Seroepidemiology of invasive pneumococcal disease in Queensland, 1990 to 1997

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Abstract

Serotypes responsible for 842 cases of invasive pneumococcal disease in Queensland between February 1990 and October 1997 were identified. Type 14 caused 37.5% of episodes in children aged 0-4 years and 19.2% of adult cases. Types 6A, 6B, 14, 18C, and 19F were significantly more frequent in young children while types 3, 4, 7F, 9V and 23F predominated in adults. The regional incidence of type 14 and 7F disease differed significantly in Southeast and Far North Queensland. Coverage for 87% of children aged less than 5 years in this study would be provided by a recently advocated polysaccharide-protein conjugate vaccine containing capsular antigens of types 4, 6B, 9V, 14, 18C, 19F and 23F. Similarly, more than 90% of adults would be covered by the currently available 23- valent polysaccaride vaccine.

Introduction

Invasive pneumococcal disease, particularly among indigenous minorities, is a major public health problem in Australia.[1-4] A laboratory based pneumococcus surveillance programme commenced in Queensland in February 1990 and has continued, since July 1994, under the aegis of Queensland Health Scientific Services. This report details the type frequency and distribution of sterile site pneumococcal isolates in Queensland during a 6.8 year period. Serotype data of isolates from 87

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Aboriginal and Torres Strait Islander adults included in this report have been published previously.[2]

Methods

Queensland hospital laboratories participating in the study referred pneumococci cultured from normally sterile sites. Multiple isolates of the same type recovered during an invasive episode were included once. A pneumococcus transport system comprising semi-solid nutrient agar supplemented with lysed horse blood was provided. Referral guidelines were distributed. Cultures, on receipt, were checked for purity, catalogued and stored in skim milk glucose glycerol broth[5] at minus 75^{o} C. All isolates were sero- and factor typed, as appropriate, by the Quellung reaction, with antisera purchased from the Statens Seruminstitut, Copenhagen, Denmark.

Results

Pneumococci from 842 episodes of invasive disease were received from 13 Queensland hospital laboratories between February 1990 and October 1997. The surveillance periods for individual laboratories ranged from 4-80 months (0.4-6.8 years) (Table 1). Three hospitals, Princess Alexandra (PAH), Royal Brisbane (RBH) and Cairns Base (CBH), contributed two thirds of all strains. The ages of 29 RBH patients, from whom isolates were received, were unavailable.

Blood and CSF provided 98.6% of all strains. Adults comprised 64.5% and children aged less than two years 23% of the patient population (Table 2). Overall, 40 of the 90 known pneumococcal types were identified.

Type 14 was responsible for one quarter of all episodes (Table 3). It was the most frequent type encountered in children 0-4 years old (37.5% of 253 cases) (Table 4) and adults (19.2% of 525 cases) (Table 5). A diversity of types, 38 in all, caused adult disease (Table 5) while 82% of infections in young children were due to six types: 6A, 6B, 14, 18C, 19F and 19A (Table 4). Only 35 cases of invasive disease occurred in children aged 5-14 years.

Table 6 compares the frequency in children aged 0-4 years and adults of commonly identified types. A significantly higher proportion of type 6A, 6B, 14, 18C and 19F infections occurred in young children. These serotypes are associated with paediatric disease. Types 3, 4, 7F, 9V and 23F predominated in adults. Proportionately, disease due to type 7F was encountered significantly more frequently in Far North Queensland (FNQ) than in Southeast

Table 1. Surveillance hospitals, monitoring period and the number of referred pneumococcal isolates

Hospital	Surveillance period (years)	Number of referred strains	Percentage (%)
Cairns Base	Aug 1991 - Oct 1997 (6.1)	219	(26.0)
Gold Coast	Aug 1991 - Oct 1997 (6.1)	78	(9.3)
Greenslopes Repatriation	Oct 1990 - Jun 1994 (3.7)	10	(1.2)
Ipswich	Nov 1996 - Mar 1997 (0.4)	3	(0.4)
Mackay Base	Nov 1994 - Jun 1997 (2.6)	2	(0.2)
Mater Misericordiae	May 1997 - Oct 1997 (0.5)	36	(4.3)
Mount Isa Base	Apr 1995 - Oct 1997 (2.5)	18	(2.1)
Nambour General	June 1997 - Oct 1997 (1.3)	13	(1.5)
Prince Charles	Jun 1995 - Aug 1997 (2.1)	58	(6.9)
Princess Alexandra	Feb 1995 - Oct 1997 (2.8)	129	(15.3)
Royal Brisbane	Feb 1990 - Nov 1996 (6.8)	214	(25.4)
Thursday Island	Oct 1995 - Aug 1997 (1.9)	3	(0.4)
Townsville General	Jun 1995 - Oct 1997 (2.3)	59	(7.0)
Total		842	

Table 2. Sites of isolation of invasive pneumococci, by age of subjects, Queensland: February 1990 to October 1997.

	Age (years)					
Site	<2	2-4	5-14	15 & above	unknown	Total (%)
Blood	164	58	28	490	29	769 (91.3)
CSF	12	5	4	12		33 (3.9)
Blood & CSF	10	2	1	16		29 (3.4)
Other*	1	1	2	7		11 (1.3)
Total (%)	187(23)	66(8.1)	35(4.3)	525(64.5)	29	842

* Other: aspirates (joint, 1; lung, 1) 2; pleural fluid, 2; peritoneal fluid, 2; pericardial fluid, 1; dialysis fluid, 1; tissue, 1; blood & peritoneal fluid, 1; blood & pleural fluid & aspirate, 1.

Table 3. Invasive pneumococcal types isolated from patients of all ages in Queensland: February 1990 to October 1997.

Order of frequency	Type *	Number of isolates	(% of total/ cumulative %)
1	14	206	(24.5/24.5)
2	6B	72	(8.6/33.1)
3	4	66	(7.8/40.9)
4	19F	53	(6.3/47.2)
5	23F	50	(5.9/53.1)
6	9V	49	(5.8/58.9)
7	19A	47	(5.6/64.5)
8	18C	42	(5.0/69.5)
9	3	40	(4.8/74.3)
10	7F	35	(4.2/78.5)
11	6A	29	(3.4/81.9)
12	9N	24	(2.8/84.7)
13	1	17	(2.0/86.7)
14	22F	17	(2.0/88.7)
15	8	16	(1.9/90.6)
16	10A	11	(1.3/91.9)
17	11A	10	(1.2/93.1)
18	12F	10	(1.2/94.3)
19	16F	8	(0.9/95.2)
20	15F	6	(0.7/95.9)
21	18A	6	(0.7/96.6)
Subtotal		814	
Other types †		28	
Total		842	

* Types included in the currently available 23–valent pneumococcal polysaccharide vaccine are underlined.

† Types 15C, 34, 38 (3 strains each); 18B, 33F, 48 (2 strains each); 5, 13, 15A, 15B, 17F, 18F, 20, 21, 22A, 23A, 31, 35B, 45 (1 strain each).

Table 5. Invasive pneumococcal types isolated from adults aged 15 years and over in Queensland: February 1990 to October 1997.

Order of frequency	Type *	Number of isolates	(% of total/ cumulative %)
1	14	101	(19.2/19.2)
2	4	51	(9.7/28.9)
3	23F	40	(7.6/36.5)
4	3	37	(7.0/43.5)
5	9V	34	(6.5/50.0)
6	7F	31	(5.9/55.9)
7	6B	29	(5.5/61.4)
8	19A	28	(5.3/66.7)
9	19F	23	(4.4/71.1)
10	9N	17	(3.2/74.3)
11	18C	16	(3.0/77.3)
12	1	15	(2.9/80.2)
13	22F	15	(2.9/83.1)
14	8	14	(2.7/85.8)
15	6A	13	(2.5/88.3)
16	12F	8	(1.5/89.8)
17	10A	7	(1.3/91.1)
18	11A	7	(1.3/92.4)
19	16F	6	(1.1/93.5)
20	15F	5	(1.0/94.5)
21	18A	5	(1.0/95.5)
Subtotal		502	
Other types †		23	
Total		525	

* Types included in the currently available 23-valent pneumococcal polysaccharide vaccine are underlined.

† Types 34, 38 (3 strains each); 33F, 48 (2 strains each); 5, 13, 15A, 15B, 15C, 17F, 18F, 18B, 20, 22A, 23A, 31, 35B (1 strain each).

Table 4. Invasive pneumococcal types isolated from children aged 0 to 4 years in Queensland: February 1990 to October 1997.

Order of frequency	Type	Number of isolates	(% of total/ cumulative %)
1	14	95	(37.5/37.5)
2	6B	42	(16.6/54.1)
3	19F	26	(10.3/64.4)
4	18C	16	(6.3/70.7)
5	19A	15	(5.9/76.6)
6	6A	14	(5.5/82.1)
7	4	13	(5.1/87.2)
8	9V	7	(2.8/90.0)
9	23F	7	(2.8/92.8)
Subtotal		235	
Other types *		18	
Total		253	

* Types 9N, 10A (3 strains each); 1, 12F, 15C, 22F (2 strains each); 7F, 8, 11A, 45 (1 strain each)

Queensland (SEQ) while the reverse was true for type 14 cases (Table 7).

Overall, 91.6% of isolates in this study are included in the currently available 23-valent polysaccharide vaccine (Table 3) while 91.2% of isolates from adults have vaccine coverage (Table 5). Since types 6A (not in the vaccine) and type 6B are cross protective,[6] coverage for this age group is 93.6%.

Discussion

The high frequency of invasive disease in all ages due to type 14 is an important but not surprising finding. Type 14 pneumococcal disease is globally endemic. Of more than 10,000 strains cultured from blood and CSF in mainly European countries during 1982 to 1987, type 14 ranked first and third in children and adults respectively.[7] In the USA between 1978 and 1994 27% of 3884 sterile site isolates from children under six years old were type 14,[8] while in Finland, a study in children aged 0-15 years during 1985 and 1989 identified type 14 in 19% of 365 typed episodes with 82% of strains from subjects under two years old.[9] In developing countries such as Bangladesh and Papua New Guinea and in indigenous populations in

Table 6. Comparison in children aged 0-4 years (n=253) and adults (n=525) of the frequency of type-specific pneumococcal disease in Queensland: February 1990 to October 1997.

Type	Number of isolates		χ^2,1df	P
	Children	Adults		
1	2	15	2.513*	NSS
3	0	37	17.197*	.001
4	13	51	4.682	.05
6A	14	13	4.764	.05
6B	42	29	25.259	.001
7F	1	31	10.770*	.01
8	1	14	3.535*	NSS
9N	3	17	2.110*	NSS
9V	7	34	3.992*	.05
14	95	101	30.375	.001
18C	16	16	4.647	.05
19F	26	23	10.056	.01
19A	15	28	0.116	NSS
23F	7	40	6.253*	.02

* Yates' correction applied.

NSS not statistically significant.

Table 7. Comparison of the regional incidence of types 7F and 14 in Southeast (n=541) and Far North Queensland (n=299): February 1990 to October 1997.

Type	Number of isolates (%)		χ2,1df	P
	SEQ	FNQ		
7F	6 (1.1)	29 (9.7)	33.466	.001
14	153 (28.3)	52 (17.4)	12.378	.001

SEQ Southeast Queensland

FNQ Far North Queensland

Australia, type 14 causes 9-12% of invasive pneumococcal disease in children less than five years old.[3,10,11] A recent marked increase in invasive type 14 disease has been reported in Sweden.[12]

Although type 23F disease is generally associated with children,[13,14] it also commonly invades older age groups,[7,15] as seen in the current study. Unlike most other types protective antibody levels to type 23F continue to increase until adolescence and possibly longer.[16] This finding may, in part, explain the relative frequency of type 23F disease in older subjects.

Type 7F is one of several epidemic types whose frequency has diminished over time while type diversity has increased.[17-21] It has been suggested that these changes are associated with improved socioeconomic conditions including less crowding and prompt treatment and isolation of cases of active disease.[15] The predominance of type 7F disease in FNQ (9.7% of 299 cases) compared with SEQ (1.1% of 541 cases) may reflect the presence of risk factors similar to those in developing countries. In central Australia and Western Australia type 7F is the second (9.4% of 203 episodes) and fourth (6.5% of 153 episodes) ranked type respectively in pneumococcal disease[3] (VISN Study Group, Western Australia, unpublished material). The prevalence of type 7F invasion in eastern states is similar to that of SEQ. Of 989 invasive pneumococci identified in Victoria in 1994 to 1997 only 1.5% belonged to type 7F (Hogg G and Strachan J, unpublished material) while in New South Wales 1.3% of 154 recent isolates are of this type (McIntyre P and others, unpublished material).

Whilst type 14 disease showed a Queensland-wide distribution, significantly greater frequency occurred in SEQ. This was due, at least in part, to the commoness of type 14 disease in patients admitted to RBH during a 6.8 year surveillance period. At this hospital type 14 isolations comprised 31% of all referrals with peaks in 1990 (42%) and 1994 (49%). Type 14 disease also predominated in other SEQ hospitals including Gold Coast (29%) and Prince Charles (34.5%) during shorter monitoring periods.

Our study indicates that more than 90% of pneumococcal strains in adults in Queensland are represented in the current 23-valent polysaccahride vaccine. Children less than 5 years respond poorly to polysaccharide antigens, particularly those belonging to capsular groups 6, 19 and 23 and type 14.[22,23] Types 6A, 6B, 14, 19F and 23F were responsible for 73% of 253 paediatric episodes in the current study. A pneumococcal protein conjugate vaccine containing capsular antigens 4, 6B, 9V, 14, 18C, 19F and 23F for use in children in industrialised countries has been advocated.[24] With cross-protection between types 6A and 6B this formulation would provide 87% coverage for our children aged under five years.

The laboratory surveillance of invasive pneumococcal disease should have an ongoing public health commitment in order to monitor satisfactory vaccine coverage and significant changes in type specific invasion.

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