Annual report of the Australian Meningococcal Surveillance Programme, 2002

The Australian Meningococcal Surveillance Programme

Abstract

Since 1994,The National Neisseria Network, a nationwide collaborative laboratory program, has examined and analysed isolates of *Neisseria meningitidis* from cases of invasive meningococcal disease in Australia. The phenotypes (serogroup, serotype and serosubtype) and antibiotic susceptibility of 393 isolates of *N. meningitidis* from invasive cases of meningococcal disease were determined in 2002. Most disease was caused by serogroup B (210 isolates, 63%) or serogroup C (162 isolates, 41%) meningococci. An increased number of isolates in Victoria (129 from 78 in 2001) accounted for most of the increased national total. A diversity of phenotypes circulated in the different states and territories. Serogroup B strains predominated in all jurisdictions except Victoria, Tasmania and the Australian Capital Territory and were isolated from sporadic cases of invasive disease. Serogroup B phenotypes B:4:P1.4(7) and B:15:P1.7 were the most common and widely distributed. The common serogroup C phenotype in Victoria, C:2a:P1.4(7), was also common in Tasmania. Elsewhere in Australia it was detected only in low numbers. Other C:2a serosubtypes were prominent in other jurisdictions. About two-thirds of all isolates showed decreased susceptibility to the penicillin group of antibiotics (MIC 0.06 to 0.5 mg/L). Two isolates, one each from Darwin and Sydney, had MICs of 1 mg/L. From 1999, reports have also included diagnoses made by non-culture-based methods in these analyses. Data relating to 187 laboratory-confirmed but culture-negative cases supplemented information on culture confirmed cases in this report. *Commun Dis Intell* 2003;27:196–208.

Keywords: antibiotic resistance, meningococcal disease, Neiserria meningitidis

Introduction

A national laboratory-based program for the examination of isolates of *Neisseria meningitidis* from cases of invasive meningococcal disease (IMD), the National Neisseria Network (NNN), has operated since 1994 through the collaboration of reference laboratories in each jurisdiction. The NNN supplies information on the phenotype (serogroup, serotype and subserotype), and increasingly on the genotype, and the antibiotic susceptibility of meningococci from cases of IMD. Additional data from non-culture-based laboratory testing, derived from nucleic acid amplification assays (NAA) and serological examination, are included in the analyses. These data supplement those from clinical notification schemes. The characteristics of the meningococci responsible for IMD are important both for individual patient management and to tailor the public health response. The prospect of additional vaccines e.g. porin-based vaccines for serogroup B meningococcal disease, increases the need for precise data on circulating meningococcal subtypes.

Annual reports summarising data gathered since the inception of the program were published in *Communicable Diseases Intelligence*.[1–8] The following report analyses the characteristics of meningococci isolated in the calendar year 2002.

Methods

The NNN is a long term collaborative program for the laboratory surveillance of the pathogenic *Neisseria, N. meningitidis and N. gonorrhoeae.*[1–9] A network of reference laboratories in each state and territory (see acknowledgements) undertakes meningococcal isolate surveillance throughout Australia.

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Isolate-based surveillance

Each case was based upon isolation of a meningococcus from a normally sterile site and defined as IMD according to Public Health Laboratory Network definitions. 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-based subset of the program categorises cases on the basis of site of isolation of the organism. Where an isolate is grown from both blood and cerebrospinal fluid (CSF) cultures in the same patient, the case is classified as one of meningitis. It is recognised that 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, is underestimated. However, the above approach has been used since the beginning of this program 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, the Netherlands. Increasingly, sequencing of products derived from amplification of the porin genes *porA* and *porB* has been used to supplement and supplant serotyping analyses based on the use of monoclonal antibodies. For the purposes of continuity and comparability, the typing data from both approaches have been unified in the accompanying tables by converting sequence data to the more familiar serotyping/serosubtyping nomenclature.

Antibiotic susceptibility was assessed by determining the minimal inhibitory concentration (MIC) to antibiotics used for therapeutic and prophylactic purposes. This program uses the following parameters to define the various levels of penicillin susceptibility/resistance when determined by a standardised agar plate dilution technique:[9]

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. However, precise MIC/outcome correlations are difficult to obtain because of the nature of IMD.

Non-culture-based laboratory-confirmed cases

Additional laboratory confirmation of suspected cases of IMD is increasingly available by means of non-culture-based methods including NAA and serological techniques. NAA testing is essentially by polymerase chain reaction (PCR) techniques[10] and has been progressively introduced in the different jurisdictions. Data from the results of these investigations were included for the first time in the 1999 report. The serological results are based on results of tests performed using the methods and test criteria of the Manchester PHLS reference laboratory, United Kingdom, as assessed for Australian conditions.[11,12,13] Where age, sex and outcome data for patients with non-culture-based diagnoses were available these were also recorded. The site of a sample of a positive NAA 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

A total of 393 invasive isolates of meningococci were examined in 2002, 55 more than the 338 isolates examined in 2001, but closely approximating the 388 isolates seen in 2000. There were 129 isolates from patients whose infections were acquired in Victoria (33% of all isolates), 110 in New South Wales (28%), 76 (19%) from Queensland, 35 (9%) from Western Australia, 20 (5%) from Tasmania, 13 (3%) from South Australia, and 5 (1%) each from the Northern Territory and the Australian Capital Territory (Table 1). The increase in the number of isolates in 2002 was principally due to increases in the number of culture positive cases in Victoria, from 77 culture positive isolates in 2001. Slight increases in numbers of isolates compared to 2001 were noted in New South Wales (10 more) Tasmania (4 more) and Western Australia (3 more). In South Australia numbers decreased by 9 to 13 cases in 2002 with slight decreases in the Northern Territory and Queensland (3 and 2 less respectively). Numbers in the Australian Capital Territory remained unchanged from 2001.

Table 1. *Neisseria meningitidis* isolates, Australia, 2002, by state or territory and serogroup

State/territory	Serogroup										Total	
	B		C		A	Y		W135		NG*		
	n	%	n	%	n	n	%	n	%	n	n	%
ACT	1	20.0	4	80.0	0	0	0.0	0	0.0	0	5	1.3
NSW	71	64.6	34	30.9	0	2	1.8	2	1.8	1	110	28.0
NT	4	80.0	1	20.0	0	0	0.0	0	0.0	0	5	1.3
Qld	41	53.9	29	38.2	0	4	5.3	1	1.3	1	76	19.3
SA	9	69.2	4	30.8	0	0	0.0	0	0.0	0	13	3.3
Tas.	6	30.0	14	70.0	0	0	0.0	0	0.0	0	20	5.1
Vic.	47	36.4	72	55.8	0	4	3.1	6	4.7	0	129	32.8
WA	31	88.6	4	11.4	0	0	0.0	0	0.0	0	35	8.9
Total	**210**	**53.4**	**162**	**41.2**	**0**	**10**	**2.5**	**9**	**2.3**	**2**	**393**	**100.0**

* Not viable for serogrouping or not serogroupable

Seasonality

Sixty-six (17%) cases occurred between 1 January and 31 March, 84 (21%) between 1 April and 30 June, 131 (33%) between 1 July and 30 September and 112 (28%) between October and 31 December 2002. A winter peak of meningococcal disease is usual.

Age group

The age distribution of patients infected with invasive isolates in each state or territory is shown in Table 2. Nationally, the peak incidence of meningococcal disease traditionally occurred in those four years and under. Those aged less than one year or in the 1–4 age group accounted for 43 (10.9%) and 65 (16.5%) cases respectively. These numbers are essentially unchanged from 2001 although as a proportion of all cases in these two age groups, is lower than last year. A secondary peak in the 1–19 year age range was substantially increased to 95 (24.2%) from the 54 cases (16%) recorded in 2001. A further 45 cases (11.5%) occurred in those aged 20–24 years. The number (140) and proportion (35.7%) of culture positive cases in the 15–24 year age range in 2002 was considerably greater than the 89 (26%) cases in 2001 but similar to the 126 (32%) cases recorded in 2000.

Serogroup, serotype and serosubtype (phenotype) distribution

The distribution of the isolates by serogroup is shown in Tables 1 and 2. Nationally, 210 serogroup B isolates represented 53.5 per cent of all strains, similar in number, but a smaller proportion compared with culture positive cases in 2001.The 162 serogroup C strains (41.2%) was an increase in the number (122) and proportion (36%) detected in 2001 and also in 2000 (128, 33%). The number of serogroup W135 and serogroup Y strains both increased, compared to 2001 but accounted for a small proportion of cases. No serogroup A isolates were identified.

Some important differences in the distribution of serogroups were evident when data were disaggregated by region. Serogroup B meningococci predominated in national data (53%) and in all jurisdictions except Victoria, Tasmania and the Australian Capital Territory. When examined regionally, Western Australia (89% of isolates), South Australia (69%), the Northern Territory (80%), Queensland (54%) and New South Wales (65%) had high proportions of serogroup B strains. However in Victoria, serogroup B isolates were 36 per cent of the total and in Tasmania 30 per cent. Group B disease comprised mainly unlinked and apparently sporadic cases.

Table 2. *Neisseria meningitidis* isolates, Australia, 2002, by state or territory, serogroup and age*

State/territory		Age group (years)										Total
		<1	1–4	5–9	10–14	15–19	20–24	25–44	45–64	65+	NS	
ACT	B	0	0	0	0	1	0	0	0	0	0	**1**
	C	0	0	0	0	1	0	1	2	0	0	**4**
	Total	**0**	**0**	**0**	**0**	**2**	**0**	**1**	**2**	**0**	**0**	**5**
NSW	B	15	15	11	4	9	4	2	6	5	0	**71**
	C	1	4	2	0	9	6	5	4	3	0	**34**
	Total	**16**	**19**	**13**	**4**	**19**	**11**	**8**	**11**	**9**	**0**	**110**
NT	B	1	2	0	0	0	0	1	0	0	0	**4**
	C	0	0	0	0	0	1	0	0	0	0	**1**
	Total	**1**	**2**	**0**	**0**	**0**	**1**	**1**	**0**	**0**	**0**	**5**
Qld	B	7	9	3	2	7	5	6	1	1	0	**41**
	C	0	3	6	2	10	2	5	0	1	0	**29**
	Total	**9**	**12**	**9**	**4**	**18**	**8**	**12**	**2**	**2**	**0**	**76**
SA	B	3	1	0	0	2	0	1	1	1	0	**9**
	C	0	0	0	0	1	2	1	0	0	0	**4**
	Total	**3**	**1**	**0**	**0**	**3**	**2**	**2**	**1**	**1**	**0**	**13**
Tas.	B	0	2	0	0	3	1	0	0	0	0	**6**
	C	0	2	1	0	4	0	4	2	1	0	**14**
	Total	**0**	**4**	**1**	**0**	**7**	**1**	**4**	**2**	**1**	**0**	**20**
Vic.	B	8	10	3	2	14	4	2	3	1	0	**47**
	C	1	8	5	3	22	13	11	5	4	0	**72**
	Total	**10**	**19**	**8**	**5**	**38**	**18**	**14**	**11**	**6**	**0**	**129**
WA	B	4	7	3	2	7	3	3	1	1	0	**31**
	C	0	1	0	1	1	1	0	0	0	0	**4**
	Total	**4**	**8**	**3**	**3**	**8**	**4**	**3**	**1**	**1**	**0**	**35**
Australia	n	43	65	34	16	95	45	45	30	20	0	**393**
	%	10.90	16.50	8.60	4.10	24.20	11.50	11.50	7.60	5.10	0.00	
Serogroup B	n	38	46	20	10	43	17	15	12	9	0	**210**
Australia	%	18.1	21.9	9.5	4.8	20.5	8.1	7.1	5.7	4.3	0.0	**53.5**
Serogroup C	n	2	18	14	6	48	25	27	13	9	0	**162**
Australia	%	1.2	11.1	8.6	3.7	29.6	15.4	16.7	8.0	5.6	0.0	**41.2**
Other	n	3	1	0	0	4	3	3	5	2	0	**21**
Australia	%											**5.3**

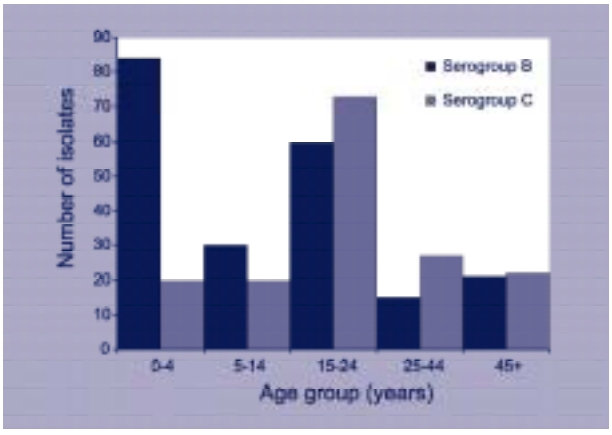
* Includes serogroup B and C data and totals only.

NS Age not stated.

Serogroup C strains were most prominent in the Australian Capital Territory and Tasmania where four of five isolates and 14 of 20 isolates, respectively, were serogroup C. The proportion of serogroup C infections in Victoria increased to 56 per cent and their number almost doubled to 72 from the 38 isolated in 2001. The number (34) and proportion (31%) of serogroup C isolates remained essentially unchanged in New South Wales in 2002. There were 29 group C isolates (38%) in Queensland, four (31%) in South Australia, four (11%) in Western Australia, and one in the Northern Territory.

Serogroup distribution has been typically age-associated, with serogroup B disease concentrated in younger age groups and serogroup C infections predominating in adolescents and young adults. In 2002, 84 (78%) of all isolates in those aged less than four years were serogroup B compared with 20 serogroup C isolates (18%) (Table 2, Figure 1). In those aged 5–14 years, serogroup B meningococcal cultures represented 60 per cent of isolates and serogroup C strains represented 40 per cent. Nationally, serogroup C isolates were more common in all age groups over 14 years (Figure 1) and represented 52 per cent of cases aged 15 years or above.

Figure 1. Number of serogroup B and C isolates, Australia, 2002, by age



However, some jurisdictional differences in the distribution of serogroup B and C meningococcal isolates were again evident in 2002 (Table 2, Figures 2, 3 and 4). In Western Australia and the Northern Territory, serogroup B isolates predominated in all age groups and in all centres serogroup B was more commonly encountered in those four years of age and under. New South Wales, Queensland and South Australia followed the national pattern with regard to age-associated serogroup distribution. In Victoria, serogroup C isolates were especially prominent in older, i.e. adolescent and young adult, age groups but were also seen more often in younger age groups than in other jurisdictions. In Tasmania, 11 of the 14 serogroup C isolates were in patients aged 15 years or more.

Figure 2. Number of serogroup B and C isolates, Victoria, 2002, by age

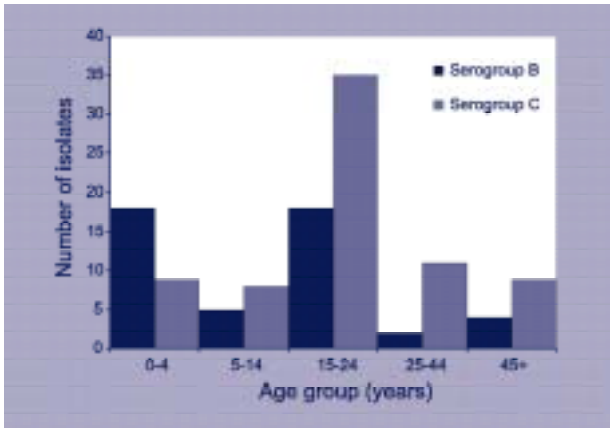


Figure 3. Number of serogroup B and C isolates, New South Wales, 2002, by age

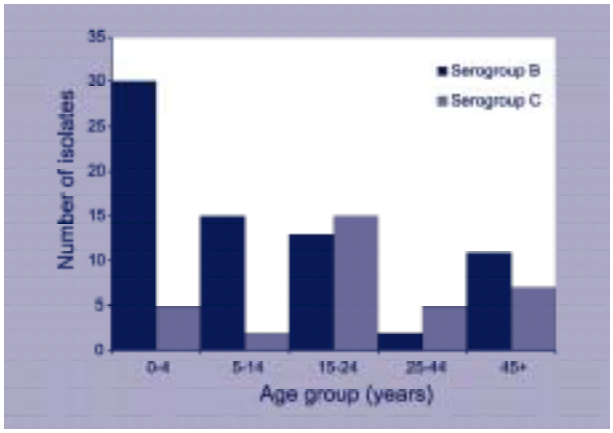
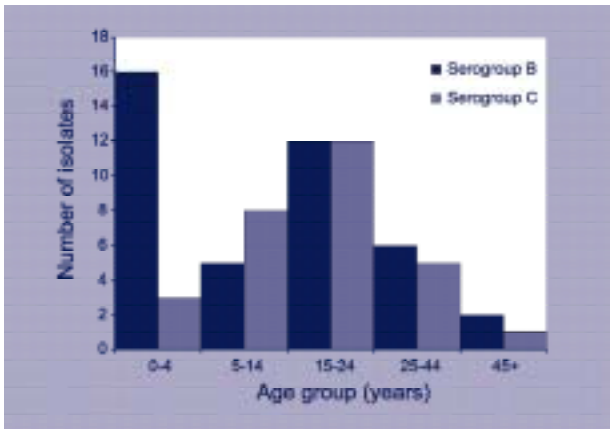


Figure 4. Number of serogroup B and C isolates, Queensland, 2002, by age



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 in general quite heterogeneous, but also more difficult to characterise by serological methods and a number could not be phenotyped. Two main phenotypes circulated in Australia in 2002. The B:4:P1.4(7) phenotype was prominent in New South Wales and Victoria and was also present in Queensland, Western Australia and the Northern Territory. The other main phenotype circulating was B:15:P1.7 and strains were present in Victoria, New South Wales, Queensland, South Australia, and Western Australia. This distribution of serogroup B strains was similar to that in 2001.

Serogroup C meningococci are less diverse that serogroup B strains and nearly all strains were of serotype 2a. Phenotype C:2a:P1.4(7), which appeared in Victoria in 1999, continues to require special comment. There were 10 such isolates in Victoria in 1999, 24 in 2000, 19 in 2001 and 55 in 2002. This phenotype had hitherto been uncommon elsewhere in Australia, but was seen in all other jurisdictions in 2002. Numbers were low however, except for Tasmania. The other common serogroup C phenotypes were C:2a:P1.5 and C:2a:P1.5,2, the former being common in Queensland and New South Wales and present also in Victoria, Tasmania and Western Australia. Victoria and Tasmania also encountered phenotype C:2a:P1.5.10. Serotype 2b strains were not detected.

Site of isolation

There were 71 isolates from CSF either alone or with a blood culture isolate and 311 from blood cultures alone. There were 10 isolates from synovial fluid and one from skin. Trends in relative rates of isolation have been followed in these reports (Figure 2). The ratio of CSF isolates to blood culture isolates was 0.23:1, lower than that recorded in recent years.

Outcome data for cases with sterile site isolates

Outcome data (survived or died) were available for only 147 patients (37%). Twenty-six deaths were recorded in this group (17.6% Table 4). Outcomes were available for 82 (39%) serogroup B infections and 61 (37%) serogroup C infections. There were 9 (11%) deaths in serogroup B infections and 17 (27.8%) in serogroup C infections.

Where outcomes were known, there were four deaths in 25 patients (16%) with meningitis. One of these patients was infected with a serogroup B, and three with a serogroup C strain. Twenty-two deaths were recorded in 122 bacteraemic patients (18%). There were 71 cases of serogroup B meningococcal bacteraemia with eight deaths (11%) and another 47 cases were caused by serogroup C strains among whom 14 fatalities were recorded (29.8%). No fatalities were recorded in serogroup Y (1 case) and W135 (3 cases) bacteraemias.

Antibiotic susceptibility surveillance of invasive meningococcal isolates

Penicillin

Three hundred and ninety-one isolates were available for determination of their susceptibility to penicillin. Using defined criteria, 127 strains (33%) were fully sensitive to penicillin and 262 (67%) less sensitive (MIC 0.06 to 0.5 mg/L). These proportions are similar to those observed in recent years. Nine isolates had MICs of 0.5 mg/L and two (one each from Darwin and Sydney) had MICs of 1 mg/L. An increase in geometric mean penicillin MICs of *N. meningitidis* has been reported by the AMSP in an examination of strains isolated between 1994 and 1999.[14]

Other antibiotics

All isolates were susceptible to ceftriaxone (and by extrapolation to other third generation cephalosporins) and to the prophylactic antibiotics rifampicin and ciprofloxacin.

Table 3. Commonly isolated serotypes and serosubtypes and phenotypes of *Neisseria meningitidis* of interest, Australia, 2002, by state or territory

State/territory	Serogroup B				Serogroup C			
	Serotype	n	Serosubtype	n	Serotype	n	Serosubtype	n
ACT	4	1	1.4	1	2a	4	1.4	1
NSW	4	32	1.4	22	2a	28	1.5	16
			1.5	2			1.5,2	3
			1.63	1			1.4	3
			1.7	2			1.2	1
			1.14	2			nst	5
			nst	3	nt	6	1.15	1
	15	7	1.7	4			1.16	1
	nt	23	1.14	5			1.2	1
			1.15	3			1.5,2	2
			1.4	3			nst	1
			nst	9				
	1	4	nst	3				
			1.14	1				
NT	4	1	1.7,4	1	2a	1	1.4	1
	14	1	nt	1				
	nt	2	nt	2				
Qld	15	9	1.7	5	2a	26	1.4	4
	4	3	1.14	2			1.5	18
			1.4	1			nst	4
	1	3	1.14	1	26	1	nst	1
			nst	2	nt	1	1.15	1
	nt	26	1.4	12				
			1.6	3				
			1.7	1				
			nst	8				
SA	15	3	1.7	3	2a	3	nst	3
	14	1	nst	1	1	1	1.14	1
	1	1	1.14	1				
	nt	4	1.7	1				
		nst	3					
Tas.	ND	6	ND	6	2a	14	1.7–2,4	9
							1.5,2	4
							1.5–1,10–8	1
Vic.	4	19	1.4	15	2a	70	1.4	55
			1.12,13	1			1.5	2
			1.14	1			1.5,2	5
			1.15	1			1.5,10	7
			1.15,10	1				
	15	12	1.7	11				
			nst	1				
	1	5	1.14	3				
			nst	2				
	2b	2	nst	2				
	nt	8	1.2	5				
WA	15	4	1.7	4	2a	2	1.5	2
	14	3	1.2	1			1.15	1
	4	2	1.4	1			1.4	1
	nt	20	1.4	10				
			1.14	2				
			nst	6				

nt Not typeable.

nst Not serosubtypeable.

ND Not determined.

Numbers and sources of non-culture diagnoses of invasive meningococcal disease in 2002

One hundred and eighty-seven additional cases of IMD were diagnosed by non-culture methods in 2002 (Table 5). In five instances where both serology and PCR testing were performed, both tests were positive. However it was more usual to have samples suitable for testing by only one of the above techniques.

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 142 cases positive by PCR, 61 were from CSF or CSF and blood, 75 from blood only and 6 from other sites. This is a different distribution from that obtained with culture-based diagnosis. Diagnoses based on blood cultures alone yielded four times the number of isolates derived from culture of CSF. With PCR-based diagnosis, the ratio of diagnoses from blood to CSF positive was 1.2:1. The sources of positive PCR examination other than CSF or blood samples were synovial fluid (5) and pericardial fluid (1). In one case with a positive PCR from joint fluid, a CSF sample from the same patient was also positive and is recorded in the Table 5 under that heading. The pericardial fluid which was positive by PCR was also positive on serology.

Serogroup and age distribution of non-culture-based invasive meningococcal disease

In addition to diagnosis, PCR can also be used to ascertain the serogroup involved in the disease process. In most centres this is still restricted to serogroup B and C determinations. There were 142 cases where a PCR-based diagnosis was made and in 124 of these the serogroup was also determined (Table 6).

For those 45 cases diagnosed by serology alone (Table 7) age distribution was different with most diagnoses—(40/46)—in those aged 10 years or more. This reflects in part the difficulty in obtaining serum samples from young children. The categorisation of IMD by site of infection cannot be determined by serology. In 2002, an additional serological test to identify serogroup C infections was introduced.[13] This test was requested for 20 patients and was positive, i.e. a serogroup C infection was confirmed, in eight of these.

Outcome data for invasive meningococcal disease based on non-culture-based diagnosis

For IMD diagnosed by PCR based tests, the outcome was known in 46 cases, with nine deaths recorded. There were five deaths where blood PCR alone was positive (three of serogroup C and two where the serogroup was not determined). There were four instances of deaths where PCR was positive on a CSF sample, two each with serogroups B and C. Of the 37 cases where survival was recorded, the diagnosis was made on CSF samples in 11 cases due to serogroup B infections and in one case due to serogroup C organisms. For the 24 cases diagnosed as having IMD on PCR of a blood sample, 10 were with serogroup B and six were with serogroup C meningococci. The serogroup was not determined in the remainder. The other case where survival was recorded was in a case of septic arthritis, but the serogroup was not determined.

Table 4. Outcome of meningitic and septicaemic cases of meningococcal infection, culture positive cases, Australia, 2002, by serogroup

Disease type	Outcome	Serogroup					Total
		B	C	Y	W135	NG*	
Meningitis	Survived	10	11	0	0	0	21
	Died	1	3	0	0	0	4
	Total	11	14	0	0	0	25
Septicaemia	Survived	63	33	1	3	0	100
	Died	8	14	0	0	0	22
	Total	71	47	1	3	0	122
All cases	Total	82	61	1	3	0	147
	Died	9	17	0	0	0	26

* NG: Not viable for serogrouping or not serogroupable.

Table 5. Source of non-culture-based diagnosis of invasive meningococcal disease, Australia, 2002

Diagnostic method	Number
All non-culture-based diagnoses	187
PCR positive*	142
CSF PCR positive	53
CSF and blood PCR both positive	8
Blood PCR positive	75
Other†	6
Serology positive in the absence of positive PCR	45

* Including those with positive serology.

† Five joint fluids and one pericardial fluid.

Table 6.Serogroup and age distribution of invasive meningococcal disease diagnosed by polymerase chain reaction, Australia, 2002

Serogroup	Age group (years)										Total
	<1	1–4	5–9	10–14	15–19	20–24	25–44	45–64	65+	Unknown	
B	10	14	5	2	15	8	12	6	0	0	72
C	0	1	5	3	13	9	12	6	2	0	51
Y	0	0	0	0	0	0	0	1	0	0	1
ND	0	7	0	1	1	0	1	1	1	6	18
All	10	22	10	6	29	17	25	14	3	6	142

ND serogroup not determined.

Table 7. Age distribution of serologically diagnosed cases of invasive meningococcal disease, Australia, 2002

Serologically diagnosed	Age group (years)										Total
	<1	1–4	5–9	10–14	15–19	20–24	25–44	45–64	65+	Unknown	
Cases	1	5	0	4	12	12	8	4	0	0	46

Discussion

The total of 393 isolates examined by NNN laboratories in the Australian Meningococcal Surveillance Programme in 2002 was the highest number recorded since the program commenced in 1994. In 2001, 338 isolates were recovered and the annual numbers prior to this year have ranged between 323 and 388 cases. Disaggregation of the data by jurisdiction provides additional insights into case distribution. The number of isolates available in Victoria increased from 41 in 1998 to 94 in 1999 and 108 in 2000, declined to 77 in 2001 and increased to 129 in 2002. Changes in numbers in other jurisdictions were not marked so that the increase in the number of isolates nationally in 2002, was principally due to increases in Victoria.

Care must be taken before these data on isolation rates are applied to determine trends in disease rates. The number of isolates available for examination will always be less than the number of clinically notified cases because clinical surveillance case definitions allow for inclusion of culture negative cases under certain criteria. The number of culture negative cases will also vary according to the implementation of and adherence to the 'early treatment' practices now advocated for management of IMD. The increasing use of non-culture-based methods has closed this gap between laboratory confirmed and clinically diagnosed cases, but the introduction and use of non-culture-based diagnostic methods has varied in different jurisdictions over time. For these reasons, there should be care taken in comparing trend data from different states and territories in recent years on the basis of laboratory confirmation. The 187 cases confirmed by non-culture-based methods, when added to the 393 positive cultures, saw a total of 580 laboratory confirmed cases in 2002. Provisional data from the National Notifiable Diseases Surveillance System recorded a total of 675 cases of IMD in Australia in 2002.

The ratio of cases of meningitis to bacteraemia in culture confirmed cases (0.23:1) maintained an existing trend (Figure 2) remarked on in previous reports. Differences in meningitis/septicaemia rates were previously noted when these were derived from culture-based and non-culture-based methods. It was observed that the initial introduction of PCR based diagnosis saw positive CSF samples representing 2.5 times the number of diagnoses from blood. In 2002, this ratio was reversed with PCR examinations on blood yielding 1.3 times the rate of diagnoses from CSF. Since 2000, there has been an increasing trend towards positive diagnosis by NAA using blood samples.

The predominant disease pattern throughout the country remained sporadic infection with serogroup B meningococci. However, the proportion of serogroup C cases in aggregated data (41%) increased from 36 per cent in 2001. In 1998 this proportion was 25 per cent. The increase in recent years has been noted particularly in Victoria and Tasmania, but also in Queensland. There was little change in the number and proportion of serogroup C cases in New South Wales, South Australia or Western Australia.

No serogroup A meningococci were isolated and the proportion of serogroup Y and W135 strains increased only slightly.

In recent reports, it has been noted that the age distribution of IMD showed a primary peak in those aged four years or less with a secondary peak in adolescents and young adults. It was further observed that the primary peak (0–4 years) was predominantly with serogroup B infections and that serogroup C infection were more common among the young adults. In 2000, those aged 15–24 years had more IMD infections than those aged less than five years in aggregated data. Larger numbers of cases in young adults in New South Wales and Victoria influenced this pattern. In 2001, the age distribution of IMD was more typical with children aged less than five years the most frequently infected, although in Queensland and Tasmania the highest proportion of cases was still in young adults. In 2002, the proportion of cases among young adults was again higher than among infants. Infections in Victoria accounted for 40 per cent of infections in this age group nationally, most of these (45 of 56) were serogroup C strains. Serogroup B infections accounted for nearly 80 per cent of IMD infections in infants (Figures 1, 2, 3 and 4).

The subtypes of meningococci circulating within Australia have been determined mainly by phenotypic methods, by genotyping systems in Victoria. These data illustrate the similarities and differences in meningococci present in different jurisdictions and trend data show changes in

distributions of these subtypes. Patterns vary with time and influence decisions of public health relevance.[15] One particular phenotype, B:4:P1.4(7), has been associated with hyperendemic disease in New Zealand for many years. A monovalent porin vaccine, specific for this strain, has been developed and is undergoing clinical trials. This phenotype, or those closely related to it, have been present in Australia for some time and in New South Wales represented at least 20 per cent of all isolates. Use of *por* gene sequencing techniques may be required to establish the real incidence of infection due to this subtype throughout Australia. Phenotype B:15:P1.7 continues to be widely distributed. The frequency of C:2a:P1.4(7) strains in Victoria has continued to expand, accounting for much of the increase in serogroup C disease in that state and in 2002 more than 40 per cent of all isolates were of this type. In 2002, the 'Victorian' phenotype was increasingly identified elsewhere in Australia, albeit in low numbers. In Tasmania, it became the dominant phenotype. The phenotypes C:2a:P1.5 and C.2a:P1.5,2 continued to be frequently identified in New South Wales, Queensland and Victoria. Genetic recombination events in meningococci are frequent may manifest themselves as subtypes causing epidemic or hyperendemic IMD. Responses to these events are based on an intimate knowledge of relevant aspects of the organism. If the porin vaccine directed against the New Zealand hyperendemic strain proves to be effective, there may be a place for it in Australia also, given the high rate of infection with both serogroup B and C meningococci with this porin subtype.

Mortality data from this surveillance system needs to be interpreted with caution. Information on outcome was assessable in only 147 (37%) of culture positive cases and the 26 deaths recorded giving a mortality rate of 17.6 per cent, may not accurately represent the true rate. Although a higher mortality for serogroup C infections has been consistently recorded in NNN data, other factors, such as age, and time from onset to presentation and treatment, may also explain the difference in outcomes due to infection with different serogroups.

Penicillin MICs of 1 mg/L were detected in two strains in 2002. Penicillin MICs at or about 1 mg/L would still be expected to respond clinically to the currently recommended dose of penicillin,[16] although correlations between MIC and clinical outcome are difficult to establish because of the fulminant nature of fatal cases of meningococcal disease.

All isolates were susceptible to the third generation cephalosporins and the prophylactic agents rifampicin and ciprofloxacin.

Since 1994, the NNN has examined about 3,000 strains of invasive meningococcal isolates from all states and territories. The continuing evolution and development of laboratory techniques over this period mean that it is not always possible to make comparisons of data gathered in different years. The NNN data are used to supplement information collected separately by clinically based surveillance of IMD. The NNN data remain an essential component of IMD surveillance in Australia as decisions on public health management including vaccine policies are developed. These issues are likely to become increasingly complex. For further details the relevant NNN member in each jurisdiction should be contacted.

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References

1. National Neisseria Network. Meningococcal isolate surveillance Australia, 1994. *Commun Dis Intell* 1995:19:286–289.
2. National Neisseria Network. Meningococcal isolate surveillance Australia, 1995. *Commun Dis Intell* 1996;20:422–424.
3. Australian Meningococcal Surveillance Programme. Annual report of the Australian Meningococcal Surveillance Programme, 1996. *Commun Dis Intell* 1997;21:217–221.
4. Australian Meningococcal Surveillance Programme. Annual report of the Australian Meningococcal Surveillance Programme, 1997. *Commun Dis Intell* 1998;22:205–211.
5. Australian Meningococcal Surveillance Programme. Annual report of the Australian Meningococcal Surveillance Programme, 1998. *Commun Dis Intell* 1999;23:317–323.
6. Australian Meningococcal Surveillance Programme. Annual report of the Australian Meningococcal Surveillance Programme, 1999. *Commun Dis Intell* 2000;24:181–189.
7. Australian Meningococcal Surveillance Programme. Annual report of the Australian Meningococcal Surveillance Programme, 2000. *Commun Dis Intell* 2001;25:113–121.
8. Australian Meningococcal Surveillance Programme. Annual report of the Australian Meningococcal Surveillance Programme, 2001. *Commun Dis Intell* 2002; 26:407–418.
9. Australian Gonococcal Surveillance Programme. Penicillin sensitivity of gonococci in Australia: development of an Australian Gonococcal Surveillance Programme. *Br J Vener Dis* 1984;60: 226–230.
10. Porrit RJ, Mercer JL, Munro R. Detection and serogroup determination of *Neisseria meningitidis* in CSF by polymerase chain reaction (PCR). *Pathology* 2000;32:42–45.
11. Gray SJ, Borrow R, Kaczmarski EB. Meningococcal serology. In: Pollard AJ, Martin MCJ, eds. *Meningococcal disease methods and protocols*. Humana Press, Totawa, New Jersey, 2001 pp 61–87.
12. Robertson PW, Reinbott P, Duffy Y, Binotto E, Tapsall JW. Confirmation of invasive meningococcal disease by single point estimation of IgM antibody to outer membrane protein of *Neisseria meningitidis*. *Pathology* 2001:33:375–378.
13. Robertson PW, Tapsall JW, Lahra MM, Yi Z. Enhanced serological diagnosis of invasive meningococcal disease (IMD). Abstract 222, 13th International Pathogenic Neisseria Conference, Oslo, Norway, September 2002. Available from: http://neisseria.org/ipnc/2002.shtml
14. Tapsall JW, Shultz TR, Limnios EA, Munro, R, Mercer J, Porritt R, *et al*. Surveillance of antibiotic resistance in invasive isolates of *Neisseria meningitidis* in Australia 1994 – 1999. *Pathology* 2001;33:359–361.
15. Moura AS, Pablos-Mendoz A, Layton M, Weiss D. Epidemiology of meningococcal disease, New York City, 1989–2000. *Emerging Infectious Diseases* 2003;9:355–361.
16. Public Health Laboratory Service. Antimicrobial resistance in 2000: England and Wales. London: Public Health Laboratory Service, 2002, p 32.