

# Annual report of the Australian Meningococcal Surveillance Programme, 1998

*The Australian Meningococcal Surveillance Programme*<sup>1</sup>

## Abstract

The National Neisseria Network 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 323 isolates of *Neisseria meningitidis* from invasive cases of meningococcal disease were determined in 1998. Ninety per cent of the invasive isolates were either serogroup B or C. Serogroup B strains predominated in all States and Territories and were isolated from sporadic cases of invasive disease. Serogroup B phenotypes were diverse. Serogroup C isolates were most prominent in New South Wales, especially in adolescents and young adults. C:2a:P1.5 was the most frequently encountered phenotype and C:2b:P1.5,2 strains were also distributed widely. About three-quarters of all isolates showed decreased susceptibility to the penicillin group of antibiotics (MIC 0.06 to 0.5 mg/L). Four isolates showed reduced susceptibility to rifampicin, one to ciprofloxacin and one to chloramphenicol. *Commun Dis Intell* 1999;23:317-323.

## Introduction

Invasive meningococcal diseases continued to attract considerable public attention in 1998. The manifestations of meningococcal disease may range from the mild and even subclinical to the rapidly progressive and fatal. Many of the reasons for these different responses remain unknown.

However, 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.<sup>1,2</sup> The public health response to a suspected outbreak or cluster of cases is also influenced by certain features of the meningococci concerned, for example vaccines

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are available for some serogroups of meningococci but not for others, and certain phenotypes have been linked to disease outbreaks.

A national programme for the examination of strains of *Neisseria meningitidis* (*N. 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 phenotype (the serogroup, the serotype and subserotype) and antibiotic susceptibility of invasive isolates to clinical data. In certain instances other laboratory investigations, mainly molecular studies, are undertaken to provide further epidemiological information.

Reports summarising data gathered since the inception of the programme were published in *CDI*.<sup>3-7</sup> The following report deals with the calendar year 1998.

## Methods

The National Neisseria Network (NNN) is a collaborative programme for the laboratory surveillance of the pathogenic *Neisseria*, *N. meningitidis* and *N. gonorrhoeae*.<sup>3-7</sup> A network of reference laboratories in each State and Territory (see acknowledgments) performs meningococcal isolate surveillance. 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 sought. The isolate surveillance programme categorises cases on the basis of site of isolation of the organism. Where an isolate is grown from both blood and CSF cultures in the same patient, the case is classified as one of meningitis. It is recognised that the total number of cases and particularly the number of cases of meningitis, for example, where there was no lumbar puncture or else where lumbar puncture was delayed and culture was sterile, was underestimated. 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 protein 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 (MIC) 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 323 invasive isolates of meningococci was examined in 1998. There were 113 isolates from patients whose infections were acquired in New South Wales (35% of all isolates), 81 (25%) from Queensland, 42 (13%) from Western Australia, 40 (12.5%) from Victoria, 24 (7.5%) from South Australia, 13 (4%) from Tasmania, 9 (3%) from the Northern Territory and 1 (0.3%) from the Australian Capital Territory (Table 1).

### Seasonality

Thirty-eight (11.7%) of cases occurred between 1 January and 31 March, 79 (24.5%) between 1 April and 30 June, 132 (40.9%) between 1 July and 30 September and 74 (22.9%) between 1 October and 31 December. A winter peak of meningococcal disease is usual.

### Age group

The age distribution of patients infected with invasive isolates in each State and Territory is shown in Table 1. Nationally, the peak incidence of meningococcal disease occurred in those 4 years and under. Those aged less than 1 year or in the 1-4 year age group accounted for 11.8% and 30% of cases respectively. A secondary peak

**Table 1.** *Neisseria meningitidis* isolates, 1998, by State or Territory and age group

	Age group (years)										NS	All
	<1	1-4	5-9	10-14	15-19	20-24	25-44	45-64	65+			
Qld	5	26	7	4	9	6	17	7	6	0	81	
NSW	15	32	6	5	25	10	9	6	4	1	113	
ACT	0	1	0	0	0	0	0	0	0	0	1	
Vic	6	12	3	2	5	4	5	3	1	0	41	
Tas	4	5	0	1	1	0	1	0	1	0	13	
SA	5	4	1	2	1	2	1	1	2	2	24	
WA	1	14	2	0	10	7	4	2	2	0	42	
NT	2	3	1	1	0	0	0	1	1	0	9	
Total n	38	97	20	15	51	29	30	20	20	3	323	
%	11.8	30	6.2	4.6	15.7	9	9.3	6.2	6.2	1	100	

NS Not stated

**Table 2. *Neisseria meningitidis* isolates, 1998, by State or Territory and serogroup**

State/ Territory	Serogroup										Total		
	B		C		A	Y		W135		NG*		n	%
	n	%	n	%		n	%	n	%	n	%		
Qld	56	70.4	12	13.6	0	6	7.5	2	2.5	5	6	81	25
NSW	53	47	50	44	0	6	5.5	4	3.5	0		113	35
ACT	1	100	0		0	0		0		0		1	0.3
Vic	29	72.5	7	17.5	0	4	10	0		0		40	12.5
Tas	9	69	2	15.5	0	0		0		2	15.5	13	4
SA	14	58.3	7	29.1	0	11	4.2	2	8.4	0		24	7.5
WA	36	87	4	8	0	1	2.5	1	2.5	0		42	13
NT	8	89	1	11	0	0		0		0		9	2.5
Total	204	64	81	25	0	18	6	99	3	7	2	323	100

\*NG = non-groupable

was noted in the 15-19 year age group when 51 cases accounting for 15.7% of the total were recorded. A further 29 cases (9%) occurred in those aged 20-24 years.

Western Australia differed from the national pattern in that the number of cases of invasive disease in those aged 15-24 years was higher than for those aged 4 years or less. In Queensland, South Australia and Victoria, the secondary peak in the young adult group was half or less than in the infant group. New South Wales approximated the national average age distribution of disease.

### Serogroup, serotype and serosubtype (phenotype) distribution

The distribution of the isolates by serogroup is shown in Table 2. Nationally, 204 serogroup B isolates represented 64% of all strains, the same proportion as in 1997. The 81 serogroup C strains (25%) were less than the number and proportion detected in 1997. There was an increase in the number (18) and proportion (6%) of serogroup Y strains in 1998. Nine serogroup W135 meningococci were also identified. Seven isolates were not serogroupable. No serogroup A isolates were encountered in 1998.

**Table 3. Most frequently isolated serotypes and serosubtypes and phenotypes of *N. meningitidis* of interest, by State and Territory in 1998**

State/Territory	Serogroup			
	B		C	
	Serotype:serosubtype		Serotype:serosubtype	
Qld	4:P1.4	4 (3, 6)*	2b:P1.5,2	3 (0, 10)*
	NT:P1.4	3 (9, 4)	2a:P1.5	4 (1, 4)
	15:P1.7	1 (3)	2a:P1.5,2	0 (3, 4)
	2b:P1.10	1 (2)	2b:P1.2	0 (3)
NSW	4:P1.4	5 (17, 11)	2a:P1.5	23 (39, 15)
	NT:NST	8 (13, 9)	2b:P1.5,2	6 (8, 10)
	2b:P1.10	4 (11, 8)	2a:P1.5,2	8 (3, 2)
	15:P1.7	1 (7)	2b:P1.2	0 (2, 0)
Vic	NT:P1.4	11 (8, 13)	2a:P1.5	1 (1)
	15:P1.7	1 (3)	2b:P1.10	2 (1)
	4:P1.4	2 (3, 2)	2b:P1.2	2 (1)
	2b:P1.10	1 (2)		
SA	15:P1.7	3	2b:P1.5,2	2
	4:NST	3		
	4:P1.4	1		
Tas	2b:nst	2	2b:P1.2	1 (2)
ACT	Single isolate only			
NT	2b:nst	5	2a:nst	1

\* The numbers of isolates of each phenotype in 1997 and 1996 are shown in parenthesis

The regional data show some important differences in the distribution of serogroups.

Serogroup B predominated in aggregated national data and especially in Western Australia (87% of isolates), Victoria (72%), the Northern Territory (89%) and Queensland (70%). In contrast, in New South Wales the 53 group B strains accounted for 47% of isolates and in South Australia group B isolates were nearly 60% of the total. Group B disease comprised unlinked and apparently sporadic cases. Serogroup C isolates were again concentrated in New South Wales. Fifty group C meningococci or 62% of all serogroup C strains isolated in Australia were from infections there. Group C meningococci represented 44% of the New South Wales isolates and about 30% of South Australian meningococci. Numbers and proportions of group C strains were much lower in other States and Territories. There was a single group C isolate in the Northern Territory, 2 in Tasmania, 11 (14%) in Queensland, 7 (17%) in Victoria and 4 (8%) in Western Australia. No clusters of serogroup C infection were identified.

The distinct serogroup distribution in New South Wales had an age specific pattern. Serogroup B isolates predominated in the 0-4 year age group (29 of 47) isolates whereas serogroup C strains were most prominent (20 of 35) in the adolescent and young adult age group (15-24 years).

There was considerable phenotypic heterogeneity amongst invasive isolates as determined by serotyping and serosubtyping. The predominant serotypes/serosubtypes in each State and Territory are shown in Table 3, Western Australia excepted. Serogroup B meningococci are more difficult to characterise by serological methods and a number could not be phenotyped. B:4:P1.4 strains were present in New South Wales, Queensland, Victoria and South Australia, and B:15:P1.7 strains in New South Wales, Queensland, Victoria, and South Australia.

There was less heterogeneity amongst serogroup C meningococci. All isolates were either serotype 2a or 2b and the serosubtypes present were either P1.5 or P1.2 or else a combination of both. There were 28 serogroup C strains of phenotype 2a:P1.5 (54% of all group C strains phenotyped). Twenty-three of these were found in New South Wales. Strains of this phenotype were also isolated

in Queensland and Victoria. The phenotype 2b:P1.5,2 was also prominent.

Serogroup Y strains were either serotype 14 or else not serotypeable.

#### Site of isolation

There were 84 isolates from CSF either alone or with a blood culture isolate and 235 from blood cultures alone. There were four isolates from other sterile sites including synovial fluid and skin lesions.

#### Outcome data for 1998

Outcome data (survived or died) were available for 202 patients (62.5%). Eighteen deaths were recorded (9%) (Table 4). Outcomes were available in 122 serogroup B infections (59%) and 61 serogroup C infections (74%). There were four deaths in serogroup B infections and 10 in serogroup C infections ( $p < 0.002$ ). Where outcomes were known, there were four deaths in 44 patients (9%) with meningitis. Two patients were infected with serogroup B and two with serogroup C strains. Fourteen deaths were recorded in 157 bacteraemic patients (9%). There were 86 cases of serogroup B meningococcal bacteraemia with 2 deaths and another 47 cases were caused by serogroup C strains among whom 8 fatalities were recorded. Three of 8 patients with serogroup Y septicaemia died. There was one fatal case of septicaemia with serogroup W135.

#### Antibiotic susceptibility surveillance of invasive meningococcal isolates

##### Penicillin

Three-hundred and two isolates of the 323 strains were tested for their susceptibility to penicillin. Using defined criteria, 75 strains (25%) were fully sensitive to penicillin and 227 (75%) less sensitive (MIC 0.06 - 0.5 mg/L). These proportions differ little from 1997 data. The penicillin MICs recorded ranged between 0.015 and 0.5 mg/L. Only four isolates had MICs of 0.5 mg/L.

##### Other antibiotics

All 302 isolates which were tested for susceptibility to ceftriaxone (and by extrapolation to other third generation cephalosporins), were susceptible to these therapeutic agents. A single isolate had decreased susceptibility to chloramphenicol. Four meningococci had raised MICs to

**Table 4. Outcome of meningitic and septicaemic cases of meningococcal infection by serogroup, 1998**

Disease type	Outcome	Serogroup					Total
		B	C	Y	W135	NG*	
Meningitis	Survived	34	4	1	1	0	40
	Died	2	2	0	0	0	4
	Total	36	6	1	1	0	44
Septicaemia	Survived	84	47	5	5	2	143
	Died	2	8	3	1	0	14
	Total	86	55	8	6	2	157
All cases**	Total	122	61	10	7	2	202
	Died	4	10	3	1	0	18 (9%)

\* Non groupable

\*\* Includes one serogroup Y strain from a joint aspirate from a patient who survived.

rifampicin (MICs of 1 mg/L) and one to ciprofloxacin (MIC 0.25 mg/L) (sulphonamide testing was not performed).

## Discussion

The total of 323 isolates examined by NNN laboratories in the Australian Meningococcal Surveillance Programme in 1998 was less than the 343 available in 1997. From 1994 onwards, the number of isolates examined each year by the NNN has increased. This has been in part at least the result of improved surveillance, although increases in disease incidence have also occurred. The decrease in overall numbers in 1998 reverses this trend, but this did not occur in all jurisdictions. The numbers of isolates available in New South Wales and Victoria were between 70% and 75% of the total examined in 1997. In Western Australia and Queensland the numbers of isolates increased, from 23 to 42 and 62 to 81 respectively. Although considerable public attention was focussed on meningococcal disease in South Australia in 1998, the number of cases was essentially unchanged from 1997. The number of isolates available for examination will always be less than the number of clinically notified cases because clinical surveillance case definitions include culture negative cases. A number of clinical cases were confirmed only by non-culture based laboratory examinations. These procedures include nucleic-acid-based amplification assays (NAA) and serological examination. These cases were not included in this year's analysis of isolate-based surveillance. Some of the techniques in use can provide additional data on the serogroup of the isolate. It is anticipated that laboratory confirmation of invasive meningococcal disease by non-culture based methods will continue to increase. NNN laboratories may be contacted for advice regarding these tests.

The ratio of cases of meningitis to bacteraemia was significantly lower in 1998, accentuating a trend noted in 1997 (Figure 1). From 1994 to 1996, the ratio of cases of meningitis to bacteraemia was close to 1.0:1 in NNN data. In 1997 this ratio decreased to 0.6:1 and in 1998 further declined to 0.3:1. NNN case definitions, which are based on site of isolation, tend to overestimate the number of bacteraemic cases. This is because those cases of clinical meningitis where only a blood culture was positive were regarded as bacteraemias in NNN data. It has been recognised anecdotally that there is an increasing reluctance on the part of clinicians to perform lumbar puncture early in cases of suspected meningitis or to omit the investigation altogether. However, NNN case definitions have been constant over the past 5 years. Another factor which may impact on this changing picture, is the continuing emphasis on early antibiotic treatment for meningococcal disease. It is more feasible to obtain a blood culture when intravenous antibiotics are administered than to perform a lumbar puncture, so this may also influence data on categorisation. However, it would appear that the reluctance or inability to obtain CSF early in the disease, rather than a shift in disease manifestations, is the principal reason for the change in isolation pattern observed. Again, non-culture based diagnosis may assist in the clarification of disease manifestations.

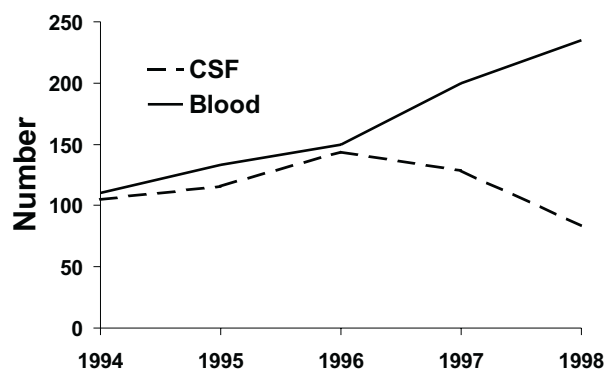
The predominant disease pattern observed was one of sporadic infection with serogroup B meningococci. The proportion of serogroup C cases was less in 1998 than in 1997, which has relevance to decisions regarding the use of conjugate group C vaccines.<sup>9</sup> Serogroup C cases were also sporadic in nature in 1998. Serogroup C disease was most often encountered in New South Wales, but infrequently in other States and Territories. No serogroup A meningococci were isolated in 1998. Also of interest was the increased number and proportion of cases of serogroup Y infection. Although distributed in low numbers in a number of States, they represented about 5% of all infections. Serogroup Y infections have increased in some parts of the United States of America in recent years.<sup>10</sup>

Children aged 4 years or less were the group most frequently infected. A secondary incidence peak was noted in young adults and adolescents, especially in Western Australia and New South Wales. Serogroup C disease occurred more often in the young adult age group. This picture of serogroup B and C disease occurring as sporadic cases is typical of the pattern of meningococcal disease in developed countries. Clusters of cases of serogroup C infection have been present in recent years but were not seen in 1998.<sup>5,6</sup>

Phenotyping data obtained on the basis of serotyping and serosubtyping was again available from all but one centre in 1998. The heterogeneity of serogroup B isolates present in Australia was confirmed. 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 encountered in low numbers in a number of States.

Of some interest in the reports from 1996 and 1997<sup>5,6</sup> was the appearance and spread of the phenotypes C:2a:P1.5 and C:2a:P1.5,2. These phenotypes have been implicated in hyperendemic meningococcal disease in Canada for a number of years<sup>9</sup> and have also been reported in Europe. They were responsible for clusters of cases in Western Sydney in 1996 and 1997. The C:2a:P1.5 phenotype was responsible for 23 cases of invasive disease in New South Wales in 1998, but no case clusters were recognised. This phenotype was also present in Queensland and Victoria in 1998.

**Figure 1. Numbers of meningococcal isolates from CSF and blood culture, 1994 to 1998**



Overall, the mortality recorded in assessable cases was 9%, higher than the 6% observed in previous years. A higher mortality rate was observed with serogroup C and serogroup Y infections than with serogroup B cases, but outcome data was incomplete. Although serogroup C strains have been associated with increased mortality overseas, other factors for which data were not available may explain this difference, such as age and time from onset to presentation and treatment. The increase in mortality was observed in a number of States.

Continuing interest has been shown in the decrease in susceptibility of meningococci to penicillin in many parts of the world. Further, other isolates have occasionally been shown to be resistant to other antibiotics which are used currently for either therapeutic or prophylactic purposes in meningococcal disease. This programme therefore includes routine examination of the antibiotic susceptibility of invasive isolates as part of its surveillance. Trend data indicates that 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%) and no further change was recorded in 1998. The isolation of a meningococcus with an MIC in the less sensitive range does not mean that therapeutic failure will occur, but the increase in the number and proportion of strains in this category is rather 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. There were four isolates with rifampicin MICs of 1 mg/L or more in 1998. One isolate was chloramphenicol resistant and another had decreased susceptibility to ciprofloxacin.

The programme has examined a total of more than 1,400 strains from all States and Territories since 1994 and has assisted in clarifying and expanding information on invasive meningococcal isolates in Australia. The nature and high public recognition of meningococcal disease suggests that these efforts should continue. For further details the relevant NNN member should be contacted (see acknowledgments for contact numbers).

### *Acknowledgments*

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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## Changes to the Editorial team

The production team for *CDI* has recently farewelled the Editor Eddie O'Brien, and welcomed our new Editor, Jenny Thomson. Eddie's valuable input, skills and expertise, as well as his cheerful interaction as a team member will be missed. We wish Eddie well in his new

position and thank him for his contribution to *CDI*. Jenny Thomson comes to us with qualifications and experience that will greatly benefit *CDI*. We welcome Jenny to the team and look forward to her ongoing input to the quality and development of the publication.

## Australian recommendations for the influenza vaccine composition for the year 2000 season

The meeting of the Australian Influenza Vaccine Committee (AIVC) was convened on 7 October 1999 and reconvened on 9 November.

Having considered the information on international surveillance by the WHO, and recent epidemiological data and strain characterisation presented at both AIVC meetings, the Committee decided that the composition of vaccines for the year 2000 season should be as follows:

- **A (H3N2):** a A/Sydney/5/97 (H3N2) - like strain, 15 µg HA per dose
- **A (H1N1):** a A/New Caledonia/20/99 (H1N1) - like strain, 15 µg HA per dose
- **B:** a B/Beijing/184/93 - like strain, 15 µg HA per dose

It was also determined that the following viruses are suitable vaccine strains:

- A/Sydney/5/97 (IVR-108 and RESVIR-13) are A/Sydney/5/97 (H3N2)-like strains
- A/New Caledonia/20/99 (IVR-116) is an A/New Caledonia/20/99 (H1N1)-like strain
- B/Yamanashi/166/98 is a B/Beijing/184/93-like strain