

# Invasive pneumococcal disease in Australia, 2002

Paul Roche,<sup>1</sup> Vicki Krause,<sup>2</sup> Ross Andrews,<sup>3</sup> Louise Carter,<sup>4</sup> David Coleman,<sup>5</sup> Heather Cook,<sup>2</sup> Megan Counahan,<sup>3</sup> Carolien Giele,<sup>6</sup> Robyn Gilmore,<sup>7</sup> Sharon Hart,<sup>8</sup> Robyn Pugh<sup>9</sup> with laboratory data supplied by Geoff Hogg,<sup>10</sup> Denise Murphy,<sup>11</sup> and Michael Watson<sup>12</sup> for the Pneumococcal Working party of the Communicable Diseases Network Australia

## Abstract

There were 2,271 cases of invasive pneumococcal disease (IPD) notified to the National Notifiable Diseases Surveillance System in Australia in 2002; a rate of 11.5 cases per 100,000 population. The notification rate varied between states and territories and by geographical region with the highest rates in the north of the country. Invasive pneumococcal disease was reported most frequently in children aged less than five years (57.3 per 100,000 population). Enhanced surveillance for IPD in 2002 was carried out in all states and territories, providing additional data on 1,929 (85%) of all notified cases. Rates of IPD in Indigenous Australians were 2.7 times the rate in non-Indigenous Australians. The clinical presentation of IPD was most commonly pneumonia (44%) and bacteraemia (35%). There were 175 deaths attributed to IPD resulting in an overall case fatality rate of 9.2 per cent. Forty-two per cent of all cases had a recognised risk factor for IPD. Seventy-five per cent of all pneumococcal isolates serotyped were serotypes in the seven-valent conjugate vaccine and 93 per cent were serotypes in the 23-valent polysaccharide pneumococcal vaccine. The clinical presentation and rates of risk factors varied between Indigenous and non-Indigenous cases and non-vaccine serotypes occurred more frequently among Indigenous children and adults. *Commun Dis Intell* 2003;27:466–477.

*Keywords:* disease surveillance, pneumococcal disease, polysaccharide pneumococcal vaccine, *Streptococcus pneumoniae*

## Introduction

Infection with *Streptococcus pneumoniae* is responsible for significant morbidity and mortality worldwide, especially in the very young, the elderly and those with predisposing risk factors. It is a leading cause of otitis media, pneumonia, bacteraemia, meningitis and a less frequent cause of other conditions including septic arthritis and mastoiditis. Invasive pneumococcal disease (IPD) is defined as a clinical condition in which *S. pneumoniae* infects a normally sterile site such as blood, cerebrospinal fluid (CSF) or pleural fluid. IPD presents most commonly as pneumonia in adults and bacteraemia in children. The risk of disease is highest among people who are immunocompromised or have a chronic illness.

In developed countries, the incidence rate of IPD is bimodal, with a peak in children under two years and another peak in adults over 65 years. The incidence rates can be many times higher in developing countries and in some populations of developed countries, including Australian and American Indigenous people. Rates in Indigenous children from Central Australia between 1994 and 1998 were 1,534 cases per 100,000 population<sup>1</sup> while between 1983 and 1990, rates of IPD among White Mountain Apache children were as high as 1,820 cases per 100,000 population.<sup>2</sup> Case fatality rates for IPD vary depending on the age and the focus of the disease.<sup>3</sup>

1. Surveillance and Epidemiology Section, Department of Health and Ageing, Canberra, Australian Capital Territory
2. Centre for Disease Control, Department of Health and Community Services, Darwin, Northern Territory
3. Communicable Diseases Section, Department of Human Services, Melbourne, Victoria
4. Communicable Diseases Control Unit, Department of Health and Community Care, Canberra, Australian Capital Territory
5. Communicable Disease Surveillance, Department of Health and Human Services, Hobart, Tasmania
6. Communicable Disease Control Branch, Department of Health, Perth, Western Australia
7. Communicable Diseases Branch, Department of Health, Sydney, New South Wales
8. Communicable Disease Control Branch, Department of Human Services, Adelaide, South Australia
9. Communicable Disease Unit, Queensland Health, Brisbane, Queensland
10. Microbiological Diagnostic Unit, University of Melbourne, Melbourne, Victoria
11. Queensland Health Pathology and Scientific Services, Brisbane, Queensland
12. Department of Microbiology, Children's Hospital at Westmead, Westmead, New South Wales

Corresponding author: Dr Paul Roche, Surveillance and Epidemiology Section, Department of Health and Ageing, GPO Box 9848 (MDP6), Canberra ACT 2601. Telephone: +61 2 6289 8152. Facsimile: +61 2 6289 7791. Email: paul.roche@health.gov.au

Since the 1970s, large outbreaks of severe pneumococcal disease caused by penicillin resistant organisms occurred in South Africa and Papua New Guinea and subsequently the rates of penicillin resistance in pneumococci increased worldwide. In Australia, the rate of penicillin resistant pneumococci increased from one per cent in 1984 to 25 per cent in 1997. Reduced susceptibilities to other antimicrobials has also emerged in recent years with the rate of reduced susceptibility to third generation cephalosporins in Australia reaching 13 per cent in 1997.<sup>4</sup> The emergence of multi-drug resistant pneumococci has been an important factor for the development and use of new pneumococcal vaccines.

Ninety serotypes of *S. pneumoniae* identified by the polysaccharide composition of their capsule have been described. Immunity to pneumococcal infection is thought to be serotype specific. Vaccines containing pneumococcal polysaccharides from a varying number of serotypes have been available for many years, with a 23-valent polysaccharide vaccine produced in 1983 being licensed in Australia in 1986 (Table 1). Polysaccharide vaccines are poorly immunogenic in young children.<sup>5</sup> A vaccine in which polysaccharides from seven serotypes coupled to a protein carrier (mutated diphtheria toxoid) was developed to provide an effective vaccine for children and in a trial in the United States of America (USA) in infants aged 2 to 15 months demonstrated an efficacy of 93.9 per cent.<sup>6</sup> This conjugate vaccine was licensed for use in Australia in January 2001 and vaccination of children at high risk commenced in July 2001 (Table 1).

IPD was a notifiable disease in all Australian states and territories in 2002 and data were reported to the National Notifiable Diseases Surveillance System (NNDSS). In addition, the Commonwealth Government funded an enhanced surveillance program for IPD in five jurisdictions and three reference laboratories in 2002.

### Methods and materials

#### Case definition

A case of invasive pneumococcal disease was defined as the isolation from or the detection in blood, cerebrospinal fluid or other sterile site of *Streptococcus pneumoniae*.

#### Data collection

Invasive pneumococcal disease has been a notifiable disease in some Australian states and territories for several years. In 2001, the Communicable Diseases Network Australia agreed to make IPD notifiable in all states and territories and data were forwarded to the National Notifiable Diseases Surveillance System. Since this required changes to legislation, the data in 2001 was incomplete in some states and territories, but was complete for all jurisdictions for the first time in 2002.

NNDSS data in 2002 comprised core data, which is a set of data collected on all cases of all notifiable diseases, as well as enhanced data specific for IPD. A list of the data fields collected in core and enhanced datasets are shown in Table 2.

**Table 1. Recommendations for pneumococcal vaccination, Australia, 2002**

Vaccine	23-valent polysaccharide vaccine	7-valent conjugate vaccine
Pneumococcal serotypes	1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, 33F	4, 6B, 9V, 14, 18C, 19F, 23F
Date implemented	1998	July 2001
Target populations	All individuals aged 65 years and over Individuals with asplenia Immunocompromised patients Aboriginal and Torres Strait Islander people aged 50 years and over Immunocompetent individuals with chronic illness including chronic cardiac, renal or pulmonary disease, diabetes and alcohol-related problems	Tier 1: Indigenous children less than 5 years living in Central Australia Tier 2: Indigenous children aged less than 2 years particularly in rural and remote settings Tier 3: Indigenous children under 2 years living in other settings Non-Indigenous children less than 2 years living in Central Australia Non-Indigenous children with conditions predisposing to pneumococcal infection
Data source	NHMRC Immunisation Handbook 7th edition, 2000	ATAGI recommendations, 2001

There were differences between jurisdictions in the collection of enhanced IPD data. While enhanced data were collected on all cases in the Northern Territory, South Australia, Tasmania, Victoria and Western Australia, other jurisdictions collected enhanced data on limited age groups or in limited areas. In Queensland, enhanced data was collected on cases aged less than five years or more than 50 years in all areas except north Queensland, where enhanced data were collected on all cases. In New South Wales enhanced data were collected on all cases aged less than five years or more than 50 years. In the Australian Capital Territory, enhanced data collection was limited to data on the site of infection and pneumococcal serotype.

NNDSS data for 2002 were analysed by date of disease onset while data in the enhanced datasets were analysed by date of notification.

Clinical presentations were coded as pneumonia, meningitis, bacteraemia, other or unknown. Pneumonia was defined as blood culture positive for *S. pneumoniae* with clinical and/or radiological signs of pneumonia. Meningitis was defined as CSF

and/or blood culture positive with supportive CSF findings. Bacteraemia was defined as blood culture positive with no localising signs. 'Other' included detection of *S. pneumoniae* in pleural, peritoneal or joint fluid. More than one clinical presentation could be recorded for each case.

### Data analysis

The rates presented in this report were calculated using population data produced by the Australian Bureau of Statistics (ABS). The Estimated Resident Population (ABS 3201.0) in each state and territory and in Australia as a whole, as at 30 June 2002, was used as the denominator in rate calculations. Estimates of the Indigenous Australia population were based on projections from the 2001 census (ABS 3231.0). The ABS calculated projections based on assumptions about future births, deaths and migrations in the Indigenous population and a 'low' and 'high' estimate were reported. The 'low' estimate has been used in this report, consistent with the reporting of other national communicable diseases.

**Table 2. Enhanced invasive pneumococcal disease surveillance data, supplied by states and territories, used in this report**

Data type	Data fields
Demographic	Date of birth Age Indigenous status: (Aboriginal, Torres Strait Islander, Aboriginal and Torres Strait Islander, other, unknown) Location (optional) Postcode
Risk factors	Premature birth (gestation less than 37 weeks) Congenital abnormality Anatomical or congenital asplenia Immunocompromised (e.g. HIV, lymphoma, transplant, multiple myeloma, nephrotic syndrome, etc.) Chronic illness (e.g. cardiac disease, pulmonary disease, CSF leak, diabetes)
Clinical data	Clinical presentation (pneumonia, meningitis, bacteraemia, other, unknown) Date of onset Death due to invasive pneumococcal disease
Microbiology data	Specimen collection date Date laboratory results issued (report date) Date notification received Specimen type (blood, CSF, pleural fluid, joint fluid, other sterile site) Specimen culture positive or <i>S. pneumoniae</i> detected by nucleic acid tests Antibiotic susceptibility (penicillin, cefotaxime/ceftriaxone) Pneumococcal serotype
Vaccination history	Source of vaccination history (validated, not validated, information not collected) Pneumococcal vaccination dates, number of doses and type of vaccine Vaccination status (fully vaccinated for age, partially vaccinated for age, not vaccinated, not applicable, unknown)

The significance of differences in proportions were calculated using the Chi-square test with Yates correction using Epi Info 6.

*Results*

**Notifications to the National Notifiable Diseases Surveillance System**

There were 2,271 notifications of IPD to the NNDSS in 2002. The numbers of notification and the notification rate per 100,000 population are shown in Table 3. There was an overall increase in the number of notifications compared with 2001. As noted above, this was principally a product of under-reporting in 2001 due to delays in making IPD a notifiable disease in some jurisdictions.

The differences in numbers of notifications between 2002 and 2001 varied by jurisdiction. In states and territories where IPD had been a notifiable disease

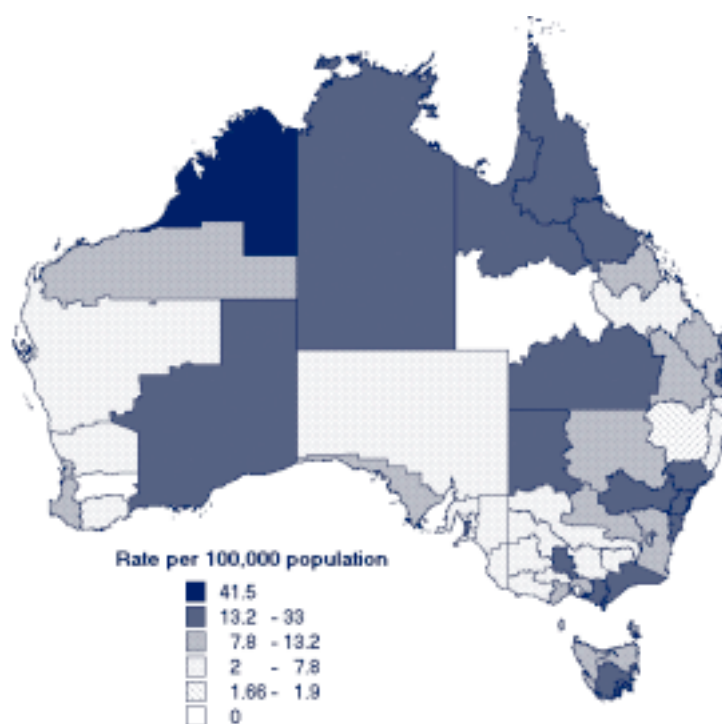
before 2001, there were small increases noted in some (Queensland, 2%; Western Australia, 1% Tasmania, 3%), while in the Northern Territory there was a marked decrease (33%). This marked decrease is explicable by the large number of IPD reported in the Northern Territory in 2001 (n=97) which was aberrantly high compared to notifications in previous years. Notifications in the Northern Territory in 1998, 1999 and 2000 were 77, 77 and 70, respectively (Heather Cook, personal communication). In other jurisdictions, where IPD had not been a notifiable disease before 2001, there were marked increases in the numbers of notifications in 2002 compared with 2001 (Table 3).

The rates of IPD disease ranged between 9.3 and 13.3 cases per 100,000 population except in the Northern Territory where the rate was 32.8 cases per 100,000 population. When the notification rates of IPD were examined by geographical distribution, variation within states was evident (Map).

**Table 3. Notifications and notification rate per 100,000 population, invasive pneumococcal disease, Australia, 2002**

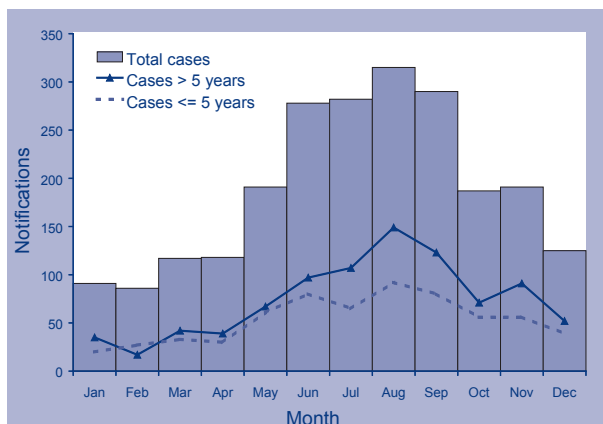
	ACT	NSW	NT	Qld	SA	Tas	Vic	WA	Australia
Notifications	30	841	65	437	174	63	454	207	2,271
Rate per 100,000 population	9.3	12.7	32.8	11.8	11.4	13.3	9.3	10.7	11.5
Notifications in 2001	18	434	97	425	114	61	327	205	1,681
(% change in 2002)	(+66%)	(+94%)	(-33%)	(+3%)	(+52%)	(+3%)	(+39%)	(+1%)	(+35%)

**Map. Notification rates of invasive pneumococcal disease, Australia, 2002, by Statistical Division of residence**



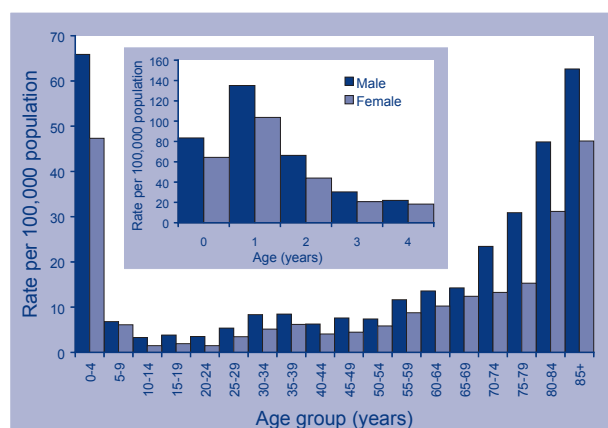
The frequency of cases varied by season with 875 (38%) cases reported in winter months (June to August). The effect of season was more evident on notifications of IPD among children and adults aged more than five years than in younger children aged five years or less (Figure 1).

**Figure 1. Notifications of invasive pneumococcal disease, Australia, 2002, by month of report and age group**



As previously noted, IPD in Australia is largely a disease of the very young and very old. The highest rates of disease were in children aged less than five years (57.3 cases per 100,000 population) and adults aged more than 85 years (51.7 cases per 100,000 population, Figure 2). Among children aged less than five years, the highest rates were recorded in children aged one year (male, 135 and female, 103 per 100,000 population). In all age groups there were more male than female cases (overall male to female ratio 1.3:1).

**Figure 2. Notification rates of invasive pneumococcal disease, Australia, 2002, by age and sex**



## Enhanced invasive pneumococcal disease surveillance data

Enhanced data were available for 1,929 cases or 85 per cent of notified cases—a similar proportion of cases to that reported on in the last annual report. The percentage of notified cases with enhanced data was lower in New South Wales and Queensland since additional data were only collected for children aged less than five years or adults aged more than 50 years. Since NNDSS data for 2002 was analysed by date of disease onset while data in the enhanced datasets was by date of notification, the enhanced dataset included 35 additional cases in South Australia and three additional cases in Western Australia compared with NNDSS notifications. In all other jurisdictions all notified cases in 2002 were followed up for the collection of enhanced data.

## Demographics

The demographic characteristics of cases on which enhanced data were collected are shown in Table 4. In all jurisdictions, except Tasmania, the male to female ratio was between 1.1 to 1.6:1, similar to the 1.3:1 ratio recorded in NNDSS data. In Tasmania, the ratio was 3.2:1. The reasons for this strong preponderance of males among cases from Tasmania were unclear.

The age distribution of the enhanced data is biased by the limited enhanced surveillance in Queensland and New South Wales, where children aged less than five years and adults aged over 50 years only, were followed up.

The enhanced data identified 135 cases of IPD among Indigenous people, which represented seven per cent of all cases, a similar proportion to that in 2001. This represented a national rate of 31 cases per 100,000 population in Indigenous people compared with the national rate of 11.5 cases per 100,000 population. The rates of IPD in Indigenous people were highest in the Northern Territory (85.6 per 100,000 population) and Western Australia (51 per 100,000 population). These rates are estimates only, as under-reporting of Indigenous status continues to be a problem.

## Clinical presentation

The clinical presentation was reported in 92 per cent (1,774/1,929) of cases (Table 5).

Pneumonia was the most common clinical presentation (878 cases, 4.5 per 100,000 population) followed by bacteraemia (697 cases, 3.5 per 100,000 population) and meningitis (0.47 per 100,000 population). Presentations of IPD in other



sites accounted for 106 cases (0.54 per 100,000 population). These rates were similar to those reported in 2001.

Clinical presentation varied by age with pneumonia being the most common presentation among the over 65 years (348, 63%) while bacteraemia was the most common presentation among children under five years (378, 49%).

The proportion of IPD presenting as pneumonia was significantly higher in Indigenous children (60%) compared with non-Indigenous children (21%),

while presentations of bacteraemia were conversely more common in non-Indigenous children (60%) than Indigenous children (38%, Table 6).

IPD resulted in 175 deaths in Australia in 2002, a case fatality rate of 9.2 per cent (Table 7). The case fatality rate was significantly higher in cases aged more than 65 years (19.4%) compared with children aged less than five years (1.3%,  $p < 0.0001$ ). The case fatality rate was higher but not significantly different in non-Indigenous cases (9.5%) compared with Indigenous cases (5%).

**Table 5. Clinical presentations of invasive pneumococcal disease, Australia, 2002, by jurisdiction**

Clinical presentation*	State or territory							Total
	NSW	NT	Qld	SA	Tas	Vic	WA	
Pneumonia (n)	336	42	97	113	44	127	119	878
%	50	65	33	51	59	28	52	44
Meningitis (n)	31	2	7	12	6	18	17	93
%	5	3	2	6	8	4	4	5
Bacteraemia (n)	264	17	136	81	25	111	63	697
%	40	26	46	37	32	24	28	35
Other (n)	24	4	48	12	1	12	5	106
%	3	6	16	6	1	3	2	5
Unknown (n)	12	0	5	0	0	186	23	226
%	2		2			41	10	11

\* Totals may exceed case total and percentages exceed 100 per cent since cases may have had more than one type of clinical presentation.

**Table 4. Demographic profile of invasive pneumococcal disease cases reported by enhanced surveillance systems, Australia, 2002, by jurisdiction**

		ACT	NSW*	NT	Qld*	SA	Tas	Vic	WA	Total
Number		30	668	65	228	211	63	454	210	1,929
Sex	Male:female ratio	1.1:1	1.3:1	1.3:1	1.6:1	1.1:1	3.2:1	1.3:1	1.4:1	1.5:1
Age	<5 years (n)	19	265	21	159	91	16	125	66	761
		63%	39.7%	32%	69.7%	43%	25%	28%	31%	39%
	5 to 64 years	7	130	39	48	71	29	192	100	616
		23.3%	19.3%	60%	20.6%	33.6%	46%	42%	47.6%	31%
	≥65 years	4	273	5	21	49	18	137	44	551
		13.3%	40.9%	7.7%	9.2%	23.2%	29%	30%	20.9%	30%
Indigenous status	Indigenous	1	15	49	29	6	0	3	32	135
		3.3%	2.2%	75.4%	12.7%	2.8%		0.6%	15.2%	7%
	Non-Indigenous	17	614	16	171	191	41	385	162	1,597
		56.7%	92%	24.6%	75%	90.5%	65%	85%	77%	83%
	Unknown	12	38	0	28	14	22	66	16	197
		40%	5.8%		11.8%	6.6%	35%	14.4%	7.6%	10%

\* In New South Wales and Queensland enhanced data were only collected on cases aged less than five years or more than 50 years, except north Queensland where enhanced data were collected on all cases.

**Risk factors for pneumococcal disease**

Overall, 42 per cent (813/1,929) of cases had a recognised risk factor for pneumococcal disease. The most common of these was chronic illness, which included chronic respiratory, cardiac and renal disease. Immunocompromising conditions such as long-term immunosuppressant use were common among IPD cases. Risk factor categories were defined by the national surveillance working group. Other risk factors were recorded but varied between jurisdictions. More than one risk factor could be recorded for each case. The proportion of cases with an identified risk factor was significantly

higher in cases aged five years and above (63%) compared with cases aged less than five years (19%, Chi=147, p<0.0001).

The frequency of risk factors for IPD in Indigenous and non-Indigenous people are shown in Table 8. The rates of premature birth and chronic illness were significantly higher in Indigenous children aged less than five years compared with non-Indigenous children. Among cases aged five years or more, the number of immunocompromised patients were significantly higher among non-Indigenous cases than Indigenous cases.

**Table 6. Clinical presentations of invasive pneumococcal disease in Indigenous and non-Indigenous children aged less than five years, Australia, 2002**

	Indigenous (n=45)		Non-Indigenous (n=647)		Significance of difference*
	n	%	n	%	
Pneumonia	27	60	137	21	p<0.0001
Meningitis	1	2	45	7	ns
Bacteraemia	17	38	391	60	p<0.005
Other	2	4	26	4	ns

\* Chi-square test with Yates correction.

**Table 7. Case fatality rates for invasive pneumococcal disease, Australia, 2002, by jurisdiction**

	NSW	NT	Qld	SA	Tas	Vic	WA	Total
Cases	668	65	228	211	63	454	210	1,899
Deaths	99	4	4	12	11	26	19	175
Total case fatality rate (%)	14.8	6.1	1.8	5.7	17.0	5.7	9.0	9.2
Deaths in cases aged <5 years	4/265	0/21	0/159	1/91	1/16	2/125	2/66	10/743
Total cases aged <5 years (%)	1.5	0.0	0.0	1.0	6.0	1.6	3.0	1.3
Deaths in cases aged >65 years	71/273	1/5	2/21	6/49	4/18	16/137	6/44	106/547
Total cases aged >65 years (%)	26.0	20.0	9.5	12.2	22.0	11.6	13.6	19.4
Deaths in Indigenous people	0/15	3/49	2/29	0/6	0	0/3	2/32	7/134
Total Indigenous cases (%)	0.0	6.0	6.9	0.0			6.2	5.0
Death in non-Indigenous	99/653	1/16	2/199	12/205	11/62	26/451	17/178	168/1,764
Total non-Indigenous + 'unknown' cases (%)	15.2	6.2	1.0	5.9	17.0	5.7	9.5	9.5

**Table 8. The frequency of risk factors for invasive pneumococcal disease, Australia, 2002, by age group and Indigenous status**

	Cases aged less than five years			Cases aged five years or more		
	Indigenous (n=45)	Non-Indigenous (n=647)	Significance of difference	Indigenous (n=88)	Non-Indigenous (n=1,022)	Significance of difference
Premature birth	8 (17%)	37 (6%)	p<0.0005	—	—	—
Congenital abnormality	2 (4%)	15 (2.3%)	ns	1 (1.1%)	2 (0.2%)	ns
Asplenia	0	1 (0.2%)	ns	1 (1.1%)	5 (0.5%)	ns
Immunocompromised	0	18 (2.8%)	ns	6 (6.8%)	171 (16.7%)	p<0.05
Chronic illness	11 (24%)	23 (3.5%)	p<0.0001	38 (43%)	393 (38.4%)	ns

### Pneumococcal serotypes causing disease in Australia

Pneumococcal serotypes were identified in 84 per cent (1,624/1,929) of the cases under enhanced surveillance in 2002. Of these, 75 per cent (1,221/1,624) of serotypes were those in the 7-valent conjugate pneumococcal vaccine and 93 per cent (1,517/1,624) were serotypes in the 23-valent polysaccharide pneumococcal vaccine (Table 9).

The frequency of vaccine serotypes in the conjugate and polysaccharide was further analysed in the target age groups for these vaccines and by Indigenous status (Table 10). The proportion of 7-valent conjugate vaccine serotypes was significantly lower in Indigenous children aged less than 2 years (45.8%) than in non-Indigenous children (87.6%,  $p < 0.0001$ ). Similarly, the proportion of 23-valent polysaccharide vaccine serotypes in Indigenous cases aged two years and above was significantly lower (88.2%) than in non-Indigenous cases (94.8%,  $p < 0.05$ ).

**Table 9. Proportion of pneumococcal serotypes in cases of invasive pneumococcal disease, covered by the 7-valent and 23-valent pneumococcal vaccines,\* Australia, 2002, by jurisdiction**

Vaccine	ACT	NSW	NT	Qld	SA	Tas	Vic	WA	Total
7-valent (n)	16/23	415/534	25/59	164/219	133/160	41/58	293/376	134/195	1,221/1,624
%	69.6	77.7	42	75	83	70	78	68.7	75
23-valent (n)	20/23	501/534	54/59	201/219	153/160	48/58	363/376	177/195	1,517/1,624
%	87	94	92	92	95	83	96	91	93

\* As a proportion of serotyped isolates.

**Table 10. The proportion of pneumococcal serotypes isolated from cases of invasive pneumococcal disease, which were serotypes in the 7-valent and 23-valent pneumococcal vaccine, Australia, 2002, by age and Indigenous status**

	No. (%) serotypes in pneumococcal vaccines					
	Cases aged less than two years with serotypes in 7-valent conjugate vaccine			Cases aged two years or more with serotypes in 23-valent vaccine		
	Indigenous	Non-Indigenous	Significance of difference*	Indigenous	Non-Indigenous	Significance of difference*
ACT	–	4/4 100%	–	1/1 100%	15/17 88.2%	ns
NSW	2/2 100%	114/129 88%	ns	3/3 100%	443/454 98%	ns
NT	4/7 57%	4/5 80%	ns	33/37 89%	9/10 90%	ns
Qld	4/10 40%	68/80 85%	$p < 0.005$	12/16 75%	81/85 95%	ns
SA	–	38/43 88%	–	3/3 100%	95/101 94%	ns
Tas	–	11/11 100%	–	–	34/43 79%	–
Vic	–	52/60 87%	–	3/3 100%	300/313 96%	ns
WA	1/5 20%	21/24 87.5%	$p < 0.01$	20/22 91%	118/132 89%	ns
Australia	11/24 45.8%	312/356 87.6%	$p < 0.0001$	75/85 88.2%	1,095/1,155 94.8%	$p < 0.05$

\* Differences tested by Chi square test with Yates correction; ns: not significant.



### Vaccination status of invasive pneumococcal disease cases

Data on pneumococcal vaccination were available for half of the cases in 2002. Of the 973 cases with a vaccination history, the majority (687, 69%) were reported as unvaccinated (Tables 11a and 11b). IPD was reported in 9 children aged two years or less who had received vaccination with the 7-valent conjugate vaccine and 151 in older children and adults who had received the 23-valent polysaccharide pneumococcal vaccine.

An analysis of cases recorded as 'fully vaccinated for age' is shown in Tables 12a and 12b. Of the nine infants recorded as fully vaccinated for age, only one was judged to be a 'vaccine failure' that is, having IPD caused by a *S. pneumoniae* serotype in the 7-valent vaccine. This case occurred in the Northern Territory in an Indigenous child with significant risk factors for IPD.

Of the 151 cases of IPD occurring in older children and adults with a history of vaccination within the 23-valent polysaccharide vaccine, 103 were judged to be vaccine failures (Table 12b). The majority of these cases occurred in elderly people with significant risk factors for IPD. History of pneumococcal vaccination in these cases was poorly documented and infection may have occurred many years after vaccination.

### Discussion

In 2002, the completeness of IPD reporting improved Australia-wide with notifications received from all jurisdictions for the entire year. The overall increase in notifications relative to 2001 can be accounted for by this improvement in surveillance completeness. In the Northern Territory, however, the number of notifications decreased. It is too early to ascribe this decline to the impact of the childhood pneumococcal vaccination.

**Table 11a. Vaccination status of invasive pneumococcal disease cases aged less than two years, Australia, 2002, by age group and jurisdiction**

Vaccination status	NSW	NT	Qld	SA	Tas	Vic	WA	Total
Fully vaccinated for age	2	5	2	0	0	0	0	9
Partially vaccinated for age	4	2	2	26	1	1	4	40
Not vaccinated	81	7	6	–	7	42	13	156
Unknown	73	0	104	37	2	35	16	267
<b>Vaccine given</b>								
7-valent	3	7	4	–	1	1	4	20
23-valent	–	*	–	–	–	–	–	–
Unknown	3	0	0	26	0	0	0	29

\* One child had two doses of 7vPCV and one dose of PPV.

**Table 11b. Vaccination status of invasive pneumococcal disease cases aged two years or more, Australia, 2002, by age group and jurisdiction**

Vaccination status	NSW	NT	Qld	SA	Tas	Vic	WA	Total
Fully vaccinated for age	59	10	12	12	8	40	10	151
Partially vaccinated for age	1	5*	1	67	–	–	–	74
Not vaccinated	267	35	8	1	25	123	72	531
Unknown	181	1	93	68	20	213	95	670
<b>Vaccine given</b>								
7-valent	–	2	–	1	–	–	–	3
23-valent	60	15	11	9	8	40	10	154
Unknown	0	1	2	69	0	0	0	72

Data not available from the Australian Capital Territory.

\* Partially vaccinated defined in the Northern Territory for cases >2 years as PPV vaccination more than five years before disease onset.

Recent publications have demonstrated the effectiveness of the pneumococcal vaccines in reducing IPD at a population level. An analysis of the burden of IPD nearly two years after the introduction of the conjugate vaccine in the USA has demonstrated a 69 per cent reduction in IPD in children less than two years of age. Interestingly there was also a decline in IPD in older age groups, which was taken as evidence for decreased transmission from children. This decline, together with prevention of disease caused by drug resistant strains and by disease caused by vaccine-related serotypes, provides reasons for optimism for the control of IPD in communities where children receive pneumococcal vaccination.<sup>7</sup> In Native American children the same conjugate vaccine has shown a primary efficacy of 76.8 per cent in communities with very high burden of IPD, comparable to those experienced in Central Australian Indigenous communities.<sup>2</sup> In addition, evidence has been presented recently that there is a small but significant impact of vaccination on otitis media with reductions of 7.8 per cent in visits to medical practitioners, reductions of 5.7 per cent in antibiotic prescriptions for otitis media, and reductions in repeated episodes of otitis media and tube replacements.<sup>8</sup> Continued application

of the conjugate vaccine in Australian Indigenous communities may also reduce IPD burden in the unvaccinated groups and the burden of non-invasive pneumococcal disease, for example otitis media.

Nevertheless there are continuing questions about the impact of vaccines, particularly whether vaccine pressure will result in disease caused by non-vaccine serotypes and a gradual diminution of vaccine efficacy.<sup>9</sup> Whitney and colleagues reported that while disease caused by vaccine and vaccine related serotypes decreased (by 78% and 50% respectively), disease caused by non-vaccine serotypes increased by 27 per cent, although this increase did not reach statistical significance.<sup>7</sup> In the high-prevalence Native American setting which had a relatively high proportion of non-vaccine serotypes circulating, there was an increase in IPD caused by non-vaccine serotypes following the introduction of the 7-valent vaccine, but again this difference was not significant.<sup>2</sup> It is essential to continue the surveillance of serotypes causing disease in Indigenous communities to monitor whether IPD from non-vaccine serotypes are increasing, compromising the impact of the 7-valent vaccine.

**Table 12a. Details of the cases of invasive pneumococcal disease that occurred in those fully vaccinated for age with the 7-valent conjugate pneumococcal vaccine, Australia, 2002, by jurisdiction**

	NSW	NT	Qld	Total
Number	2	5	2	9
Age range (years)	0–1	0–1	0–1	0–1
Indigenous	2 (100%)	5 (100%)	2 (100%)	9 (100%)
Risk factors present	0	4 (80%)	2 (100%)	6 (67%)
7-valent vaccination confirmed	2	5	2	9
Serotypes in 7-valent vaccine/ number with known serotype	0/2	2/4	0/2	2/8
Number of vaccine failures*	0	1	0	1

\* Where vaccination was confirmed and disease was caused by a serotype in the appropriate vaccine.

**Table 12b. Details of the cases of invasive pneumococcal disease that occurred in those fully vaccinated for age with the 23-valent polysaccharide vaccine, Australia, 2002, by jurisdiction**

	NSW	NT	Qld	SA	Tas	Vic	WA	Total
Number	59	10	12	12	8	40	10	151
Age range (years)	53–93y	2–82y	30–73y	24–87y	58–80y	14–89y	50–86y	2–93y
Indigenous	2	10	8	1	0	0	5	26
Risk factors present	51	7	11	11	8	31	4	123
23-valent vaccination confirmed	57	10	11	9	8	38	6	139
Serotypes in 23 valent vaccine/ no. with known serotype	45/52	8/9	9/12	7/8	3/7	34/35	4/8	110/131
Number of vaccine failures*	43	8	7	5	3	34	3	103

\* Where vaccination was confirmed and disease was caused by a serotype in the appropriate vaccine.

Pneumococcal disease in Australia is also a disease of the elderly with 26 per cent of cases aged 65 years and over and rates of 51.7 cases per 100,000 population in those aged 85 years or over. Current recommendations in Australia are for all non-Indigenous Australians over 65 years and all Indigenous Australians over 50 years to receive 23-valent polysaccharide pneumococcal vaccination. Re-vaccination is recommended every five years.<sup>10</sup> In Victoria, vaccine has been offered free to all residents aged 65 years or more since 1998<sup>11</sup> and coverage in a recent survey was estimated to be between 47 and 51 per cent.<sup>12</sup> The Northern Territory has additionally recommended the 23-valent vaccine for all Aboriginal people 15 years and older since mid-2000 with coverage rates calculated, via a vaccine register capturing 50 per cent of distributed vaccine, to be 21 per cent in the 15–49 year age group and 50 per cent in those 50 years or older.<sup>13</sup> Coverage in the rest of Australia in 2002 was estimated to be between 25 and 28 per cent.

Two recent systematic reviews of pneumococcal polysaccharide vaccine effectiveness in adults<sup>14,15</sup> found protective effects of the vaccine against disease and mortality in non-industrialised countries, but no protective effect except possibly against pneumococcal bacteraemia in industrialised countries. Similar results were evident in a retrospective cohort study in elderly Americans.<sup>16</sup> Likewise, recent studies of the 23-valent polysaccharide vaccine among Native American adults also shows a low effectiveness in these communities with high pneumococcal disease burden and high rates of chronic diseases.<sup>17</sup> However, evidence from other case control and cohort studies indicates a vaccine effectiveness of 50–80 per cent in preventing pneumococcal bacteraemia or invasive disease in the elderly.<sup>18</sup> Difficulties in the diagnosis of pneumococcal pneumonia, variation in IPD epidemiology, and circulating serotypes, decreased vaccine efficacy in the presence of certain and multiple risk factors, and uncertainties over the duration of vaccine-induced immunity complicate debate over effectiveness. While vaccine induced antibody responses appear to decline after three years and can be boosted by re-vaccination, the clinical efficacy of re-vaccination has not been demonstrated.<sup>19</sup> A cost effectiveness analysis in Australia<sup>20</sup> indicated that extending pneumococcal vaccination for all persons aged 50 to 64 years and to all Indigenous people aged between 15 and 49 years would be cost effective. Enhanced surveillance of IPD in the adult Australian population will assist with evaluating present recommended vaccine schedules and funded programs.

The use of pneumococcal vaccines has been promoted as a means to reduce the need for the use of antibiotics and so reduce the spread of antibiotic resistant pneumococci.<sup>21</sup> After two years of use of the conjugate vaccine in American children, declines in rates of disease caused by penicillin resistant and penicillin susceptible strains were not significantly different, although there was a small decline in the overall proportion of resistant strains.<sup>7</sup> The impacts of vaccination on antibiotic resistance in the pneumococci will not be evident until the vaccine is more widely available. Reports on antibiotic resistance from the enhanced IPD surveillance in Australia, in 2002, will be reported separately.

Surveillance of IPD in children aged less than five years will continue in Australia, supported by laboratory surveillance of serotypes and antibiotic resistance. A reduction in the disease burden in Indigenous children as the vaccine coverage in the target population increases seems likely with a possible reduction in Indigenous adults as well. On-going surveillance will be essential to monitor serotype replacement and the impact of vaccination on antibiotic susceptibility.

### Acknowledgments

The authors acknowledge the contribution to surveillance data collection by Catherine Ferreira, Department of Human Services, Victoria.

### References

1. Krause VL, Reid SJC, Merianos A. Invasive pneumococcal disease in the Northern Territory of Australia, 1994–1998. *Med J Aust* 2000;173:S27–S31.
2. O'Brien KL, Moulton LH, Reid R, Weatherholtz R, Oski J, Brown L, *et al.* Efficacy and safety of seven-valent conjugate pneumococcal vaccine in American Indian children: group randomised trial. *Lancet* 2003;362:355–361.
3. Gilbert GL. Retreat of the pneumococcus? *Med J Aust* 2000;173 Suppl:S20–S21.
4. Turnidge J, Bell J, Collignon P. Rapidly emerging antimicrobial resistances in *Streptococcus pneumoniae* in Australia. *Med J Aust* 1999;170:152–155.
5. Douglas R, Miles H. Vaccination against *Streptococcus pneumoniae* in childhood: lack of demonstrable benefit in young Australian children. *J Infect Dis* 1984;149: 861–869.

6. Black S, Shinefield H, Fireman B, Lewis E, Ray P, Hansen JR. Efficacy, safety and immunogenicity of heptavalent pneumococcal conjugate vaccine in children. *Pediatr Infect Dis J* 2000;19:187–195.
7. Whitney CG, Farley MM, Hadler J, Harrison LH, Bennett NM, Lynfield R, *et al*. Decline in invasive pneumococcal disease after the introduction of protein-polysaccharide conjugate vaccine. *N Engl J Med* 2003;348:1737–1746.
8. Fireman B, Black SB, Shinefield HR, Lee J, Lewis E, Ray P. Impact of the pneumococcal conjugate vaccine on otitis media. *Paediatr Infect Dis J* 2003;22:10–16.
9. Pelton S, Klein J. The future of pneumococcal conjugate vaccines for prevention of pneumococcal diseases in infants and children. *Paediatrics* 2002;110:805–814.
10. National Health and Medical Research Council. *The Australian Immunisation Handbook*. 7th edition. Canberra: Australian Government Publishing Services; 2000.
11. Andrews RM, Lester RA. Improving pneumococcal vaccination coverage among older people in Victoria. *Med J Aust* 2000;173 Suppl:S45–S47.
12. Roche P, McIntyre P, Spencer J. Pneumococcal disease in Australia: current status and future challenges. A report of the workshop held at the national Centre for Immunisation Research and Surveillance, 8–9 November 2002. *Commun Dis Intell* 2003;27:79–88.
13. Stewart D, Markey P. Review of the NT adult pneumococcal vaccine database. *NT Disease Control Bulletin* 2002;9:23–27.
14. Watson L, Wilson B, Waugh N. Pneumococcal polysaccharide vaccine: a systematic review of clinical effectiveness in adults. *Vaccine* 2002;20:2166–2173.
15. Mangtani P, Cutts F, Hall A. Efficacy of polysaccharide pneumococcal vaccine in adults in more developed countries: the state of the evidence. *Lancet Infect Dis* 2003;3:71–78.
16. Jackson LA, Neuzil KM, Yu O, Benson P, Barlow WE, Adams AL, *et al*. Effectiveness of pneumococcal polysaccharide vaccine in older adults. *N Engl J Med* 2003;348:1747–1755.
17. Benin AL, O'Brien KL, Watt JP, Reid R, Zell ER, Katz S, *et al*. Effectiveness of the 23-valent polysaccharide vaccine against invasive pneumococcal disease in Navajo adults. *J Infect Dis* 2003;188:81–89.
18. Fedson DS. Efficacy of polysaccharide pneumococcal vaccine in adults in more developed countries: another view of the evidence. *Lancet Infect Dis* 2003;3:272–273.
19. Artz A, Ershler WB, Longo DL. Pneumococcal vaccination and re-vaccination of older adults. *Clin Micro Rev* 2003;16:308–318.
20. Andrews R, Whitfield K, Kelly H, McIntyre P, Butler J. Economic analysis of various options for population level funded influenza and pneumococcal immunisation programs; 2002.
21. Dagan R. Antibiotic resistance and the potential impact of pneumococcal conjugate vaccines. *Commun Dis Intell* 2003;27 Suppl:S134–S142.