Invasive pneumococcal disease among children in Victoria

Min Liu,[1,2] Ross Andrews,[2,3] Joanne Stylianopoulos,[4] Catherine Ferreira,[2] Geoff Hogg,[4] Nyree Pyper[2]

Abstract

This study analysed notification data from the first year of enhanced surveillance of invasive pneumococcal disease (IPD) in Victoria (1 July 2001 – 30 June 2002), with a focus on risk factors for infection and vaccination status among children under five years of age. Overall, there were 397 notifications (8.2 per 100,000 population), 131 (33%) were children under five years of age. The highest notification rates were among those aged less than two years (72.6 per 100,000 population). Among children aged less than five years: bacteraemia without a primary focus of infection was the most common clinical presentation (64%); 89 per cent were hospitalised with the median length of stay being three days; four children (3%) died. There were 107 cases of a known serotype, 92% (n=98) were either in or closely related to those included in the 7-valent conjugate pneumococcal vaccine (7vPCV). Most cases (98%) were not eligible for free 7vPCV under the currently funded program in Victoria. Only one child had been vaccinated. The results from the first year of enhanced IPD surveillance in Victoria suggest consideration should be given to extending the publicly funded program to include all children under two years of age. *Commun Dis Intell* 2003;27:362–366.

Keywords: invasive pneumococcal disease; enhanced surveillance; risk factors; vaccine; serotype; children

Introduction

Streptococcus pneumoniae causes morbidity and mortality in both developing and developed countries, predominantly among young children and the aged.[1] Invasive pneumococcal disease (IPD), that is where *S. pneumoniae* is isolated from a normally sterile site, usually presents as pneumonia, meningitis or bacteraemia (without a primary focus of infection). *S. pneumonia*e has gradually become more resistant to penicillin and other antibiotics.[2]

Victoria is participating in a national program of enhanced IPD surveillance under the auspices of the Communicable Diseases Network Australia (CDNA).[3] Since May 2001, all medical practitioners and laboratories in Victoria have been required to notify the Department of Human Services (DHS) of all IPD diagnoses pursuant to the Health (Infectious Diseases) Regulations 2001.

A 7vPCV (Prevenar™, Wyeth-Lederle Vaccines) has been licensed and approved for use among children six weeks to nine years of age in Australia,[4] but public funding for the vaccine in Victoria is only available to Indigenous children under two years of age or children under five years of age with one of the following medical risk factors:[5]

- impaired immunity;
  - congenital immune deficiency including symptomatic IgG subclass or isolated IgA deficiency;
  - disease associated with immunosuppressive therapy or radiation therapy;
  - compromised splenic function due to sickle haemoglobinopathies or congenital or acquired asplenia;
  - HIV infection;
  - renal failure or relapsing or persistent nephrotic syndrome;
- anatomical abnormalities;
  - cardiac disease associated with cyanosis or cardiac failure;
  - proven or presumptive cerebrospinal fluid leak.

This article describes the epidemiology of IPD in Victoria based on the first 12 months of notification data, with a focus on risk factors for infection and vaccination status of children under five years of age.

1. Public Heath Training Scheme, Department of Human Services, Victoria
2. Communicable Diseases Section, Department of Human Services, Victoria
3. National Centre for Epidemiology and Population Health, Australian National University, Canberra
4. Microbiological Diagnostic Unit, Public Health Laboratory, University of Melbourne, Victoria

Corresponding author: Dr Min Liu, 589 Collins Street, Melbourne, Victoria 3000. Telephone: +61 3 9616 1506. Facsimile: +61 3 9616 1500. Email: min.liu@dhs.vic.gov.au

Methods

A case of IPD was defined as a clinical condition where *S. pneumoniae* was isolated from blood, cerebrospinal fluid or other normally sterile site or detected by nucleic acid testing, e.g. polymerase chain reaction, in a normally sterile site.

All notifications of IPD received by DHS from 1 July 2001 to 30 June 2002 were included. The treating practitioner of each notified case was contacted by telephone or facsimile to confirm clinical details, risk factors for infection and vaccination status as a component of a national program of enhanced IPD surveillance.[3] The primary diagnostic laboratory was encouraged to forward cultures from normally sterile sites to the Microbiological Diagnostic Unit, Public Health Laboratory, Melbourne University, for serotyping.

Risk factor data for notifications related to children under five years of age included: immunocompromising conditions (e.g. HIV/AIDS, organ transplant, multiple myeloma, asplenia, chronic drug therapy); chronic illness (e.g. chronic respiratory, heart, liver or renal disease, diabetes); prematurity (<37 weeks gestation); low birth weight (<2,500 g); congenital or chromosomal abnormality; cigarette smoker in the household. More than one risk factor could be reported. Cases were classified according to the identified risk factors as: immunocompromised; any other identified risk factor; no identified risk factor; or as unspecified (if no records were available). Immunocompromised cases who also had other risk factors were classified as immunocompromised.

For all children under five years of age, vaccination status was checked against the Australian Childhood Immunisation Register (ACIR). In order to be considered vaccinated or partially vaccinated, a pneumococcal vaccine must have been given at least two weeks prior to illness onset. The Australian Bureau of Statistics Estimated Residential Population for Victoria, as at 30 June 2001, was used as the source for denominator data when calculating notification rates.

Results

All ages

From 1 July 2001 to 30 June 2002, DHS received 397 notifications of IPD, ranging from 18 cases in February 2002 to a peak of 56 cases in August 2001. There were 213 notifications for males (56%) and 184 females (44%). The notification rate was 8.2 cases per 100,000 population. Thirty-three per cent of the notifications (n=131) were for children under five years of age. Age-specific rate notification rates were highest among those aged less than five years (42.1 per 100,000 population) and those aged 85 years or more (35.6 per 100,000 population) (Figure). For the younger age group, rates were highest among children aged less than two years (72.6 per 100,000 population). There were 22 deaths due to IPD (6%), the highest case fatality rate was among those aged 65 years or more (10%, 12 deaths).

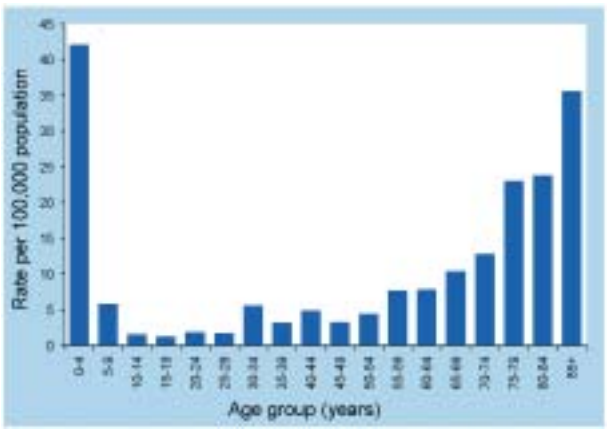
Four notifications (1%) were Aboriginal persons (aged from 39–46 years), 325 (82%) were not Aboriginal or Torres Strait Islander persons whilst Indigenous status was not specified for the remaining 68 cases (17%).

Children under five years of age

Of the 131 notifications among children aged less than five years, 84 (64%) had bacteraemia without a primary focus of infection, 27 (21%) presented with pneumonia and 13 (10%) with meningitis (one child presented with pneumonia and meningitis). The foci of infection were not specified for the remaining eight cases (6%). One hundred and seventeen cases were hospitalised (89%), seven (5%) were not hospitalised whilst hospitalisation status was not established for the remaining seven (5%). The median length of stay for hospitalised cases was three days (range 0–86 days) and the interquartile range was 2–3 days.

Four deaths were reported among children aged less than five years (3% case fatality rate). A 17-month-old child with serotype 18C had bacteraemia without primary focus. The second fatality was an infant aged two months who had serotype 19A identified from a post mortem lung culture. The cause of death was confirmed as bilateral broncho-pneumonia by the Coroner and the Chief Pathologist. The third fatality was a two-year-old child who presented with meningitis and had serotype 19F identified from cerebrospinal fluid. The fourth fatality was a 15-month-old child with a positive blood culture and clinical meningitis features for whom the serotype was unknown. Of the three deaths due to known serotypes, two were a type contained in the 7vPCV. No risk factor information was obtained for the child

Figure. Age-specific notification rate of invasive pneumococcal disease, Victoria, 1 July 2001 to 30 June 2002



diagnosed post mortem, while none of the other children were immunocompromised or identified as having any other risk factor.

Serotypes

Serotypes were identified for 107 cases (82%), one isolate was unable to be typed (1%) and cultures were not forwarded for serotyping for the remaining 23 cases (18%). Of the 107 with a known serotype, 95 (89%) were serotypes contained in the 7vPCV, while another 3 (3%) were serotype 6A for which the vaccine is likely to confer protection since it is closely related to a serotype contained within the 7vPCV.[6] Eight of the nine remaining cases were caused by serotypes contained in the 23 valent polysaccharide pneumococcal vaccine (7F, 11A, 15B and 19A) but only one of these was old enough (>2 years) to have received that vaccine (Table 1).[7]

Vaccination status and risk factors

One child, who had biliary atresia and was awaiting a liver transplant, had recurrent bacteraemia within the study period (both episodes were serotype 14). The first episode occurred at 10 months of age, the child received a first dose of 7vPCV five days prior to illness onset so was not expected to have developed an immune response within that time. The second episode occurred at age 11.5 months and by that time, the child had received two doses at least two weeks prior to illness onset (the second dose of 7vPCV was given 12 days after the first).

Three cases (2%) were in a risk group eligible for the free vaccine in Victoria, all were immunocompromised. One of these was infected with a serotype not contained in the 7vPCV—the child, aged four months, had received a bone marrow transplant and had serotype 11A isolated from a blood culture. The other two children were both infected with serotypes contained in the 7vPCV (14 and 18C)—one child, aged three years, was receiving treatment for leukaemia while the other child, aged four years, had acute lymphatic lymphoma. All three children had bacteraemia without a primary focus of infection.

Twenty-six children (20%) had a risk factor for IPD other than those for which the vaccine is currently funded, 89 (68%) had no identified risk factor, and there was insufficient information available to enable

Table 1. Vaccine and non-vaccine serotypes of invasive pneumococcal disease identified among children aged less than 5 years, Victoria, 1 July 2001 to 30 June 2002

Vaccine	Serotype	Age (years)					Total		Cumulative
		<1	1	2	3	4	n	%	%
7vPCV	14	12	13	7	3	4	39	36	36
	6B	7	9	1	1		18	17	53
	18C	2	5	3	2	1	13	12	65
	19F		5	3		2	10	9	75
	4		3	1	2	1	7	7	81
	23F	3		1	1		5	5	86
	9V	1				2	3	3	89
Related*	6A	1	1	1			3	3	92
Subtotal		26	36	17	9	10	98	92	92
23vPPV	19A	2	3				5	5	96
	11A	1					1	1	97
	15B	1					1	1	98
	7F					1	1	1	99
Neither	18B		1				1	1	100
Total		30	40	17	9	11	107	100	100
Others		12	8	0	3	2	25		N/A

7vPCV refers to serotypes contained in the 7 valent conjugate pneumococcal vaccine.

* Serotype 6A is not contained in the 7vPCV but is closely related to Serotype 6B.

23vPPV refers to serotypes contained in the 23 valent polysaccharide pneumococcal vaccine but not in the 7vPCV.

Other includes one isolate for a child aged <1 year that was not typable and 24 isolates that were not forwarded for serotyping.

N/A Not applicable with respect to proportions of vaccine and non-vaccine serotypes.

identification of any risk factors for the remaining 12 children (9%) (Table 2). Information on smoking in the household was poorly reported with 67 per cent (n=88) recorded as unknown or not stated, even so this was the most prevalent risk factor reported (10 children, 8% of 130). It is likely that more cases with this risk factor would have been identified if interviews had also been conducted with the parent/guardian. Chronic illness and gestation related risk factors were more completely reported with the proportions unknown or not stated ranging from 30–34 per cent. The congenital or chromosomal abnormalities identified were: Arnold-Chiari syndrome; anomalous pulmonary venous drainage; biliary atresia; cardiac murmur/pulmonary stenosis; Down's syndrome; Hirschsprung's disease; infantile osteopetrosis and translocation of chromosome 3&6.

Discussion

IPD first became notifiable in Victoria on 15 May 2001. This is the first report including a full 12 months data since that time and includes the information collected through enhanced surveillance in Victoria. This report has focussed on children less than five years of age because this is a group with high rates of disease and includes a subgroup for which the 7vPCV is publicly funded.[5]

Other jurisdictions, such as metropolitan New South Wales and the United States of America have reported rates approaching, or in excess of, 100 cases per 100,000 children under two years of age.[8,9] In Victoria, the notification rate for children aged less than five years (42.1 cases per 100,000 population) was slightly lower than the national rate reported recently (47.3 cases per 100,000 population).[3] For children less than two years of age, the notification rate (72.6 cases per 100,000 population) represented a 23 per cent increase on data collated prior to IPD becoming a notifiable condition in Victoria.[10] However, it is likely that the true disease burden remains under-reported. Failure to test or failure to test prior to commencement of antibiotics are factors that have been identified as contributing to under-reporting.[11] Failure to notify all diagnosed cases to DHS could also be a factor given that this was the first year the condition was notifiable.

Even though the notification rate was highest in children under two years of age and serotyping showed that 92 per cent of cases in this age group were of a type included in/or closely related to those in the 7vPCV, only one child had been vaccinated. Of all the cases detected in children under five years of age, only three (2%) were eligible for free vaccine under the current program.

Table 2. Risk factors of invasive pneumococcal disease identified among children aged less than 5 years, Victoria, 1 July 2001 to 30 June 2002

Risk factor	Age (years)					Total*	
	<1	1	2	3	4	n	%
Immunocompromised	1	0	0	1	1	3	2
Any other identified risk factor (see below)	10	7	2	5	2	26	20
No identified risk factor	25	37	14	6	7	89	68
Unspecified	4	4	1	0	3	12	9
Total	40	48	17	12	13	130	100
Any other identified risk factor including:	10	7	2	5	2	26	20
Chronic illness	2	3	1	2	1	9	7
Premature birth	2	2	2	0	1	7	5
Low birth weight	1	1	2	1	0	5	4
Congenital or chromosomal abnormality	5	2	1	0	0	8	6
Smoker in household	5	2	0	2	1	10	8

* Total refers to children (n=130) not notifications (one child had two episodes during study period)

† More than one risk factor could be identified for each notified case

The 7vPCV is currently funded for those groups in Australia at highest risk of pneumococcal disease: Indigenous children to the age of two years and non-Indigenous children to the age of five years in specified risk groups.[4] Our data showed that, within Victoria, the disease burden was predominantly among children outside the funded risk groups (98%). Whilst it is acknowledged that risk factor information collated through the enhanced surveillance may be incomplete, it is not believed that the information collected from treating practitioners is likely to substantially under-estimate the proportion of children eligible for the 7vPCV under the currently funded program.

The 7vPCV contains serotypes that most frequently cause invasive antibiotic-resistant disease.[12] Both the efficacy and cost-effectiveness of the vaccine have shown that it has the potential to have a significant public health impact on the incidence of IPD.[13,14] Assuming 92 per cent of all cases in children were caused by serotypes contained in the 7vPCV, then, given vaccine efficacy of 94 per cent, we could expect that a universal vaccination program in Victoria could prevent 86 per cent of invasive pneumococcal disease in children old enough to complete the primary course.

In the United States of America, conjugate pneumococcal vaccine has been recommended for all children under two years of age.[15] A recent report on invasive pneumococcal disease in north Queensland, an area with a much higher proportion of Indigenous children than Victoria, suggested that there may be a case for extending the publicly funded 7vPCV program to include all non-indigenous children under two years of age.[16] The results from the first year of enhanced surveillance in Victoria support this view.

Acknowledgements

We wish to thank staff at the Department of Human Services, the Microbiological Diagnostic Unit, Public Health Laboratory, the University of Melbourne, primary diagnostic laboratories, medical practitioners and hospitals throughout Victoria who contributed to the surveillance. In particular, we wish to acknowledge Kerry-Ann O'Grady, Joanna Gaston and Megan Counahan, DHS, for data management and comments on the manuscript. The National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases (NCIRS) provided funding to support a pilot program of enhanced IPD surveillance, additional funding was also provided by the Commonwealth Department of Health and Ageing during the first year of the program. NCIRS also provided a PhD scholarship for Ross Andrews. The Commonwealth Department of Health and Ageing also supported Laboratory Typing.

References

1. Forrest JM, McIntyre PB, Burgess MA. Pneumococcal disease in Australia. *Commun Dis Intell* 2000;24:89-92.
2. Musher DM. *Streptococcus pneumoniae*. In: Mandell GL, Douglas RG and Bennett JE, eds. *Principles and practice of infectious diseases*. 4th edn. Philadelphia: Churchill Livingstone, 2000:1811–1826.
3. Roche P, Krause K for the Enhanced Pneumococcal Surveillance Group of the Pneumococcal Working Party of the Communicable Diseases Network Australia. Invasive pneumococcal disease in Australia, 2001. *Commun Dis Intell* 2002;26:505–519.
4. National Health and Medical Research Council Health Advisory Committee. National Childhood Pneumococcal Vaccination Program: recommendations of the Australian Technical Advisory Group on Immunisation for a childhood pneumococcal vaccination program. National Health and Medical Research Council; October 2001
5. Victorian Government Department of Human Services, Public Health Division. Childhood pneumococcal disease immunisation information. Department of Human Services; May 2002 (0210202).
6. Fedson DS, Musher DM, Eskola J. Pneumococcal vaccine. In: Plotkin SA, Orenstein WA, eds. *Vaccines*. 3rd edn. Philadelphia: WB Saunders, 1999:553–607.
7. National Health and Medical Research Council. The *Australian Immunisation Handbook*. 7th edn. Canberra: Australian Government Publishing Service, 2000:183–187.
8. McIntyre PB, Gilmour RE, Gilbert GL, Kakakios AM, Mellis CM. Epidemiology of invasive pneumococcal disease in urban New South Wales, 1997–1999. *Med J Aust* 2000;173:S22–S26.
9. Centers for Disease Control and Prevention. Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Morb Mortal Wkly Rep* 1997;46:1–24.
10. Hogg GG, Strachan JE, Lester RA. Invasive pneumococcal disease in the population of Victoria. *Med J Aust* 2000;173:S32–S35.
11. Fedson DS, Scott JA, Scott G. The burden of pneumococcal disease among adults in developed and developing countries: what is and is not known. *Vaccine* 1999;17:S11–S18.
12. Poland GA. The prevention of pneumococcal disease by vaccines: promises and challenges. [Review] *Infect Dis Clin North Am* 2001;15:97–122.
13. Peters TR, Edwards KM. The pneumococcal protein conjugate vaccines. *J Paediatr* 2000;137:416–420.
14. Lieu TA, Ray GT, Black SB, Butler JC, Klein JO, Breiman RF, *et al*. Projected cost-effectiveness of pneumococcal conjugate vaccination of healthy infants and young children. *JAMA* 2000;283:1460–1468.
15. Centres for Disease Control and Prevention. Preventing pneumococcal disease among infants and young children: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Morb Mortal Wkly Rep* 2000;49(RR–9):1–38.
16. Hills SL, Hanna JN and Murphy D. Invasive pneumococcal disease in North Queensland, 2001. *Commun Dis Intell* 2002;26:520–524.