Annual report of the Australian Meningococcal Surveillance Programme, 1999

The Australian Meningococcal Surveillance Programme[1]

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 368 isolates of *Neisseria meningitidis* from invasive cases of meningococcal disease were determined in 1999. Ninety percent 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 generally diverse, but in New South Wales phenotype B:4:P1.4(7) became more prominent. The number of serogroup C isolates increased significantly in Victoria and remained prominent in New South Wales, especially in adolescents and adults. Phenotype C:2a:P1.2, infrequently isolated prior to 1999, was the most frequently encountered serogroup C phenotype. A number of infections with a phenotype new to Australia, C:2a:P1.4(7), were noted in Victoria and to a lesser extent in New South Wales. Phenotype C:2a:P1.5 was less frequently encountered than in previous years. 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. Data relating to 92 laboratory-confirmed but culture-negative cases were included in this report. Some differences in the patterns of disease were revealed when culture-based and non-culture-based data were compared. *Commun Dis Intell* 2000;24:181-189.

Keywords: meningococci, surveillance, invasive, phenotype, genotyping, diagnosis, antibiotic susceptibility

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ISSN 0725-3141
Volume 24
Number 7
July 2000

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Introduction

Invasive meningococcal diseases remained a focus of public health and general attention in 1999. Invasive meningococcal disease (IMD) presents mainly as septicaemia and/or meningitis and occasionally as single organ disease such as arthritis. Manifestations of IMD may range from the mild and even subclinical to the rapidly progressive and fatal. While some of the reasons for these different responses have been elucidated, many remain unknown. however, both the host response and the 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.[1,2]

The public health response to IMD is also influenced by a number of the features of the subtypes of the meningococci involved. These features may be used to confirm or exclude the presence of an outbreak or cluster of cases suspected on clinical grounds, and to influence the public health response to such an outbreak. For example, vaccines are available for some serogroups of meningococci but not for others and the presence of different subtypes of meningococci excludes case clustering if this is suspected epidemiologically.

A national programme for the examination of isolates of *Neisseria meningitidis* from cases of IMD was commenced in 1994 through the collaboration of reference laboratories in each State and Territory. This laboratory-based activity is designed to supplement data from existent clinical notification schemes by adding information on the phenotype (the serogroup, the serotype and subserotype), and on occasion the genotype, and the antibiotic susceptibility of invasive isolates to clinical data.

Annual reports summarising data gathered since the inception of the programme have been published in *Communicable Diseases Intelligence (CDI)*.[3-7] The following report analyses the characteristics of meningococci isolated in the calendar year 1999. Non-culture based laboratory testing, based on nucleic acid based amplification assays and serology, is increasingly used to confirm IMD.[9] This report includes some data from IMD confirmed by these means.

Methods

The National Neisseria Network (NNN) is a collaborative programme for the laboratory surveillance of the pathogenic Neisseria, *N. meningitidis* and *N. gonorrhoeae*.[3-8] A network of reference laboratories in each State and Territory (see acknowledgments) performs meningococcal isolate surveillance.

Isolate-based 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 subset of the 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 (e.g. where there was no lumbar puncture or else where lumbar puncture was delayed and the culture 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 the 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:[8]

sensitive MIC 0.03 mg/L

less sensitive MIC 0.06 - 0.5 mg/L

relatively resistant MIC 1 mg/L

Contents, *continued*

Strains with MICs that 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.

Non-culture-based laboratory-confirmed cases

Additional laboratory confirmation of suspected cases of IMD is increasingly available by means of non-culture based methods such as nucleic acid based amplification assays (NAA) and serological techniques. NAA testing is essentially by use of polymerase chain reaction (PCR) techniques.[9] Data arising from these investigations are included for the first time in this 1999 report. The serological results are based on tests performed using the methods and test criteria of the Manchester PHLS reference laboratory, UK.[10,11] Demographic data on non-culture based cases were obtained by telecommunication with the laboratory or public health unit involved. Where age, sex and outcome data for patients with non-culture based diagnoses are available these are also recorded. The site of a sample of a positive PCR test is also used to define the clinical syndrome. This separation is not possible for cases diagnosed serologically.

Results

Numbers of isolates from culture-confirmed cases

In total 368 invasive isolates of meningococci were examined in 1999. There were 122 isolates from patients whose infections were acquired in New South Wales (33% of all isolates), 94 (26%) from Victoria, 66 (18%) from Queensland, 39 (11%) from Western Australia, 24 (6%) from South Australia, 11 (3%) from Tasmania, 7 (2%) from the Northern Territory and 5 (1%) from the Australian Capital Territory (Table 1).

Seasonality

Fifty-eight (16%) of cases occurred between 1 January and 31 March, 69 (19%) between 1 April and 30 June, 142 (39%) between 1 July and 30 September and 95 (26%) 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 2. 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 15% and 19% of cases respectively. A secondary peak was noted in the 15-19 year age group when 59 cases accounting for 16% of the total were recorded. A further 35 cases (9.5%) occurred in those aged 20-24. Victoria differed from the national pattern in that the number of cases of invasive disease in those aged 15-24 (30) was higher than for those aged 4 years or less (20).

Serogroup, serotype and serosubtype (phenotype) distribution

The distribution of the isolates by serogroup is shown in Table 1. Nationally, 232 serogroup B isolates represented 63% of all strains, the same proportion as in 1997 and 1998. The 120 serogroup C strains (33%) were more than the number (81) and proportion (25%) detected in 1998. The number (9) and proportion (2.5%) of serogroup Y strains in 1999 was half that recorded in 1998. Six serogroup W135 meningococci were also identified. One was not viable and not serogrouped. No serogroup A isolates were encountered in 1999.

Some important differences in the distribution of serogroups were evident when data were disaggregated by region. Serogroup B predominated in national data (63%) and in all jurisdictions. When examined regionally, Western Australia (85% of isolates), the Australian Capital Territory (80%), Tasmania (73%), South Australia (70%) and Queensland (69%) had high proportions of serogroup B strains. In New South Wales the 70 group B strains accounted for 57% of isolates, in Victoria serogroup B isolates were 53% of the total and in the Northern Territory 57% of 7 strains were serogroup B. Group B disease comprised unlinked and apparently sporadic cases.

A substantial increase in serogroup C infections occurred in Victoria in 1999 in that 42 isolates (45% of the total) were group C. In 1998 there were 7 (17.5%) serogroup C strains in Victoria. Serogroup C isolates were less prominent in

Table 1. ***Neisseria meningitidis*** **isolates, Australia, 1999, by State or Territory and serogroup**

State/ Territory	Serogroup											Total	
	B		C		A	Y		W135		NG*			
	n	%	n	%	n	n	%	n	%	n	%	n	%
ACT	4	80.0	1	20.0	0	0		0		0		5	1
NSW	70	57.4	45	36.9	0	5	4.1	2	1.6	0		122	33
NT	4	57.2	3	41.8	0	0		0		0		7	2
Qld	46	69.6	15	22.7	0	2	3.0	2	3.0	1	1.5	66	18
SA	17	70.0	6	25.0	0	1	5.0	0		0		24	6
Tas	8	72.7	2	18.2	0	0		1	9.1	0		11	3
Vic	50	53.1	42	44.7	0	1	1.1	1	1.1	0		94	26
WA	33	84.6	6	15.3	0	0		0		0		39	11
Total	232	63.0	120	33.0	0	9	2.5	6	1.5	1	0.5	368	100

* NG = not viable for serogrouping

Table 2. ***Neisseria meningitidis*** **isolates, Australia, 1999, by State or Territory and age group**

	Age group (years)										
	<1	1-4	5-9	10-14	15-19	20-24	25-44	45-64	65+	NS*	All
ACT	0	1	0	0	2	0	2	0	0	0	5
NSW	27	20	9	6	15	11	14	11	8	1	122
NT	2	2	0	0	1	1	1	0	0	0	7
Qld	9	16	6	1	10	8	7	6	3		66
SA	1	5	1	4	3	2	4	1	2	1	24
Tas	2	1	2	0	0	0	3	1	0	2	11
Vic	8	12	5	6	21	9	12	10	6	5	94
WA	5	13	5	0	7	4	0	4	1	0	39
Total n	54	70	28	17	59	35	43	33	20	9	368
%	15	19	7.5	4.5	16	9.5	11.5	9	5.5	2.5	100

* Not stated

New South Wales in 1999 where 45 strains accounted for 37% of all isolates. Eighty-seven group C meningococci or 73% of all serogroup C strains isolated in Australia were from infections in New South Wales and Victoria. In the Northern Territory 3 of the 7 strains were group C. Numbers and/or proportions of group C strains were lower in other States and Territories. There were 15 group C isolates (23%) in Queensland, 2 in Tasmania, 6 (25%) in South Australia, 6 (15%) in Western Australia and a single isolate in the Australian Capital Territory. No clusters of serogroup C infection were identified.

Serogroup distribution was again age associated (Figures 1a-c). Serogroup B strains predominated in younger age groups (less than 14 years) in all centres and in all age groups for centres other than New South Wales and Victoria. In these States group C meningococci were seen more often than in other centres, and represented the highest proportion of any serogroup in those aged between 15 and 44 years. In Victoria this trend was also present in those aged over 45 years. This differential distribution of serogroups by age has been noted previously in these reports.

There was again 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. Serogroup B meningococci are more difficult to characterise by serological methods and a number could not be phenotyped. B:4:P1.4(7) strains predominated in New South Wales and were also present in Queensland and Victoria. B:15:P1.7 strains were also seen in New South Wales, Queensland, Victoria, Western Australia and South Australia.

Figure 1b. Serogroup B and C infections, Victoria, 1999, by age

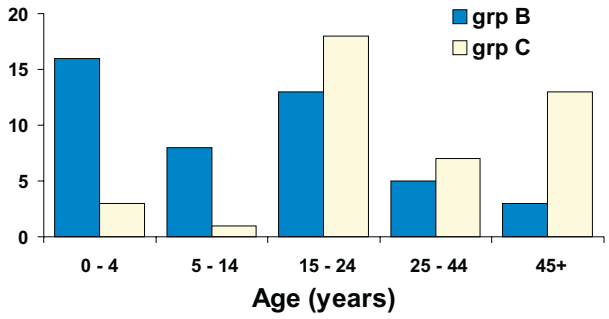


Figure 1a. Serogroup B and C infections, centres other than Victoria and New South Wales, 1999, by age

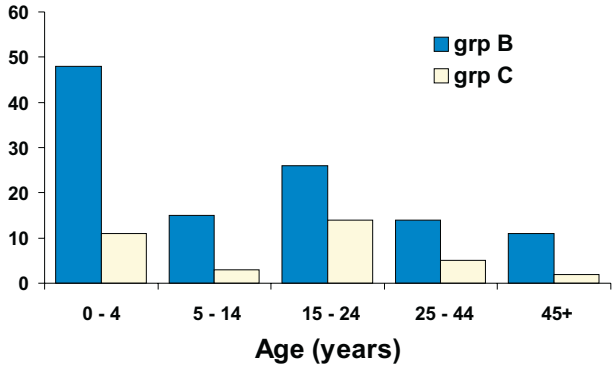


Figure 1c. Serogroup B and C infections, New South Wales, 1999, by age group

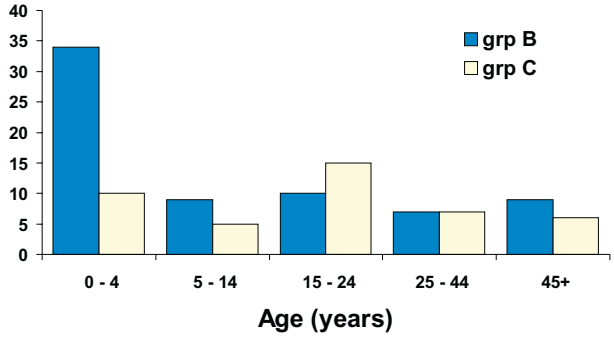


Table 3. Commonly isolated serotypes and serosubtypes and phenotypes of *N. meningitidis* of interest, Australia, 1997 to 1999, by State and Territory.

	Serogroup B			Serogroup C		
State/Territory	Serotype:serosubtype	n =	('97,'98)*	Serotype:serosubtype	n =	('97,'98)*
Qld	4:P1.4(7)	5	(4, 3)	2b:P1.5,2	2	(3, 0)
	NT:P1.4	6	(3, 9)	2a:P1.5	1	(4, 1)
	15:P1.7	5	(1, 3)	2a:P1.5,2	1	(0, 3)
	2b:P1.10	0	(1,2)	2b:P1.2	1	(0, 3)
NSW	4:P1.4(7)	28	(5, 17)	2a:P1.5	11	(23, 39)
	NT:nst**	10	(8, 13)	2b:P1.5,2	2	(6, 8)
	2b:P1.10	1	(4, 11)	2a:P1.5,2	7	(8, 3)
	15:P1.7	7	(1, 7)	2a:P1.2	9	
Vic	NT:P1.4	14	(11, 8)	2a:P1.2	13	
	15:P1.7(16)	6	(1, 3)	2a:P1.4(7)	10	
	4:P1.4	4	(2, 3)	2b:P1.2	1	(2, 1)
	2b:P1.10	1	(1, 2)	2a:P1.5	2	(1, 1)
SA	15:P1.7	1	(3)	2b:P1.5,2	1	(2)
	4:nst	1	(3)	2a:P1.5,2	1	
	4 :P1.4	0	(1)	2a:nst	1	
	NT:nst	5				
Tas	NT:nst	2		2b:P1.2	1	(1, 2)
ACT	Single isolate only	1				
NT	2b:nst	1	(5)	2a:P1.5	1	
	NT:nst	2		2a:P1.5,2	1	
WA	NT:P1.4	9		2a:nst	4	

* The numbers of isolates of each phenotype in 1997 and 1998 are shown in parentheses

** nst = non serosubtype tested

There was less heterogeneity amongst serogroup C meningococci. All isolates were either serotype 2a or 2b. Two phenotypes present in 1999 in New South Wales and Victoria that are worthy of note were C:2a:P1.2 and C:2a:P1.4(7). The former phenotype was uncommonly encountered in previous years but the 22 isolates of this phenotype in 1999 represented 19% of all serogroup C strains. The latter phenotype was especially prominent in Victoria. The other group C serosubtypes present were either P1.5, P1.5,2 or P1.2. There were 16 serogroup C strains of phenotype 2a:P1.5, 14% of all group C strains phenotyped. Most of these were found in New South Wales, but the number and proportion of this phenotype was much less than in 1998 (28 strains, 54%). Strains of this phenotype were also isolated in Queensland, the Northern Territory and Victoria.

Site of isolation

There were 111 isolates from CSF either alone or with a blood culture isolate and 251 from blood cultures alone. There were six isolates from synovial fluid.

Outcome data for cases with sterile site isolates for 1999

Outcome data (survived or died) were available for 320 patients (87%). Twenty-nine deaths were recorded (9.1%) (Table 4). Outcomes were available in 87% of serogroup B infections and 86% of serogroup C infections. There were 13 (6.4%) deaths in serogroup B infections and 16 (14.9%) in serogroup C infections ($p < 0.05$). Where outcomes were known, there were 11 deaths in 96 patients (11.4%) with meningitis. Six patients were infected with serogroup B and 5 with serogroup C strains. Eighteen deaths were recorded in 220 bacteraemic patients (8.2 %). There were 129 cases of serogroup B meningococcal bacteraemia with 7 deaths and another 82 cases were caused by serogroup C strains among which 11 fatalities were recorded. No fatalities were recorded with serogroup Y or W135 infections.

Antibiotic susceptibility surveillance of invasive meningococcal isolates

Penicillin

Three hundred and fifty two isolates of the 368 strains were tested for their susceptibility to penicillin. A single isolate was regarded as resistant with an MIC of 1 mg/L. Using defined criteria, 90 strains (25.5%) were fully sensitive to penicillin and 261 (74%) less sensitive (MIC 0.06 to 0.5 mg/L). These proportions are virtually the same as for 1998. Only three isolates had MICs of 0.5 mg/L.

Table 4. Outcome of 316 meningitic and septicaemic cases of meningococcal infection, Australia, 1999, by serogroup.

		Serogroup				Total	
Disease Type	Outcome	B	C	Y	W135	n =	%
Meningitis	Survived	66	18	0	1	85	88.5
	Died	6	5	0	0	11	11.5
	Total	72	23	0	1	96	
Septicaemia	Survived	122	71	4	5	202	91.8
	Died	7	11	0	0	18	8.2
	Total	129	82	4	5	220	
All cases*	Total	203	107	4	6	320	
	Died	13	16	0	0	29	9.1

* Includes 2 serogroup B and 2 serogroup C strains from joint aspirates from patients who survived.

Other antibiotics.

All 352 isolates which were tested for susceptibility to ceftriaxone (and by extrapolation to other third generation cephalosporins) were susceptible to these therapeutic agents. Three meningococci had raised MICs to the prophylactic antibiotic rifampicin (MICs of 1 mg/L or more, including one with a MIC >100mg/L). Sulphonamide testing was not performed.

Numbers and sources of non-culture diagnoses of IMD in 1999

There were 92 diagnoses of invasive meningococcal disease in 1999 where PCR and/or serology were positive in the absence of positive cultures (Table 5). In 13 cases both serology and PCR testing were performed and both tests were positive. however, it was more usual to have available samples suitable for testing by only one of the above techniques. Thus there were 41 cases where PCR testing in isolation was positive and 38 cases where serology testing was positive.

With PCR testing it was also possible to categorise the disease type by source of specimen in a manner similar to that used for culture-positive cases (Table 5). Of the 54 cases positive by PCR, 36 were from CSF and 18 from blood. This is a distinct difference from the distribution of culture-based diagnosis. Culture-based diagnosis of blood yielded 2.5 times the number of cultures derived from CSF.

Table 5. Source of non-culture based diagnosis of invasive meningococcal disease 1999

All non culture based diagnoses	92
PCR and serology positive	13
PCR positive alone	41
CSF PCR positive (including those with positive serology)	36
Blood PCR positive (including those with positive serology)	18
Serology positive alone	38

With PCR based diagnosis the ratio of blood to CSF positive was 0.5:1.

Serogroup and age distribution of non-culture based IMD

In addition to diagnostic PCR, this technique can also be used to ascertain whether serogroup B or C meningococci were involved in the disease process. (At present this is not available for serogroups other than B or C). There were 54 cases where a PCR-based diagnosis was made and in 49 of these the serogroup was also determined as B or C (Table 6).

For those cases diagnosed by serology alone, age distribution was different with most diagnoses – 35 of 38 in those aged 10 years or more (Table 7). This reflects in part the difficulty in obtaining serum samples from young children. The categorisation of IMD by site of organism capture cannot be determined with serology. Additionally, serogroup determination is not possible.

Outcome data for IMD based on non-culture based diagnosis

Non-culture based diagnosis is currently less well established than that for IMD based on positive culture. For IMD diagnosed by PCR based tests, the outcome is known in 24 cases. All 9 diagnosed by PCR on blood survived (3 each of serogroup B and C and 3 where no serogroup was determined). Of a further 15 patients with PCR positive on a CSF sample, 12 patients survived (8 group B, 3 group C, 1 undetermined serogroup) and 3 died (one each with serogroup B and C and one with an undetermined serogroup). One death and 11 survivors were recorded amongst the 38 cases diagnosed serologically.

Discussion

The total 368 isolates examined by NNN laboratories in the Australian Meningococcal Surveillance Programme in 1999 was the highest since the inception of the programme in 1994. The number of isolates examined each year by the NNN increased each year from 1994 until 1998 when it decreased slightly. The numbers of isolates examined between 1997 and 1999 ranged between 323 and 368 i.e. small aggregate differences only. Importantly however,

Table 6. Invasive meningococcal disease diagnosed by polymerase chain reaction, Australia, 1999, by serogroup and age group

Serogroup	Age group (years)									Total
	<1	1-4	5-9	10-14	15-19	20-24	25-44	45-64	64+	
B	6	10	0	2	10	3	5	1	0	37
C	0	2	1	1	5	0	3	0	0	12
U*	0	3	0	1	0	0	0	1	0	5
All	6	15	1	4	15	3	8	2	0	54

* U = undetermined

Table 7. Cases of invasive meningococcal disease diagnosed by serology alone, Australia, 1999, by age group

Age group (years)	Cases
<1	0
1-4	2
5-9	1
10-14	4
15-19	11
20-24	7
25-44	7
45-64	4
>65	2
Total	38

greater differences in the annual number of isolates are revealed when data are examined by jurisdiction. The number of isolates available in Victoria in 1999 (94) was more than twice the 41 examined in 1998. In Queensland the number of isolates decreased from 81 to 66. Isolate numbers in other centres varied little from 1998 totals. 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.

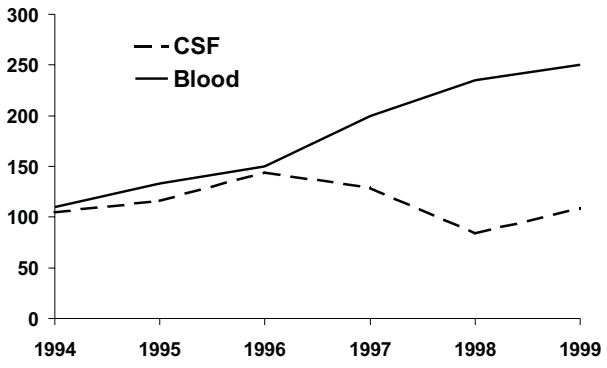
Eighty-six clinical cases were confirmed only by non-culture based laboratory examinations in 1999. These procedures include NAA assays using PCR and/or serological examination. These cases were included separately in this report. Some of the PCR techniques in use can provide additional data on the serogroup of the isolate. It is anticipated that laboratory confirmation of invasive meningococcal disease by non-culture based methods will continue to increase. In general serologically diagnosed disease is usually milder – patients survive to have serological tests. One corollary of this is that serological tests diagnose some previously unrecognised but milder IMD syndromes. NNN laboratories may be contacted for advice regarding these tests.

The ratio of cases of meningitis to bacteraemia was 0.44:1 in 1999 in culture confirmed cases, continuing a trend noted first in 1997 (Figure 2). From 1994 to 1996, the ratio of cases of meningitis to bacteraemia was close to 1:1 in NNN isolate-based data. In 1997 this ratio decreased to 0.6:1 and in 1998 further declined to 0.36:1. NNN cases are based on the site of isolation of the organism and thus tend to overestimate the number of bacteraemic cases for several reasons.[7] NNN case definitions have remained constant to allow year-to-year comparisons. The PCR-based diagnostic data included in this report has a markedly different disease ratio, with meningitis featuring prominently in disease syndromes. Again however, there is an inherent bias in these data in that PCR was initially only performed on CSF samples and sensitivity of PCR techniques in blood samples is less than that for CSF.

The predominant disease pattern throughout the country remained sporadic infection with serogroup B meningococci. The proportion of serogroup C cases in aggregated data in 1999 increased to 32.5% from 25% in 1998. however, the numbers of isolates from the more populous States introduce some distortions. The increase in 1999 was due to increased numbers of serogroup C cases in Victoria - from 7 in 1998 to 42 in 1999. Serogroup C infections have been prominent in New South Wales from 1996 onwards, but until 1999 were infrequently encountered in other States and Territories. In New South Wales in 1998 and 1999, serogroup C strains have declined as a proportion of all isolates tested. Serogroup C cases were also sporadic in 1999. No serogroup A meningococci were isolated in 1999. The number and proportion of cases of serogroup Y infection decreased in 1999.

Children aged 4 years or less remained the group most frequently infected. A secondary incidence peak in young adults and adolescents was again present. Serogroup C disease occurred more often in the young adult age group

Figure 2. Numbers of meningococcal isolates from CSF and blood culture, 1994 to 1999



(Figures 1a – c) as previously noted in NNN reports, and was responsible for an upsurge in adult cases in Victoria. This picture of serogroup B and C disease occurring as sporadic cases is typical of the pattern of meningococcal disease in developed countries. Occasional clusters of cases of serogroup C infection have been noted in recent years but were not seen in 1999.

Phenotyping data obtained on the basis of serotyping and serosubtyping was again available from all centres in 1999. These data reinforce the considerable differences that exist in meningococcal subtypes causing IMD in different jurisdictions. The heterogeneity of serogroup B isolates present in Australia was once more evident (Table 3). Of interest amongst the group B strains were phenotypes B:4:P1.4(7) and B:15:P1.7 associated with hyperendemic disease in New Zealand and Europe respectively. B:4:P1.4(7) strains were encountered in higher numbers in 1999 and in New South Wales this phenotype represented about 23% of all isolates. The distribution of phenotype B:15:P:1.7 was little changed from 1998.

Earlier reports noted the appearance and spread of the phenotypes C:2a:P1.5 and C:2a:P1.5,2, particularly in New South Wales. These phenotypes, although present in small numbers in several States and Territories in 1999, declined in prominence. Of particular interest was the emergence in Victoria of a phenotype C:2a:P1.4(7) that appears to be an example of 'swapping' of outer membrane protein genes. This phenotype was also seen in a small number of cases in New South Wales. Additionally phenotype B:4:P1.5 was recognised. While it remains speculative how these events arose, it emphasises the considerable recombination potential of meningococci. Also more prominent in 1999 was the number of isolates of phenotype C:2a:P1.2 in both New South Wales and Victoria, again illustrating the temporal and geographic variation in meningococcal subtypes that occurs in Australia.

The overall mortality recorded in 304 assessable culture-positive cases was 9.4%, similar to the 9% observed in 1998. A higher mortality rate was again observed with serogroup C cases. Although serogroup C strains have been associated with increased mortality overseas, other factors, such as age, and time from onset to presentation and treatment - on which data were not available - may also explain this difference.

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 that 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 indicate 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 or 1999. 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 strains in this category is rather an epidemiological marker of the slow progression to resistance. A single isolate with an MIC of 1 mg/L was found in 1999. All isolates were fully sensitive to third generation cephalosporins. Chloramphenicol testing is no longer performed in this programme.

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 three isolates with rifampicin MICs of 1 mg/L or more in 1999. All isolates were quinolone susceptible.

The NNN programme has examined a total of about 1,800 strains from all States and Territories since 1994. It is a continuing, long-term collaborative study that has evolved to accommodate the situation that exists in Australia. As such it has assisted in clarifying and expanding information on invasive meningococcal isolates in Australia. It is emphasised that this is an independent laboratory based and structured programme designed to augment those data which should properly be collected separately by clinically based surveillance systems. The nature and high public recognition of meningococcal disease suggests that the efforts of this programme 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.

The Commonwealth Department of Health and Aged Care provided a grant for the National Neisseria Network.

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