Invasive pneumococcal disease in Australia, 2001

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Abstract

There were 1,681 cases of invasive pneumococcal disease (IPD) notified to the National Notifiable Diseases Surveillance System in Australia in 2001; a rate of 8.6 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. Pneumococcal disease was reported most frequently in children aged less than 5 years (47.3 cases per 100,000 population). Enhanced surveillance for IPD was carried out in the Northern Territory, Western Australia, South Australia, Victoria, Tasmania and metropolitan areas of New South Wales, encompassing 72 per cent of the population and providing additional data on 86 per cent of all notified cases. Enhanced surveillance data revealed high rates of pneumococcal disease in Indigenous Australians. Rates of IPD in Indigenous children aged less than 5 years were as high as 483 cases per 100,000 population in the Northern Territory. The clinical presentation of IPD was most commonly pneumonia (56%) and bacteraemia (36%). There were 125 deaths attributed to IPD resulting in an overall case fatality rate of 8.6 per cent. More than half (54%) of all cases had a recognised risk factor for IPD. Eighty-six per cent of serotypes identified in non-Indigenous children compared with only 55% of serotypes in Indigenous children were in the 7-valent vaccine. Antibiotic susceptibility testing showed reduced susceptibility to penicillin in 12 per cent, and to third generation cephalosporins in 5 per cent of isolates. These are the first national data available on IPD in Australia and will assist in evaluating the impact of the newly introduced conjugate vaccine and guide overall pneumococcal vaccine strategies. *Commun Dis Intell* 2002;26:505–519.

Keywords: Streptococcus pneumoniae, *antibiotic susceptibility, pneumococcal disease, surveillance, penicillin, cephalosporins*

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* is isolated from a normally sterile site, e.g. blood, cerebrospinal fluid 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 (e.g. due to HIV, asplenia) or have a chronic illness (e.g. chronic cardiovascular, pulmonary, renal or liver disease or diabetes).

In developed countries, the incidence rate of IPD is bimodal, with a peak in children under 2 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. Indigenous children from Central Australia have the highest rates in the world with the most recently reported incidence of 1,534 cases per 100,000 population.[1] Case fatality rates for IPD vary from 12–14 per cent depending on the age and the focus of the disease.[2]

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Since the 1970s, large outbreaks of severe pneumococcal disease caused by penicillin resistant organisms occurred in South Africa and Papua New Guinea and subsequently increased rates of penicillin resistance in pneumococci have been documented 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.[3] The emergence of multi-drug resistant pneumococci has been an important reason for the development of new pneumococcal vaccines.

Ninety serotypes of *S. pneumoniae*, which are unique in the polysaccharide composition of their capsules, have been described. Immunity to 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 have shown 50–80 per cent effectiveness in preventing invasive pneumococcal disease in immunocompetent adults,[4] but are poorly effective in children.[5] 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 of age demonstrated an efficacy of 93.9 per cent.[6] This conjugate vaccine was licensed for use in Australia in January 2001 and the Australian Technical Advisory Group on Immunisation (ATAGI) recommended vaccination of children at high risk, commencing in July 2001 (Table 1).

The ATAGI group recommended that the impact of the new conjugate vaccine on IPD in Australia be monitored by means of national surveillance of all incident cases. The Communicable Diseases Network Australia agreed to make IPD a notifiable disease in all Australian jurisdictions from January 2001. In 2001, State and Territory health authorities made changes to legislation to make reporting of all cases of IPD mandatory in each jurisdiction. The Pneumococcal Working Party of the Communicable Diseases Network Australia convened a working group to devise an appropriate surveillance dataset for IPD. This surveillance working group recommended that data be collected to establish baseline nationwide data on IPD and evaluate the impact of the new 7-valent conjugate vaccine and 23-valent polysaccharide vaccine on the clinical presentation, serotype and antibiotic resistance (to penicillin and third generation cephalosporins).

This paper reports on data from 2001 and combines National Notifiable Diseases Surveillance System (NNDSS) data with additional data collected on cases of pneumococcal disease in six jurisdictions.

Methods and materials

Case definition

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

National Notifiable Diseases Surveillance System

While IPD has been a notifiable disease in some States and Territories for several years, it became a notifiable disease in all Australian States and Territories only in 2001. This required changes to public health legislation in all States and Territories, resulting in different starting dates for collection of data from the individual jurisdictions. In some States and Territories, there was a retrospective collection of data for the whole year.

Data on IPD cases sent to the NNDSS included basic demographic data — age, sex and date of birth, residential postcode (except in the NT) and indigenous status — and the dates of onset, report and data transmission.

Enhanced data collections were available from prospective surveillance schemes in the Northern Territory, South Australia, Western Australia, Victoria and metropolitan New South Wales. Enhanced data for IPD for 2001 was collected retrospectively in Tasmania. The enhanced data set fields are shown in Table 2.

Table 1. Recommendations for pneumococcal vaccination, Australia, 2001

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 • Immuncompromised 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

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 IPD
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 *S. pneumoniae* 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 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 2001, was used as the denominator in rate calculations. Estimates of the Indigenous Australian population were based on projections from the 1996 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, which is consistent with the reporting of other national communicable diseases.

Results

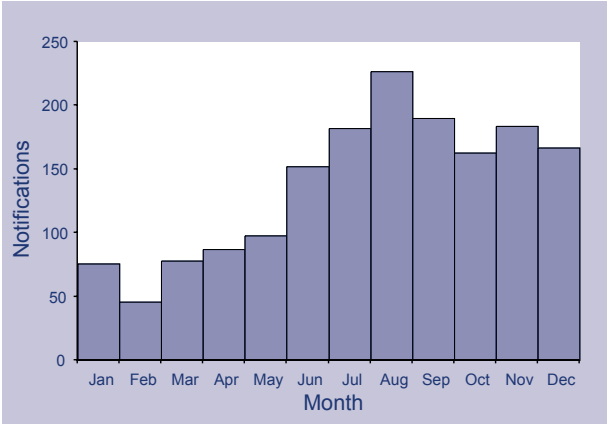
Notifications to the National Notifiable Diseases Surveillance System

There were 1,681 notifications of IPD to the NNDSS in 2001. The number of notifications and the notification rate per 100,000 population of IPD in Australian States and Territories are shown in Table 3. Since legislation to make IPD a notifiable disease came into force at different times during 2001, the number of cases in some jurisdictions may be under-estimated.

While the largest number of cases were found in New South Wales, Queensland and Victoria, the highest rates were found in the Northern Territory, which had a rate 5.6 times the national rate. Notifications of pneumococcal disease to NNDSS by month of report are shown in Figure 1. There was a peak of IPD in the second half of the year in late winter and early spring, with the largest numbers of notifications being in August 2001 (227 cases, Figure 1).

The geographical distribution of IPD by Statistical Division (Map), shows the rates of IPD in each Statistical Division shaded to indicate areas above >10% and <10% below the national rate (8.6 per 100,000 population). The highest rates occur in the Northern Territory, Far North Queensland and Western Australia. Areas of above average incidence were also noted in Queensland (South West, Wide Bay, Moreton and Brisbane), New South Wales (Hunter and the Central West), Victoria (Gippsland, Barwon and Lodden) and Tasmania (Northern and Mersey Lyall).

Figure 1. Notifications of invasive pneumococcal disease, Australia, 2001, by month of report



In Australia in 2001, IPD was largely a disease of the very young and very old. The highest rates of disease were among children aged less than 5 years (47.3 cases per 100,000 population) and adults aged more than 85 years (38.7 cases per 100,000 population, Figure 2). Among children aged less than 5 years, the highest rates of disease were in those aged 12 months (males 103 and female 91 cases per 100,000 population). Overall, there were more male cases and there was a male to female ratio of 1.2:1.

Figure 2. Notification rates of invasive pneumococcal disease, Australia, 2001, by age and sex

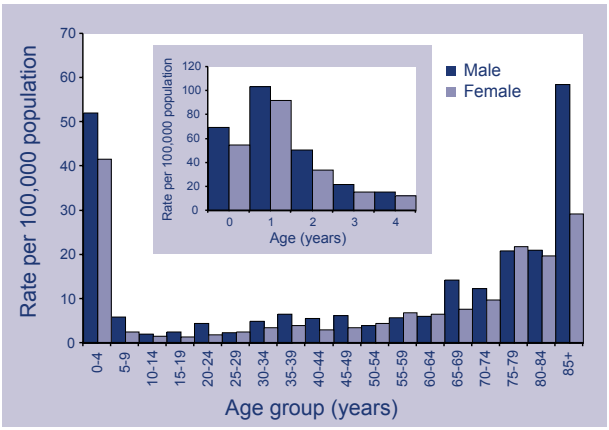
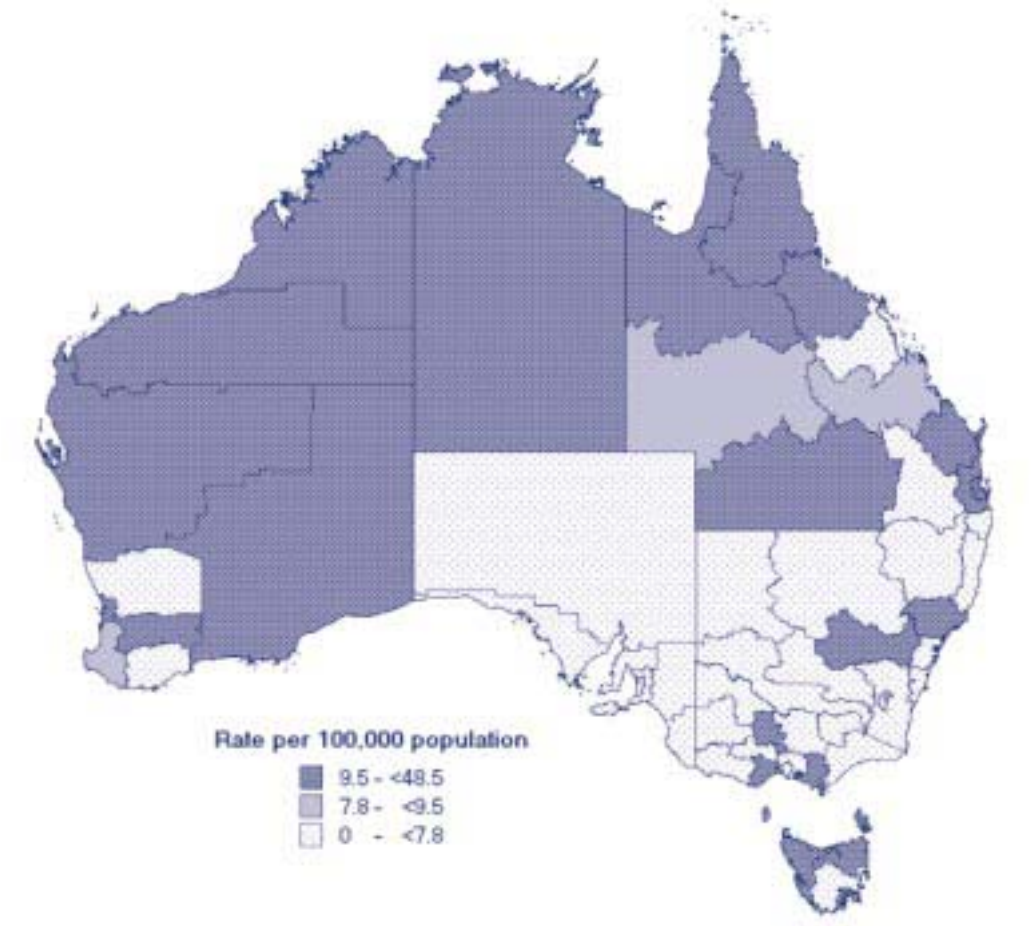


Table 3. Notifications and notification rate per 100,000 population, invasive pneumococcal disease, Australia, 2001*

	ACT	NSW	NT	Qld	SA	Tas	Vic	WA	Australia
Notifications	18	434	97	425	114	61	327	205	**1,681**
Rate per 100,000 population	5.6	6.6	48.5	11.7	7.5	12.9	6.8	10.8	**8.6**

* Notifications to the NNDSS based on onset date between 1 January 2001 and 31 December 2001. Data received as at 6 September 2002 and subject to revision.

Map. Notification rates of invasive pneumococcal disease, Australia, 2001, by Statistical Division of residence



Enhanced surveillance for invasive pneumococcal disease in 2001

Additional data were available on cases from the Northern Territory, Victoria, South Australia, Western Australia, Tasmania and the metropolitan areas of New South Wales (from Newcastle in the north to Wollongong in the south). This enhanced surveillance covered 13,947,962 people or 71.8 per cent of the Australian population (based on mid-year 2001 population estimates).

The number of cases in the enhanced IPD datasets from most states and territories were similar to the total number of IPD notifications to NNDSS. In New South Wales, the total in the enhanced dataset, which covered only metropolitan areas of the State, was higher than the total number of notifications. The NNDSS total for New South Wales is an underestimate, probably because of delays in implementing legislation making IPD a notifiable disease in that jurisdiction. In all, enhanced data were available for 1,446 cases of pneumococcal disease or 86 per cent of the notified cases.

In the following analysis, we have combined the enhanced data from all jurisdictions to describe the epidemiology of invasive pneumococcal disease in Australia. This extrapolation should be interpreted with caution given that there were variations in data collection between jurisdictions in 2001 and data were not available for Queensland, the Australian Capital Territory or rural New South Wales.

Demographics

The demographic profile of cases reported in enhanced pnemococcal surveillance schemes is shown in Table 4, In the enhanced surveillance datasets there were more cases of IPD among males than females (national male to female ratio of 1.4:1). Children aged less than 5 years made up a significant proportion of cases (35%), although this varied by jurisdiction with 59 per cent of cases in South Australia in this age group compared with 18 per cent in Tasmania (Table 4). These variations may reflect differences in clinical practice or in the ability to capture all cases, especially in the adult population, in those jurisdictions where this was the first year of notification (e.g. in South Australia).

Indigenous status was well reported in all jurisdictions although the accuracy of the data may be questioned due to the manner of acquisition (e.g. in New South Wales the status is obtained from medical records, rather than from individuals and may underestimate indigenous identification). Jurisdictions with large Indigenous populations, such as the Northern Territory reported more than two-thirds of IPD cases occurred in Indigenous people. The estimated rate of IPD in Indigenous Australians was 120 cases per 100,000 population in the Northern Territory and 60 cases per 100,000 population in Western Australia. Rates of IPD in Indigenous children, aged less than 5 years were 483 and 256 cases per 100,000 population in the Northern Territory and Western Australia respectively.

Clinical presentation

The clinical presentation of IPD was reported for 1,415/1,446 (98%) of cases. Clinical presentations were coded as pneumonia, meningitis, bacteraemia, other or unknown. Pneumonia was defined as blood culture positive for *S. pneumoniae* with consistent 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 and joint fluid. More than one clinical presentation could be recorded for each case.

The clinical presentations reported by enhanced surveillance in 2001 are shown in Table 5.

Table 4. Demographic profile of invasive pneumococcal disease cases reported by enhanced surveillance systems, metropolitan New South Wales, the Northern Territory, South Australia, Tasmania, Victoria and Western Australia, 2001, by jurisdiction

Data		NSW (metro)	NT	SA	Tas	Vic	WA	Total
Number of records		643	99	116	62	322	204	**1,446**
Sex	Male:female	1.4:1	1.8:1	1.4:1	1.6:1	1.2:1	1.2:1	**1.4:1**
Age	<5 years	205 32%	33 33%	69 59%	11 18%	111 34%	83 41%	**512** **35%**
	5 to 64 years	217 33%	61 61%	26 22%	29 47%	116 36%	80 39%	**529** **37%**
	>65 years	221 35%	5 5%	21 18%	22 35%	95 30%	41 20%	**405** 28%
Indigenous status	Indigenous	9 1.4%	68 69%	3 3%	0 0%	2 0.6%	37 18%	**119** **8%**
	Non-indigenous	634* 98.6%	30 30%	91 78%	47 76%	280 87%	160 78%	**1,242** **86%**
	Unknown	0	1 1%	22 19%	15 24%	40 12%	7 4%	**85** **6%**
	Estimated indigenous population 2001	121,142† (1.8%)	56,364 (28%)	24,313 (1.6%)	16,644 (3.5%)	24,586 (0.5%)	61,505 (3.2%)	**427,094** **(2.2%)**

* Based on medical records

† The estimated indigenous population for New South Wales is the total for the State.

Table 5. Clinical presentations of invasive pneumococcal disease, metropolitan New South Wales, the Northern Territory, South Australia, Tasmania, Victoria and Western Australia, 2001, by jurisdiction

Data	No. of cases (% of cases)	NSW (metro)	NT	SA	Tas	Vic	WA	Total
Clinical presentation*	Pneumonia	365 57%	78 78%	49 42%	36 58%	157 49%	106 52%	**791** **56%**
	Meningitis	40 6%	7 7%	7 6%	6 10%	13 4%	13 6%	**86** **6%**
	Bacteraemia	223 35%	14 14%	58 50%	6 10%	138 43%	70 34%	**509** **36%**
	Other	13 2%	1 1%	8 7%	3 5%	49 15%	9 4%	**83** **6%**
	Unknown	2 0.3%	–	1 1%	13 21%	–	15 7%	**31** **2%**

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

Pneumonia was the most common clinical presentation, particularly among the elderly, while bacteraemia and meningitis were more common among children. The rate of pneumococcal pneumonia in the enhanced surveillance population was 5.7 cases per 100,000 population. The rate of pneumococcal bacteraemia was 3.6 cases per 100,000 population and pneumococcal meningitis was 0.6 per 100,000 population. The relative proportions of the clinical presentations of IPD in children aged less than 5 years were different in Indigenous and non-Indigenous children (Table 6).

Indigenous children presented with pneumococcal pneumonia more frequently than non Indigenous children, while non-Indigenous children presented with bacteraemia more frequently than Indigenous children.

The case fatality rate by age group and Indigenous status is shown in Table 7. With the exception of South Australia, there was a higher case fatality rate in elderly patients with IPD, aged more than 65 years, than in children aged less than 5 years. The case fatality rate for Indigenous people with IPD was comparable to that in non-Indigenous people.

Risk factors for pneumococcal disease

Data on relevant risk factors were collected on 1,376/1,446 (95%) cases of IPD in enhanced surveillance systems. Overall, 749 (55%) 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 patients. Risk factor categories were defined by the national surveillance working party. Other risk factors were recorded but varied between jurisdictions. More than one risk factor could be recorded for each patient. The proportion of cases with an identified risk factor was significantly higher in cases aged 5 years and above (45%) compared with cases aged less than 5 years (15%, Chi^2 =68.5, p<0.0001). The proportions of patients in each age group with an identified risk factor varied widely between jurisdictions. The method of ascertainment of risk factor data varied from jurisdiction to jurisdiction with some interviewing cases directly and others dependent on medical records. The frequency of risk factors for IPD in Indigenous people and different age groups are shown in Table 8.

The rates of premature birth and chronic illness were significantly higher in Indigenous children with IPD compared with non-Indigenous children. Chronic illness was also more frequent in older Indigenous people with IPD than in non-Indigenous patients, but the proportion immunocompromised was higher in older non-Indigenous IPD cases than in Indigenous cases (Table 8).

Table 6. Clinical presentations of invasive pneumococcal disease in Indigenous and non-Indigenous children aged less than 5 years, Australia, 2001*

	Number of cases (%)		
	Indigenous (n=36)	Non-Indigenous (n=255)	Significance of difference†
Pneumonia	26 (72%)	81 (31%)	p<0.0001
Meningitis	4 (11%)	19 (7%)	ns
Bacteraemia	7 (19%)	149 (58%)	p<0.0001
Other invasive disease	0 (0%)	26 (10%)	p<0.05

* Analysis did not include New South Wales

† Chi^2 with Yates correction

ns Not significant

Table 7. Case fatality rates for invasive pneumococcal disease, metropolitan New South Wales, the Northern Territory, South Australia, Tasmania, Victoria and Western Australia, 2001, by jurisdiction

Data	NSW (metro)	NT	SA	Tas	Vic	WA	Total
Total cases	643	99	116	62	322	204	**1,446**
Total deaths	75	3	9	3	19	16	**125**
Total case fatality rate (%)	11.6	3	7.7	4.8	5.9	7.8	**8.6**
Deaths in aged < 5y/ Total cases aged <5y (%)	1/205 *0.5*	0/33 *0*	1/69 *1*	0/11 *0*	0/111 *0*	3/83 *3.6*	**5/512** ***1***
Deaths in aged >65y/ Total cases aged >65y (%)	59/221 *27*	2/5 *40*	5/21 *24*	0/22 *0*	10/95 *10.5*	6/41 *14.6*	**82/405** ***20***
Deaths in Indigenous people Total Indigenous cases (%)	Nd	2/68 *3*	0/3 *0*	0/0 *0*	0/2 *0*	3/37 *8*	**5/110** ***4.5***
Death in non-Indigenous/ Total non-Indigenous + 'unknown' cases (%)	Nd	1/31 *3*	9/113 *8*	3/62 *4.8*	19/320 *5.9*	13/167 *7.8*	**45/693** ***6.5***

Nd Data not available

Table 8. The frequency of risk factors for invasive pneumococcal disease, Australia, 2001, by age group and Indigenous status*

	Cases aged less than 5 years			Cases aged 5 years or more		
	Indigenous (n=32)	Non-Indigenous (n=245)	Significance of difference†	Indigenous (n=63)	Non-Indigenous (n=399)	Significance of difference†
Premature birth	6 (19%)	10 (4%)	p<0.005	NA	NA	ns
Congenital abnormality	1 (3%)	21 (9%)	ns	0	5 (1%)	ns
Asplenia	0	0	–	0	3 (0.7%)	ns
Immunocompromised	2 (6%)	21 (8%)	ns	6 (10%)	81 (20%)	p<0.005
Chronic illness	12 (38%)	30 (12%)	p<0.001	41 (65%)	168 (42%)	p<0.005

* Analysis did not include New South Wales

† Chi^2 test with Yates correction

NA Not applicable

ns Not significant

Pneumococcal serotypes causing disease in Australia

The pneumococcal serotypes were identified in 1,179 (82%) of the 1,446 cases under enhanced surveillance in 2001. Overall, 75% (889/1,179) of serotypes were those in the 7-valent conjugate pneumococcal vaccine and 93% (1,097/1,179) were those in the 23-valent polysaccharide pneumococcal vaccine. The frequency of pneumococcal serotypes was analysed in the target group for the 7-valent vaccine (children aged less than 2 years) and the target group for the 23-valent vaccine (those aged more than 2 years, Table 9).

Overall, a large majority (126/154, 82%) of pneumococcal serotypes reported in children aged less than 2 years were covered by the 7-valent conjugate vaccine. Among all other age groups, 463/513 (90%) of pneumococcal isolates were serotypes covered by the 23-valent polysaccharide pneumococcal vaccine.

A significantly smaller proportion of serotypes in Indigenous children aged less than 2 years (12/22 55%), were serotypes contained in the 7-valent conjugate vaccine compared with serotypes isolated in non-Indigenous children (114/132, 86%, $p<0.005$). Likewise, a significantly smaller proportion of isolates from Indigenous people aged more than 2 years with IPD (62/80 74%), were contained within the 23-valent pneumococcal vaccine, compared with isolates from non-Indigenous people (401/433, 93%, $p<0.0001$, Table 9).

Vaccination status of IPD cases

Data on pneumococcal vaccination were available for only a minority of cases of IPD in 2001. No data were available from New South Wales and in only a minority of cases in Western Australia and Tasmania. Data from the Northern Territory and Victoria indicate that the majority of cases were not vaccinated (Table 10).

The majority of cases who had received pneumococcal vaccine had received the 23-valent polysaccharide vaccine, while a small number had received the 7-valent conjugate vaccine. Since vaccination with the conjugate vaccine commenced in Australia in July 2001 and was targeted at specific groups of children (Table 1), these data represent a baseline against which to compare data in future years when conjugate vaccination becomes more widespread.

Three cases of IPD in Victoria occurred in children aged less than 2 years who were fully vaccinated for age. Only one of the children was verified as having received the conjugate vaccine. This non-Indigenous child was 12 months of age at the time of disease onset and had *S. pneumoniae* serotype 14 isolated from blood culture. The child had biliary atresia. The other two Victorian children were aged 9 months and 17 months and the vaccine history was not verified. One had a serotype 14 isolated from blood culture and the other a serotype 19A also isolated from blood culture. No risk factors were identified in these two children.

Table 9. The proportion of pneumococcal serotypes isolated from cases of invasive pneumococcal disease, which were serotypes in the 7-valent and 23-valent pneumococcal vaccine, the Northern Territory, South Australia, Tasmania, Victoria and Western Australia, 2001, by age and Indigenous status*

	Cases aged less than 2 years with serotypes in 7-valent conjugate vaccine			Cases aged 2 years or more serotypes in 23-valent vaccine		
	Indigenous (n=32)	Non-Indigenous (n=245)	Significance of difference†	Indigenous (n=63)	Non-Indigenous (n=399)	Significance of difference†
Northern Territory	8/12 67%	12/12 100%	ns	38/53 72%	15/16 94%	ns
South Australia	2/2 100%	34/36 94%	ns	0/1 0%	50/54 93%	ns
Tasmania	0/0	3/5 60%	–	0/0 87%	26/30	–
Victoria	0/0	53/61 87%	–	2/2 100%	182/195 93%	ns
Western Australia	2/8 25%	12/18 67%	ns	22/24 92%	128/138 93%	ns
Total	**12/22 55%**	**114/132 86%**	**p<0.005**	**62/80 76%**	**401/433 93%**	**p<0.0001**

* Data for New South Wales not available

† Chi^2 test with Yates correction

ns Not significant

Table 10. Vaccination status of invasive pneumococcal disease cases, the Northern Territory, South Australia, Tasmania, Victoria and Western Australia, 2001, by age group and jurisdiction

	Invasive pneumococcal disease cases aged less than 2 years of age					
Vaccination status	**NT**	**SA**	**Tas**	**Vic**	**WA**	**Total**
Fully vaccinated for age	0	0	0	3	0	**3**
Partially vaccinated for age	1	2	0	1	0	**4**
Not vaccinated	43	45	2	67	5	**163**
Unknown	–	–	9	11	29	**49**
Vaccine						
7-valent	1	2	–	4	–	**7**
23-valent	0	0	–	0	–	**0**
Unknown	0	0	–	0	–	**0**
	Invasive pneumococcal disease cases aged 2 years of age or more					
Vaccination status	**NT**	**SA**	**Tas**	**Vic**	**WA**	**Total**
Fully vaccinated for age	18	4	1	24	1	**48**
Partially vaccinated for age	6	9	0	2	0	**17**
Not vaccinated	50	35	3	140	80	**308**
Unknown	0	17	36	73	56	**182**
Vaccine						
7-valent	1	0	0	0	0	**1**
23-valent	22	4	1	21	1	**49**
Unknown	1	9	0	5	0	**15**

Details of the 48 cases of IPD that occurred in individuals aged 2 years and over, who were reported as fully vaccinated are shown in Table 11.

Vaccine failure with the 23-valent vaccine, where polysaccharide vaccination was confirmed and disease was caused by one of the 23-valent vaccine serotypes was suggested in 26 cases. Surveillance of vaccine failures is continuing.

Antibiotic resistance in pneumococcal cases

Antibiotic susceptibilities of *S. pneumoniae* isolates from 1,245 patients were tested against penicillin and from 1,041 patients against third-generation cephalosporin (cefotaxime or ceftriaxone, Table 12).

Reduced susceptibility to penicillin was found in 147/1,245 (12%) of all isolates tested, with 38 (3%) isolates fully resistant and 109 (9%) isolates with 'intermediate' resistance (Table 13). There was a variable prevalence in penicillin resistance by jurisdiction with Western Australia reporting 17 per cent of isolates with reduced susceptibility and Tasmania reporting all isolates as fully susceptible. Reduced susceptibility to third-generation cephalosporins was found in 56 (5%) of all isolates tested. Only one per cent (10 isolates) were reported as 'fully resistant', while 46 (4%) had intermediate resistance. All isolates from Tasmania were fully sensitive to the cephalosporins, while the Northern Territory reported 28 per cent of their isolates as having intermediate resistance.

The characteristics of cases with reduced susceptibility to antibiotics were analysed for all jurisdictions except metropolitan New South Wales. Pneumococcal serotypes associated with reduced penicillin susceptibility were also analysed. The results are shown in Table 13.

While the overall prevalence of penicillin resistance is low, there is evidence in some jurisdictions that penicillin resistance is more frequent in Indigenous cases and children. An analysis of patients with reduced susceptibility to third generation cephalosporins revealed that all such patients also had disease caused by vaccine serotypes with reduced susceptibility to penicillin. In the Northern Territory, 3/5 cases with reduced cephalosporin susceptibility were Indigenous children aged less than 5 years while 3/9 cases in Western Australia were Indigenous. Two of these were aged less than 5 years. All other cases with reduced cephalosporin susceptibility were non-Indigenous. One third (25/76) of the drug resistant isolates were serotype 9V, 21 per cent (16/76) were serotype 19F and 12% (9/76) were serotype 6B.

Table 11. Details of the 48 cases of invasive pneumococcal disease which occurred in recipients of the 23-valent pneumococcal vaccine, the Northern Territory, South Australia, Tasmania, Victoria and Western Australia, 2001, by jurisdiction*

	NT	SA	Tas	Vic	WA
Number	18	4	1	24	1
Age range (years)	>= 60 y	>=46y	85	>=24y	75
Indigenous	17/18	0/4	0/1	0/24	1/1
Risk factors present	15/18	3/4	0/1	18/18	0/1
23-valent vaccination confirmed	18/18	4/4	1/1	19/24	0/1
Serogroups (%) in 23-valent vaccine	10/17	4/4	No serotype information	16/17	1/1
Number of vaccine failure†	10	4	0	12	0

* Data not available for New South Wales

† Where polysaccharide vaccination was confirmed and disease was caused by a serotype in the 23-valent vaccine

Table 12. *S. pneumoniae* resistance to penicillin and third generation cephalosporins, metropolitan New South Wales, the Northern Territory, South Australia, Tasmania, Victoria and Western Australia, 2001, by jurisdiction

Antibiotic	Susceptibility	NSW	NT	SA	Tas	Vic	WA	Total
Penicillin	Resistant (n)	28	1	0	0	4	5	**38**
	(%)	*4*	*1*	*0*		*3*	*3*	***3***
	Intermediate (n)	53	8	15	0	7	26	**109**
	(%)	*8*	*8*	*13*		*5*	*14*	***9***
	Susceptible (n)	552	89	99	63	138	158	**1,098**
	(%)	*88*	*91*	*87*	*100*	*92*	*83*	***88***
	Total tested (n)							
	(%)	633	98	114	62	149	189	**1,245**
Cefotaxime/ ceftriaxone	Resistant (n)	8	0	1	0	1	0	**10**
	(%)	*1*	*0*	*1*	*0*	*1*	*0*	***1***
	Intermediate (n)	30	5	2	0	0	9	**46**
	(%)	*5*	*28*	*3*	*0*	*0*	*5*	***4***
	Susceptible (n)	588	13	63	59	82	180	**985**
	(%)	*94*	*72*	*96*	*100*	*99*	*95*	***95***
	Total tested	626	18	66	59	83	189	**1,041**

Penicillin resistance was defined as 'fully resistant' (MIC > 1mg/L) or intermediate (MIC 0.1–1.0mg/L). Ceftriaxone resistance was defined as MIC >1mg/L or intermediate as MIC 0.1–1mg/L.

Table 13. Characteristics of invasive pneumococcal disease cases with reduced susceptibility to penicillin and cephalosporins, Australia*, 2001

	Reduced susceptibility	
	Penicillin	3rd generation cephalosporins
Total number of cases with reduced susceptibility†	66	18
No. aged less than 5 years with reduced susceptibility/ Total tested aged less than 5 years (%)	30/188 16%	6/153 4%
No. Indigenous cases with reduced susceptibility/ Total Indigenous tested	14/104 13%	6/43 14%
Proportion of serotypes in 7-valent vaccine	62/66 94%	18/18 100%
Proportion of serotypes in 23-valent vaccine	66/66 100%	18/18 100%
Proportion of cases vaccinated (all with 23-valent pneumococcal vaccine)	9/29 31%	4/9 44%

* Data not available for New South Wales

† Includes cases resistant and with intermediate susceptibility as defined above.

Discussion

This report is the first attempt to describe the epidemiology of invasive pneumococcal disease in Australia from a national perspective. The totals and rates described are likely to be underestimates as the capture of cases through the NNDSS was incomplete in this the first year that IPD was a nationally notifiable disease. In this early period of surveillance, there may have been a failure to report all diagnosed cases and to collect appropriate clinical specimens. It would appear that rates of pneumococcal disease in Australia were lower than in the USA in 2000 (20.7 cases per 100,000 population).[7]

Invasive pneumococcal disease in Australia is generally a disease of the very young and the very old and with a continuing high rate of disease in Indigenous children. There appears to be a geographical effect on disease incidence with the highest rates among Indigenous children in the inland desert areas of the country.[1] The clinical presentations of pneumococcal disease were typical of the age groups affected, however, pneumonia was a more common manifestation in Indigenous children than non-Indigenous children. The overall case fatality rate of 8.6 per cent represents a crude rate of 0.89 per 100,000 population. This estimate is higher than estimates of 0.3 fatalities per 100,000 population from the Australian Institute of Health and Welfare mortality database[8] and well below the projected death rate for pneumococcal disease in the USA (2.3 per 100,000 population).[7] Of importance, is the observation that case fatality rates were not significantly higher in Indigenous Australians, despite the high rates of disease and risk factors in that community.

More than half of all cases of pneumococcal disease in Australia occurs in people with recognised risk factors. The proportion of patients with risk factors is larger in older age groups. In the Northern Territory where a more comprehensive set of risk factors such as smoking (active or passive), previous pneumonia or IPD disease or excessive alcohol consumption was recorded, 83 per cent of cases were identified as having a risk factor. These data highlight that better strategies are needed to target and successfully immunise those with recognised risk factors. Some risk factors not included in the National Health and Medical Research Council guidelines,[9] include smoking and excessive alcohol consumption. In some populations, universal immunisation may be the most effective method of disease control.

While a large proportion of pneumococcal serotypes causing disease in Australia are contained in the 7-valent and 23-valent vaccines, this proportion was significantly lower in Indigenous people. Among Indigenous children with pneumococcal disease aged less than 2 years, only 55 per cent had disease caused by serotypes in the 7-valent vaccine, while among older Indigenous people with IPD only 76 per cent had disease due to serotype of *S. pneumoniae* in the 23-valent vaccine. Cross-reactive immunity induced by vaccine serotypes has been noted to confer immunity to non-vaccine serotypes. Otitis media caused by serotype 6A was reduced by vaccination with the 7-valent conjugate vaccine which contains serotype 6B.[10] The proportion of disease caused by non-vaccine serotypes of *S. pneumoniae* should also be closely monitored, especially in Indigenous communities.

In the USA, historical changes in pneumococcal serotype distribution over 70 years (1928 to 1978) have recently been analysed.[11] The authors found a significant decrease in the proportion of 'epidemic' pneumococcal serotypes 1, 2, 3 and 5, and an increase in serotypes contained in the 7-valent vaccine. This trend is thought to be explained by changes in antibiotic use, socioeconomic conditions, an ageing population and blood-culturing practices. As the 7-valent vaccine becomes more widely used, there may be strong selective pressure on the circulation of vaccine serotypes. Although replacement by non-vaccine serotypes in vaccine recipients of a 9-valent pneumococcal conjugate vaccine has been reported,[12] no increase in non-vaccine serotypes causing disease was observed in the 3.5 year 7-valent vaccine efficacy trial.[6] Longer-term surveillance of pneumococcal serotypes is required to confirm these preliminary findings.

The level of reduced susceptibility to penicillin among pneumococcal isolates collected in this study (12%) is similar to that recorded for invasive isolates in Australia in 1997 (13%).[3] The level of reduced susceptibility to ceftriaxone (5%) was also similar to that in the same study (6%). Changes in treatment practice over this period and differences in the sample population, site of isolation, and diagnostic methods between the two studies should be noted. The levels of antibiotic resistance in this study is also markedly lower than in the USA, where the proportion of penicillin resistant isolates increased between 1995 and 1998, from 21 per cent to 25 per cent, the proportion resistant to cefotaxime increased from 10 per cent to 14 per cent and multi-drug resistance increased from 9 per cent to 14 per cent.[13]

Antibiotic resistance in the pneumococci has been increasing worldwide[3] and the development of multi-resistance (penicillin, macrolides, tetracyclines and cotrimoxazole) have posed a threat to treatment. Infections with penicillin resistant *S. pneumoniae* in Australia, have been shown to result in longer hospitalisation and longer resolution times, further resulting in higher treatment costs.[14] Control of penicillin resistance among invasive pneumococcal isolates may be influenced by reducing the use of antibiotics which has been shown to reduce the carriage rates of resistant pneumococci.[15] The higher rates of resistance among Indigenous children is a cause for concern, however most isolates with reduced antibiotic susceptibility in the present study were vaccine serotypes contained in the 7-valent vaccine and all were serotypes in the 23-valent vaccine. The impact of widespread vaccination is expected to be important in controlling the spread of drug resistant pneumococcal disease.

Although the pneumococcal vaccination history of the majority of cases reported in the enhanced surveillance was unknown, only a small number of cases were fully vaccinated for age. There was only one vaccine failure reported with the 7-valent vaccine during this period.

Generally, this report represents the epidemiology of pneumococcal disease on the eve of the introduction of the conjugate vaccine in Australia. In the coming years, it will be important to monitor the impact of the 7-valent conjugate vaccine on the epidemiology of pneumococcal disease in Australia. The vaccination schedule (Table 1) focuses on high-risk Indigenous children with the primary goal of reducing the incidence of disease in this group. Enhanced surveillance for pneumococcal disease in all Australian jurisdictions from July 2001, will measure changes in clinical presentation, serotype frequency and the prevalence of antibiotic resistance. Additionally, monitoring disease in those age groups recommended for the 23-valent vaccine will be important, as will the nationwide disease rates in other age groups to better guide 23-valent vaccine strategies and recommendations.

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