morris R, *et al.* Immunogenicity and reactogenicity of a pneumococcal conjugate vaccine administered combined with a Haemophilus influenzae type b conjugate vaccine in United Kingdom infants. *Pediatr Infect Dis J* 2000;**19**:854–62.
  - 33 **Dagan R**, Eskola J, Leclerc C, *et al.* Reduced response to multiple vaccines sharing common protein epitopes that are administered simultaneously to infants. *Infect Immun* 1998;**66**:2093–8.
  - 34 **Haemophilus influenzae b (Hib) vaccine introduction.** [http://www.euro.who.int/vaccine/20030808\\_3](http://www.euro.who.int/vaccine/20030808_3), WHO Regional Office for Europe, editor. 13 November, 2004.
  - 35 **Whitney CG**, Farley MM, Hadler J, *et al.* Decline in invasive pneumococcal disease after the introduction of protein-polysaccharide conjugate vaccine. *N Engl J Med* 2003;**348**:1737–46.
  - 36 **Flannery B**, Schrag S, Bennett NM, *et al.* Impact of childhood vaccination on racial disparities in invasive Streptococcus pneumoniae infections. *JAMA* 2004;**291**:2197–203.
  - 37 **Ramsay ME**, McVernon J, Andrews NJ, *et al.* Estimating Haemophilus influenzae type b vaccine effectiveness in England and Wales by use of the screening method. *J Infect Dis* 2003;**188**:481–5.
  - 38 **Givon-Lavi N**, Fraser D, Dagan R. Vaccination of day-care center attendees reduces carriage of Streptococcus pneumoniae among their younger siblings. *Pediatr Infect Dis J* 2003;**22**:524–32.