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SHORT REPORT
Long-term impact of vaccination on *Haemophilus influenzae* type b (Hib) carriage in the United Kingdom

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SUMMARY

A recent resurgence in serious infections due to *Haemophilus influenzae* type b (Hib) has been observed in the United Kingdom. More information on Hib transmission in the population is required in order to better understand the mechanism of this increase. The Public Health Laboratory Service (subsumed into the Health Protection Agency since April 2004) conducted four cross-sectional studies of asymptomatic oropharyngeal Hib carriage in children attending day-care nurseries in England and Wales in 1992, 1994, 1997 and 2002. These demonstrated a marked reduction in the prevalence of Hib colonization over time since vaccine introduction (3·98% in 1992; 0·70% in 1994; 0% in 1997; 0% in 2002), which did not explain the increase in invasive disease reports from 1999 onwards. We believe that a reduction in antibody levels over the first 5 years of life in immunized children in recent years has fuelled the rise in reported cases in the absence of an obvious increase in transmission.

The United Kingdom has observed a concerning increase in invasive disease caused by *Haemophilus influenzae* type b (Hib) over the last 4 years, predominantly in fully immunized children. Many factors have been implicated in this rise including loss of an initial 'catch-up' immunization campaign's effect, and the use of less immunogenic Hib vaccines [1–3]. Further information is required on the longer-term impact of widespread immunization on asymptomatic Hib carriage prevalence in the United Kingdom.

The Public Health Laboratory Service has conducted a series of carriage studies in pre-school children in England and Wales since the introduction of Hib vaccine into the routine infant immunization schedule in 1992. Personnel in six public health laboratories (Bangor, Manchester, Ipswich, Newcastle, Gloucester, Swansea) recruited children in local playgroups, nursery schools and child welfare clinics on two occasions, in June/July 1992 and 1994. A third survey was performed in Bangor and Manchester in June/July 1997, and a fourth in Oxfordshire and Gloucestershire in 2002. In a separate study of pneumococcal carriage, 103 children of the same age had swabs sent for Hib isolation in June 2002 [Pnc Euro Study (Herts), R. George, personal communication]. Children recruited in 1992 were not eligible for vaccination; children swabbed in 1994 would have been offered a single dose of Hib conjugate vaccine between 1 and 4 years of age as part of an initial 'catch-up' immunization programme and those studied in 1997 and 2002 would have been offered routine Hib vaccine at 2, 3 and 4 months of age.

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Table. *Hib carriage prevalence*

	1992 [*n* (%)]		1994 [*n* (%)]		1997 [*n* (%)]		2002 [*n* (%)]	
(*a*) By year of collection and age								
Age (years)								
1–1·99	0/17	(0)	0/27	(0)	0/4	(0)	0/69	(0)
2–2·99	9/349	(2·58)	0/279	(0)	0/129	(0)	0/96	(0)
3–3·99	30/904	(3·32)	7/888	(0·79)	0/229	(0)	0/134	(0)
4–4·99	22/261	(8·43)	4/369	(1·08)	0/96	(0)	0/85	(0)
Total	61/1531	(3·98)	11/1563	(0·70)	0/458	(0)	0/384	(0)
(*b*) By year of collection and location								
Location								
Bangor	9/306	(2·94)	1/292	(0·34)	0/191*	(0)		
Gloucester	8/249	(3·21)	4/222	(1·80)			0/78*	(0)
Ipswich	5/296	(1·69)	1/282	(0·35)				
Manchester	10/258	(3·88)	2/266	(0·75)	0/267*	(0)		
Newcastle	27/303	(8·91)	3/292	(1·02)				
Oxford							0/203	(0)
Pnc Euro Study (Herts)							0/103*	(0)
Swansea	2/119	(1·68)	0/209	(0·0)				
Total	61/1531	(3·98)	11/1563	(0·70)	0/458	(0)	0/384	(0)
(95% CI)		(3·06–5·09)		(0·35–1·26)		(0–0·80)		(0–0·96)

* Denotes use of chocolate agar for initial plating.

After obtaining parental consent, throat swabs were collected and inserted into *Haemophilus* transport medium. They were then plated on to enriched Columbia Hib antiserum agar plates which were incubated at 37 °C and in 5% CO_2. Due to a shortage of antiserum in 1997 and 2002, some swabs were initially plated on to chocolate agar. Presumptive Hib colonies were subcultured and referred to the *Haemophilus* Reference Unit in Oxford for serotyping, and confirmatory genotyping.

The results of these studies demonstrate the expected decline in Hib carriage prevalence (see Table). The 95% confidence intervals for the 1992 estimate did not overlap with those from any other year. In 2002, a year of increased invasive disease incidence, combined data from separate studies still revealed no carriers among 384 children. No carriage studies have been conducted in teenagers and adults, but in the absence of historical population-based data for comparison, would be almost impossible to interpret.

No evidence was found of an increase in the prevalence of asymptomatic Hib colonization in preschool children over the four time-periods studied, with no carriers detected in the last two surveys. We believe the factor contributing most to the increase in Hib disease in children in the United Kingdom has been a reduction in antibody levels throughout the first 5 years of life [2, 3]. This increase in the size of the susceptible pool appears to have fuelled an increase in cases without an apparently higher rate of transmission in the age group at risk. Prior to 2002, there was no evidence of an increase in invasive Hib incidence in any European Union countries outside the UK [4]. The only exception has been a recent report from The Netherlands of a three-fold rise in Hib cases in 2002 [5]. We will be interested to hear whether the experience in The Netherlands is maintained, and to monitor trends in other European Union countries.

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