Annual reports

Australian Meningococcal Surveillance Programme annual report, 2015

Monica M Lahra, Rodney P Enriquez for the National Neisseria Network

Abstract

In 2015, there were 174 laboratory-confirmed cases of invasive meningococcal disease analysed by the Australian National Neisseria Network. This number was higher than that reported in 2013 and 2014, which were the lowest and second-lowest totals reported, respectively, since inception of the Australian Meningococcal Surveillance Programme in 1994. Probable and laboratory confirmed invasive meningococcal disease (IMD) is notifiable in Australia. There were 182 IMD cases notified to the National Notifiable Diseases Surveillance System in 2015, again, higher than in 2013 and 2014, which were the lowest and second-lowest totals of IMD cases recorded, respectively, by this system. Meningococcal serogrouping was able to be determined for 168/174 (97%) laboratory confirmed IMD cases. Of these, 64.2% (108 cases) were serogroup B infections, the lowest reported since 2003. Further, the number and proportion of cases of serogroup C IMD, (1.2%, 2 cases), was the lowest yet reported. By contrast, in 2015 in Australia, there was a marked increase in the number and proportion of serogroup W IMD (21.4%, 36 cases), and an increase in serogroup Y IMD (13.1%, 22 cases). The number and proportion of IMD cases caused by serogroups W and Y was the highest reported since the inception of the Australian Meningococcal Surveillance Programme in 1994. Molecular typing results were available for 140 of the 174 IMD cases. Of the 31 serogroup W IMD strains that were able to be genotyped, 25/31 (81%) were sequence type (ST)-11, and have the *porA* antigen encoding gene type P1.5,2, the same genotype as the hypervirulent serogroup W strain of that has been circulating in the United Kingdom and South America since 2009. In 2015, the most common serogroup B *porA* genotype circulating in Australia was P1.7-2,4. The primary IMD age peak was observed in adults aged 45 years or more, which was the first time that this was noted by the AMSP, whilst secondary disease peaks were observed in those aged 4 years or less, and in adolescents (15–19 years). Serogroup B cases predominated in all jurisdictions and age groups, except for those aged 45 years or over where serogroups W and Y predominated. All IMD isolates tested were susceptible to ceftriaxone and ciprofloxacin. One isolate was resistant to rifampicin. Four isolates were resistant to penicillin. Decreased susceptibility to penicillin was observed in 86% of isolates. *Commun Dis Intell* 2014;40(4):E503–E511.

Keywords: antibiotic resistance; disease surveillance; meningococcal disease; *Neisseria meningitidis*

Introduction

The National Neisseria Network (NNN) in Australia is an established, collaborative network of reference laboratories in each state and territory that contribute to the laboratory surveillance system of the pathogenic *Neisseria* species *(N. meningitidis* and *N. gonorrhoeae)*. Since 1994 the NNN has coordinated laboratory data from the examination of *N. meningitidis* cases of invasive meningococcal disease (IMD) for the Australian Meningococcal Surveillance Programme (AMSP).[1] The AMSP is funded by the Australian Government Department of Health. The NNN laboratories supply phenotypic and genotypic data of invasive meningococci for the AMSP. These data supplement the notification data from the National Notifiable Diseases Surveillance System (NNDSS), which includes cases of probable IMD as well as laboratory confirmed IMD. The characteristics of meningococci responsible for IMD, and the associated demographic information, are important considerations for management of individual patients and their contacts; and to inform public health responses for outbreaks or case clusters, locally and nationally. The introduction of the publicly funded conjugate serogroup C meningococcal vaccine onto the National Immunisation Program in 2003 has seen a significant and sustained reduction in the number of cases of serogroup C IMD after 2003.[2] However, IMD remains an issue of public health concern in Australia. In this report please note a nomenclature change for serogroup W135, which will be hereafter referred to as serogroup W in line with the accepted international nomenclature system for *N. meningitidis*.[3]

Methods

Case confirmation of invasive meningococcal disease

Case confirmation is based on isolation of *N. meningitidis*, or a positive nucleic acid amplification testing (NAAT) from a normally sterile site, defined as laboratory definitive evidence of IMD

by the Communicable Diseases Network Australia criteria.[4] Information regarding the site of infection, age and sex of the patients is collated by the NNN for the AMSP.

IMD cases are categorised on the basis of the site from which *N. meningitidis* was isolated, or from which meningococcal DNA was detected (blood, joint fluid, vitreous fluid). When *N. meningitidis* is detected from both blood and cerebrospinal fluid (CSF) from the same patient, the case is classified as one of meningitis.

Phenotyping and genotyping of *Neisseria meningitidis*

Phenotyping is limited to the determination of the serogroup by detection of soluble polysaccharide antigens. Genotyping of both isolates and DNA extracts is performed by sequencing of products derived from amplification of the porin genes *porA, porB* and *FetA*.

Antibiotic susceptibility testing

Isolates were tested to determine their minimum inhibitory concentration (MIC) values to antibiotics used for therapeutic and prophylactic purposes: ceftriaxone, ciprofloxacin; and rifampicin. This program uses the following parameters to define the various levels of penicillin susceptibility or resistance when determined by a standardised agar plate dilution technique: sensitive (MIC $\leq$ 0.03 mg/L); less sensitive (MIC 0.06–0.5 mg/L) and resistant (MIC $\geq$ 1 mg/L).

Results

In 2015, there were 174 laboratory-confirmed cases of IMD analysed by the NNN, and 182 cases notified to the NNDSS. Thus, laboratory data were available for 96% of notified cases of IMD in Australia in 2014 (Figure 1). This number was higher than that reported in 2013 and 2014, which were the lowest and second-lowest totals reported, respectively, by both the NNDSS, and the AMSP. With regard to the number of cases of IMD in Australia, there has been an overall decrease from the peak reported in 2002. As in previous years, the peak incidence for IMD was in late winter and early spring (1 July to 30 September) (Table 1).

The highest number of laboratory confirmed cases was from Victoria (54 cases), which was higher than 2014 (33 cases), and the highest number of cases reported in this state since 2008 (61 cases).

New South Wales also recorded a rise in IMD cases in 2015 compared with 2014 (41 cases in 2015, compared with 36 cases in 2014). In contrast, Queensland recorded a fall in the number of IMD cases in 2015 (30 cases) compared with 2014 (39 cases), and this was the lowest number of cases

Figure 1: Number of invasive meningococcal disease cases reported to the National Notifiable Diseases Surveillance System compared with laboratory confirmed data from the Australian Meningococcal Surveillance Programme, Australia, 2015

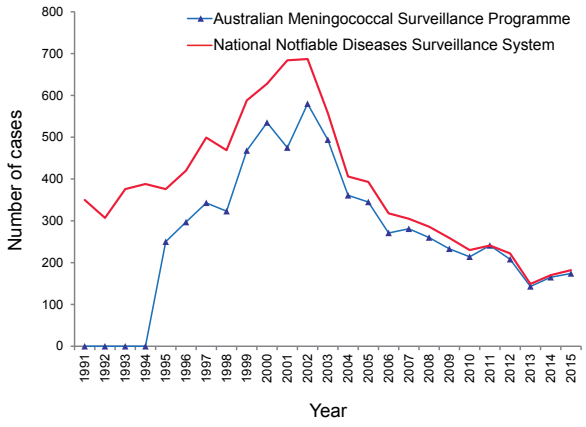


Table 1: Laboratory confirmed cases of invasive meningococcal disease, Australia, 2015, by quarter

Serogroup	1 January to 31 March	1 April to 30 June	1 July to 30 September	1 October to 31 December	2015
B	20	32	35	21	108
C	1	0	0	1	2
Y	1	5	12	4	22
W	2	6	16	12	36
NG	0	2	0	2	4
ND	0	0	0	2	2
Total	24	45	63	42	174

NG: Non-groupable.

ND: Not determined.

reported in this State since the inception of the AMSP in 1994. Numbers for the other states were similar to 2014 (Table 2).

Age distribution

Nationally, for the first time in AMSP reporting, the peak incidence of IMD occurred in adults aged 45 years or more. This age group represented 61/174 (35%) IMD cases in 2015 (Table 3). The number of IMD cases and the proportion of cases within this age group was almost double that in 2014 (21%, 34 cases). Previously, the primary peak incidence of IMD was in children less than 5 years of age; however in 2015 they represented 23% of IMD cases, the lowest percentage of cases noted by the AMSP in this age group in any year. Between 2003 and 2014, the proportion of IMD that occurred in those less than 5 years of age in Australia ranged from 28% to 36% of cases. A secondary disease peak has also been observed in previous years among adolescents aged 15–19 years. Of the total cases of IMD, 33 (19%) were in those aged 15–19 years in 2015, which was similar to the proportion reported in the period 2006 to 2011, and 2013 to 2014 (17%, 20% respectively).

Anatomical site of samples for laboratory confirmed cases

In 2015, diagnosis was made by a positive culture in 117/174 (67%) cases and 57/174 (33%) cases were confirmed by NAAT testing alone (Table 4).

There were 53 diagnoses of meningitis based on cultures or NAAT examination of CSF either alone or with a positive blood sample. There were

Table 2: Number of laboratory confirmed cases of invasive meningococcal disease, Australia, 2015, by state or territory and serogroup

State or territory	Serogroup						Total
	B	C	Y	W	NG	ND	
ACT	1	0	1	0	0	0	2
NSW	20	2	7	9	3	0	41
NT	1	0	0	0	0	0	1
Qld	19	0	3	5	1	2	30
SA	29	0	1	0	0	0	30
Tas.	0	0	0	1	0	0	1
Vic.	29	0	8	17	0	0	54
WA	9	0	2	4	0	0	15
Australia	108	2	22	36	4	2	174
%	62.1	1.1	12.6	20.7	2.3	1.1	

NG: Non-groupable
ND: Not determined

Table 4: Number of laboratory confirmed cases of invasive meningococcal disease, Australia, 2015, by anatomical source and method of confirmation

Specimen type	Isolate of MC	PCR positive	Total
Blood	92	23	115
CSF +/- blood	20	33	53
Other‡	5	1	6
Total	117	57	174

PCR Polymerase chain reaction.

Table 3: Laboratory confirmed cases of invasive meningococcal disease, Australia, 2015, by age and serogroup

Serogroup	Age group										Total
	<1	1–4	5–9	10–14	15–19	20–24	25–44	45–64	65+	NS	
B	9	20	3	3	27	11	9	12	12	2	108
C	1	0	0	1	0	0	0	0	0	0	2
Y	0	1	1	0	1	2	1	4	12	0	22
W	2	2	1	0	4	4	2	10	11	0	36
NG	2	1	0	0	1	0	0	0	0	0	4
ND	2	0	0	0	0	0	0	0	0	0	2
Total	16	24	5	4	33	17	12	26	35	2	174
% B of within age group	56.3	83.3	60.0	75.0	81.8	64.7	75.0	46.2	34.3		

NS: Age not stated.
NG: Non-groupable.
ND: Not determined.

115 diagnoses of septicaemia based on cultures or NAAT examination from blood samples alone (Table 4). There were 3 IMD diagnoses by positive joint fluid culture, 1 IMD diagnosis by positive eye vitreous fluid culture, 1 IMD diagnosis by positive cyst fluid culture, and 1 IMD diagnosis by NAAT where the site was not stated.

Serogroup data

Number of cases of serogroup B, C, Y, W invasive meningococcal disease

The serogroup was determined for 168 of 174 laboratory confirmed cases of IMD (97%) in 2015 (Tables 2 and 3). The overall decrease since 2002 was initially predominantly due to a reduction in the number of cases of IMD caused by serogroup C from 2003 to 2007 following the introduction of the serogroup C vaccine. After 2009 a decline in the number of IMD cases caused by serogroup B was reported, from 194 cases in 2009, to 104 cases in 2013. In 2014, there was an increase in the number of IMD cases caused by serogroup B (n=129), but in 2015 the number of IMD cases caused by serogroup B was similar to 2013. The number of IMD cases caused by serogroup C (n=2) in 2015 was the lowest total reported by the AMSP. The number of cases of IMD caused by serogroup Y (n=22) in 2015 was the highest reported (13 cases in 2014). In contrast, the number of cases of serogroup W IMD has increased in recent years (7-16 cases in 2011-2014, compared with 4-9 cases in 2007-2010), and in 2015 there were 36 cases, the highest number reported by the AMSP, and more than double the number reported in 2014 (n=16).

Proportions of serogroup B, C, Y, W invasive meningococcal disease

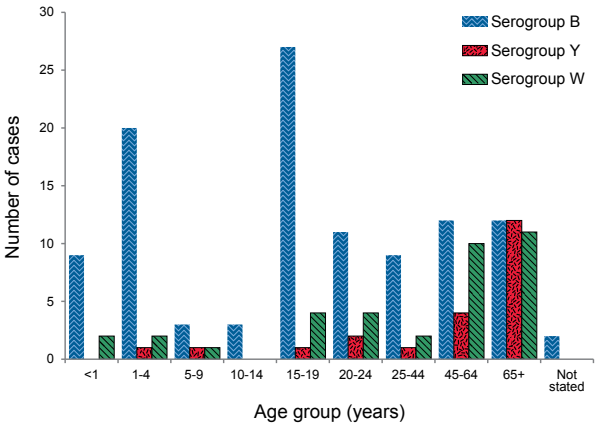
Of the 168 IMD strains for which the serogroup was determined in 2015, 64.3% were serogroup B, which is the lowest overall proportion since 2003. In the years 2006 to 2012 it was 84% to 88%, and in 2013 to 2014 it was 75% to 80%. The proportion and number of IMD caused by serogroup C in 2015 was lowest since the inception of the Australian Meningococcal Surveillance Programme (1.2%).

Whilst the number and proportion of IMD attributable to serogroup B and C declined in 2015, the number and proportion of cases of serogroup Y and W have increased. In 2012 to 2014 serogroup Y accounted for 7.7% to 10.8% of IMD, higher than the proportion reported in the period 2007 to 2011: 3.5% to 5.0%. In 2015 the proportion of IMD cases caused by serogroup Y (13.1%) was the highest yet reported and the predominance (16/22, (73%) was in those aged 45 years or over.

The proportion of cases of IMD caused by serogroup W in Australia ranged from 1.8% to 4.5% in the period 2007 to 2011, and was 8.6% to 9.9% in 2013 to 2014. In 2015, this rose to 21.4% of the total cases of IMD in Australia.

In 2015 the proportion of cases of IMD caused by serogroup B in children less than 5 years, was the lowest since 2000 (Table 3, Figure 2). In young adults 20–24 years, serogroup B IMD was lower than in 2014 (83%), and lower than 2007 to 2010 and 2012 (72% to 88%) but similar to 2011 and 2013 (61% to 67%). The proportion of cases of IMD caused by serogroup B in those aged 15–19 has remained relatively stable since 2008. Serogroup B IMD was prominent in IMD in all age groups excepting 65 years or over where, serogroup Y was equally prevalent, and serogroup W slightly less so. The age group with the highest prevalence of serogroup Y IMD was those aged 65 years or over, and accounted for 12/22 total serogroup Y IMD cases (55%) in 2015. Serogroup W cases were more evenly distributed over the age groups than serogroup Y; however the age group with the highest prevalence of serogroup W IMD was those aged 65 years or over (11/37 cases, 30%), followed by those aged between 45 and 64 years (8/37 cases, 22%).

Figure 2: Number of serogroups B, Y and W cases of confirmed invasive meningococcal disease, Australia, 2015, by age



Genotyping

In 2015, genotyping results were available for 140/174 (81%) IMD cases (Tables 5 and 6). The predominant *porA* genotypes for serogroup B IMD cases were again P1.7-2,4 (29 cases, 35% of serogroup B IMD cases that were typeable) and P1.7,16-26 (14 cases, 17% of serogroup B IMD cases that were typeable) (Figure 3). In 2014, the genotype P1.7-2,4 accounted for 18% (14 cases) of serogroup B IMD cases that were typeable, and

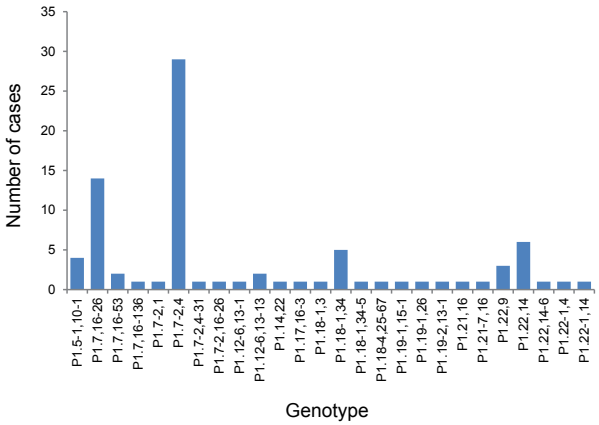
between 2011 and 2014 was the most common genotype detected for serogroup B IMD cases that were typeable (18% to 30%).The predominant *porA* genotype for serogroup Y IMD cases was P1.5-1,10-1 (14 cases, 70% of serogroup Y IMD cases that were typeable). This was higher than in 2014 (6 cases, 50% of serogroup Y IMD cases that were typeable) but the overall numbers were low.

Table 5: Laboratory confirmed cases of invasive meningococcal disease, Australia, 2015, by *porA* genotype

Genotype	B	C	Y	W	NG	Total
P1.5,2	0	0	0	31	0	31
P1.5,2-1	0	1	0	0	0	1
P1.5-1,2-2	0	0	0	1	0	1
P1.5-1,10-1	4	0	14	0	0	18
P1.5-1,10-4	0	0	1	1	0	2
P1.5-1,10-8	0	0	1	0	0	1
P1.5-2,10-1	0	0	3	0	0	3
P1.5-2,10-29	0	0	1	0	0	1
P1.7,16-26	14	0	0	0	0	14
P1.7,16-53	2	0	0	0	0	2
P1.7,16-136	1	0	0	0	0	1
P1.7-2,1	1	0	0	0	0	1
P1.7-2,4	29	0	0	0	0	29
P1.7-2,4-31	1	0	0	0	0	1
P1.7-2,16-26	1	0	0	0	0	1
P1.12-6,13-1	1	0	0	0	0	1
P1.12-6,13-13	2	0	0	0	0	2
P1.14,22	1	0	0	0	0	1
P1.17,16-3	1	0	0	0	0	1
P1.18-1,3	1	0	0	1	0	2
P1.18-1,34	5	0	0	0	1	6
P1.18-1,34-5	1	0	0	0	0	1
P1.18-4,25-67	1	0	0	0	0	1
P1.19,15-1	1	0	0	0	0	1
P1.19-1,26	1	0	0	0	0	1
P1.19-2,13-1	1	0	0	0	0	1
P1.21,16	1	0	0	1	0	2
P1.21-7,16	1	0	0	0	0	1
P1.22,9	3	0	0	0	0	3
P1.22,14	6	0	0	0	0	6
P1.22,14-6	1	0	0	0	0	1
P1.22-1,4	1	0	0	0	0	1
P1.22-1,14	1	0	0	0	0	1
Total	83	1	20	35	1	140

Of the 31 serogroup W IMD strains that were able to be genotyped, 25/31 (81%) were sequence type (ST)-11, and had the *porA* antigen encoding gene type P1.5,2; the same genotype as the hypervirulent serogroup W strain reported in the United Kingdom and South America since 2009[6,7] (Table 7).

Figure 3: Number of *porA* genotypes* for serogroup B in cases of invasive meningococcal disease, Australia, 2015



* Where data available.

Antibiotic susceptibility testing

Testing for antimicrobial susceptibility was performed for 117/174 (67%) IMD cases in 2015. All isolates tested were susceptible to ceftriaxone and ciprofloxacin. There was 1 isolate that was resistant to rifampicin (MIC=1 mg/L). Using the defined criteria, 12/117 (10.3%) isolates were fully sensitive to penicillin (MIC 0.03 mg/L or less), and 101 (86%) isolates were less sensitive to penicillin (MIC=0.06–0.5 mg/L). Four isolates were resistant to penicillin (MIC ≥ 1 mg/L).

Discussion

In 2015, there were 174 cases of laboratory confirmed IMD, representing 96% of the number of notifications to the NNDSS.[2] Whilst this was higher than the number of IMD cases reported in 2014, it represents the second lowest number of IMD cases reported in Australia since laboratory based surveillance (AMSP) began in 1994, and since notification data collection commenced in 1991, and represents about one-third of the peak number of IMD cases reported in Australia in 2002 (n=580). The introduction of the serogroup C vaccine to the national immunisation schedule in 2003 has resulted in a very large and sustained reduction in the number and proportion of sero-

Table 6: Distribution of *porA* genotype laboratory confirmed cases of invasive meningococcal disease, Australia, 2015, by state or territory

Genotype	ACT	NSW	NT	Qld	SA	Tas.	Vic.	WA
P1.5,2		9 W		3 W		1 W	15 W	3 W
P1.5,2-1		1 C						
P1.5-1,2-2							1W	
P1.5-1,10-1		3 B,6 Y		1 B,1 Y			6 Y	1 Y
P1.5-1,10-4		1Y		1 W				
P1.5-1,10-8								1 Y
P1.5-2,10-1				1 Y			2 Y	
P1.5-2,10-29	1 Y							
P1.7,16-26		3 B		4 B	1 B		5 B	1 B
P1.7,16-53				2 B				
P1.7,16-136				1 B				
P1.7-2,1				1 B				
P1.7-2,4		4 B		5 B	13 B		5 B	2 B
P1.7-2,4-31							1 B	
P1.7-2,16-26		1 B						
P1.12-6,13-1					1 B			
P1.12-6,13-13					2 B			
P1.14,22				1 B				
P1.17,16-3							1 B	
P1.18-1,3					1 W		1 B	
P1.18-1,34				1 NG	2 B		3 B	
P1.18-1,34-5				1 B				
P1.18-4,25-67		1 B						
P1.19,15-1					1 B			
P1.19-1,26				1 B				
P1.19-2,13-1							1 B	
P1.21,16							1 B	1 W
P1.21-7,16		1 B						
P1.22,9		1 B					2 B	
P1.22,14		1 B		2 B			1 B	2 B
P1.22,14-6							1 B	
P1.22-1,4								
P1.22-1,14				1 B				

Table 7: Laboratory confirmed cases of serogroup W invasive meningococcal disease, Australia, 2015, by whole genome sequence type

	Whole genome sequence type							
W genotype	ST11	ST22	ST23	ST184	ST1287	Not typeable	Not tested	Total
P1.5,2	25	0	0	0	2	1	3	31
P1.5-1,2-2	0	1	0	0	0	0	0	1
P1.5-1,10-4	0	0	1	0	0	0	0	1
P1.18-1,3	0	0	0	1	0	0	0	1
P1.21,16	0	0	0	1	0	0	0	1
Not typeable	0	0	0	0	0	1	0	1
Total	25	1	1	2	2	2	3	36

group C IMD cases in this country. In 2015, the number and proportion of serogroup C IMD cases was the lowest ever reported by the AMSP. In 2015 the majority of IMD cases continue to be caused by serogroup B strains; however the overall proportion IMD caused by serogroup B was the lowest since 2003. In early 2014, a recombinant multicomponent meningococcal B vaccine became available in Australia.[8] This vaccine is not on the immunisation register but is available for purchase privately. Therefore uptake is elective and the impact of its introduction is yet to be determined in this country.

All IMD isolates were susceptible to ceftriaxone and ciprofloxacin; and there was 1 isolate that was resistant to rifampicin, and 4 isolates that were resistant to penicillin. The proportion of IMD isolates with penicillin MIC values in the less sensitive category in 2015 was 86%. In previous years the range was 62% to 75% in 1996–2006; 67% to 79% in 2007–2009; and 78% to 88% in 2010–2014, thus indicating an ongoing increasing trend in penicillin MIC values of IMD isolates. The incidence of penicillin resistance in *N. meningitidis* in Australia however, remains low.

In 2015, a number of changes in IMD epidemiology were observed in Australia. There was a notable increase in the number of IMD cases caused by serogroups W and Y, the highest yet reported by the AMSP, and these were the predominant serogroups causing IMD in those aged 65 years or over. In addition, in 2015, the primary peak of IMD was observed for the first time in adults aged 45 years or more, because of the increased number of serogroup W and serogroup Y IMD cases in this age group. Secondary disease peaks were observed in those aged 4 years or less, and in adolescents (15–19 years).

In 2015, 21% of all IMD notifications were serogroup W, with the highest proportion of cases in New South Wales (22%), Victoria (17%), and Queensland (17%). Whole genome sequencing found that the predominant circulating strain of serogroup W in Australia in 2015, (25/31, 81%), was sequence type (ST)-11, and had the *porA* antigen encoding gene type P1.5,2. This is the same genotype as the hypervirulent serogroup W strain that emerged in the United Kingdom and South America in 2009[6,7] and has spread to now account for 25% of IMD in the United Kingdom in 2014–2015, and 59% of all cases in Chile in 2012. This serogroup W strain is now considered endemic in these regions, is associated with atypical presentations, more severe clinical disease and a higher case fatality rate.[7] In these regions, the initial increase in IMD was seen in older adults, but was subsequently reported in all age groups, particularly in adolescents and infants.[9] In response, vaccination programs have been implemented in both the United Kingdom and in Chile.[6,10] The increase in cases of serogroup W IMD is of significant concern and the NNN is working on further investigations with the Australian Government Department of Health and the Communicable Diseases Network Australia and is closely monitoring the phenotypic and genotypic features of *N. meningitidis* causing IMD in Australia. Additional investigations including whole genome sequencing of all Serogroup W are in place to enhance surveillance practices. The AMSP data are used for informing treatment protocols and to inform the need for and monitor the effect of disease prevention strategies.

Acknowledgements

Meningococcal isolates were received in the reference centres from many laboratories throughout Australia. The considerable time and effort involved in forwarding these isolates 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 Australian Government Department of Health provided funding for the National Neisseria Network.

Members of the AMSP in 2015 were: John Bates, Helen Smith and Vicki Hicks, Public Health Microbiology, Forensic and Scientific Services, Coopers Plains, Queensland; Monica Lahra, Rodney Enriquez; Tiffany Hogan; Ratan Kundu and Athena Limnios, Department of Microbiology, SEALS, The Prince of Wales Hospital, Randwick, New South Wales; Dr Michael Maley, Robert Porritt and Joanne Mercer, Department of Microbiology and Infectious Diseases, SSWPS, Liverpool, New South Wales; Kerrie Stevens, The Microbiological Diagnostic Unit Public Health Laboratory, Department of Microbiology and Immunology, University of Melbourne, Parkville, Victoria; Andrew Lawrence, Microbiology and Infectious Diseases Department, SA Pathology, Adelaide, South Australia; Jane Bew, Leanne Sammels and Tony Keil, Department of Microbiology, Princess Margaret Hospital for Children, Subiaco, Western Australia; Belinda McEwan Belinda Chamley and Dr McGregor Department of Microbiology and Infectious Diseases, Royal Hobart Hospital, Hobart, Tasmania; Rob Baird, Kevin Freeman and microbiology staff, Microbiology Laboratory, Territory Pathology, Royal Darwin Hospital, Tiwi, Northern Territory; Angelique Clyde-Smith and Peter Collignon, Microbiology Department, Canberra Hospital, Garran, Australian Capital Territory.

Participants in the 2015 AMSP to whom isolates and samples should be referred, and enquiries directed, are listed below.

Australian Capital Territory

P Collignon, S Bradbury
Microbiology Department
The Canberra Hospital
Yamba Drive
Garran ACT 2605
Telephone: +61 2 6244 2414
Email: peter.collignon@act.gov.au

New South Wales

MM Lahra, RP Enriquez, EA Limnios,
TR Hogan, RL Kundu
Microbiology Department, SEALS, The Prince of Wales Hospital
Barker Street, Randwick NSW 2031
Telephone: +61 2 9382 9084
Facsimile: +61 2 9382 9310
Email: monica.lahra@health.nsw.gov.au

M Maley, J Mercer, R Porritt
Department of Microbiology and Infectious Diseases
SSWPS
Locked Mail Bag 7090
Liverpool BC NSW 1871
Telephone: +61 8738 5124
Facsimile: +61 2 8738 5129
Email: Joanne.Mercer@sswahs.nsw.gov.au or Robert.Porritt@sswahs.nsw.gov.au

Northern Territory

R Baird, K Freeman
Microbiology Laboratory
Territory Pathology
Royal Darwin Hospital
Tiwi NT 0810
Telephone: +61 8 8922 8167
Facsimile: +61 8 8922 7788
Email: rob.baird@nt.gov.au

Queensland

J Bates, H Smith, V Hicks
Public Health Microbiology
Forensic and Scientific Services
39 Kessels Road
Coopers Plains Qld 4108
Telephone: +61 7 3274 9101
Facsimile: +61 7 3274 9175
Email: john_bates@health.qld.gov.au

South Australia

A Lawrence
Microbiology and Infectious Diseases
SA Pathology
Frome Road, Adelaide, SA 5000
Telephone: +61 8 2223503
Facsimile: +61 8 2223543
Email: andrew.lawrence@health.sa.gov.au

Tasmania

B McEwan, B Chamley
Department of Microbiology and Infectious Diseases
Royal Hobart Hospital
48 Liverpool Street
Hobart Tasmania 7000
Telephone: +61 3 6222 8656
Email: belinda.mcewan@dhhs.tas.gov.au

Victoria

K Stevens
Microbiological Diagnostic Unit Public Health Laboratory
Department of Microbiology and Immunology
The University of Melbourne
Parkville Victoria 3052
Telephone: +61 3 8344 5701
Facsimile: +61 3 8344 7833
Email: kerries@unimelb.edu.au

Western Australia

AD Keil, J Bew, L Sammels
Department of Microbiology
Princess Margaret Hospital for Children
1 Thomas Street
Subiaco WA 6008
Telephone: +61 8 9340 8273
Facsimile: +61 8 9380 4474
Email: tony.keil@health.wa.gov.au or jane.bew@health.wa.gov.au

Author details

Monica M Lahra[1,2]
Rodney Enriquez[1]

1. Neisseria Reference Laboratory and World Health Organisation Collaborating Centre for STD, Sydney. Department of Microbiology, South Eastern Area Laboratory Services, The Prince of Wales Hospital, Randwick, New South Wales.
2. School of Medical Sciences, Faculty of Medicine, The University of New South Wales, New South Wales

Corresponding author: Professor Monica Lahra, Microbiology Department, SEALS, Director, Neisseria Reference Laboratory and WHO Collaborating Centre for STD, Level 4, Campus Centre, The Prince of Wales Hospital, RANDWICK NSW, 2031. Email: monica.lahra@health.nsw.gov.au

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