

JCVI Statement: *Haemophilus influenzae* type b (Hib) Disease and Hib Vaccine

Executive Summary

Hib disease used to cause about 30 deaths per year in children aged under 4 years, and left around 80 children with permanent brain damage.

The Hib vaccination programme has been very successful in combating this disease – it cut rates of infection by 98%. Since it was introduced in 1992, the vaccine has prevented an estimated 270 deaths and 720 cases of permanent brain damage.

There has been a small but constant rise in Hib cases since 1998. Factors which may have contributed to this increase are:

- the huge reduction in Hib disease seen in the mid 1990's was likely to be due to the combination of the impact of a Hib vaccine catch-up campaign in children aged 1- 4 years, and the impact of Hib vaccine given in routine childhood immunisation. The impact of the catch-up campaign will have waned over time. Therefore the rate of Hib disease seen now may reflect the true level of protection given by Hib vaccine as part of the routine childhood programme alone;
- A DTaP/Hib vaccine (containing a particular acellular pertussis component) used in 2000 –2001 may not have provided the same high level of protection against Hib disease as the vaccines used before this period, or subsequently.
- The small decline in the rate of children receiving Hib vaccine is leaving more children unprotected against the disease.

In order to halt and reverse the rise in cases of Hib disease, JCVI has recommended that children aged between 6 months and 4 years should be offered an additional dose of Hib vaccine. A successful campaign is expected to result in a reduction in this disease to the low levels previously seen. Careful consideration is being given to the best ways to prevent any future return of Hib disease.

Background

1. Before Hib vaccine was introduced, infections due to Hib disease used to be an important cause of morbidity and mortality, especially in young children. It resulted in about 30 deaths per year in England and Wales, and a further 80 cases of permanent brain damage.

2. The most common illness caused by invasive Hib disease was meningitis (inflammation of the lining of the brain), frequently accompanied by bacteraemia (where Hib infection is found in the blood), which occurs in about 60% of cases. Epiglottitis (swelling of part of the windpipe causing noisy and painful breathing which may lead to blockage of the airway) occurs in about 15% of cases. Septicaemia (blood poisoning) on its own occurred in 10% of cases¹.

3. Hib disease was rare in children under three months of age, but rose progressively during the first year of life, reaching a peak incidence between 6 and 12 months of

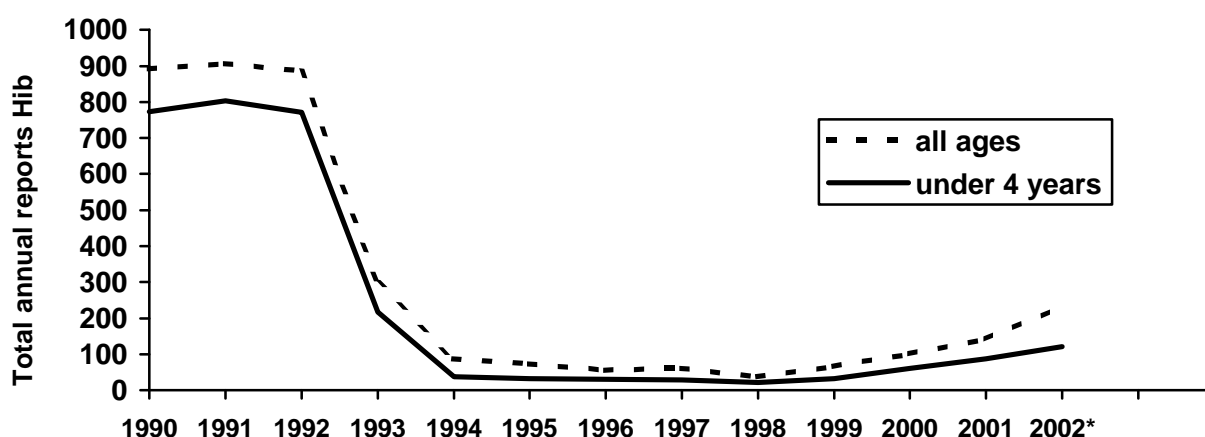
age^{1,2}. Thereafter, the incidence declined steadily up to 4 years of age after which infection was uncommon¹. Hib disease was the most common cause of meningitis in children aged under 4².

Introduction of Hib vaccine to the UK immunisation schedule

Following trials which had demonstrated its safety and short-term efficacy^{3,4}, Hib vaccine was introduced to the routine childhood immunisation programme in October 1992. It was offered to children aged two, three and four months of age (“the UK accelerated schedule”) to provide protection before the peak incidence of Hib disease.

In order to protect all of the at-risk group as quickly as possible, a Hib catch-up campaign was introduced from 1 year up to 4 years of age from October 1992 to October 1993. Catch-up campaigns provide rapid protection in large groups of the population and can rapidly reduce rates of disease^{5,6}. The Hib catch-up was hoped to reduce carriage of the disease and thereby transmission of Hib in the childhood population².

The Impact of the Vaccine on Hib Disease



Laboratory reports of Hib disease in England and Wales (1990-2002).

*provisional data

Source PHLS, HRU/CDSC

The Hib vaccine has been very successful in reducing Hib disease in the UK⁷ and elsewhere⁸.

The impact of the Hib immunisation campaign is illustrated in the above graph. The graph also indicates a significant reduction in cases of Hib in older unvaccinated age groups. This is likely to reflect the fact that in addition to the direct protection given to vaccinated children, others are indirectly protected by reduced exposure to infection (herd immunity)⁹. It has been estimated that since the vaccine was introduced in 1992, about 270 deaths and 720 cases of permanent brain damage have been prevented in young children.

The graph also identifies a small but consistent increase in rates of Hib disease since 1998 in all age groups.

Protection Against Hib Disease

The Hib vaccine has proved excellent in controlling this disease. The mechanism of protection given by the vaccine involves both circulating antibody¹⁰ and immunological memory¹¹. The precise role and relative importance of each mechanism is not clear. However it is also known that in a child protected with Hib vaccine, their antibody levels are likely to be further boosted by natural exposure to Hib bacteria, and this may help in providing long term protection against infection.^{12,13}

The level of antibody produced in response to Hib vaccine can depend on how it is administered. A good antibody response is produced when the vaccine is given when mixed with DTwP (diphtheria/ tetanus/ wholecell pertussis) in a combined vaccine; or when given at the same time as DTaP (diphtheria/ tetanus/ acellular pertussis) vaccine but in separate limbs; or when given singly. However a weaker antibody response is seen when the Hib vaccine is mixed with a particular DTaP vaccine prior to injection^{14,15}. This observation is more apparent when the particular DTaP/Hib is given in the UK accelerated schedule^{14,16} than in more extended schedules.

The reason for this weaker response is not fully understood but appears likely to be due to an effect caused by the mixing of the Hib component with the particular DTaP vaccine prior to injection. Also the importance of this reduction of antibody level on the overall protection given to the child is not fully understood. This is because protection is due to a combination of antibody levels and immunological memory.

Current Incidence of Hib Disease

The surveillance data shows that there has been a small, but consistent, increase since 1998¹⁷. It is likely that there are multiple and complex reasons for the increase¹⁸. However the following factors may have contributed:

1. The rate of Hib disease now may reflect the true level of protection given by the Hib vaccine in the UK childhood schedule.

The major reduction in Hib disease seen during the 1990's was due to a combination of the impact of the Hib catch-up campaign, and of the impact of Hib vaccine being introduced into the routine childhood immunisation schedule. Initially the impact of the Hib catch-up programme would have been the major factor. Within one year of the catch up campaign being introduced, all children between the age of 1 and 5 years had high levels of Hib antibodies following vaccination. However the impact of this campaign may now have waned as these children have grown up and are no longer in the at-risk group. Therefore the rate of Hib disease now seen may be a true reflection of the impact of Hib vaccine in the routine childhood schedule alone. This rate of disease is higher than when the impact of the catch-up campaign was still observed together with the impact of the routine programme combined.

2. A vaccine used in 2000 –2001 provided a lower level of protection against Hib disease.

Due to a widespread shortage of DTwP/Hib vaccine used in the UK childhood programme, a DTaP/Hib vaccine was used. This combination vaccine produced lower levels of Hib antibodies than the usual vaccine, however other measures of the immune response had indicated that this would be sufficient for protection. A new study has shown that vaccinated children who received two or three doses of DTaP/Hib as part of their routine childhood immunisation schedule, had a higher risk of contracting Hib disease than those who had received two or three doses of DTwP/Hib (M Ramsay; personal communication).

3. Hib vaccination rates have declined slightly in recent years from 95.1% of children being immunised by the age of 2 to 90.8% being immunised in July to September 2002. This results in more children being left unprotected against this disease.

All of the above data has been carefully considered by JCVI.

The JCVI Recommendation

The Committee has now recommended that all children aged from six months to four years should be offered an additional dose of Hib vaccine.

The rationale for this is that:

- Hib vaccine is known to produce an excellent antibody response in children aged one or above;
- Children aged under twelve months of age used to be at greatest risk from Hib disease, and cases of Hib still occur in this age group. An additional dose of Hib is expected to boost the antibody levels of these children to ensure adequate protection during this period;
- the Hib catch up campaign in 1992-1993 demonstrated the significant and rapid decline in rates of Hib disease when children under four were given Hib vaccine;
- carriage and thereby transmission of Hib in childhood in older groups is expected to fall, as was seen during the previous campaign.

The catch-up campaign will allow time for the impact of routine vaccination to be further assessed and the most appropriate schedule and vaccines for future use to be considered.

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