

Annual report of the Australian Meningococcal Surveillance Programme, 1997

*The Australian Meningococcal Surveillance Programme*¹

Abstract

The National Neisseria Network (NNN) has undertaken meningococcal isolate surveillance by means of a collaborative laboratory based initiative since 1994. The phenotype (serogroup, serotype and serosubtype) and antibiotic susceptibility of 343 isolates of *Neisseria meningitidis* from invasive cases of meningococcal disease were determined in 1997. Ninety six percent of the invasive isolates were serogroup B or C. Serogroup B strains predominated in all States and Territories and were isolated from sporadic cases of invasive disease. Phenotypes B:4:P1.4 and B:15:P1.7 were prominent. Serogroup C isolates were most often encountered in New South Wales, especially in adolescents and young adults, and in that State were nearly as numerous as serogroup B strains. C:2a:P1.5 was the most frequently encountered phenotype and C:2b:P1.2 strains were also distributed widely. A number of clusters of cases of serogroup C disease were noted, mainly with phenotype C:2a:P1.5. About three quarters of all isolates showed decreased susceptibility to the penicillin group of antibiotics (MIC 0.06 to 0.5 mg/L). Three isolates showed reduced susceptibility to rifampicin and one was chloramphenicol resistant. *Commun Dis Intell* 1998;22:205-211.

Introduction

Invasive meningococcal diseases, manifested mainly as bacteraemia and/or meningitis, remain a conspicuous cause of morbidity and mortality in Australia¹ and in 1997 attracted considerable public attention. The host response and outcome

of disease in an individual patient, and the patterns of the infection within a community may be materially altered by the characteristics of the infecting organism. The public health response to an outbreak or cluster of cases is also influenced by certain features of the invasive meningococci, for example vaccines are available for some

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serogroups but not for others, and some phenotypes have been linked to disease outbreaks.

A national programme for the examination of strains of *Neisseria meningitidis* from cases of invasive meningococcal disease was commenced in 1994 with the co-operation and participation of reference laboratories in each State and Territory. This laboratory-based activity is designed to supplement data from existing clinical notification schemes by adding information on the serogroup, the serotype and subserotype (the phenotype) of invasive isolates as well as antibiotic sensitivity data to clinical data. In certain instances, other laboratory investigations are undertaken, such as pulsed field gel electrophoresis (PFGE), which, with other molecular techniques, determine the genotype of meningococci and provides further epidemiological information.

Reports summarising data gathered since the inception of the programme have been published in *CDI*.²⁻⁴ The following report deals with the calendar year 1997.

Methods

The National Neisseria Network (NNN) is a collaborative programme for the laboratory surveillance of the pathogenic Neisseria, *N. meningitidis* and *N. gonorrhoeae*.²⁻⁵ Meningococcal isolate surveillance is performed by a collaborative network of reference laboratories in each State and Territory (see acknowledgements for participants). Each case was based upon isolation of a meningococcus from a normally sterile site. Information on the site of infection, the age and sex of the patient and the outcome (survived/died) of the infection was obtained by each laboratory from clinicians and public health units. The isolate surveillance programme categorises cases on the basis of site of isolation of the organism. It is recognised that the total number of isolates was an underestimate of the number of cases, particularly of meningitis where lumbar puncture was not performed or was delayed and culture was sterile. However the above approach has been used since the beginning of this programme and is continued for comparative purposes.

Phenotyping of invasive isolates of meningococci by serotyping and serosubtyping was based on the detection of outer membrane proteins antigens using a standard set of monoclonal antibodies obtained from Dr. J. Poolman, National Institute for Public Health (RIVM), The Netherlands.

Antibiotic susceptibility was assessed by determining the minimal inhibitory concentration to antibiotics used for therapeutic and prophylactic purposes. This programme

uses the following parameters to define the various levels of penicillin susceptibility/resistance when determined by a standardised agar plate dilution technique:

sensitive,	MIC ≤ 0.03 mg/l;
less sensitive,	MIC = 0.06 - 0.5 mg/l;
relatively resistant	MIC ≥ 1 mg/l.

Strains with MICs which place them in the category of 'sensitive' or 'less sensitive' would be considered to be amenable to penicillin therapy when used in currently recommended doses.

Results

Number of isolates

A total of 343 isolates of invasive meningococci were examined in 1997. There were 153 isolates from patients whose infections acquired in New South Wales (44.6% of all isolates), 62 (18.0%) from Queensland, 56 (16.3%) from Victoria, 24 (7.0%) from Western Australia, 20 (5.8%) from South Australia, 9 (2.5%) from Tasmania, 12 (3.5%) from the Northern Territory and 7 (2.0%) from the ACT (Table 1).

Seasonality

Fifty four (15.7%) of cases occurred between January 1 and March 31, 83 (24.2%) between April 1 and June 30, 105 (30.6%) between July 1 and September 30 and 101 (29.5%) between October 1 and December 31. A winter peak of meningococcal disease is normal.

Distribution of disease by sex and age

Overall there was slight excess of invasive meningococcal disease in males, 178 cases compared with 165 cases in females (M:F ratio 1.08:1). The ratio was highest for males in those patients ages 4 years or less (83 cases in males, 59 in females, M:F ratio 1.4:1) and those aged 15 to 24 years (48 cases in males, 37 in females, M:F ratio 1.3:1). In those aged 45 years or more, there were 30 cases in females and 14 in males (M:F ratio 0.46:1).

The age distribution of patients infected with invasive isolates in each State and Territory is shown in Table 2. Nationally, the peak incidence of meningococcal disease occurred in children aged less than 5 years, with 41.5% of all cases in this age group. Another peak was noted in the 15 - 19 years age group, where 53 cases (15.5% of the total) were recorded. A further 32 cases (9.0%) occurred in those aged 20 -24 years. New South Wales differed from the national pattern in that the number of cases of invasive disease in those aged 15 - 24 years was the same as that

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Table 1. *Neisseria meningitidis* isolates, Australia, 1997, by State or Territory and serogroup

State/ Territory	Serogroup										Total N
	B		C		Y		Other ¹		NG ²		
	N	%	N	%	N	%	N	%	N	%	
ACT	5	72	1	14	1	14	0	0	0	0	7
NSW	78	51	72	47	3	2	0	0	0	0	153
NT	8	67	4	33	0	0	0	0	0	0	12
Qld	43	69	14	23	0	0	3	5	2	3	62
Tas	5	50	3	30	0	0	1	10	1	10	10
SA	14	70	4	20	2	10	0	0	0	0	20
Vic	44	79	9	16	0	0	0	0	3	5	56
WA	22	96	1	4	0	0	0	0	0	0	23
Total	219	64	108	32	6	1.6	4	0.8	6	1.6	343

1. Other includes serogroup Z and serogroup W135. There were no serogroup A isolates

2. NG = non-groupable

Table 2. *Neisseria meningitidis* isolates, Australia, 1997, by State or Territory and age.

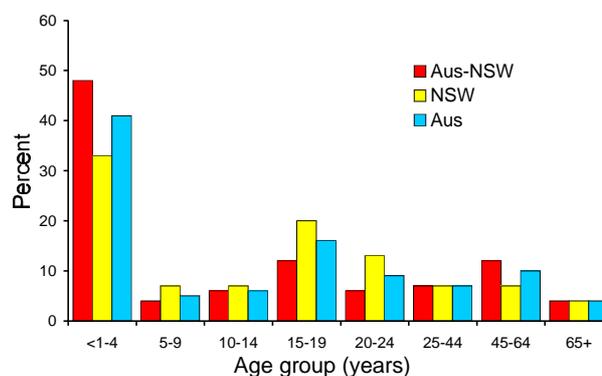
State/Territory	Age group (years)										All
	< 1	1-4	5-9	10-14	15-19	20-24	25-44	45-64	65+	NS	
ACT	2	2	0	0	0	0	0	3	0	0	7
NSW	21	30	10	11	30	20	10	11	6	4	153
NT	3	1	2	1	0	0	0	2	1	2	12
Qld	12	21	2	5	9	4	2	6	1	0	62
SA	7	3	0	1	0	1	3	3	2	0	20
Tas	2	0	1	0	2	1	1	1	1	0	9
Vic	9	18	2	2	6	4	7	6	2	0	56
WA	4	7	1	2	6	2	1	1	0	0	24
Total N	60	82	18	22	53	32	24	33	13	6	343
%	17.5	24	5.2	6.4	15.5	9.3	7	9.6	3.8	1.7	100

for those aged less than 5 years, each group accounting for one third of the infections in that State. In contrast, in Queensland and Victoria about half the cases were less than 5 years old, with a lower secondary peak in the young adult group (Figure 1).

Serogroup, Serotype and Serosubtype (phenotype) Distribution

The distribution of the isolates by serogroup is shown in Table 1. Overall, the 219 serogroup B isolates represented 64% of all strains and the 108 serogroup C strains were 31.5% of the total. Serogroup Y, Z and W135 strains (6, 2 and 2 respectively) were also identified. Four isolates were not serogroupable and 2 were nonviable. No serogroup A isolates were encountered in 1997.

The regional data show some important serogroup differences between centres, and New South Wales in particular had a distinct serogroup distribution. Serogroup B predominated in aggregated national data and especially in Western Australia (all but one of the 24 strains), Victoria (79% of isolates), and South Australia and Queensland (70%). In contrast, in New South Wales the 78 group B strains accounted for only 51% of isolates. Group B

Figure 1. Percentage of isolates of invasive meningococci in each age group, 1997, for all Australia, New South Wales and Australia excluding New South Wales

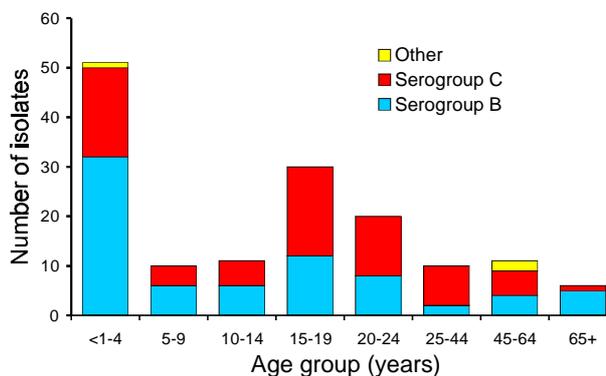
disease comprised unlinked and apparently sporadic cases.

With serogroup C isolates there was again a contrast between New South Wales and the other regions. Seventy two of the 108 group C strains isolated in Australia were from New South Wales. Group C meningococci represented 47% of the New South Wales isolates whereas proportions of group C strains were much lower in other States and Territories, ranging from 34% in the Northern Territory (4 cases) and Tasmania (3 cases) to 16% (9 cases) in Victoria. Only one group C strain was isolated from Western Australia.

Additionally, the distinct serogroup distribution in New South Wales had an age specific pattern. Figure 2 shows the number of cases of invasive disease in New South Wales by age and serogroup. Serogroup B isolates predominated in the 0 - 4 year age group isolates (32 of 51) and generally conformed to the national pattern, whereas serogroup C strains were most prominent (30 of 50) in the adolescent and young adult age group (15 - 24 years). This latter picture was not present in other States and Territories.

There was considerable phenotypic heterogeneity amongst invasive isolates as determined by serotyping and serosubtyping and the strains from New South Wales also showed a different phenotypic pattern to that observed in other States. The predominant

Figure 2. Number of isolates of invasive meningococci, New South Wales, 1997, by age and serogroup



serotype/serosubtypes in each State and Territory are shown in Table 3. Serogroup B meningococci are more difficult to characterise by serological methods, and a number were not successfully phenotyped. B:4:P1.4 strains were present in New South Wales, Queensland, Victoria, Western Australia and the ACT and B:15:P1.7

Table 3. Most frequently isolated serotypes and serosubtypes of *Neisseria meningitidis*, Australia, 1997, by State and Territory.

State/Territory	Serogroup			
	B		C	
	Serotype:serosubtype	N	Serotype:serosubtype	N ¹
ACT	4:P1.4	1	2b:P1.2	1
NSW	4:P1.4	17 (11)	2a:P1.5	39 (15)
	NT:NST	13 (9)	2b:P1.5,2	8 (10)
	2b:P1.10	11 (8)	2a:P1.5,2	3 (2)
	15:P1.7	7	2b:P1.2	2 (0)
NT	4:P1.5	2	2a:P1.5,2	2
			2a:P1.5	2 (2)
Qld	4:P1.4	3 (6)	2b:P1.5,2	0 (10)
	NT:P1.4	9 (4)	2a:P1.5	1 (4)
	15:P1.7	3	2a:P1.5,2	3 (4)
	2b:P1.10	2	2b:P1.2	3
SA	15:P1.7	16 (3)	one isolate only	
	2b:NST	(2)		
	NT:P1.10	(2)		
Tas	Various		2b:P1.2	2
Vic	NT:P1.4	8 (13)	2a:P1.5	1
	15:P1.7	3	2b:P1.10	1
	4:P1.4	3 (2)	2b:P1.2	1
	2b:P1.10	2		
WA	15:P1.7	5	2a:P1.5	1
	NT:P1.4	5 (5)		
	4:P1.4	1		

1. The numbers of isolates of each phenotype in 1996 are shown in parenthesis

strains in New South Wales, Queensland, Victoria and Western Australia.

There was less heterogeneity amongst serogroup C meningococci. There were 44 serogroup C strains of phenotype 2a:P1.5, comprising 40% of all group C strains. Thirty nine of these were found in New South Wales and, of these, 19 were in the young adult group. Strains of this type were also isolated in Queensland, Victoria and the Northern Territory. The single serogroup C strain in Western Australia was also a 2a:P1.5 phenotype. In New South Wales this phenotype was associated with several clusters of invasive disease. Another cluster of cases was associated with strains of phenotype C:2a:P1.5.2, this phenotype also appearing in Queensland and the Northern Territory.

Site of isolation

There were 129 isolates from CSF either alone or with a blood culture isolate and 200 from blood culture alone. Fourteen isolates were from other sterile sites including synovial fluid and skin lesions.

Outcome data for 1997

Outcome data (survived or died) were available for 240 patients. Sixteen deaths were recorded (6.6%) (Table 4).

There were two deaths in 86 patients (2.3%) with meningitis. Both patients were infected with serogroup B strains. Thirteen deaths were recorded in 146 bacteraemic patients (8.9%). There were 89 cases of serogroup B meningococcal bacteraemia with six deaths and another 44 cases were caused by serogroup C strains among whom five fatalities were recorded. Two of four patients with septicaemia with serogroup Y meningococci died.

Other antibiotics.

The 339 isolates which were tested for susceptibility to ceftriaxone and, by extrapolation, to other third generation cephalosporins, were susceptible to these therapeutic agents. Two hundred and sixteen isolates were examined for chloramphenicol resistance and a single strain from New South Wales was resistant at a MIC of 8 mg/L.

Three hundred and thirty nine isolates were also tested for susceptibility to the prophylactic agents rifampicin and ciprofloxacin. Two isolates from Queensland had raised MICs to rifampicin (MICs of 1 mg/l). All isolates tested were sensitive to ciprofloxacin. Sulphonamide testing was not performed.

Discussion

The number of isolates examined by NNN laboratories in the Australian Meningococcal Surveillance Programme increased to 343 in 1997 from the 297 in 1996. These are 69% of the 496 notifications of meningococcal disease for 1997 and 70% of the 426 notifications for 1996. The number of isolates examined in 1994 was 216, which was 56% of the 383 notifications for that year. Most of the increase since 1994 has been the result of improved surveillance. The numbers of invasive isolates in most States and Territories in 1997 changed only slightly from those in 1996. However in New South Wales the number of isolates available for further examination increased from 95 in 1996 to 153 in 1997. Two factors in New South Wales contributed to this increase; the number of clinical cases notified increased from 166 in 1996 to 219 in 1997 and isolates from a higher proportion of culture positive cases were available. The number of isolates available for

Table 4. *Neisseria meningitidis* isolates, Australia 1997, outcome of meningitic and septicaemic cases by serogroup

Disease Type	Outcome	Serogroup				Total
		B	C	Y	NG ¹	
Meningitis	Survived	64	19	1	0	84
	Died	2	0	0	0	2
	Total	66	19	1	0	86
Septicaemia	Survived	83	44	2	4	133
	Died	6	5	2	0	13
	Total	89	49	4	4	146
All cases ²	Survived	150	66	3	5	224
	Died	8	6	2	0	16
	Total	158	72	5	5	240

1. Non groupable

2. Includes two serogroup B, two serogroup C and one non-groupable strain from joint aspirates and one serogroup B and one serogroup C from skin lesions, all of whom survived, and a serogroup C sterile site aspirate in a fatal case.

Antibiotic susceptibility surveillance of invasive meningococcal isolates

Penicillin

Using defined criteria, 92 of 339 strains tested (27%) were fully sensitive to penicillin and 247 (73%) less sensitive (MIC 0.06 to 0.5 mg/l). MICs recorded ranged between 0.015 and 0.5 mg/l.

examination will always be less than the number of clinically notified cases because surveillance case definitions include culture negative cases. The increased number of cases in New South Wales and changing meningococcal phenotypes accounted for most of the differences from previous reports.

The dominant pattern observed in most centres was one of sporadic serogroup B disease. This was the pattern also in New South Wales, but additionally in that State there was

increased serogroup C disease, most noticeably in young adults and adolescents. The serogroup C disease was also mainly sporadic, but clusters of cases, typical of group C meningococcal disease, were also noted. This serogroup C activity in young adults was responsible for the different age distribution of disease in New South Wales. Serogroup B and serogroup C isolates together accounted for 95.5% of all invasive meningococci. No serogroup A meningococci were isolated in 1997. This picture is typical of the pattern of meningococcal disease in developed countries.

Phenotyping data, obtained on the basis of serotyping and serosubtyping was again available in 1997. Of interest amongst the group B strains were phenotypes B:4:P1.4 and B:15:P1.7, associated with hyperendemic disease in New Zealand and Europe respectively. B:4:P1.4 strains were most frequently encountered in New South Wales, and were also present in low numbers in other States and the ACT. B:15:P1.7 isolates represented a high proportion of strains from Western Australia and were also widely distributed.

Of special interest in the 1996 report was the recognition of the phenotypes C:2a:P1.5 and C:2a:P1.5.2 in all States and Territories except South Australia and Western Australia. These phenotypes have been implicated in hyperendemic meningococcal disease in Canada for a number of years⁶ and have also been reported in Europe. Studies here indicate that the C:2a:P1.5 isolates in New South Wales are of the ET 37 (15) complex seen overseas (Jane Jelfs, South Western Area Pathology Service, personal communication). They were responsible for a cluster of cases in Western Sydney in 1996 and continued to be isolated throughout 1997. The C:2a:P1.5 phenotype was responsible for 39 cases of invasive disease in New South Wales in 1997, a number of these occurring as clusters. This phenotype was also present in Queensland, Victoria and the Northern Territory. The Western Australian isolate of this phenotype was probably acquired in New South Wales. The C:2a:P1.5,2 phenotype was seen in a small cluster of cases in 1997.

Overall, the outcome data in 1997 (6.8% mortality) were similar to those recorded in 1996 (6% mortality) and are in the expected range where early diagnosis, and appropriate antibiotic therapy and supportive measures are available.⁷

A decrease in susceptibility of meningococci to penicillin has been noted in many parts of the world. Isolates have occasionally been shown to be resistant to other antibiotics which are used currently in the therapeutic or prophylactic management of meningococcal disease. This programme

therefore includes routine examination of the antibiotic susceptibility of invasive isolates as part of its surveillance. By using consistent methods over the past four years the data now provide evidence of an emerging trend in Australia.

Since 1994 there has been an increase in the proportion of invasive meningococci showing some decrease in penicillin susceptibility. In 1994, 52% of strains were in the 'less sensitive' range (MIC 0.06 - 0.5 mg/L). In 1995, 155 (63%) of 247 strains tested were 'less sensitive'. The proportion of less sensitive isolates increased further to 74% of 297 isolates in 1996. This proportion remained unchanged in 1997 (73%). The isolation of a meningococcus with a MIC in the less sensitive range does not mean that therapeutic failure will occur, but the increase in the number and proportion of stains in this category is an epidemiological marker of the slow progression to resistance.

The definition of what constitutes 'resistance' to the prophylactic agent rifampicin varies. This programme has chosen to monitor the number of isolates with MICs of 1 mg/l or more. In 1997, two isolates from Queensland had rifampicin MICs of 1 mg/L or more, compared with three strains in 1996. One isolate in New South Wales was chloramphenicol resistant.

The Australian Meningococcal Surveillance Programme (AMSP) has examined a total of more than 1100 strains from all States and Territories since 1994 and has assisted in clarifying and expanding information on invasive meningococcal isolates in Australia. The programme is investigating the utility of other means of enhancing laboratory diagnosis of meningococcal disease, notably PCR based diagnosis using cerebrospinal fluid, and serology for retrospective diagnosis. Other methods of strain differentiation, most notably pulsed field gel electrophoresis are available. For further details, contact the relevant NNN member (see acknowledgements).

Acknowledgements

Isolates were received in the reference centres from many laboratories throughout Australia. The considerable time and effort involved in forwarding these strains is recognised and these efforts are greatly appreciated. These data could not have been provided without this assistance and the help of clinical colleagues and Public Health personnel.

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