Annual report of the Australian Meningococcal Surveillance Programme, 2003

The Australian Meningococcal Surveillance Programme

Abstract

This tenth report by the National Neisseria Network, a nation-wide collaborative laboratory program, describes 494 laboratory-confirmed cases of meningococcal disease in Australia, diagnosed in 2003. The phenotypes (serogroup, serotype and serosubtype) and antibiotic susceptibility of 303 isolates of *Neisseria meningitidis* from invasive cases of meningococcal disease were determined, and an additional 191 cases were confirmed by non-culture-based methods. The age distribution of invasive meningococcal disease showed a typical primary peak in those aged four years or less which was predominantly serogroup B meningococci. A secondary peak in adolescents and young adults contained a larger proportion of serogroup C infections. Nationally, the majority of isolates were serogroup B (183 isolates, 60.4%) or serogroup C (102 isolates, 33.6%) meningococci. The number of serogroup C isolates in Victoria decreased from 72 in 2002 to 33 in 2003 and in Tasmania the number of serogroup C isolates decreased from 14 to five. Smaller decreases in serogroup C isolate numbers were recorded in most other jurisdictions but the number increased in the Australian Capital Territory from four to seven isolates. Serogroup B isolate numbers also decreased nationally but by a smaller amount. However in South Australia serogroup B infections more than doubled, and there were also increases in the Northern Territory and Australian Capital Territory. The serogroup C phenotype C:2a:P1.4 remained prominent in Victoria but elsewhere in Australia it was detected only in low numbers. About two thirds of all isolates showed decreased susceptibility to the penicillin group of antibiotics (MIC 0.06 to 0.5 mg/L). A single isolate from the Australian Capital Territory was penicillin resistant at 1 mg/L and two, one each from South and Western Australia were rifampicin resistant. *Commun Dis Intell* 2004;28:194–206.

Keywords: antibiotics, antimicrobial resistance, cephalosporin, ceftriaxone, ciprofloxacin, penicillin, Neisseria meningitidis*, meningococcal, surveillance*

Introduction

The National Neisseria Network (NNN) is a collaborative national program of reference laboratories in each state and territory of Australia. NNN provides surveillance data relevant to the public health control of invasive meningococcal disease (IMD), namely diagnosis, antimicrobial resistance surveillance, and organism typing, including both isolate-based and non-culture derived methodologies. The first reports from the meningococcal surveillance program, which began in 1994, relied on data derived from examination of isolates from culture-positive cases of IMD, in particular, their phenotype and antibiotic susceptibility. Increasingly, data derived from non-culture-based methods, notably the genotype and diagnoses based on nucleic acid amplifications assays (NAA), have been included. The information is provided to supplement that from clinical notification schemes.

During 2003, a publicly funded program to vaccinate children and adolescents with serogroup C conjugate vaccine, commenced in Australia, but at different times in different States and Territories. This report analyses information gathered by the NNN on laboratory-confirmed cases of IMD in the calendar year 2003. The format of previous annual reports published in *Communicable Diseases Intelligence*[1–9] has been followed for comparative purposes, but this report includes additional data on IMD diagnosed by non-culture methods.

Methods

The NNN is a long term collaborative program for the laboratory surveillance of the pathogenic *Neisseria*, *Neisseria meningitidis* and *N. gonorrhoeae*.[1–10] A network of reference laboratories in each state and territory (see acknowledgements) performs and gathers laboratory data on cases of IMD 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 (porin) 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 has 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.[10]

sensitive	MIC $\leq$ 0.03 mg/L;
less sensitive	MIC 0.06 – 0.5 mg/L;
relatively resistant	MIC $\geq$ 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

Increasingly, additional laboratory confirmation of suspected cases of IMD is made available by means of non-culture-based methods including NAA and serological techniques. NAA testing is essentially by polymerase chain reaction techniques[11] 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 Public Health Laboratory Service reference laboratory, United Kingdom, as assessed for Australian conditions.[12–14] Where age, sex and outcome data for patients with non-culture-based diagnoses are 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

Number of isolates from culture-confirmed cases

A total of 303 invasive isolates of meningococci were examined in 2003, 90 less than the 393 examined in 2002, and 35 less than the 338 seen in 2001. The decrease in the number of isolates in 2003 was principally due to the lower number of culture positive cases in Victoria where there has been considerable volatility in the number of isolates in recent years. In 2001 in Victoria, there were 77 culture positive isolates, and 129 in 2002, decreasing again to 69 (22.6% of all isolates in Australia) in 2003. The number of isolates in Tasmania (10, 3%) was half that recorded in 2002. Smaller decreases in numbers were also seen in New South Wales (93, 30%, from 110 in 2002), Western Australia (25, 9%, from 35) and Queensland (69, 20%, from 76). The number of culture-positive cases in the Australian Capital Territory (11, 3%) and the Northern Territory (7, 2%) both increased from the five seen in each jurisdiction in 2002 and in South Australia the number almost doubled from 13 to 25, (9%) (Table 1).

Seasonality

Fifty-six (19%) of cases occurred between 1 January and 31 March, 57 (19%) between 1 April and 30 June, 111 (36%) between 1 July and 30 September and 79 (26%) between 1 October and 31 December. A winter peak of meningococcal disease is usual.

Table 1. *Neisseria meningitidis* isolates, Australia, 2003, by serogroup and state or territory

State or territory	Serogroup										Total	
	B		C		A	Y		W135		NG*		
	n	%	n	%	n	n	%	n	%	n	n	%
ACT	3	27	7	63	0	0	0	1	10	0	11	3.4
NSW	61	66	25	27	0	5	5	1	1	1	93	30.4
NT	6	86	0		0	0		1	14	0	7	2.3
Qld	33	52	28	44	1	1	4	0		0	63	20.6
SA	20	80	2	8	0	1	4	1	4	1	25	9.2
Tas	5	50	5	50	0	0		0		0	10	3.3
Vic	33	48	33	48	0	2	3	1	1	0	69	22.6
WA	22	88	2	8	0	1	4	0		0	25	8.2
Australia	183	60	102	34	1	10	3	5	1.5	2	303	100

* Not viable for serogrouping or not serogroupable.

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 was again in those aged four years and under. Those aged less than one year or in the 1–4 year age group accounted for 40 (13.2%) and 53 (17.5%) cases respectively. The combined total of culture positive cases in these two groups (93) is less than that in 2002 (108). However, these two age groups comprised a slightly higher proportion of all cases in 2003. A secondary disease peak is also usual in the 15–19 year age group. The total of 52 cases (17.1%) in this age group in 2003 was substantially less than the 95 (24.2%) seen in 2002, but almost the same as the 54 cases (16%) recorded in 2001. The total of 35 cases (11.5%) in those aged 20–24 years was the same proportion as the 45 cases seen in 2002. Those aged 15–24 years together accounted for 87 (28.6%) cases, that is, almost the same proportion as the four years and under age group.

Serogroup, serotype and serosubtype (phenotype) distribution

The distribution of the isolates by serogroup is shown in Tables 1 and 2. Nationally, 183 serogroup B isolates represented 60.4 per cent of all strains, lower in number, but an increase in the proportion of all cases when compared with 2002 data (210 cases, 53.5%). The 102 serogroup C strains isolated (33.6% of all cases) was a substantial decrease in both the number and proportion seen in recent years. In 2002, there were 162 serogroup C cases (41.2% of all culture positive IMD), while in 2001 there were 122 serogroup C isolates (36%) detected and in 2000, 128 (33%) isolates. The other culture positive cases were serogroup W135 (5, 1.6%), serogroup Y (10, 3.3%) and a single case of serogroup A IMD from Queensland.

When data were disaggregated by state and territory, some differences in disease distribution were again noted and changes in patterns observed in recent years were recorded. Serogroup B meningococci predominated in Western Australia (22, 88%), the Northern Territory (6, 86%), and New South Wales (61, 66%). While these proportions differ little from data obtained in 2002, the number of strains isolated was less in 2003. In South Australia, serogroup B isolates also predominated with an increased number of 20 strains representing 80 per cent of all meningococcal isolates. In Victoria (33 isolates, 48%) and Tasmania (5, 50%) the number of serogroup B strains isolated decreased in 2003 but was higher as a proportion of all meningococci grown. In Queensland, both the number (33) and proportion (52%) of serogroup B strains detected decreased.

The number of serogroup C isolated nationally decreased from 162 in 2002 to 102 in 2003 and as a proportion of all culture positive cases of IMD from 41 per cent to 34 per cent. The largest reduction in the number of serogroup C isolates was in Victoria where 33 strains were isolated in 2003 and 72 in 2002. Serogroup C strains were 48 per cent of all Victorian isolates in 2003 and 55 per cent in 2002. The number of serogroup C strains also decreased in all other jurisdictions except the Australian Capital Territory. In the Australian Capital Territory the number of strains rose from four in 2002 to seven in 2003. The other notable reduction in the number of serogroup C isolates was in Tasmania, from 14 isolates in 2002 to five in 2003. In other states, the reduction in serogroup C isolates from 2002 figures was more modest. In New South Wales the 25 isolates (27%) were nine fewer than in 2002 and in Queensland, the Northern Territory, South Australia and Western Australia the reduction in the number of serogroup C isolates from 2002 was one or two only.

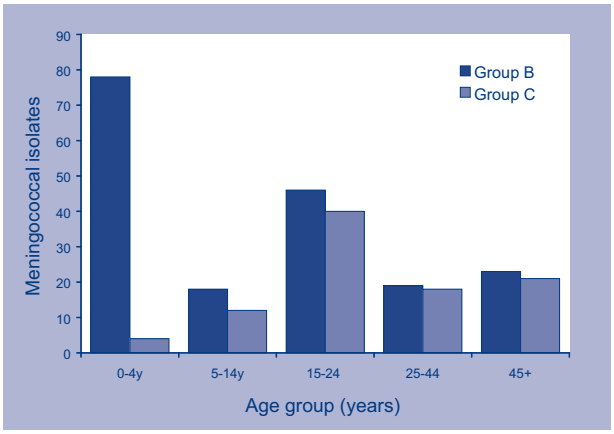
Table 2. Serogroup B and C meningococcal isolates, Australia, 2003, by state or territory

State or territory		Age group (years)										Total
		<1	1–4	5–9	10–14	15–19	20–24	25–44	45–64	65+	NS	
ACT	Total	0	1	1	2	4	0	0	2	1	0	11
	B	0	0	1	1	0	0	0	1	0	0	3
	C	0	1	0	1	4	0	0	1	0	0	7
NSW	Total	18	20	5	3	14	5	11	8	9	0	93
	B	15	19	2	2	7	1	6	6	3	0	61
	C	3	1	3	1	5	4	5	1	2	0	25
NT	Total	2	1	1	0	0	0	2	1	0	0	7
	B	2	1	1	0	0	0	1	1	0	0	6
	C	0	0	0	0	0	0	0	0	0	0	0
Qld	Total	8	3	4	4	14	10	8	8	4	0	63
	B	8	1	2	1	8	4	5	3	1	0	33
	C	0	2	1	2	6	6	3	5	3	0	28
SA	Total	3	7	0	2	5	3	2	0	3	0	25
	B	2	7	0	2	4	1	2	0	2	0	20
	C	0	0	0	0	0	2	0	0	0	0	2
Tas	Total	0	3	1	0	1	1	3	0	0	1	10
	B	0	1	0	0	1	1	1	0	0	1	5
	C	0	2	1	0	0	0	2	0	0	0	5
Vic	Total	6	8	3	4	10	14	10	10	4	0	69
	B	4	6	2	2	6	7	2	2	2	0	33
	C	1	2	1	2	4	6	8	7	2	0	33
WA	Total	3	10	2	0	4	2	2	1	1	0	25
	B	3	9	2	0	2	2	2	1	1	0	22
	C	0	0	0	0	2	0	0	0	0	0	2
Australia	n	40	53	17	15	52	35	38	30	22	1	303
	%	13.2	17.49	5.6	4.9	17.1	11.55	12.54	9.9	7.26	0.33	
Serogroup B Australia	n	34	44	10	8	28	16	19	14	9	1	183
	%	18.5	24.04	5.56	4.37	15.3	8.79	10.38	7.65	4.91	0.54	60.39
Serogroup C Australia	n	4	8	6	6	21	18	18	14	7	0	102
	%	3.92	7.84	5.88	5.88	20.58	1.64	17.64	13.72	6.86	0	33.66
Other Australia	n	2	1	1	1	3	1	1	2	6	0	18
												5.94

NS Not stated.

Serogroup distribution was typically age-associated, with serogroup B disease concentrated in younger age groups and serogroup C infections increasing as a proportion of all isolates in adolescents and young adults (Table 2). In 2003, 78 of 93 (84%) isolates in those aged less than four years were serogroup B and the 12 serogroup C isolates comprised 13 per cent of cultures nationally in this age group (Figure 1). In those aged 5–14 years, 18 serogroup B meningococcal cultures represented 56 per cent of the 32 isolates and the 12 serogroup C strains 38 per cent. There were 87 isolates in those aged 15–24 years in 2003 of which 44 (50.5%) were serogroup B and 39 (44.8%) were serogroup C. In 2002, there were 140 isolates in this age group of which 60 (43%) were serogroup B and 73 (52%) were serogroup C. In older age groups serogroup B (42) and serogroup C (39) isolates were in about equal numbers nationally.

Figure 1. Number of serogroup B and C isolates, Australia, 2003, by age



Jurisdictional differences in the distribution of serogroup B and C meningococcal isolates were also evident in 2003 with notable changes in the 15–24 year age groups when compared with 2002 data (Table 2). In all centres except Tasmania and the Australian Capital Territory serogroup B markedly predominated in those aged four years or less. In Western Australia, South Australia and the Northern Territory, serogroup B isolates predominated in most age groups. In New South Wales, serogroup B was especially prominent in these younger age groups in that only four of 38 cases were of serogroup C. A distinct shift in the number and proportion of serogroup C isolates was observed in the adolescent and young adult (15–24 year) age group in Victoria. In 2002, 35 of 56 (62%) isolates in this age group were serogroup C whereas in 2003, 10 of 24 (42%) isolates were serogroup C. In Queensland however, the number and proportion of serogroup B and C isolates in the 15–24 year age group was identical in both years.

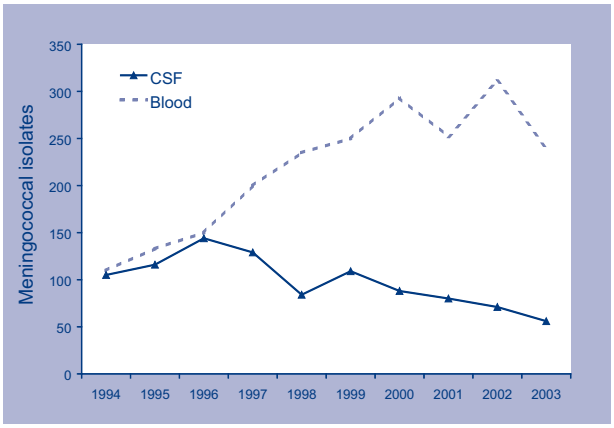
Considerable phenotypic heterogeneity amongst invasive isolates was again present. The predominant serotypes/serosubtypes in each state and territory are shown in Table 3. Serogroup B meningococci are in general more heterogeneous, but also more difficult to characterise by serological methods and a number could not be phenotyped. Twenty-five isolates of the B:4:P1.4 phenotype were identified in Victoria, New South Wales, Queensland and the Australian Capital Territory. Historically, the other common phenotype circulating has been B:15:P1.7 but only nine strains of this type were seen, seven of them in New South Wales. Of interest were four B serotypes of 2a or 2b, all with a separate serosubtype. These serotypes are more often seen in serogroup C organisms. If these subtypes become more common, extensive genotypic investigation would be warranted.

All except one of the typeable serogroup C isolates was of serotype 2a. Phenotype C:2a:P1.4, prominent in Victoria in recent years, was again commonly seen and 29 of the 33 serogroup C strains were of this phenotype. There were 10 such isolates in Victoria in 1999, 24 in 2000, 19 in 2001 and 55 in 2002. The same phenotype was also seen in most other jurisdictions. In the Australian Capital Territory and Tasmania this subtype was seen exclusively in those strains fully phenotyped, but was only found infrequently in Queensland and New South Wales. Serotype 2b strains were rare.

Site of isolation

There were 55 isolates from CSF either alone or with a blood culture isolate and 238 from blood cultures alone. There were seven isolates from synovial fluid and one each from skin, eye and peritoneum. 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, the same as in 2002 but lower than that recorded in preceding years.

Figure 2. Numbers of meningococcal isolates from cerebrospinal fluid and blood culture, Australia, 1994 to 2003



Outcome data for cases with sterile site isolates

Outcome data (survived or died) were available for 214 of the 303 patients from whom isolates were obtained (71%). Sixteen deaths were recorded in this group (7.5%) (Table 4). Outcomes were available for 123 (67%) serogroup B infections and 76 (75%) serogroup C infections. There were 5 (4%) deaths in serogroup B infections and 11 (14.4%) in serogroup C infections.

Table 3. Commonly isolated serotypes and serosubtypes and phenotypes of *Neisseria meningitidis* of interest, 2003, by state or territory

State or territory	Serogroup B				Serogroup C			
	Serotype	n	Serosubtype	n	Serotype	n	Serosubtype	n
ACT	4	1	1.4	1	2a	7	1.4	6
NSW	4	17	1.4	8	2a	20	1.5	8
			1.6,3	3			1.5,2	3
			1.14	2			1.2	2
			nst**	4			1.4	3
	2a	3	1.2	1			nst	4
			1.5	1	2b	1	1.5,2	1
			1.5,2	1	1	2	1.15	1
	15	9	1.7,(16)	7	NT	3	1.15	2
	1	7	1.14	2			1.5,2	1
			1.7	1				
	nt*	24	4	4				
			1.14	4				
			1.15	2				
			1.7	1				
			nst	12				
NT	14	4	nst	4				
Qld	4	7	1.4,(7)	6	2a	23	1.5	13
			nst	1			1.2	1
	1	5	1.4,(7)	2			1.4	3
	14	2	1.5	1			nst	4
			nst	1	nt	5	1.5	3
	15	2	1.7	1			nst	2
			nst	1				
	nt	16	1.4,(7)	6				
			1.15	2				
			nst	5				
SA	1	5	1.14	3	2a	2	nst	1
			1.7	2				
	15	3	1.4	1				
			1.7	1				
	nt	9	1.4	1				
			1.14	3				
			1.15	2				
Tas	ND	5			2a	4	1.4	4
Vic	4	12	1.4	10	2a	33	1.4	29
			1.5,2	1			1.5,10	3
			1.16	1			1.14	1
	14	2	1.14	2				
	15	2	1.4	1				
	2b	1	1.16	1				
	nt	16	1.15	8				
			1.14	3				
			nst	4				

Table 3. Commonly isolated serotypes and serosubtypes and phenotypes of *Neisseria meningitidis* of interest, 2003, by state or territory, continued

State or territory	Serogroup B				Serogroup C			
	Serotype	n	Serosubtype	n	Serotype	n	Serosubtype	n
WA	1	2	1.1,7	1	2a	2	1.4	1
			1.5	1			nst	1
	14	1	nst	1				
	15	1	1.7	1				
	nt	16	1.4	6				
			1.5	1				
			1.15	1				
			nst	8				

nt Not serotypeable.

nst Not serosubtypeable.

Table 4. Outcome data (survived, died) for culture positive cases of invasive meningococcal disease, 2003, by syndrome and serogroup

Disease type	Outcome	Serogroup					Total
		B	C	Y	W135	NG	
Meningitis	Survived	23	12	2	0	0	37
	Died	2	0	0	0	0	2
	Total	25	12	2	0	0	39
Septicaemia	Survived	93	50	5	5	2	155
	Died	3	11	0	0	0	14
	Total	96	61	5	5	2	169
All cases	Survived	118	65	8	5	2	198
	Died	5	11	0	0	0	16
	Total	123	76	8	5	2	214

NG Not groupable.

There were two deaths in 39 patients (5%) with meningitis where outcome was recorded. Both of these patients were infected with a serogroup B strain. Fourteen deaths were recorded in 169 bacteraemic patients (8.2%). There were 96 cases of serogroup B meningococcal bacteraemia with three deaths (3.1%) and 61 cases were caused by serogroup C strains among whom 11 fatalities were recorded (18%). No fatalities were recorded with serogroup Y (5 cases) or W135 (5 cases) bacteraemia.

Antibiotic susceptibility surveillance of invasive meningococcal isolates

Penicillin

Three hundred isolates were available for determination of their susceptibility to penicillin. Using defined criteria, 99 strains (33%) were fully sensitive to penicillin and 200 (67%) less sensitive (MIC 0.06 to 0.5 mg/L). These proportions are similar to those observed in recent years. One isolate from a blood culture had an MIC of 1 mg/L and six isolates had MICs of 0.5 mg/L.

Other antibiotics

All isolates were susceptible to ceftriaxone (and by extrapolation to other third generation cephalosporins) and to ciprofloxacin. A single isolate from South Australia was rifampicin resistant at an MIC of 32 mg/L and another from Western Australia displayed high level resistance.

Number and sources of non-culture diagnoses of invasive meningococcal disease in 2003

One hundred and ninety-one additional cases of IMD were diagnosed by non-culture methods in 2003. This is a similar number to that diagnosed by these means in 2002. One hundred and sixty-nine cases were diagnosed by NAA (Table 5) and another 22 solely by serology using enzyme immunoassay (EIA).

With NAA, it was also possible to categorise the disease type by source of specimen in a manner similar to that used for culture positive cases. Of the 169 cases positive by NAA, 75 were from CSF or CSF and blood, 91 from blood only and three from joint fluid. This is a different IMD syndrome 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 NAA based diagnosis, the ratio of positive diagnoses from blood to CSF was 1.2:1. The site of infection could not be determined by laboratory testing in serologically diagnosed cases.

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

In addition to diagnostic NAA, molecular techniques can also be used to ascertain the serogroup involved in the disease process. In most centres this is still limited to serogroup B and C determinations. Of the 169 cases where a NAA-based diagnosis was made, a serogroup was also determined in 145 instances (Table 5); 101 cases diagnosed by NAA were with serogroup B, 43 with serogroup C and one with W135. An additional EIA can also be performed to identify serogroup C infection serologically. Eight of the 22 serologically identified cases were confirmed as serogroup C.

The serogroup and age distribution of NAA diagnosed cases is shown in Table 6. Nationally, the number of cases in children aged less than four years was 44 (26%) a lower proportion than that diagnosed by culture-based procedures (30.3%). In 40 of these cases, the serogroup was determined and 38 were serogroup B infections. The proportion of cases diagnosed by NAA testing in the 15–24 year age group (31.3%) was slightly higher than the proportion diagnosed by culture-based methods (29.4%) in the same group. Using NAA, 56 cases were detected in this age group. However, the proportion of serogroup C (n=24) cases found equalled the number of serogroup B (n=25) cases detected. Eight of the 22 serologically-confirmed cases were in the 15–24 year age group and two were in those aged four years or less.

Table 5. Nucleic acid amplifications test-based diagnosis of invasive meningococcal disease, Australia 2003, by serogroup and state or territory

State or territory	Serogroup				Total
	B	C	W135	ND	
ACT	0	3	0	0	3
NSW	42	13	0	5	60
NT	5	0	0	0	5
Qld	15	7	0	7	29
SA	6	0	0	0	6
Tas	3	3	0	3	9
Vic	20	14	1	9	44
WA	10	3	0	0	13
Total	101	43	1	24	169

ND Not determined.

Table 6. Nucleic acid amplifications test-based diagnoses of invasive meningococcal disease, Australia, 2003, by age, serogroup and jurisdiction

State or territory	Serogroup	Age group										Total
		<1	1–4	5–9	10–14	15–19	20–24	25–44	45–64	65+	NS	
ACT	C					1			2			3
	Total					1			2			3
NSW	B	4	12	2		8	5	1	5	5		42
	C			2	2	4	2	3				13
	Total	4	12	6	2	12	7	6	6	5		60
NT	B	2	2				1					5
	Total	2	2				1					5
Qld	B	2	2	1	3	3	2	1	1			15
	C			1		2	4					7
	Total	3	3	2	4	7	8	1	1			29
SA	B		1		3		1		1			6
	Total		1		3		1		1			6
Tas	B		1			1			1			3
	C					1		1	1			3
	Total		1	2	1	2		1	2			9
Vic	B	4	1	3	2	3		5	2			20
	C		2		2	3	4	2		1		14
	Total	4	5	4	4	7	6	11	2	1		44
WA	B		7	1		1		1				10
	C					1	2					3
	Total		7	1		2	2	1				13
Australia	B	12	26	7	8	16	9	8	10	5		101
	C		2	3	4	12	12	6	3	1		43
	Total	13	31	15	14	31	25	20	14	6		169

NS Not stated (totals include other serogroups).

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

For IMD diagnosed by NAA based tests, the outcome was known in 86 instances, with eight deaths recorded (9.3%). There were five deaths (4 of serogroup C and one of serogroup B) (14%) in the 35 cases where the CSF examined was positive by NAA. Three deaths where NAA was positive only on a blood sample were recorded out of a total of 48 cases where outcome data was available. Serogroup C was identified in two cases and serogroup B in one. Of the 78 cases where survival was recorded, the diagnosis was made by NAA using CSF samples in 30 instances. Twenty-four of these were due to serogroup B infections and five to serogroup C organisms. Forty-five cases who survived were diagnosed as having IMD using NAA with a blood sample. Twenty-four infections were with serogroup B, nine with serogroup C meningococci with a single case of W135 disease. The other cases where the serogroup was determined and survival was recorded were three cases of septic arthritis, two with serogroup C and one with serogroup B. The serogroup was not determined in 12 cases where survival was recorded.

Combined data for all laboratory-confirmed IMD by age, jurisdiction and serogroups B and C are shown in Table 7.

Table 7. All laboratory-confirmed cases of invasive meningococcal disease, Australia 2003, by age, jurisdiction and serogroup

State or territory	Serogroup	Age group										Total
ACT	B	0	0	1	1	0	0	0	1	0		3
	C	0	1	0	1	5	0	0	3	0		10
	Total	0	1	1	2	5	0	0	4	1		14
NSW	B	19	31	4	2	15	6	7	11	8		103
	C	3	1	7	3	11	7	8	2	2		44
	Total	23	33	13	6	31	13	21	15	15		170
NT	B	4	3	1			1	1	1			11
	C											0
	Total	4	3	1			1	2	1			12
Qld	B	10	3	3	4	11	6	6	4	1		48
	C		2	2	2	9	10	3	6	3		37
	Total	11	6	6	8	22	18	11	10	4		96
SA	B	2	8		5	4	2	2	1	2		26
	C						2					2
	Total	3	8		5	5	4	2	1	3		31
Tas	B		2			2	1	1	1		1	8
	C		2	1		1		3	1			8
	Total		4	3	1	3	2	4	2		1	20
Vic	B	8	7	5	4	9	7	7	4	2		53
	C	1	4	1	4	7	10	10	7	3		47
	Total	10	14	7	8	17	20	21	12	5		114
WA	B	3	16	3		3	2	3	1	1		32
	C					3	2					5
	Total	3	17	3		6	4	3	1	1		38
Australia	B	46	70	17	16	44	25	27	24	14	1	284
	C	4	10	11	10	36	31	24	19	8		153
	Other	4	6	6	3	9	6	13	3	7		57
	Total	54	86	34	29	89	62	64	46	29	1	494

NS Not stated (totals include other serogroups).

Discussion

There were 494 laboratory-confirmed cases of IMD in 2003, 303 (61.3%) by culture and 191 (38.7%) by non-culture-based methods. The 303 isolates examined by NNN laboratories in the Australian Meningococcal Surveillance Programme in 2003 was the lowest number recorded since 1996. The 393 isolates recovered in 2002 was the highest number examined in any year by the NNN. The annual numbers of isolates examined from 1997 to 2002 have ranged between 323 and 388. In the 2002 report, specific mention was made of the changes in the number of isolates from Victoria in recent years. The 41 isolates in 1998 increased to 94 in 1999 and to 108 in 2000, declined to 77 in 2001 only to increase to 129 in 2002. In 2003, a substantial reduction to 69 isolates was recorded and this accounted for most of the national reduction in numbers from the 2002 figure. Smaller decreases in numbers were noted in New South Wales (17), Western Australia (12) and Queensland (7). Isolate numbers more than doubled in the Australian Capital Territory and in South Australia and also increased in the Northern Territory.

The considerable fluctuation in isolate numbers both nationally and by jurisdiction means that data on isolation rates must be examined with caution if they are applied to determine trends in disease rates. The NNN has consistently pointed to reasons for differences in the number of isolates available for examination and the number of clinically notified cases. Clinical surveillance case definitions

allow for inclusion of culture negative cases under certain criteria and this number is also influenced by the 'early treatment' practices advocated for management of IMD. Since 1999, the NNN has included data on non-culture-based testing for IMD. The use of these tests has increased progressively, however the introduction and uptake of non-culture-based diagnostic methods has varied in different jurisdictions over time and new forms of NAA with increased sensitivity have been introduced. As a result, the diagnostic basis for IMD confirmation has progressively altered. The total of 191 instances of non-culture-based diagnoses in 2003 was similar to the 187 cases confirmed by these means in 2002. However in 2003, the proportion of all cases confirmed by culture declined to 61 per cent from the 68 per cent in 2002. A further potential bias in the data arises in the different sensitivity of various test methods and the influence of clinical practice. The ratio of cases of meningitis to those of bacteraemia in culture-confirmed cases is one example. Figure 2 shows trends in this ratio over a number of years. Currently, culture-confirmed cases of meningitic IMD are one quarter of bacteraemic cases. In contrast, when NAA were first introduced, cases were confirmed as positive from CSF samples at 2.5 times the rate of diagnoses from blood. In 2002 and now in 2003, this ratio has been reversed with NAAT on blood yielding 1.2 times the rate of diagnoses from CSF. Contributing to these trends have been the increasing use of appropriate blood samples for NAA and the reluctance of clinicians to perform lumbar puncture early in the disease process.

In earlier NNN reports, analyses have concentrated on data derived from culture-confirmed cases. The increasing use of NAA has been recognised in this report by inclusion of Table 6 which shows a breakdown of NAA diagnoses by jurisdiction, age and serogroup. Table 7 includes the same information, but shows all laboratory-confirmed cases. The data on culture-based cases alone (Table 2) continue to be included for longer-term comparative purposes. Some differences are noted when parameters derived from culture-based and non-culture-based cases are compared. A primary disease peak is usual in those aged less than four years with a secondary peak in those aged 15–24 years. In 2003, 31 per cent of cases confirmed by culture were in the younger age group and 29 per cent in the older age group. In those cases confirmed by NAA, 20 per cent were aged four years or less and 33 per cent aged 15–24 years. For all laboratory-confirmed cases, 28 per cent were in the 0–4 year age group and 30.5 per cent occurred in the older age group. Some differences were also noted in the relative proportions of serogroup B and C disease diagnosed by different methods. Serogroup B cases were 60 per cent of all cases diagnosed by both culture and NAA, but serogroup C cases diagnosed by culture were 33 per cent of all diagnoses by this method but 25 per cent of all NAA diagnoses. The final example of differences in data due to the diagnostic test method used occurs in the proportion of serogroup B and C disease recorded by age. In those aged 15–24 years, the ratio of serogroup B to serogroup C disease differs little with infection due to both serogroups in similar proportions irrespective of test method. However in the younger age group, serogroup B isolates were cultured 6.5 times more often than serogroup C meningococci whereas with NAA, serogroup B disease was diagnosed 19 times as often as serogroup C infection.

Irrespective of these differences, the predominant disease pattern throughout the country was with serogroup B meningococci (284 cases, 57.4%) and 153 (31%) serogroup C cases (Table 7). There has also been a substantial reduction in the number of serogroup C infections, most notably in Victoria. It is tempting to attribute these changes to the effect of vaccination programs with serogroup C conjugate vaccines. This type of analysis is beyond the scope of this report. As well as the limitations of the data presented here, it should be remembered that fluctuations in the rates of IMD can occur naturally. In Victoria there was also a smaller decrease in the number of serogroup B meningococci cultured and in New South Wales, Western Australia and Queensland the reduction in numbers of serogroup B isolated was greater than the decrease in numbers of serogroup C isolates. Any assessment of the impact of the vaccination program on IMD rates will thus require a continuing and detailed analysis. Other important considerations in these analyses include the possibility of replacement of serogroup C strains by other serogroups by 'vacuum filling'. In South Australia in 2003, the number of serogroup B infections more than doubled. A further concern is the ability of meningococci to undergo genetic recombination. A limited number of clonal complexes are responsible for most IMD globally. The ET–37 clonal complex or its genetic variant ET–15 for example, comprise related strains that may express a serogroup B, C, Y or W135 capsule. The possibility that a switch from serogroup C to other sialic acid containing capsular types may occur is well documented and it would seem that a small number of such isolates were again present in Australia in 2003. While a multivalent polysaccharide conjugate vaccine containing A, C, Y and W135 antigens is close to release, there is no realistic prospect of a serogroup B capsule vaccine. Rather, vaccination strategies for serogroup B meningococci are currently concentrated on porin subtype vaccines such as those currently under trial in New Zealand. For this reason close attention must be paid to analysis of serogroup B subtypes and any evidence of their clonal expansion. In addition, meningococcal heterogeneity may arise from variation within the *porA* and *porB* genes or, separately, from their recombination. The typing data contained

in this and earlier reports suggests that these phenomena are also occurring and warrant continued monitoring.

Recent NNN reports noted that the age distribution of IMD showed a primary peak in those aged four years or less and was predominantly with serogroup B meningococci while the secondary peak in adolescents and young adults contained a larger proportion of serogroup C infections. This pattern was again observed in 2003, irrespective of the diagnostic method by which the data were generated.

Mortality data were assessable in only a proportion of cases and must be interpreted with caution. Excess mortality has been linked to serogroup C infections in more complete studies and has been consistently recorded in NNN data. The NNN does not attempt collection of morbidity data associated with IMD.

A penicillin MIC of 1 mg/L was detected in a single strain in 2003. Outcome/MIC correlates are difficult to establish in IMD because of the fulminant nature of fatal cases of meningococcal disease. Additionally, methodological differences may significantly alter the MIC value reported so that little guidance for Australian conditions is available from overseas studies. Meningococci are however generally slower to develop antimicrobial resistance and NNN trend data show no recent shifts in penicillin MICs of invasive strains. All isolates were susceptible to the third generation cephalosporins and ciprofloxacin. Occasional isolates demonstrate rifampicin resistance and one isolate with an MIC of 32 mg/L and another with high level resistance were detected in 2003.

This report completes a decade of NNN analysis of laboratory-confirmed cases of IMD in Australia. Significant changes to diagnostic and analytical capacity have occurred in this period placing some limitations on the value of comparative analyses. However the data generated is an essential adjunct to clinically based surveillance systems for IMD. For further details the relevant NNN member in each jurisdiction should be contacted.

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