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Epidemiology of *Streptococcus pneumoniae* infections at the Edinburgh City Hospital: 1980–95

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SUMMARY

We present data on pneumococcal isolates collected from deep and superficial sites over a 16-year period at the Edinburgh City Hospital. The 10 most frequent serotypes overall were 6, 19, 11, 9, 3, 14, 1, 15 and 18 in children and 19, 23, 6, 6, 9, 11, 3, 15, 14, 22 and 4 in adults. Over 88% (2588/2932, 88·3%) of these pneumococci were of serotypes represented in the 23-valent polysaccharide pneumococcal vaccine. Within the 20–45 years age group, 228/434 (52·5%) of specimens were from HIV-infected individuals. The isolations showed a seasonal distribution with peaks in February and troughs in September. The annual numbers of blood culture isolates showed an upward trend. Recurrent isolations were more frequent in HIV-infected individuals (49/132, 37%) than in non-HIV-infected individuals (218/2421, 9·9%) (relative risk = 5·05, 95% confidence interval, 3·46–7·03). The prevalence of resistance to penicillin and erythromycin was lower than that reported in other parts of the UK.

INTRODUCTION

Pneumococci are a major cause of morbidity and mortality worldwide. In the UK, an estimated 60000 adults die of pneumococcal disease annually [1]. In developing countries, about one million children, half under the age of one year, die of pneumonia each year [2]. This continuing morbidity is despite the availability of effective antibiotics and a polysaccharide vaccine. Recently, there has been renewed interest in studying pneumococci. This has been due in part to the factors mentioned above, but in addition, there has been an increase in the population at risk of serious pneumococcal disease, especially those with impaired immunity, as well as an increased prevalence of strains resistant to penicillin and other antimicrobial agents [3].

Immunization with conjugated vaccines may offer a new approach to the control of these infections. Data on geographical and temporal distribution of capsular serotypes are important in order to estimate the potential efficacy of these vaccines.

We present data on pneumococcal isolates collected over a 16-year period at the Edinburgh City Hospital (ECH) before its closure. We compared our data with that from other regions in the UK to illustrate regional variations in distribution of serotypes within a single country. The study encompassed the period before and after the advent of the HIV epidemic in Edinburgh, and thus presented an opportunity to study the impact of this infection on the epidemiology of pneumococcal disease at the hospital. The aims of the study were to ascertain the serotype distribution of pneumococci, and to explore the impact of HIV infection on the epidemiology of pneumococcal infection.

MATERIALS AND METHODS

Background

The ECH was a 279 bed hospital housing the following units: ear, nose and throat surgery, care of the elderly,

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infectious diseases, oral and maxillofacial surgery, respiratory medicine, and thoracic surgery. The bacteriology laboratory had been routinely serotyping pneumococci since the late 1970s [4]. The ECH merged with the Royal Infirmary of Edinburgh in June 1994. Patient data recorded in this study included name, date of birth, ward, specimen type, date of receipt, and serotyping results.

Establishment of dataset used in this study

Data on all pneumococci isolated from specimens received between 1 January 1980 and 31 December 1995 were included. Duplicate records, defined as isolates of pneumococci of the same serotype from the same patient and recovered within 4 weeks of the first isolate, were excluded. Data on antibiotic sensitivity patterns of pneumococcal isolates from both the ECH and the Royal Infirmary of Edinburgh recorded between January 1992 and December 1995 were analysed. The merger of the two hospitals provided an opportunity to study a larger dataset.

Analysis of data

Data were analysed to elucidate the following: annual distribution of serotypes, sources of specimens, temporal variation, age distribution of patients, serotype distribution among HIV-infected patients and incidence of recurrent infections.

Statistical methods

The χ^2 test for contingency tables was used where appropriate. The analysis for linear trend in proportions (χ^2 for trend as described in Epi-Info, version 6.0, CDC, Atlanta) was used to determine whether there was a significant increase in blood culture isolates over the study period.

To investigate temporal variation for each of the individual serotypes, an analysis for time series [5] using the average percentage method was done. In this method the numbers of isolations for each month (for each serotype) were expressed as percentages of the average for the year. The percentages for corresponding months of different years were then averaged. The resulting 12 percentages gave the *seasonal index*. If their mean was not 100% (i.e. if the sum was not 1200%), they were adjusted by multiplying them by the appropriate factor. The seasonal indices were then examined to obtain the months with the highest and lowest isolations for each serotype.

RESULTS

Overall data

A total of 3090 unique records for pneumococci isolated during the study period were included in the dataset. Results of serotyping were available for 2932, of which 9 were non-typable. The distribution of serotypes is shown in Table 1. Over 88% (2588/2932, 88·3%) of the isolates were of serotypes represented in the current 23-valent pneumococcal vaccine.

Sources of specimens

The distribution of specimens from which pneumococci were isolated is shown in Table 2. The ten most common serotypes isolated from sterile sites were 1, 9, 14, 4, 3, 7, 8, 23, 6 and 19 and accounted for 189/235 (80·4%) sterile site isolates. The current 23-valent polysaccharide vaccine covered 224/235 (95·3%) of the isolates from invasive infections. The annual number of blood culture isolates, as a proportion of all specimens, showed an increasing trend (Table 3).

Temporal variation

The monthly data of all the serotypes showed a seasonal pattern, isolations being highest in February and lowest in September. However, analysis of individual serotypes showed the highest and lowest isolations of serotype 3 were February/March and September, for serotype 6 February/March and September, serotype 19 December and June and serotype 23 March and November, respectively.

There were significant variations in the annual occurrence of the different serotypes. A contingency table consisting of the annual isolations of serotype 3, 6, 19, and 23 is shown below Table 4.

The proportions of the different serotypes varied over the study period. Figure 1 shows the variation of the top four types over three major periods of the study. Of note were the absence of type 2 and the rarity of serotype 5, two types that were more common in developed countries in the past [6].

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Table 1. *The distribution of serotypes from all specimens*

Type	Number	%
19*	325	11·1
6*	321	10·9
23*	283	9·7
3*	219	7·5
9*	215	7·3
11*	175	6·0
14*	154	5·3
22*	122	4·2
15*	104	3·5
4*	95	3·2
8*	88	3·0
18*	86	2·9
1*	81	2·8
7*	68	2·3
17*	66	2·3
10*	57	1·9
33*	47	1·6
35	45	1·5
20*	44	1·5
13	41	1·4
16	40	1·4
31	36	1·2
34	34	1·2
12*	33	1·1
21	23	0·8
41	23	0·8
28	17	0·6
29	14	0·5
24	11	0·4
42	10	0·3
36	9	0·3
38	7	0·2
27	6	0·2
5*	5	0·2
32	5	0·2
39	3	0·1
25	3	0·1
37	2	0·1
40	2	0·1
48	2	0·1
Others	2	0·1
Non-typable	9	0·3
Grand total	2932	

* Represented in the 23-valent pneumococcal polysaccharide vaccine.
Others included types 43 and 47 which accounted for 0·1% (4/2932).

Table 2. *Specimen types*

Sample type	Number
Respiratory	
Sputum	2303
Nose swab	261
Throat swab	56
Sinus washings	51
Bronchial washings	30
Pleural fluid	26
Blood culture	209
Eye swab	40
Ear swab	31
Skin swab	14
Pus	13
Cerebrospinal fluid	11
Joint aspirate	11
Vaginal swab	3
Bone marrow	1
Ascitic fluid	1
Others*	29
Total	3090

* Others included swabs from unspecified sites, post-mortem samples.

Age distribution

Dates of birth were available for 1692 records of which 238 were from patients known to be HIV positive. Children (aged < 16 years) accounted for 182/1692 (10·6%) of the specimens. The age distribution is shown in Figure 2. Within the age group 20–45 years, 228/434 (52·5%) specimens yielding pneumococci received between 1 March 1986 and 31 December 1995 were from HIV-infected individuals.

The 10 most common serotypes in children were 6, 19, 23, 11, 9, 3, 14, 1, 15 and 18 in descending order whereas the order was 19, 23, 6, 9, 11, 3, 15, 14, 22 and 4 in adults. Of the 128 isolates from sterile sites in adults, the 10 most common serotypes, in descending order, were 4, 14, 9, 1, 23, 7, 20, 19, 3 and 8 accounting for 100/128 (96·8%) of all isolates from invasive infections.

HIV-infected subgroup

Data on serotypes were available for 228 records from patients with HIV infection, all adults. The 10 most common serotypes overall in this group were 6, 19, 23, 9, 15, 18, 3, 11, 4 and 16 in descending order, accounting for 163/228 (75·8%) strains. The 23-valent polysaccharide vaccine covered 204/228 (89·5%) of the isolates.

Recurrent infections

Analysis of the data in which serotypes were available (2932 records), duplicates having been excluded, revealed that 132 HIV-infected patients accounted for

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Table 3. *Trends in annual blood culture isolates (1980–95)*

	'80	'81	'82	'83	'84	'85	'86	'87	'88	'89	'90	'91	'92	'93	'94	'95	Totals
Blood cultures	8	12	9	9	7	15	9	9	13	11	17	14	20	17	18	21	209
Other specimens	223	157	168	156	134	175	202	144	139	177	172	192	234	237	170	201	2881
Totals	231	169	177	165	141	190	211	153	152	188	189	206	254	254	188	222	3090

$\chi^2 = 12{\cdot}43$; $P = 0{\cdot}0004$.

Table 4. *The annual variations of types 3, 6, 19, and 23 (1980–95)*

Serotype	'80	'81	'82	'83	'84	'85	'86	'87	'88	'89	'90	'91	'92	'93	'94	'95	Totals
6	26	27	17	15	11	20	18	16	21	35	20	19	18	20	23	14	320
3	15	19	20	21	10	13	17	11	9	10	8	23	17	9	5	9	216
19	21	13	13	12	12	19	17	17	28	18	20	27	33	29	16	29	324
23	19	10	18	15	14	14	27	15	16	17	15	24	26	17	18	14	279
Totals	81	69	68	63	47	66	79	59	74	80	63	93	94	75	62	66	1139

$\chi^2 = 77{\cdot}69$; D.F. $= 42$; $P = 0{\cdot}0017$.

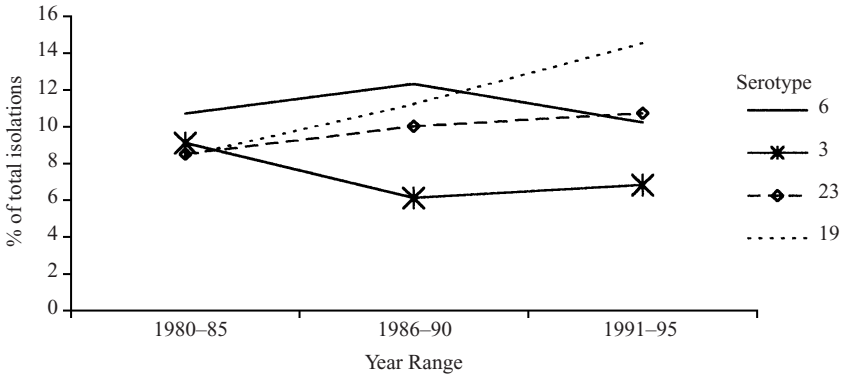

Fig. 1. Variations in prevalence of serotypes 3, 6, 19, and 23.

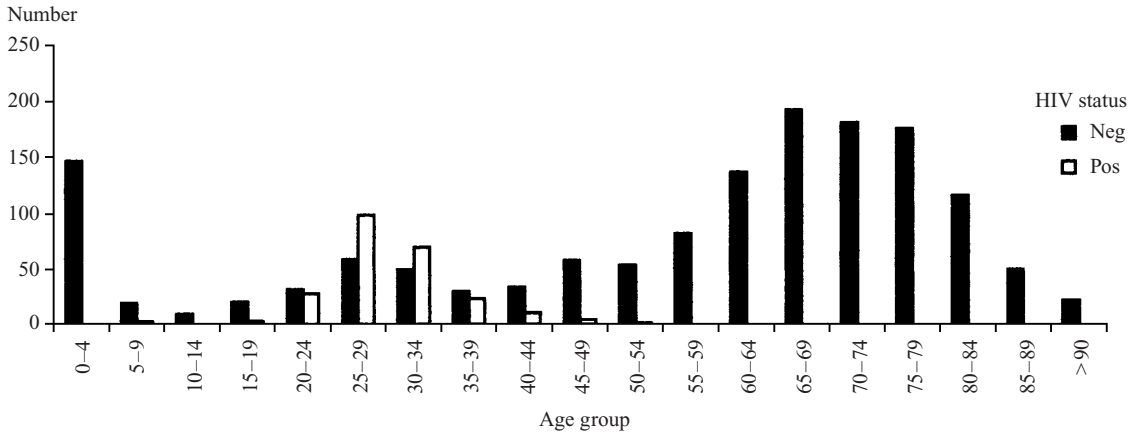

Fig. 2. Age distribution of patients.

228 isolates whereas 2421 of non-HIV-infected patients accounted for 2852 isolates. Among the HIV-infected patients, 49/132 (37%) had two or more repeat isolations more than 4 weeks apart, compared with 218/2421 (9·9%) in the non-HIV-infected group ($P < 10^{-6}$, relative risk = 5·05, 95% CI 3·46–7·03).

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Table 5. *Antimicrobial susceptibility patterns of pneumococci*

	Proportion of resistant isolates (%)			
	1992	1993	1994	1995
Penicillin	7/464 (1·5)	5/541 (0·9)	1/444 (0·2)	11/473 (2·3)
Erythromycin	4/287 (1·4)	5/295 (1·7)	4/261 (1·5)	19/420 (4·5)

Antibiotic susceptibility patterns

Penicillin and erythromycin were the commonest antibiotics tested against pneumococci in the dataset (Table 5). Data on susceptibility to chloramphenicol and trimethoprim were not complete and were excluded from the analysis.

Two of the penicillin-resistant isolates were from blood cultures and one was from bone marrow. The rest of the resistant isolates were from sputum (17), ear swabs (2), eye swabs (1) and nose swabs (1). Eleven penicillin-resistant isolates from 1995 were re-tested and found to belong to seven different serotypes (9, 19, 23, 6, 35, 10, and 14). Penicillin MICs ranged from 0·12–1·0 mg/l. Five of these strains were resistant to erythromycin and three were resistant to tetracycline. Only 2 out of 11 were multiply resistant, to penicillin, erythromycin and tetracycline. All 11 isolates were sensitive to cefotaxime, chloramphenicol, rifampicin, and vancomycin.

DISCUSSION

This study illustrates some of the epidemiological features of *S. pneumoniae* infection as seen in a district general hospital in the UK. The large dataset and long time-span help elucidate the temporal variation in the distribution of serotypes and highlight the impact of HIV infection on the epidemiology of pneumococcal infection in an area with a substantial cohort of HIV-infected IV drug abusers.

The 10 most common serotypes in the present study were similar to those reported from other parts of the UK, except for rank order [7–10]. The profile of the most common serotypes isolated from invasive infections (1, 9, 14, 4, 3, 7, 8, 23 and 6) was different from that of types causing invasive infection in similar populations in the USA [11] but very similar to those from Europe [12, 13]. Although coverage by the current 23-valent vaccine of the serotypes from invasive infections in this study was high (95·3%), careful consideration would be required in the selection of serotypes to be included in the new conjugate vaccines if these were designed to protect against the types of infections we documented. These vaccines contain a more limited number of serotypes, the majority of current formulations having seven [11, 14, 15]. Formulations of conjugate vaccines for use in adults in Europe would need to include serotypes 1, 7 and 8, types that were less frequent in the USA. The inclusion of more serotypes for a global vaccine is highly desirable, and may prove to be a less expensive option [16].

Two recent studies have shown the potential impact of these vaccines on the pattern of distribution of serotypes [17, 18], with the use of conjugate vaccines leading to a decrease in the prevalence of vaccine-related serotypes and an increase in prevalence of types not included in the vaccines. Although the clinical impact of this ecological change is at present not known, continued surveillance will be crucial.

The seasonal variation of the pattern of serotypes was similar to that described previously [19, 20]. It is thought that this correlates with the pattern of respiratory viral infections [21], which often predispose to lower respiratory tract infections. Significant shifts in the distribution of serotypes over time were observed in this study especially with types 3, 6, 19 and 23. Serotypes 3 and 6 were predominant at the beginning of the study as reported in a study from this hospital at about that time [4]. Types 19 and 23, which became prominent towards the end of the study, overtook these. Also of note were the absence of serotype 2 and the rarity of serotype 5. Other workers in this country have reported similar experiences [4, 7, 22].

There was an increasing trend in the annual rate of bacteremic infections in this study. Similar observations have been made in some, but not all other studies [13, 23, 24]. It is possible that this could have been due to an increase in hospital admissions or the number of blood cultures performed [13]. The increase in the number of individuals at risk of invasive pneumococcal disease, especially those with HIV infection, is also likely to have contributed.

Most infections occurred in patients at the extremes of age, a feature that is well known. An increase in isolations in the 20–45 years age group was also noted and was associated with patients infected with HIV. This latter feature was not observed in a previously reported study carried out at the same hospital [22]. However, there was a similar, though smaller, rise in the same age group in those not known to be HIV positive. One possible explanation may be that these patients had undiagnosed HIV infection. This peak occurred 2 years after the period when the majority of HIV-infected individuals in Edinburgh were diagnosed [25]. Others have shown that there is a significantly increased risk of concomitant HIV infection in patients aged between 20 and 45 years who develop invasive pneumococcal disease [26, 27].

The risk of repeated infections was significantly higher among HIV-infected patients in this study. This accords with the experience of other workers [28, 29]. These patients have been shown to have impaired B-lymphocyte function, resulting in an increased risk of infection with encapsulated organisms such as pneumococci [30].

The prevalence of resistance to penicillin and erythromycin of pneumococcal isolates in this study was lower than that reported elsewhere in the UK [10, 31]. The reason for such variation is not clear. Closer review of the 11 cases associated with PRPs isolated in 1995 in this study revealed no risk factors associated with acquisition of PRP [3]. The patients involved had no prior exposure to antibiotics in the few weeks leading to hospitalization, and no history of travel to a known high prevalence area. The 11 PRP strains belonged to different serotypes, and in addition, were epidemiologically unrelated.

The distribution of pneumococcal serotypes continues to change with time and surveillance will be important not only for optimizing the efficacy of conjugate vaccines, but also in the study of the natural history of pneumococcal infection following the introduction of these vaccines.

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