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The epidemiology of *Haemophilus influenzae* type b disease in the Republic of Ireland

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SUMMARY

A 2-year case-control study was conducted to describe the epidemiology of *Haemophilus influenzae* type b (Hib) and investigate Hib disease risk factors in the Republic of Ireland. Between October 1991 and September 1993, 149 laboratory confirmed incident cases were matched with community controls. Annual Hib disease incidence was 25·4 per 100000 children under 5 years, with peak incidence (65·8 per 100000) in the 6–11 months age-group. Meningitis was the predominant clinical condition. Twenty-four (16·1%) isolates were resistant to ampicillin. Crèche or day-care attendance and the presence of chronic illness emerged as risk factors for Hib disease. Empirical first line treatment for suspected Hib infection warrants alternatives to ampicillin such as cefotaxime. Completed immunization with Hib conjugate vaccine by 6 months of age is required for maximum disease prevention. Until all children are receiving Hib vaccine on schedule, those who are crèche or day-care attendees and those with chronic illness should be prioritized for timely immunization.

INTRODUCTION

The importance of *Haemophilus influenzae* type b (Hib) as a cause of serious disease in infants and children is well recognized [1–6]. Meningitis is the principal clinical disease [1, 3, 7] but other conditions such as epiglottitis, pneumonia, cellulitis, bone and joint infections and septicaemia also occur [4–6]. The major disease burden occurs in children under 5 years [3–6, 8].

Variations in Hib disease incidence rates occur between countries and regions within countries. Disease rates are higher in the United States (US) [1, 9, 10] than in western Europe [2, 4, 5, 11–13]. However, within the US, the native American and Alaskan native populations [10, 14, 15] experience particularly high Hib disease rates as do aboriginal children in Australia [6, 16]. The reasons for such differences in Hib disease incidence are not fully understood but differing genetic susceptibilities among host populations have been suggested [17, 18]. Where socio-economic risk factors for Hib disease have been studied, particularly in the US and Scandinavia, parameters such as household crowding, parental smoking, crèche or

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day-care attendance and low levels of breast feeding have been shown to be associated with occurrence of disease [19–22] and are likely to be more important than genetic factors in explaining differences in incidence rates.

The recent development and introduction of Hib conjugate vaccines [23, 24] has allowed the potential to eradicate Hib disease in children most susceptible, those under 18 months of age, and its impact is already being felt [25–27].

The purpose of this study was to document baseline incidence data on Hib disease for the Republic of Ireland (ROI) against which Hib vaccine efficacy could be evaluated after its introduction. A case-control methodology was used to investigate the hypothesis that certain risk factors not previously investigated in the ROI or the United Kingdom (UK), were more common in children with Hib disease than in controls.

METHODS

The study population comprised the inhabitants of the 26 counties of the ROI (1991 census population: 3525719) [28]. For a 2-year period between 1 October 1991 and 30 September 1993 isolates of invasive *Haemophilus influenzae* were identified by active surveillance of all microbiology laboratories throughout the ROI. Incident cases were each age-matched with two controls from the same geographical area.

A case was defined as a patient under 14 years with Hib isolated from a normally sterile site (e.g. cerebrospinal fluid (CSF), blood, joint fluid). Patients with a positive Hib antigen test and with haemophilus-like gram-negative bacilli on microscopy but from whom the organism was not isolated, were excluded. The completeness of laboratory surveillance was evaluated retrospectively by reviewing laboratory records of blood and CSF cultures.

Cultures were forwarded on chocolate agar slopes to a central laboratory where identification and serotyping of the organism were verified. Identification was performed by standard methods (PHLS Monograph). Serotyping was performed using antisera to *H. influenzae* types a–f obtained from Wellcome Diagnostics. Isolates were checked for beta-lactamase production. Antibiotic minimum inhibitory concentrations (MICs) were determined. Isolates were then stored on Protect beads and later forwarded to Baylor College of Medicine, Houston, Texas where clonal analysis was carried out using multilocus enzyme electrophoretic analysis (to be published later). Isolates from patients who had received Hib conjugate vaccine (during the second year of the study) were also forwarded to the Haemophilus Reference Laboratory, Oxford for analysis, as part of a Hib disease surveillance study following Hib immunization throughout the UK and ROI (not presented here).

Epidemiological and clinical data on laboratory identified cases were forwarded to JF by paediatricians (or other appropriate clinicians) using a structured questionnaire. This included data on patient socio-demographic characteristics together with data on potential risk factors for Hib disease being investigated in the study. A further question on Hib conjugate vaccine status was added to the questionnaire for the second year of the study as this vaccine had been introduced into the childhood immunisation schedule in the ROI on 1 October 1992 [29]. Controls were selected from the same community care area (most areas

corresponded to county boundaries) as the case. Public health physicians were forward questionnaires similar to those used with cases (but omitting the section on hospital admission). A protocol for control selection accompanied these questionnaires. This protocol included the address of the Hib case (townland (smallest administrative unit) if a rural case, or street or road if an urban case) but excluded case name. Both controls were selected from the same public health nurse (PHN) district as the case address provided. The date of birth (DOB) of the Hib case was provided and two controls with the nearest DOB before and after the case DOB were selected from the area birth register, if they resided in the PHN district already identified. Gender was not a selection criterion. Control data were collected for the time period corresponding to that of Hib disease occurrence in the case. Questionnaires were completed by PHNs or Area Medical Officers.

Denominator data for calculation of incidence rates were derived from the 1991 census [28]. Data were analysed using Epi Info version 5 [30]. The χ^2-test was used for comparison of two independent proportions and McNemar's test for paired analysis. A matched paired analysis and a multivariate logistic regression model estimated odds ratios (OR) and 95% confidence intervals (CI) for potential risk factors. Sample size was calculated using Statcalc (Epi-info version 5) based on previous studies which had documented prevalence rates for factors of interest in the present study. For example, Johnson and colleagues [31] found a difference in current smoking prevalence of 22·4% between people living in high mortality areas (50·9%) versus low mortality areas (28·5%) in Dublin. Cochi and colleagues [19] in the US also found a 26% difference in prevalence of crèche or day-care attendance between cases (65%) and controls (39%) in a risk factor study for Hib disease. In order to have an 80% chance of detecting a 15% difference in prevalence of risk factors being investigated in the present study at a 5% significance level, 139 cases and 278 controls would be required. Using retrospective laboratory data, it was estimated that the study would need to run for 2 years to generate sufficient cases.

RESULTS

Between 1 October 1991 and 30 September 1993, 164 episodes of invasive *Haemophilus influenzae* disease were identified in 163 subjects throughout the ROI. Of 151 cases with Hib disease, 149 occurred in children under 14 years. Only the first disease episode in one child with two episodes of Hib disease 3 months apart is included. There were no secondary cases of Hib disease in contacts during the study period. Data were returned on 147 (98·7%) of the 149 cases and on 286 (96·0%) of 298 potential controls. Subsequent evaluation of completeness of laboratory reporting revealed that all but two cases of invasive *Haemophilus influenzae* disease had been identified. Table 1 shows the socio-demographic profile of cases and controls.

Cases

Similar numbers of children developed Hib disease during the first (78) and second (71) years of the study despite the availability of Hib conjugate vaccine during the second year. It is widely acknowledged that Hib vaccine was not being

Table 1. *Socio-demographic characteristics of cases and controls*

Socio-demographic characteristic	Cases $n = 149$ (%)	Controls $n = 286$ (%)
Sex		
Male	78 (52·3)	149 (52·1)
Female	71 (47·7)	137 (47·9)
Age in years		
Mean	2·0	2·0
Median	1·4	1·3
Social class category*		
1–3	57 (38·3)	128 (44·8)
4–6	65 (43·6)	138 (48·3)
Unknown	27 (18·1)	20 (7·0)

* Based on parental occupation [32].

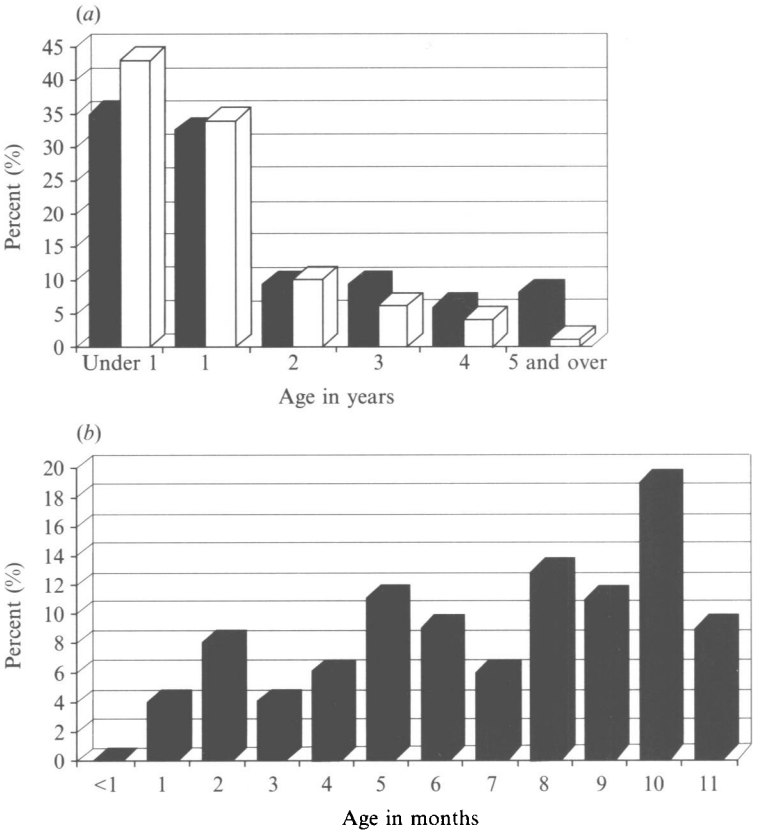

Fig. 1 (*a*). Distribution of Hib disease and Hib meningitis by age, Republic of Ireland. Based on 151 cases of Hib disease and 67 of Hib meningitis (Oct. 1991–Sep. 1993). (*b*) Distribution of Hib disease under 1 year by age, Republic of Ireland. (Values are cases as percentage of total $n = 53$). ■, All Hib disease; □, Hib meningitis.

widely administered in the ROI during the year after its introduction on 1 October 1992. Of study subjects immunized, 10 (14·2%) of 70 cases and 25 (18·4%) of 136 controls (OR = 0·74, 95% CI = 0·30–1·73) had received some doses of vaccine

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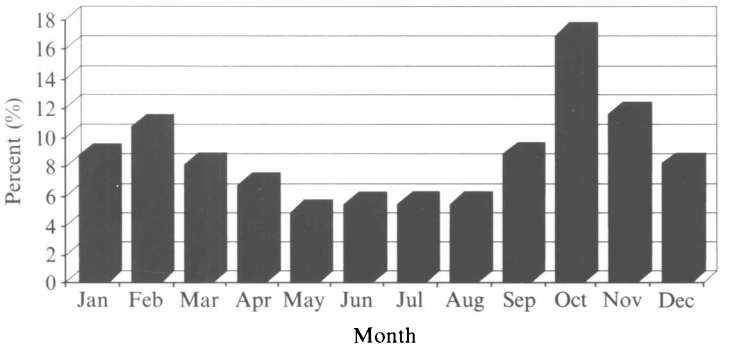

Fig. 2. Seasonal distribution of Hib disease. Republic of Ireland. Hib under 14 years (Oct. 91 Sep. 93).

Table 2. Haemophilus influenzae *type b* (*Hib*) *disease, in children under 14 years by diagnosis and disease-specific annual incidence per 100000 children under 5 years*

Principal diagnosis	Number of cases (%)	Incidence under 5 years
Meningitis	67 (45·0)	12·1
Epiglottitis	24 (16·1)	3·8
Pneumonia	15 (10·1)	2·0
Cellulitis	12 (8·1)	2·2
Osteomyelitis	6 (4·0)	1·1
Septic arthritis	5 (3·4)	0·9
Septicaemia	20 (13·4)	3·3
All Hib disease	149 (100)	25·4

Table 3. *Age-specific annual incidence of Hib disease and Hib meningitis per 100000 population*

Age-group	Hib disease	Hib meningitis
Under 6 months	33·2	21·4
6–11 months	65·8	32·9
All under 1 year	50·0	27·3
12–17 months	58·2	31·0
18–23 months	35·0	12·9
All under 2 years	48·2	24·5
24–35 months	13·3	6·6
36–47 months	12·5	3·6
48–59 months	7·7	2·5
All under 5 years	25·4	12·1

during the second year of the study and 2 cases and 10 (7·7%) controls (OR = 0·37, 95% CI = 0·04–1·82) had completed Hib immunization courses (3 doses by 6 months of age). By the time the present study ended on 30 September 1993, completed Hib vaccine uptake rates for children 12 months of age were still only 30–40% in many parts of the country. Therefore, analysis was carried out on cases for the combined 2-year period. There was a small male preponderance among cases (Table 1). The age-profile of disease is presented in Figure 1 (*a*, *b*) and

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Table 4. *Prevalence of potential risk factors for Hib disease among cases and controls and matched analysis of potential risk factors by age-group*

Potential risk factor	Prevalence of potential risk factors for Hib disease: Cases* $n = 147$ (%)	Prevalence of potential risk factors for Hib disease: Controls $n = 286$ (%)
Smoking		
Household cigarette smoking	69 (46·9)	152 (53·1)
Mean number of cigarettes smoked	26·6	22·7
Housing		
Local authority house residence	27 (18·4)	66 (23·1)
Mean number of persons in all house types	5·0	5·1
Mean number of bedrooms in all house types	3·4	3·2
Household bedroom sharing		
Sharing bedroom $\geqslant 2$ others	43 (29·3)	88 (30·8)
Sharing bedroom with 1 other	28 (19·0)	88 (30·8)
Not sharing bedroom	58 (39·5)	106 (37·1)
Siblings		
Presence of other siblings in family	112 (76·2)	226 (79·0)
Mean number of siblings in family	2·5	2·3
Presence of schoolgoing siblings in family	82 (55·8)	188 (65·7)
Mean number of siblings in school	1·6	1·7
Presence of older siblings in family	99 (67·3)	203 (71·0)
Subject is youngest in family	89 (60·5)	170 (59·4)
Crèche (or day-care)		
Crèche attendance	28 (19·0)	32 (11·2)
Mean number hours/week in crèche	25·5	25·0
Mean number children in crèche room	6·5	8·3
Recent crèche attendance†	23 (15·6)	27 (9·4)
Breast feeding		
Breast feeding of subject (at least half total feed)	40 (27·2)	89 (31·1)
Mean duration of breast feeding (weeks)	14·1	13·7
Free health service eligibility	54 (36·7)	97 (33·9)
Presence of chronic illness	16 (10·9)	13 (4·5)

almost two-thirds (63·8%) of cases occurred in the period October to March (Figure 2).

The overall annual incidence of Hib disease for the ROI was 25·4 per 100000 children under 5 years. Annual disease-specific incidence rates for children under 5 years for all forms of Hib disease are presented in Table 2. Age-specific annual incidence rates for all Hib disease and Hib meningitis are presented in Table 3. A notable feature of cases was the occurrence of Hib disease in five children with Down's syndrome, one of whom died. Four of these children were under 5 years. Based on EUROCAT, the European Registry of Congenital Anomalies, it is estimated that the population under 5 years with Down's syndrome in the ROI is approximately 440 children (Z. Johnson, C. Hayes, personal communication). Based on these data, the annual incidence of Hib disease among children under 5 years with Down's syndrome in the ROI is about 453 per 100000, some 18 times the rate for Irish children overall.

Table 4 (*cont.*)

Potential risk factor	Matched analysis of potential risk factors Hib disease‡			
	< 1 year $n = 53$	12–23 months $n = 49$	⩾ 2 years $n = 47$	All ages $n = 147$
Crèche attendance	1·75 (0·63–4·83)	**4·00 (1·18–13·53)**	1·67 (0·62–4·46)	**2·09 (1·16–3·78)**
Recent crèche attendance	1·71 (0·58–5·10)	3·25 (0·93–11·41)	1·50 (0·58–3·91)	**1·86 (1·02–3·42)**
Presence of chronic disease	**11·00 (1·26–96·12)**	Undefined	**17·00 (2·03–142·03)**	**2·90 (1·29–6·54)**
Free health card eligibility	1·62 (0·70–3·70)	0·78 (0·34–1·75)	1·14 (0·48–2·75)	1·18 (0·75–1·87)
Household bedroom sharing				
Sharing bedroom with ⩾ 2 others	1·00 (0·50–2·00)	0·50 (0·17–1·46)	1·41 (0·55–3·59)	0·93 (0·58–1·48)
Sharing bedroom with 1 other	0·75 (0·28–2·01)	0·55 (0·20–1·49)	**0·40 (0·18–0·90)**	**0·51 (0·30–0·85)**
Not sharing bedroom	0·51 (0·22–1·20)	1·62 (0·73–3·62)	1·30 (0·60–2·85)	1·19 (0·77–1·83)
Household smoking	0·71 (0·36–1·44)	0·87 (0·35–2·15)	0·86 (0·40–1·84)	0·77 (0·50–1·19)
Lower social class	0·89 (0·42–1·87)	0·58 (0·24–1·38)	1·02 (0·51–2·05)	0·87 (0·57–1·33)
Breast feeding (of any duration)	0·73 (0·29–1·81)	1·30 (0·57–2·95)	0·64 (0·29–1·41)	0·83 (0·52–1·34)
Presence of other siblings	0·93 (0·46–1·92)	0·97 (0·39–2·37)	0·52 (0·19–1·38)	0·92 (0·58–1·46)
Youngest in birth order	0·85 (0·42–1·75)	1·83 (0·76–4·37)	0·66 (0·31–1·41)	1·09 (0·71–1·66)
Local Authority housing	0·60 (0·22–1·64)	0·57 (0·20–1·67)	1·13 (0·35–3·60)	0·73 (0·40–1·33)
Presence of school age sibling(s)	0·98 (0·52–1·87)	0·74 (0·32–1·71)	**0·35 (0·16–0·76)**	0·68 (0·45–1·03)

* Risk factor data were available for 147 of 149 cases.
† ⩾ 16 h in previous 4 weeks or ⩾ 4 h in previous week.
‡ Odds ratios and 95% confidence intervals.
Figures in bold indicate a statistically significant result between case and control groups in matched analysis.

The most common clinical presentation was meningitis (Table 2). The mean age of children with meningitis was 18·1 months (median 13·0, range 1·6–90·3). The mean age of cases with epiglottitis was older, being 34·7 months (median 29·8, range 6·8–76·6).

A history of recent injury or illness in the 4-week period prior to the Hib diagnosis, was reported in 31 (21·4%) children. Except for a head injury in the previous 24 h in one child, and an eye infection in another (preceding cellulitis) the remainder of these had respiratory-type illnesses.

Two (1·3%) children died as a result of Hib infection. Six (4·0%) children were reported to have had some sequelae (all pertaining to the central nervous system) on hospital discharge.

Ampicillin resistance was identified in 24 (16·1%) Hib isolates. Three (2·0%) isolates had dual resistance to chloramphenicol and ampicillin.

Risk factors

Household cigarette smoking was common among cases (46·9%) and controls (53·1%) with the mean number of cigarettes smoked per household similar in both groups (Table 4). However, household cigarette smoking did not appear as a risk factor in this study (Table 4).

The prevalence of proxy indicators for low socio-economic status (membership of social classes 4–6 based on parental occupation [32] (Table 1), free health service eligibility and residence in local authority housing (Table 4)) were similar among families of cases and controls and did not emerge as risk factors for Hib disease (Table 4).

The mean number of residents per household was similar among cases and controls as was the mean number of bedrooms in case and control households (Table 4). The level of household overcrowding (defined in this study as a subject sharing bedroom accommodation with two or more household members) was also similar in both groups and was not a risk factor (Table 4).

The proportions of cases and controls having older siblings were similar (Table 4). Both the mean number of family siblings and the mean number of school-going siblings were also similar (Table 4). None of these family membership characteristics emerged as risk factors (Table 4).

The prevalence of breast feeding (defined as at least half total feed) was similar among cases and controls as was its mean duration (Table 4). Only 14 (9·5%) cases and 29 (10·1%) controls were reported to have been breast-fed for longer than 3 months. Breast feeding did not appear as a protective factor for Hib disease among control subjects (Table 4).

Crèche or day care attendance (defined as any regular (at least 4 h per week) supervised care of at least two unrelated children) was more prevalent among cases than controls (Table 4). Although the mean weekly duration of care was similar in both groups, cases were more likely to be recent (16 h in the previous 4 weeks or 4 h in the previous week) crèche or day-care attendees (Table 4). Both crèche or day-care attendance and recent exposure to this environment emerged as risk factors for Hib disease in matched analysis (Table 4).

The presence of chronic illness was more prevalent among cases than controls (Table 4). Sixteen (10·9%) cases suffered from the following conditions: 5 Down's Syndrome, 6 asthma and 1 child each with phenylketonuria, 'renal disorder', 'metabolic disorder', Rubenstein Tabyii Syndrome and adenoids. Thirteen (4·5%) control children suffered from the following conditions: 6 asthma, 3 eczema, and 1 each with cystic fibrosis, tuberosclerosis, bronchitis and microcephaly. Matched analysis demonstrated the presence of chronic illness, and in particular Down's syndrome, to be a risk factor for Hib disease (Table 4).

When meningitis and non-meningitic Hib disease were analysed separately the same risk factors identified in the overall analysis emerged for non-meningitic disease only. Cases with non-meningitic Hib disease were more likely than controls to be crèche or day-care attendees (OR = 3·5, 95% CI = 1·45–8·46), to have had recent crèche or day-care exposure (OR = 2·89, 95% CI = 1·23–6·80) or to have chronic illness (OR = 11·00, 95% CI = 2·38–50·94). For meningitis, no differences were observed between cases and controls for crèche or day-care attendance

(OR = 1·3, 95% CI = 0·56–2·98), recent crèche or day-care exposure (OR = 1·2, 95% CI = 0·47–2·84) or the presence of chronic illness (OR = 0·75, 95% CI = 0·20–2·83). No differences were found in any of the risk factors if different age-groups were analysed separately for these two categories of Hib disease but in some situations analysis could not be performed due to small numbers. When males and females were analysed separately no differences could be found in any of the risk factors under study.

A multivariate stepwise logistic regression model, using BMDP [33] was tested controlling for the identified significant variables and disease type (i.e. meningitis and non-meningitic Hib disease). From this analysis the only significant predictor variable in a multivariate context was shown to be crèche or day-care attendance where the estimated odds ratio for this variable was 1·95 (95% CI = 1·0–4·0).

DISCUSSION

The method of active laboratory surveillance used in this study resulted in almost complete case detection, later confirmed by retrospective evaluation. Our case definition which includes only culture positive cases is similar to that of other international studies [3, 4, 9, 15]. The inclusion by some researchers [5, 7, 8, 12] of a small proportion of additional cases (on average less than one percent) that are Hib antigen positive but culture negative should not affect comparability of data.

The annual incidence of Hib disease in Ireland was similar to that experienced in England and Wales [8], Scotland [13] and France [12], lower than that in northern Europe [2, 11], Australia and New Zealand [6] and American populations of European origin [9], and substantially lower than rates experienced in native American [14, 15] aboriginal [16] and African [34] children.

The pattern of illness in the ROI differs somewhat from that of Hib disease in the UK with meningitis comprising a smaller proportion (45%) in Irish children compared to 71% in Oxford [4], 62% in Gwynedd [5] and 56% in England and Wales [8]. Similarly, in France [12], the US [9] and parts of Scandinavia [2] meningitis is the most common clinical presentation of Hib disease. Children in Victoria, Australia [6] experienced proportionally much more epiglottitis (40%) than their Irish counterparts (16·1%) with the occurrence of a smaller proportion (18%) of diagnoses other than meningitis. The age distribution of disease in Irish children was similar to that in England and Wales [8] with 36% and 35% respectively of all Hib disease occurring in children under 1 year. In contrast the native American Apache and Navajo populations experienced 40% and 30% respectively of all Hib infections in the first 6 months of life [14]. The general trend from international data is that the younger the occurrence of Hib disease the greater is its meningitic component. In Alaska [15] where 98% of all Hib disease occurred under 18 months no case of epiglottitis, a presentation in older children, was seen. Irish children experienced a particularly high rate (39%) of clinical conditions other than meningitis and epiglottitis. In studies in England and Wales these infections comprised 26–29% of all Hib disease [5, 8] and the proportion was even lower (17%) in an earlier Oxford study [4]. Only in Dallas [9] were these infections of similar proportion to those in Ireland. Aboriginal children in

Northern Territory, Australia [16] had an exceptionally high rate (66%) of non-meningitis Hib disease (with pneumonia comprising 40% of all their disease). The absence of epiglottitis in aboriginal children contrasts sharply with the very high rate of this condition in the more southerly Australian area of Victoria [6].

Only two (1·3%) deaths occurred as a result of Hib disease in Irish children. Although slightly higher mortality rates occurred in Gwynedd (2%) [5], Denmark (2%) [11], Minnesota (3·9%) and Dallas (4%) [9], these rates from industrialized countries are substantially lower than those experienced by African children (37%) where lack of access to healthcare facilities plays a major part in poor outcome [34]. In our study 4% of children were discharged from hospital with some sequelae pertaining to the central nervous system. More long-term evaluation of Irish meningitis survivors will be required to establish the prevalence of permanent sequelae in this group.

Ampicillin resistance in beta-lactamase producing strains of Hib has long been recognized [35] and is seen to be as prevalent as 50% in highly medicalized societies [3, 12] in comparison to its rarity in the developing world [34]. The level of ampicillin resistance (16·1%) in isolates from Ireland is almost identical to that found in Gwynedd [5] and more recently in England and Wales [8]. The importance of continued monitoring of antibiotic sensitivity patterns throughout Ireland is obvious if the experience in France is considered where ampicillin resistance rose from 4% in 1980 to 55% in 1989 [12]. As in Wales [5] the appearance of organisms with dual resistance to ampicillin and chloramphenicol warrants alternative empirical treatments with antibiotics, such as cefotaxime, if Hib infection is suspected.

No secondary cases of Hib disease were detected during the present study, a finding in keeping with reports from Oxford [4], Wales [5] and the high Hib prevalence area of western Alaska [15].

Almost no impact was made on Hib disease incidence during the first year after Hib conjugate vaccine introduction (second year of study) in the ROI. There was poor vaccine uptake during this period. A vaccine coverage rate approaching 95% is required for Hib disease elimination. Coverage rates of 90% have already been achieved in the UK in 1994 [36] and such data, together with the virtual elimination of Hib disease in Finland due to immunization [25, 26] should be used as models of what can be achieved with effective vaccine delivery systems.

Two significant risk factors for primary Hib disease were identified: attendance at crèche or day-care and the presence of chronic illness. A strong relationship between age and risk of Hib disease for crèche or day-care attendance was observed with the highest risk experienced by children in the second year of life. Day-care as a risk factor for Hib disease has been documented in the US [19, 21] and Finland [20]. Istre and colleagues in Colorado [21] found the highest risk in day-care attendees over 1 year but Cochi and colleagues in Atlanta [19] found the highest risk for Hib disease in the 2–5 month age-group, declining thereafter. The highest day-care risk for Finnish children occurred in children under 2 years of age [20]. When stratified analysis was carried out for meningitis and non-meningitic disease, crèche attendance emerged as a risk factor for non-meningitic Hib disease but not for meningitis alone. No such diagnosis related difference in crèche or day-care attendance risk was found in Atlanta [19] or Finland [20]. Variations in the

level of risk of Hib disease associated with crèche or day-care attendance can be explained in part by the size and practice of these centres. The risk of Hib disease is higher the greater the number of children per room [21] and the longer the duration of stay [19].

The presence of chronic illness was another risk factor for Hib disease in Irish children. For the purpose of analysis we combined illnesses having an allergic component (e.g. asthma) and illnesses which are known to be associated with reduced immunity (e.g. Down's syndrome). A history of allergy symptoms was not associated with increased risk of Hib disease in Finland [20]. Chronic illness as a risk factor in the present study was greatest in children older than 2 years but was also seen in children in the first year of life.

No association with risk of Hib disease was observed with such family characteristics as household cigarette smoking, household crowding, presence of school-age siblings or breast-feeding, although many of these factors have been shown to be risk factors (or a protective factor in the case of breast feeding) in other studies [19, 20, 21]. The homogeneity of the Irish population may account for the similarity in distribution of many of these characteristics that have been shown to be risk factors elsewhere. Of the two risk factors identified, créche or day-care attendance may operate as an environmental factor by increasing the likelihood of children's exposure to Hib bacteria and chronic illness would appear to act as a host factor increasing the susceptibility to development of invasive Hib disease.

Until there is evidence that Hib immunization coverage rates reach 95% for eligible children in the ROI, it is essential that children with chronic illness and those who are crèche or day-care attendees receive Hib conjugate vaccine as a priority.

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