

Annual report of the Australian Meningococcal Surveillance Programme 1996

*The Australian Meningococcal Surveillance Programme*¹

Abstract

The Australian Meningococcal Surveillance Programme has undertaken meningococcal isolate surveillance by means of a collaborative laboratory-based initiative since 1994. Serogroup data have been enhanced by the addition of serotype and serosubtype information in 1996. Ninety-two per cent of the 297 invasive isolates of *Neisseria meningitidis* examined in 1996 were serogroup B or C. Serogroup B strains predominated in all States and Territories and were isolated from sporadic cases of meningococcal disease. Serogroup C isolates were prominent in New South Wales, Queensland and the Northern Territory, and were also associated with mainly sporadic cases of meningococcal disease. A number of case clusters also occurred in association with serogroup C strains. Although most sporadic cases of meningococcal disease showed a diversity of phenotypes, clusters of cases were noted with the phenotypes C:2a:P1.5 and C:2a:P1.2,5. The number of isolates with the phenotype B:4:P1.4 also increased in New South Wales and Queensland. The proportion of isolates showing decreased susceptibility to the penicillin group of antibiotics (minimal inhibitory concentration, MIC, 0.06 to 0.5 mg/L) increased to 74% in 1996. Three isolates showed reduced susceptibility to rifampicin. *Comm Dis Intell* 1997;21:217-221.

Introduction

Invasive meningococcal disease, manifest as bacteraemia and/or meningitis remains a significant cause of morbidity and mortality in Australia¹. The host response, outcome of the disease in an individual patient, and the patterns of the infection, may vary with the characteristics of the infecting organism. The public health response to an

outbreak is also influenced by the particular meningococcus e.g. vaccines are available for serogroups A and C but not for B (newer conjugate vaccines are currently being trialed).

The Australian Meningococcal Surveillance Programme (AMSP) was commenced in 1994, for the examination of strains of *Neisseria meningitidis* (*N.meningitidis*) from cases of invasive meningococcal

disease. It was established with the co-operation and participation of reference laboratories in each State and Territory. This programme is part of the National Neisseria Network.

The AMSP is designed to supplement data from the National Notifiable Diseases Surveillance Scheme by adding information on the serogroup, the serotype and subserotype of

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invasive isolates, as well as antibiotic sensitivity data.

Reports providing information gathered in the first two years of the programme were published in *Communicable Diseases Intelligence*^{2,3}. This report covers data collected for the calendar year 1996.

Methods

The National Neisseria Network (NNN) is a collaborative programme for the laboratory surveillance of the pathogenic Neisseria, *N. meningitidis* and *N. gonorrhoeae*^{2,4}.

Meningococcal isolate surveillance is performed by a collaborative network of reference laboratories in each State and Territory.

Information on the site of infection, the age and sex of the patient and the outcome (survived/died) was recorded. The surveillance programme categorised cases on the basis of site of isolation of the organism. It is recognised that this probably underestimated the number of cases of meningitis e.g. where there was no lumbar puncture, or where lumbar puncture was delayed and the culture was sterile. This approach has been adopted since the beginning of the programme.

Differentiation of meningococcal strains by serotype and serosubtype 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,

Royal Institute Veterinary Medicine, the Netherlands.

Antibiotic susceptibility was assessed by determining the minimal inhibitory concentration (MIC) to antibiotics used for therapeutic and prophylactic purposes. This programme used the following parameters to define the various levels of penicillin susceptibility/resistance when determined by a standardised agar plate dilution technique:

- sensitive, MIC \leq 0.03 mg/L;
- less sensitive, MIC = 0.06 - 0.5 mg/L; and
- relatively resistant, MIC \geq 1 mg/L.

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

Results

Phenotype Distribution

Two hundred and ninety-seven invasive isolates of *N. meningitidis* were examined in 1996 (Table 1).

Most of the isolates were serogroup B (186) representing 63% of all strains, followed by 86 serogroup C isolates representing 29%. Serogroup Y (11 strains, 4%) and serogroup W135 (9 strains, 3%) were also identified. No serogroup A isolates were identified in 1996.

The regional data show some differences between centres. Serogroup B predominated overall, and especially in the ACT (83% of

isolates) Victoria (81%) and Western Australia (79%). Serogroup C constituted a large proportion of isolates in New South Wales, Queensland and the Northern Territory (41%, 35% and 44% respectively). In South Australia three of the 16 isolates (19%) were identified as serogroup Y. The percentage of serogroup Y isolates increased from 1% in 1995 to 4% in 1996.

There was considerable heterogeneity amongst phenotypes as determined by serotyping and serosubtyping (Table 2).

Age group and sex

The highest number of isolates was for the under 5 years age group (Figure). Those aged less than one year accounted for 16% of all cases and 22% were in the 1 - 4 years age group. Another peak was noted in the 15 - 19 years age group with 51 cases (17%) recorded. A further 29 cases (10%) occurred in the 20 - 24 years age group. The male:female ratio was 1.1:1

Site of isolation

There were 144 isolates (48% of total) from cerebrospinal fluid (CSF), either alone or with a blood culture isolate, and 150 (50%) from blood cultures alone. There were two isolates from synovial fluid and one from pleural fluid.

Outcome

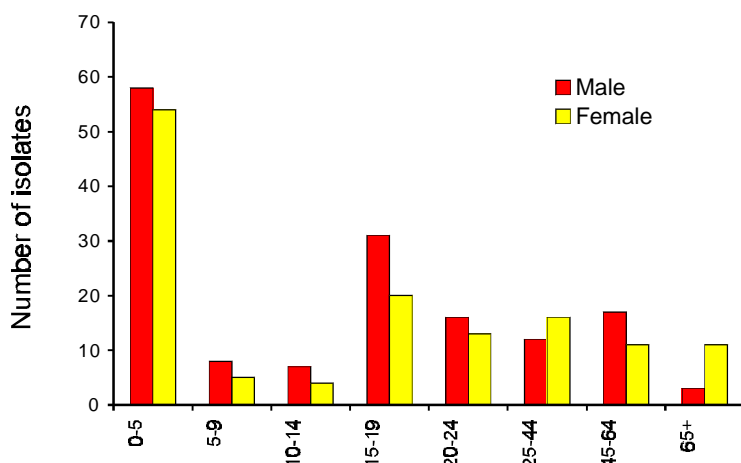
Outcome data (survived or died) including disease type and organism serogroup was available for 190 patients (Table 3). Out of the 190 patients, eleven deaths were recorded (6%). There were five deaths in 86 patients (6%) with meningitis. Six deaths (6%) were recorded in 102 bacteraemic patients. One patient with a serogroup Y strain from a synovial fluid, and another with a serogroup B strain from a pleural fluid survived.

Antibiotic susceptibility

Penicillin

Using the defined criteria (above), 72 of 282 strains tested (25%) were fully sensitive to penicillin, and 209 (74%) were less sensitive. A single isolate from New South Wales had an MIC of 1 mg/L, and the patient was treated successfully with a third-generation cephalosporin. Minimal inhibitory

Figure. *N. meningitidis* notifications, 1996, by age group and sex



concentrations recorded ranged between 0.015 and 1 mg/L. The strains from the 11 fatal cases had MICs for penicillin in the range 0.03 to 0.25 mg/L.

Other antibiotics

The 295 isolates which were tested for susceptibility to ceftriaxone (and by extrapolation to other third-generation cephalosporins), and the

156 tested for susceptibility to chloramphenicol, were susceptible to these therapeutic agents. Two hundred and ninety-five isolates were also tested for susceptibility to the prophylactic agents rifampicin and ciprofloxacin. Three isolates had raised MICs to rifampicin; two with MICs of 1 mg/L and another with an MIC of 4 mg/L. All isolates tested were sensitive to ciprofloxacin.

Sulphonamide testing was not performed.

Discussion

The number of isolates examined increased in 1996, reflecting the consolidation of the AMSP since 1994. Two hundred and ninety-seven *N. meningitidis* isolates were examined in 1996 compared to 216 in

Table 1. *Neisseria meningitidis* isolates, 1996, by State or Territory and serogroup

State or Territory	Serogroup						Total n (%)
	B n (%)	C n (%)	A	Y n (%)	W135 n (%)	NG ¹ n (%)	
Qld	36 (55)	23 (35)	0	2	4	1	66 (22)
NSW	49 (51)	40 (41)	0	5	2	1	97 (33)
ACT	5 (83)	1 (17)	0	0	0	0	6 (2)
Vic	54 (81)	10 (15)	0	0	0	3	67 (23)
Tas	8 (67)	4 (33)	0	0	0	0	12 (4)
SA	11 (68)	1 (6)	0	3	1	0	16 (5)
WA	19 (79)	3 (13)	0	1	1	0	24 (8)
NT	4 (44)	4 (44)	0	0	1	0	9 (3)
Total	186 (63)	86 (29)	0	11 (4)	9 (3)	5 (1)	297 (100)

1. NG = non-groupable

Table 2. Most frequently isolated serotypes and serosubtypes, 1996, by State and Territory

State/Territory	Serogroup B		Serogroup C	
	Serotype:serosubtype	Number	Serotype:serosubtype	Number
Queensland	4:P1.4	6	2b:P1.2,5	10
	NT:P1.4	4	2a:P1.5	4
	NT:NST	5	2b:NST	4
New South Wales	4:P1.4	11	2a:P1.5	15
	NT:NST	9	2b:P1.2,5	10
	2b:P1.10	8	-	-
Victoria	NT:P1.4	13	various	-
	14:P1.7	3	-	-
	4:P1.4	2	-	-
Western Australia	NT:NST]	7	various	-
	NT:P1.4	5	-	-
South Australia	15:P1.7,16	3	one isolate only	-
	2b:NST	2	-	-
	NT:P1.10	2	-	-
Tasmania	14:P1.7	2	2b:NST	2
Australian Capital Territory	various		2a:P1.2,5	1
Northern Territory	NT:NST	2	2a:P1.5	2

Table 3. Outcome of meningitic and bacteraemic cases by serogroup, 1996

Disease	Outcome	Serogroup					Total
		B	C	Y	W135	NG ²	
Meningitis	Died	2	3	0	0	0	5
	Total	56	28	1	1	0	86
Septicaemia	Died	3	3	0	0	0	6
	Total	69	29	1	0	3	102
All cases ¹	Died	5	6	0	0	0	11
	Total	126	57	3	1	3	190

1. Includes one serogroup B and one serogroup Y from a pleural fluid and joint fluid respectively.

2. NG = Non groupable

1994² and 250 in 1995³. The National Notifiable Diseases Surveillance System received 426 reports of meningococcal disease in 1996 (Communicable Diseases Network of Australia and New Zealand, personal communication). The number of isolates available for examination will always be less than the number of notified cases. This is because the National Health & Medical Research Council surveillance case definition includes those instances where meningococcal antigen or Gram negative diplococci are present in material from sterile sites, in the absence of a positive culture⁵.

In 1996 the overall pattern of meningococcal disease, based on serogroup analysis, was one of sporadic endemic disease with occasional localised clusters. Serogroup B and serogroup C isolates together accounted for 92% of all invasive meningococci. Serogroup B strains were again the main cause of sporadic meningococcal disease in Australia in 1996, with serogroup C isolates occurring both as sporadic cases and in disease clusters. No serogroup A meningococci were isolated in 1996. This picture is typical of the pattern of meningococcal disease in developed countries.

This report includes serotyping and serosubtyping data from the AMSP for the first time. This type of information has been available only on a limited basis in the past^{1,6}. Expanded phenotypic data allows a more detailed analysis of case clusters and apparent clusters. The recognition of the phenotypes C:2a:P1.5 and C:2a:P1.2,5 in all States and Territories except

South Australia and Western Australia was of particular interest in 1996. These phenotypes have been implicated in hyperendemic meningococcal disease in Canada for a number of years⁷ and were responsible for a cluster of cases in western Sydney in 1996. However, additional comparisons are needed to establish the relationship of these isolates to overseas strains with the same phenotype.

There also appears to have been an increase in the number of isolates of B:4:P1.4 in Queensland and New South Wales. There were also two isolates of this subtype in Victoria and one in the Northern Territory. Although serogroup B isolates predominated in the other centres, this phenotype was infrequently encountered if at all. This phenotype is involved in a continuing outbreak of meningococcal disease in Auckland, New Zealand⁸.

The age group and sex of patients from whom isolates were obtained both showed a normal distribution for meningococcal disease. Overall, the outcome data are similar to those observed in 1995 and are in the expected range where early diagnosis, and appropriate antibiotic therapy and supportive measures are undertaken⁹.

Continuing interest has been shown in the decrease in susceptibility of meningococci to penicillin in many parts of the world. Sporadic reports of beta-lactamase producing meningococci also continue to appear¹⁰. Other isolates have occasionally been shown to be resistant to other antibiotics which are currently used in meningococcal disease, either therapeutically or

prophylactically. This programme therefore includes routine examination of the antibiotic susceptibility of invasive isolates as part of its surveillance. However, interpretation of the results of *in vitro* testing of the antibiotic susceptibility of *N. meningitidis* is hampered by the absence of accurate correlations between clinical responses and *in vitro* sensitivity data in meningococcal disease. Minimal inhibitory concentration data are also method-dependent and not necessarily directly comparable when different techniques are used. However, by using consistent methods over the three years of this scheme some data are now available on the trends in Australia. In 1994, 52% of 216 strains were less sensitive to penicillin (MICs, 0.008 to 0.25 mg/L). In 1995, 63% of 247 strains tested were less sensitive to penicillin (MICs, 0.002 to 0.5mg/L). The proportion of less sensitive isolates increased further to 74% of 297 isolates in 1996 (MIC range extending to 1 mg/L). An 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 towards 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 greater. There were three isolates in 1996 with rifampicin MICs of 1 mg/L or greater; the first time such isolates have been detected in this programme.

The programme has examined more than 760 strains from all States and

Territories over the past three years and has clarified and expanded information on invasive meningococcal isolates in Australia. The programme is currently exploring the utility of other means of enhancing laboratory diagnosis of meningococcal disease, and the need for other methods of strain differentiation in Australia.

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