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Australian Meningococcal Surveillance Programme Annual Report, 2021

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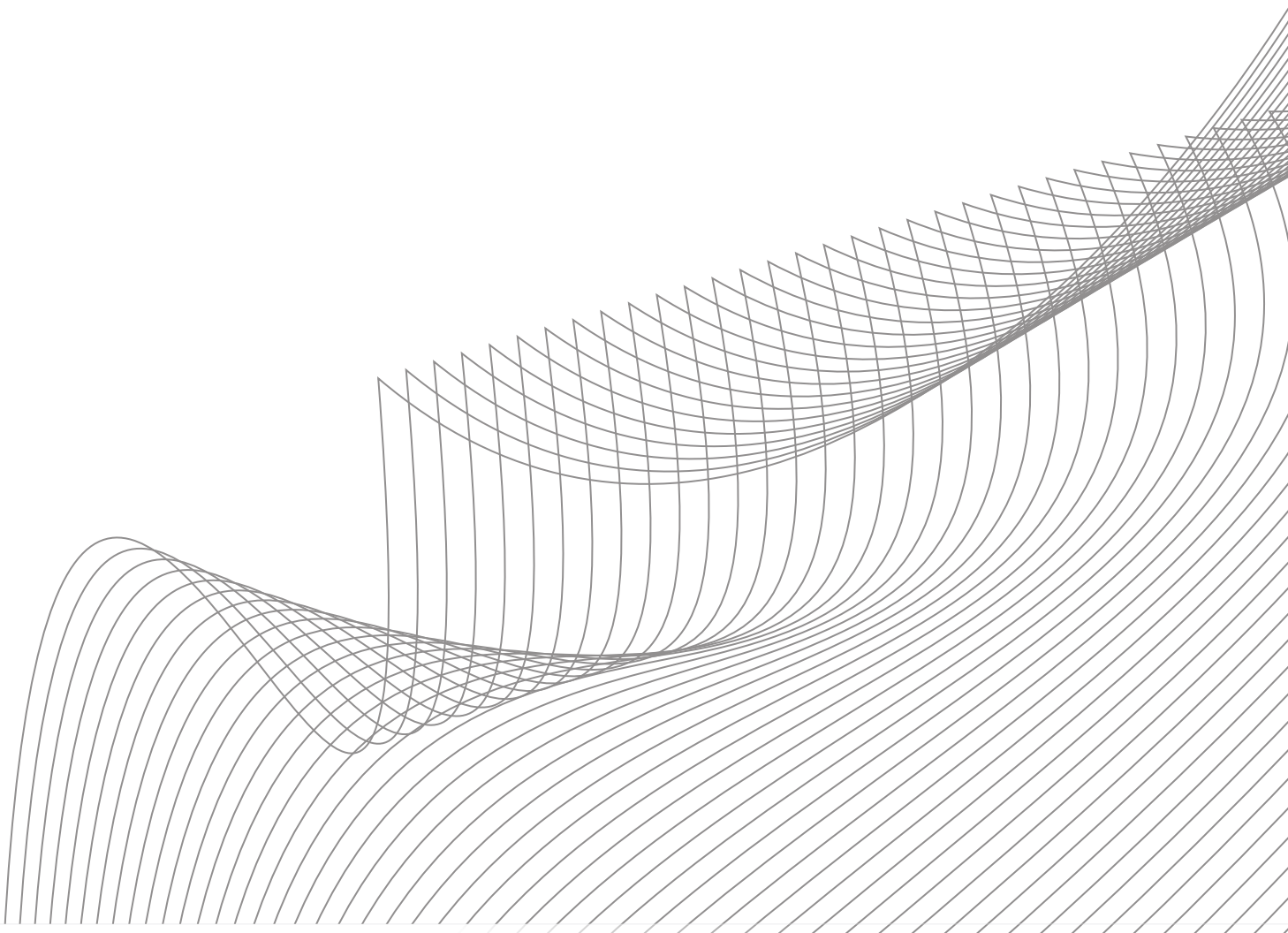

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Annual Report

Australian Meningococcal Surveillance Programme Annual Report, 2021

Monica M Lahra, CR Robert George and Tiffany R Hogan for the National Neisseria Network

Abstract

Invasive meningococcal disease (IMD) is a notifiable disease in Australia, with both probable and laboratory-confirmed cases of IMD reportable to the National Notifiable Diseases Surveillance System (NNDSS). In 2021, there were 74 notifications of IMD made, the lowest number recorded since 1991 when records began. Ninety-one percent of notified cases (67/74) were laboratory confirmed, with 69% of laboratory-confirmed cases (46/67) diagnosed by bacterial culture and 31% (21/67) by nucleic acid amplification testing. The serogroup was determined for 63/67 laboratory-confirmed cases (94%): serogroup B (MenB) accounted for 52% of infections (35/67); MenW for 22% (15/67); MenY for 19% (13/67); there were no infections attributed to MenC. Fine typing was available on 37/67 (55%) where the serogroup was determined. The greatest variability was in MenB, with nine different *porA* types represented. All MenW infections belonged to a single *porA* type (P1.5,2) with five different MLST sequence types represented: 11, 574, 1287, 12351, 13135; all belonged to clonal complex 11, the hypervirulent strain reported in recent outbreaks in Australia and overseas. All MenY were from the same *porA* antigen type, P1.5-1,10-1: MLST sequence type 1655; clonal complex 23.

Peaks occurred in children less than 5 years, reaching 24% (16/67) of reported cases, and in those aged 15–19 years reaching 16% (11/67) of reported cases. It is notable that 15% (10/67) of notifications were in persons aged 45–64 years, and an equivalent proportion (15%; 10/67) in adults aged 65 years and above. MenB infections predominated in persons aged 15–19 years (100%, 11/11), and comprised 56% (9/16) of infections in children aged less than 5 years. By contrast, Men W infections accounted for half (5/10) of IMD detections in infants less than 1 year, and 30% (3/10) of infections in persons aged 45–65 years. MenY infections predominated in adults aged 65 years and greater, resulting in 70% (7/10) of IMD in this age group.

All 46 IMD isolates had antimicrobial susceptibility testing performed. Minimum inhibitory concentration (MIC) values were categorised using Clinical Laboratory Standards Institute (CLSI) interpretative criteria: 13% (6/46) were defined as penicillin resistant (MIC value, ≥ 0.5 mg/L); 59% (27/46) had intermediate susceptibility to penicillin (MIC values, 0.125 and 0.25 mg/L) and 28% (13/46) were susceptible to penicillin. All isolates were susceptible to ceftriaxone and rifampicin. A single MenB IMD isolate from New South Wales exhibited ciprofloxacin resistance (MIC value, 0.125 mg/L).

Keywords: antimicrobial resistance; disease surveillance; invasive meningococcal disease; *Neisseria meningitidis*

Introduction

Australia's National Neisseria Network (NNN) was established in 1979 as a collaborative network of reference laboratories in each state and territory that contribute to the laboratory surveillance of the pathogenic *Neisseria*: *N. meningitidis* and *N. gonorrhoeae*. The NNN has coordinated laboratory data from cases of invasive meningococcal disease (IMD) for the Australian Meningococcal Surveillance Programme (AMSP) since 1994 and is supported by the Australian Government Department of Health and Aged Care and the jurisdictions.[1] The NNN laboratories supply data to supplement notification data from the National Notifiable Diseases Surveillance System (NNDSS), which includes cases of probable and laboratory confirmed IMD.

Notifications of IMD in Australia peaked in 2002 at 3.5 cases per 100,000 persons,[2] with the majority of disease at that time caused by MenB and MenC. In 2003 the introduction of the conjugate serogroup C meningococcal vaccine to the National Immunisation Program (NIP) was followed by significant and sustained reduction of the number of serogroup C IMD notifications, and of overall notifications to a nadir of 0.6 cases per 100,000 in 2013.[3,4] The IMD notification rate increased to 1.5 cases per 100,000 in 2017,[2] when MenACWY immunisation programmes were implemented across jurisdictions in targeted age groups. In 2018, a change in the NIP was effected, substituting monovalent MenC vaccine with the quadrivalent MenACWY vaccine. IMD notifications declined to 1.1 per 100,000 in 2018, and to 0.8 per 100,000 in 2019. In 2020, there were 0.4 cases per 100,000 recorded and a continued reduction in 2021 recorded 0.3 cases per 100,000, representing a reduction in disease rate beyond expected vaccine impact and likely attributable to the impact of public health measures implemented in the coronavirus disease 2019 (COVID-19) pandemic. IMD is a rare disease in Australia, but one of public health concern; continued monitoring of phenotypic and genotypic features of IMD strains is critical to plan and inform clinical management of cases, case clusters and outbreaks of IMD locally and nationally, and for informing and monitoring public health interventions.

Methods

Case confirmation of invasive meningococcal disease

Case confirmation is based on culture of *N. meningitidis*, or molecular diagnoses from a normally sterile site, defined as laboratory-definitive evidence of IMD according to national case definitions.[5] Information regarding the site of infection, age and sex of the patients is collated by the NNN for the AMSP.

Invasive *N. meningitidis* infections are categorised according to the site from which *N. meningitidis* was isolated, or from which meningococcal DNA was detected (blood, joint fluid, and 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.

Serogroup and genotyping of *Neisseria meningitidis*

Serogrouping is determination by detection of soluble polysaccharide antigens, with molecular testing playing an increasing role.[6] Genotyping of both isolates and DNA extracts is performed by sequencing products derived from amplification of the *porA* gene. Multi-locus sequence typing and clonal complex assignment is also reported by some jurisdictions.

Antimicrobial susceptibility testing

Meningococcal isolates are tested to determine their minimum inhibitory concentration (MIC) values for antibiotics used for treatment (ceftriaxone, penicillin) and for clearance of carriage (ciprofloxacin and rifampicin). In this report, antibiotic susceptibilities are reported according to the Clinical Laboratory Standards Institute's (CLSI) M100 guidelines;[7] this differs from historical reporting. By CLSI guidelines,

MIC breakpoints are categorised as follows, for penicillin: susceptible (MIC ≤ 0.06 mg/L); intermediate susceptibility (MIC 0.125–0.25 mg/L); and resistant (MIC ≥ 0.5 mg/L); for ceftriaxone: susceptible (MIC ≤ 0.125 mg/L); for ciprofloxacin: susceptible (MIC ≤ 0.03 mg/L), intermediate susceptibility (MIC 0.06 mg/L) and resistant (MIC ≥ 0.125 mg/L); and for rifampicin: susceptible (MIC ≤ 0.5 mg/L), intermediate susceptibility (MIC 1.0 mg/L) and resistant (MIC ≥ 2 mg/L).

Results

In 2021, there were 74 IMD cases notified to the NNDSS, of which 67 were laboratory confirmed.[2] Laboratory data were available to the AMSP for all 67 laboratory-confirmed IMD cases, as shown in Figure 1. In 2021, there was a continued decrease in notifications of IMD across all jurisdictions excluding South Australia, which reported an increase in notifications from 2020. In 2021, the peak incidence of IMD occurred in autumn through early winter (1 April to 30 June); and in spring through early summer (1 October to 31 December), as shown in Table 1.

Laboratory diagnosis of IMD

In 2021, laboratory diagnosis of IMD was by culture in 69% of laboratory-confirmed cases (46/67) and by molecular testing (nucleic acid amplification testing) in 31% (21/67), as shown in Table 2. There were 11 diagnoses of meningitis, 53 diagnoses of bacteraemia, and three IMD diagnoses from joint fluid aspirates.

Notifications by jurisdiction

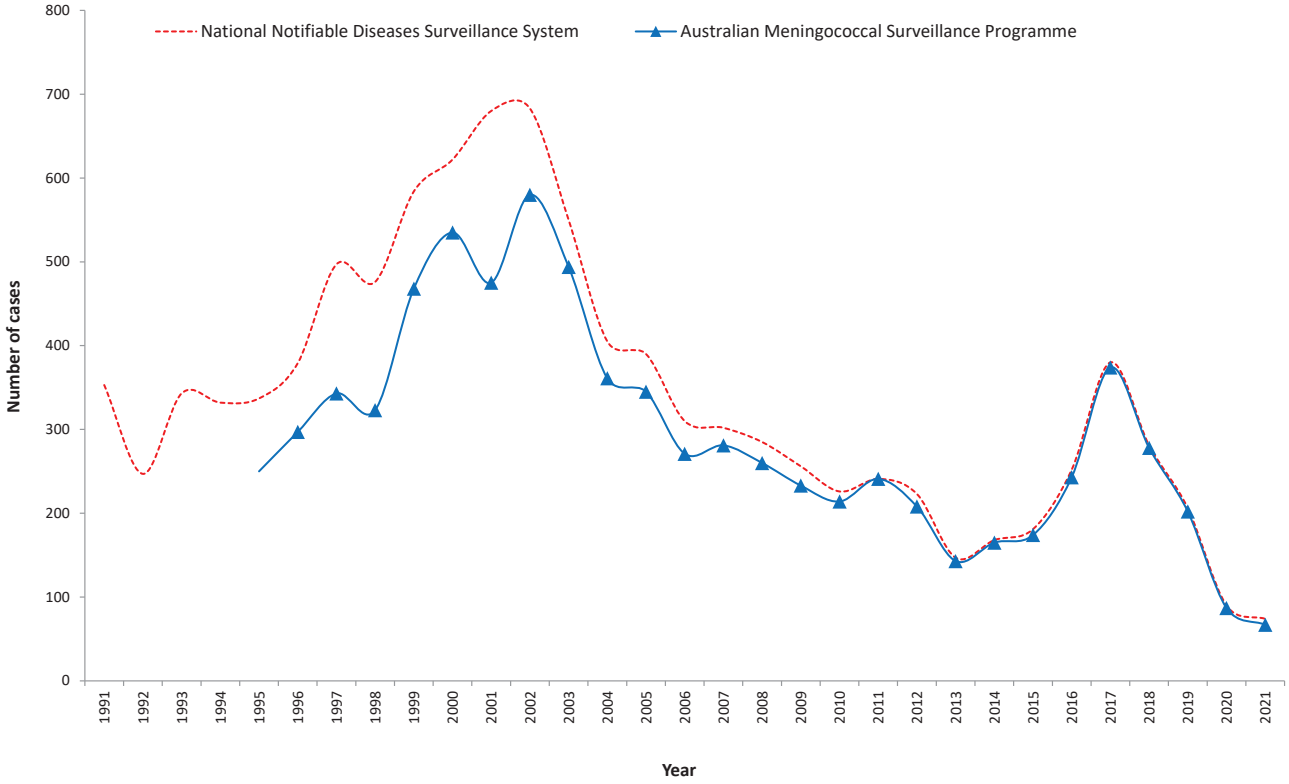
Across the jurisdictions in 2021, New South Wales reported the highest number of IMD notifications (27%; 18/67), an increased percentage of the national total but a reduction in this state's notifications from the 2020 values (24%; 21/87). Queensland had the second-highest number of notifications (21%, 14/67), a reduction from 27/87 notifications (31%) in 2020. South Australia was the only jurisdiction recording a rise in IMD cases in 2021, increasing from 5/87 cases (6%) in 2020 to 12/67 cases (18%) in 2021. The number of cases from each jurisdiction for 2021 is shown in Table 3.

MenB accounted for 52% of IMD notifications in 2021 as shown in Table 3. Over the years 2006–2012, the proportion of IMD attributable to MenB ranged within 84–88% nationwide. In 2013–2014, rates on MenB were lower (75–80%), falling to 64% in 2015, and then to 36% in 2016–2017. There was a marked increase in attributable proportion in 2018 to 44%, reaching 50% in 2019 and then 62% in 2020. In 2021, the proportion has decreased again, to 52% of IMD reported as shown in Figure 2.

MenW and MenY respectively accounted for 22% and 19% of IMD nationally in 2021, as shown in Table 3. The rise in IMD notifications in Australia since 2014 coincided with increases in numbers of infections of both MenW and MenY, as shown in Figure 1 and Figure 2. Prior to 2015, the proportion of cases of IMD caused by MenW was low, ranging within 1.1–4.8% in 1997–2012, then increasing to 8.4–9.7% in 2013–2014. By 2015, the proportion of IMD cases caused by MenW increased to 21%, reaching 44% in 2016, before declining to 36–38% in 2017–2018 and then to 18% in 2020. In 2021, the MenW proportion has risen again, to 22% (Figure 2). The proportion of cases of IMD caused by MenY prior to 2015 ranged within 1.3–4.6% in the period 1997–2010. Rates increased in 2011–2014 to 6.2–11%; then to 13% in 2015; to 17% in 2016; and then to 20% in 2017. The proportion of MenY was lower in 2018 (16%), increasing to 21% in 2019. In 2020, the proportion of MenY decreased to 16%, and in 2021 has increased again to 19% as shown in Figure 2.

There was no MenC IMD reported from Australia in 2021. Very few or no cases of any serogroup of IMD were reported from the Australian Capital Territory (0 cases); the Northern Territory (1 case); and Tasmania (2 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, 1991–2021[a]



a Source: National Notifiable Diseases Surveillance System. Data extracted 4 May 2022.

Table 1: Laboratory-confirmed cases of invasive meningococcal disease, Australia, 2021

IMD serogroup 2021[a]	1 January – 31 March	1 April – 30 June	1 July – 30 September	1 October– 31 December	2021 total
B	8	11	4	12	35
C	0	0	0	0	0
Y	4	5	2	2	13
W	2	4	4	5	15
ND	2	2	0	0	4
Total	**16**	**22**	**10**	**19**	**67**

a ND: not determined.

IMD age and serogroup distribution

In 2021, IMD was reported in all age groups. Disease peaks occurred in children less than 5 years at 24% of cases (16/67) and in persons aged 15 to 19 years comprising 16% of cases (11/67). It is notable that 15% of notifications (10/67) were in adults aged 45–64 years, with an equivalent proportion in adults 65 and above years, as shown in Table 4. Serogrouping was determined for 63/67 cases of IMD (94%), with MenB accounting for 52%, MenW for 22%,

Table 2: Number of laboratory-confirmed cases of invasive meningococcal disease, Australia, 2021, by specimen type and method of confirmation

Specimen	Bacterial culture	Nucleic acid amplification test	Total
Blood	42	11	53
CSF +/- blood	3	8	11
Joint aspirate	1	2	3
Total	**46**	**21**	**67**

Table 3: Number of laboratory-confirmed cases of invasive meningococcal disease, Australia, 2021, by state or territory, and by serogroup

State/territory	Serogroup					
	B	C	Y	W	ND[a]	Total
Australian Capital Territory	0	0	0	0	0	0
New South Wales	12	0	3	2	1	18
Northern Territory	0	0	0	1	0	1
Queensland	5	0	6	3	0	14
South Australia	6	0	0	6	0	12
Tasmania	2	0	0	0	0	2
Victoria	7	0	2	0	1	10
Western Australia	3	0	2	3	2	10
Australia	**35**	**0**	**13**	**15**	**4**	**67**
%	52.2	0.0	19.4	22.4	6.0	100%

a ND: not determined.

and MenY for 19% of national notifications, as shown in Table 3. No notifications of MenC IMD occurred nationwide.

By age group, 24% (16/67) of IMD notifications in 2021 were in children less than 5 years, a decrease from 29% in 2020. In this age group, 56% of IMD (9/16) was attributable to MenB, and 31% (5/16) to MenW (all reported from infants less than 1 year of age), as is shown in Table 4 and Figure 3.

Overall, 17% of IMD (11/67) was reported in teenagers aged 15–19 years, and all such cases (100%; 11/11) were MenB disease. Further, 83% (5/6) of IMD in adults aged 20–24 years was attributable to MenB, as shown in Table 4 and Figure 3.

Adults aged 45–64 years accounted for 15% of national IMD notifications (10/67), comprising 40% MenB (4/10); 30% MenW (3/10); and 30% MenY (3/10) reported, as shown in Table 4 and Figure 3.

In adults aged 65 years and greater, IMD accounted for a further 15% of national notifications (10/67); MenY represented 70% (7/10) of these notifications, which is a higher proportion than reported in 2020 (58%; 7/12), also shown in Table 4 and Figure 3.

Figure 2: Proportion of serogroups of laboratory-confirmed invasive meningococcal disease, Australia, 2000 – 2021 by year

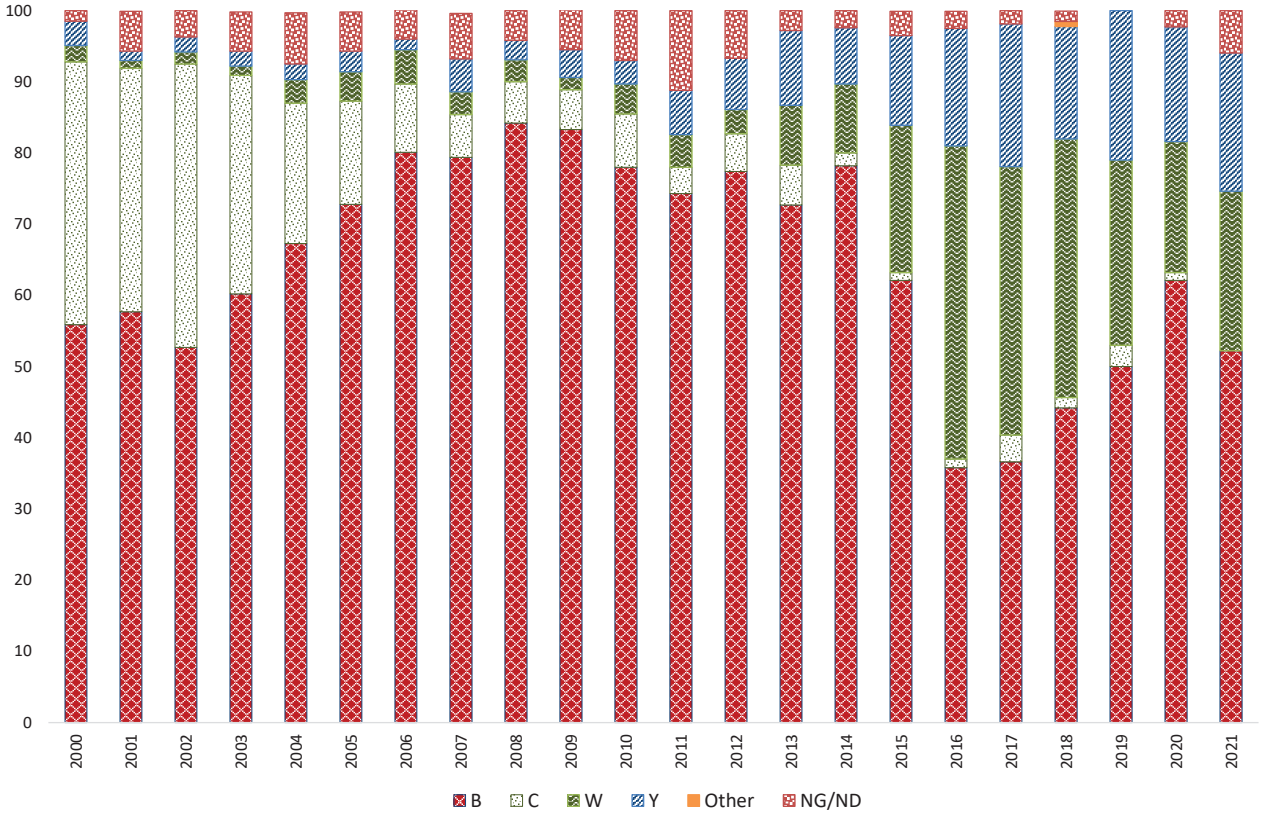


Table 4: Laboratory-confirmed cases of invasive meningococcal disease (IMD), Australia, 2021, by age and serogroup, and the proportion of IMD attributable to MenB

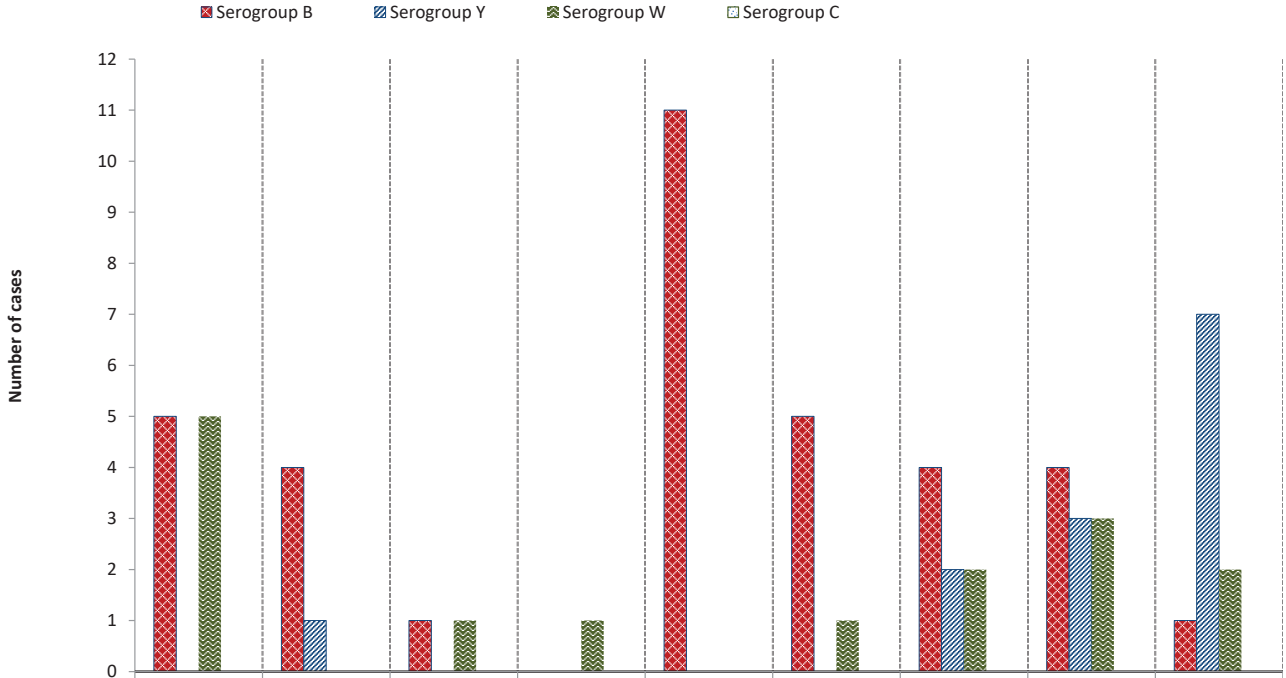
Serogroup	Age group (years)									Total
	< 1	1–4	5–9	10–14	15–19	20–24	25–44	45–64	65+	
B	5	4	1	0	11	5	4	4	1	35
C	0	0	0	0	0	0	0	0	0	0
Y	0	1	0	0	0	0	2	3	7	13
W	5	0	1	1	0	1	2	3	2	15
ND	0	1	1	2	0	0	0	0	0	4
Total	**10**	**6**	**3**	**3**	**11**	**6**	**8**	**10**	**10**	**67**
%B within age group	50%	67%	33%	0%	100%	83%	50%	40%	10%	52%

IMD and genotyping

Finetyping on MenB IMD cases was performed on 18 of 35 cases; this serogroup showed the greatest variability, with nine *porA* types represented, and with two *porA* types predominating: P1.22,14 (6/18; 33%) and P1.7-2,4 (4/18; 22%). The *porA* type P1.7,16-26, which was predominant in previous years, accounted for only one MenB notification in 2021, as shown in Figure 4 and Table 5.

Of the 15 MenW that had finetyping performed, ten were determined to be from *por*A type P1.5,2 as shown in Figure 4 and Table 5. However, five different MLST sequence types were represented: 11, 574, 1287, 12351, and

Figure 3: Number of serogroup B, C, Y and W cases of laboratory-confirmed invasive meningococcal disease, Australia, 2021, by age



	<1	1-4y	5-9y	10-14y	15-19y	20-24y	25-44y	45-64y	65+y
Serogroup B	5	4	1	0	11	5	4	4	1
Serogroup Y	0	1	0	0	0	0	2	3	7
Serogroup W	5	0	1	1	0	1	2	3	2
Serogroup C	0	0	0	0	0	0	0	0	0

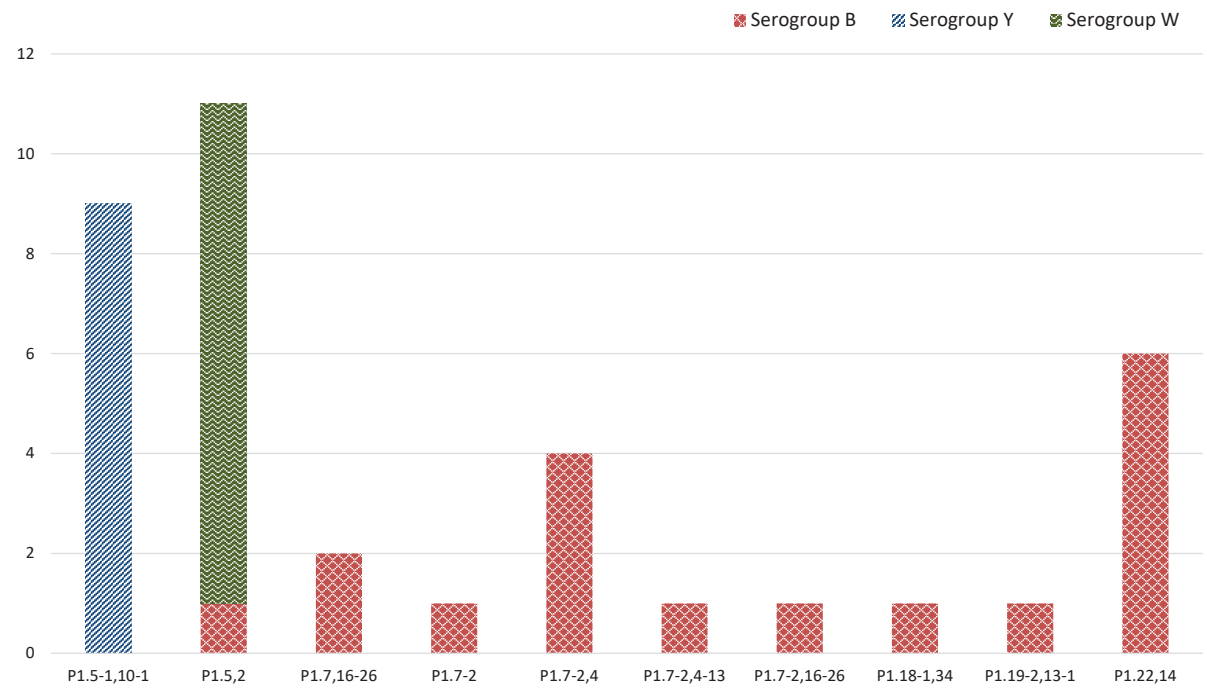
13135, with all belonging to the same clonal complex 11. The *porA* type P1.5,2 has been the predominant genotype in recent years, from the clonal complex 11, which is the same strain type as the hypervirulent serogroup W strain also reported in the United Kingdom and South America since 2009.[9,10]

Nine of the 13 MenY that had finetyping performed were determined to be from a single *porA* type, P1.5-1,10-1 (shown in Figure 4 and Table 5) and belonged to MLST sequence type 1655 and clonal complex 23. The *porA* type, P1.5-1,10-1 has been the predominant genotype circulating in Australia since 2014, when the increase in serogroup Y IMD was first noted in Australia.

Antimicrobial susceptibility testing

Isolates of *N. meningitidis* are tested against both treatment (ceftriaxone and penicillin) and clearance antibiotics (rifampicin and ciprofloxacin). In 2021, the national antimicrobial susceptibility testing (AST) data are reported according to the CLSI interpretative guidelines, changed from historical reporting (1997 to 2020). Sixty-nine percent of laboratory confirmed IMD (46/67) had *N. meningitidis* cultured, permitting antimicrobial susceptibility testing to be performed by the NNN laboratories. Ceftriaxone susceptibility testing was performed on all 46 isolates in 2021 and all were susceptible. With regards to penicillin, the distribution of penicillin MIC values is shown in Table 6. Twenty-eight percent of IMD isolates (13/46) were susceptible to penicillin (MIC ≤ 0.06 mg/L); 59% (27/46) had intermediate susceptibility to penicillin (MIC 0.125–0.25 mg/L); and 13% (6/46) were resistant to penicillin (MIC, ≥ 0.5 mg/L), as shown in Table 6. Of these isolates regarded as penicillin resistant, 5/6 were MenW IMD. In recent years, MenW has demonstrated higher penicillin MIC values and higher proportions of resistance. Regarding the clearance antibiotics for IMD,

Figure 4: The number of *porA* types represented in serogroup B, W and Y invasive meningococcal disease notifications in Australia in 2021



one isolate was resistant to ciprofloxacin (MIC 0.125 mg/L) and all isolates were susceptible to rifampicin.

Discussion

In 2021, ninety-one percent of IMD notifications in Australia (67/74) were laboratory confirmed,[3] a lower proportion than in previous years. Notably in 2021, there was an overall decrease in notifications of IMD by 23% when compared with 2020, coincident with widespread public health initiatives designed to reduce COVID-19 transmission.[11] These included physical distancing; hand hygiene and cough etiquette; use of masks; and restrictions to travel and to access to aged care facilities and hospitals. Of note, during January–March 2020, prior to the introduction of COVID-19-related restrictions, there were a total of 31 cases of IMD, whereas for the equivalent period in 2021 there were 18 cases.[11] Notifications of influenza were also reduced from 313,465 cases in 2019 to 748 cases in 2021.[11] This finding is of key relevance, as antecedent infection with influenza is a risk factor for IMD.

In Australia in 2016–2017, increased notifications of MenW and MenY IMD prompted time-limited, jurisdictional MenACWY vaccination programs for target age groups.[4,12] In July 2018, the National Immunisation Program (NIP) replaced MenC vaccine at 12 months of age with a quadrivalent ACWY vaccine. There followed a decrease in both notifications and proportion of MenW and MenY disease, accompanied by a gradual increase in the proportion of disease caused by MenB (from 44% to 62% in 2018–2020; but lower in 2021 to 52% of IMD). Prior to the introduction of the MenC vaccine in 2003 in Australia, the proportion of MenB IMD was 84–88% in the years 2006–2012, and then declining. Notifications of IMD subsequently increased with the emergence of MenW and MenY disease since 2014 in Australia.[4]

With regards to serogroup infections by age group, MenB accounted exclusively for IMD in 15–19 year olds and for 83% of IMD (5/6 cases) in 20–24 year olds. A recombinant multicomponent meningococcal B vaccine has been available in Australia since 2014,[13] although this vaccine is not currently on the NIP. MenW caused 22% (15/67) of IMD in Australia, an

Table 5: Distribution of *porA* genotypes in laboratory-confirmed cases of invasive meningococcal disease, Australia, 2021, by state or territory

2021 AMSP		Number per serogroup per state / territory								
Serogroup[a]	*PorA* genotype	ACT	NSW	NT	Qld	SA	Tas	Vic	WA	Total
Y	P1.5-1,10-1	0	0	0	5	0	0	2	2	**9**
B	P1.5,2	0	0	0	0	0	1	0	0	**1**
W	P1.5,2	0	1	0	3	4	0	0	2	**10**
B	P1.7,16-26	0	0	0	0	0	0	1	1	**2**
B	P1.7-2	0	0	0	0	0	0	1	0	**1**
B	P1.7-2,4	0	0	0	2	2	0	0	0	**4**
B	P1.7-2,4-13	0	0	0	0	0	0	1	0	**1**
B	P1.7-2,16-26	0	0	0	0	0	0	1	0	**1**
B	P1.18-1,34	0	0	0	0	0	0	0	1	**1**
NT	P1.18-4,25-15	0	0	0	0	0	0	0	1	**1**
B	P1.19-2,13-1	0	0	0	0	0	0	0	1	**1**
B	P1.22,14	0	0	0	2	0	1	3	0	**6**
Total		**0**	**1**	**0**	**12**	**6**	**2**	**9**	**8**	**38**

a NT: non typeable.

Table 6: Penicillin MIC distribution of laboratory-confirmed invasive meningococcal disease isolates, Australia, 2021

Penicillin MIC distribution									
MIC mg/L	≤ 0.032	0.064	0.125	0.25	0.5	1	2	≥4	Total
Number of isolates	5	8	8	19	6	0	0	0	46
%	11%	17%	17%	41%	13%	0%	0%	0%	100%

increase from 18% in 2020, but remained lower than in 2019 (26%). Of these MenW IMD cases, 25% (5/20) occurred in those aged 45 years and older, but of growing concern is that MenW accounted for 50% (5/10) of IMD notifications in infants less than one year old. In the previous year, by contrast, MenW IMD was absent in children under five years of age, and thus continued surveillance of IMD in this age group is required. In 2021, MenY accounted for 19% of IMD nationally (13/67) and predominantly affected older age groups, accounting for 30% of notifications (3/10) in 45–64 year olds and for 70% of notifications (7/10) in those aged 65 years and older.

With regards to prevailing IMD serogroups and genotypes, the number and proportion of IMD cases caused by MenB in 2021 (35/67; 52%) was less than in 2020 (54/87; 62%); New South Wales reported the largest number of MenB notifications. Fine typing of MenB notifications exhibited nine different *porA* types from the 18 typed cases. The predominant MenB *porA* genotype in Australia was P1.22,14 (6/18), followed by genotype P1.7-2,4 (4/18), marking a change from recent years where the previous dominant MenB genotype, P1.7,16-26, accounted for only 1/18 of MenB IMD in 2021. The predominant circulating strain of MenW continues to be *porA* genotype P1.5,2 and MLST sequence type 11.

This same MenW strain previously emerged in the United Kingdom (UK) and South America in 2009,[9,10] and spread to account for 25% of IMD in the UK in 2014–2015 and 59% of all cases in Chile in 2012. MenW ST11 is hypervirulent and associated with atypical clinical presentations, more severe disease, and a higher case fatality rate.[10] The initial increase in MenW overseas and in Australia was seen in older adults, but was subsequently reported in all age groups, particularly in adolescents and infants.[14] The predominant MenY genotype since 2014 continues to be P1.5-1,10-1, whereas previously MenY genotype distribution had been more heterogeneous.[15]

Antimicrobial susceptibility testing of IMD isolates in 2021, as categorised by the CLSI interpretative criteria, detected 13% (6/67) penicillin resistance (MIC values, ≥ 0.5 mg/L) in clinical isolates. The incidence of penicillin resistance in *N. meningitidis* in Australia is greater than previous rates due to the change from historical reporting criteria. All IMD isolates tested in 2021 were susceptible to ceftriaxone and rifampicin, however there was one NSW isolate resistant to ciprofloxacin (MIC 0.125 mg/L). Ciprofloxacin resistance has been reported globally but remains an uncommon finding, except in China where the rapid clonal expansion of ciprofloxacin-resistant *N. meningitidis* led to its withdrawal as the primary clearance agent for IMD contacts.[16]

There has been an ongoing decrease in IMD notifications from 1.5 cases per 100,000 in 2017; to 1.1 per 100,000 in 2018; 0.8 cases per 100,000 in 2019; 0.4 cases per 100,000 in 2020; and 0.3 cases per 100,000 in 2021. The year 2021 has also seen an increase in the proportion of isolates attributable to MenW and MenY. This was coincident both with widespread public health initiatives designed to reduce COVID-19 transmission and following changes in the NIP. The NNN is continuing to lead further investigations with the Australian Government Department of Health and Aged Care and is closely monitoring the phenotypic and genotypic features of *N. meningitidis* causing IMD in Australia. Additional investigations by the NNN, including whole genome sequencing of IMD isolates, are in progress to enhance IMD surveillance in Australia. The AMSP data are used for informing treatment guidelines and disease prevention strategies; and to monitor the effect of interventions.

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