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Antimicrobial susceptibility of invasive *Neisseria meningitidis,* 2023

The purpose of this report is to outline the laboratory findings for meningococcal isolates received at ESR in 2023, to inform clinical and public health interventions to treat and prevent invasive meningococcal disease.

The antimicrobial susceptibility of 32 viable meningococcal isolates received at ESR from cases of invasive disease were tested. Ceftriaxone, ciprofloxacin, penicillin and rifampicin minimum inhibitory concentrations (MICs) were determined by Etest on Mueller-Hinton agar + 5% sheep blood. MICs were interpreted according to Clinical and Laboratory Standards Institute (CLSI) breakpoints.[1] Meningococci with penicillin MICs ≥0.5 mg/L were categorised as resistant while those with MICs of 0.12 and 0.25 mg/L were categorised as intermediate. Group, PorA and strain data was generated by the Invasive Pathogens Laboratory, ESR.

The 32 meningococcal isolates tested for susceptibility included 21 group B isolates, five group Y isolates, three group W isolates, one group C isolate and two non-groupable isolates. The most common group B strains in 2023 were the B:P1.7-12,14 strain[a], with nine isolates identified, and the B:P1.7-2,4 strain, with five isolates identified.

All 2023 isolates were susceptible to ceftriaxone and rifampicin (Table 1). One 2023 group C isolate was ciprofloxacin resistant.

Table 1. Antimicrobial susceptibility, MIC range and MIC_{90} of *N. meningitidis* from invasive disease cases, 2023

Antimicrobial	Percent (number)			MIC range (mg/L)	MIC_{90} (mg/L)
	Susceptible	Intermediate	Resistant		
Penicillin#	31.3 (10)	68.8 (22)	0.0 (0)	0.03-0.25	0.25
Ciprofloxacin	96.9 (31)	0.0 (0)	3.1 (1)	0.002-0.12	0.008
Ceftriaxone	100 (32)	-^	-^	<0.002-0.008	0.004
Rifampicin	100 (32)	0.0 (0)	0.0 (0)	0.008-0.25	0.12

penicillin susceptible, MIC ≤0.06 mg/L; intermediate, MIC 0.12-0.25 mg/L; resistant, MIC ≥0.5 mg/L
^ there is no intermediate or resistant category for ceftriaxone

Testing found that 68.8% (22/32) of isolates were penicillin non-susceptible (i.e. penicillin intermediate or resistant with MICs ≥0.12 mg/L). However, no isolates were categorised as penicillin resistant (i.e. MICs ≥0.5 mg/L) (Table 1).

a The B:P.1.7-12,14 strain belongs to multilocus sequence type clonal complex 1572.

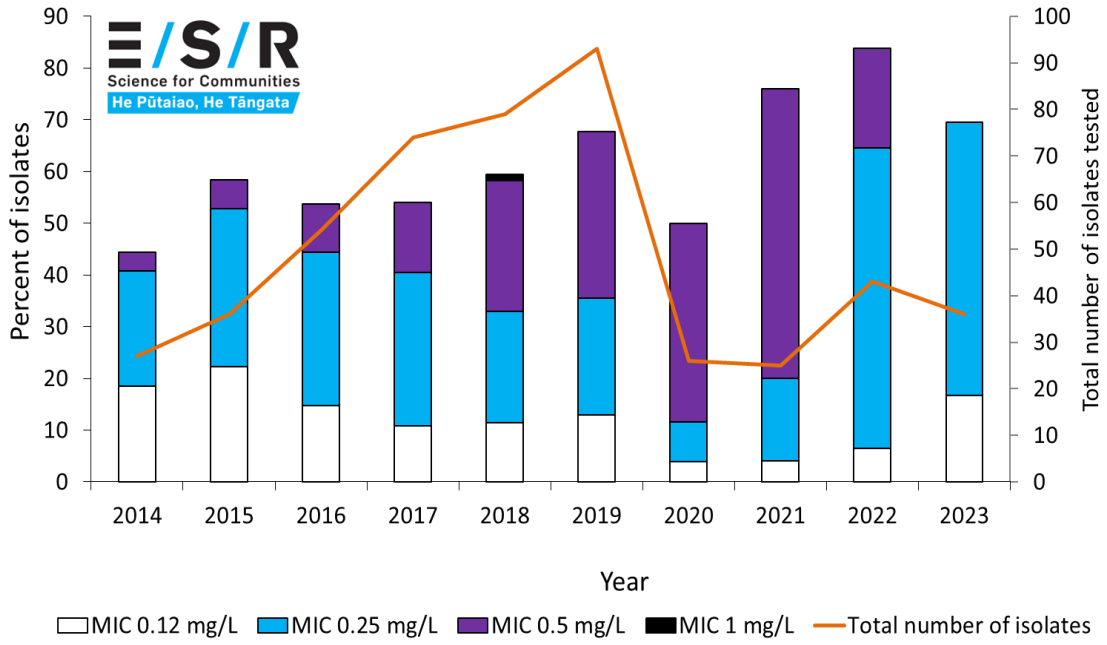
The prevalence of penicillin non-susceptibility in each of the meningococcal groups was:

- 71.4% (15/21) group B isolates, including
  - 100.0% (9/9) of the B:P1.7-12,14 strain
  - none (0/5) of the B:P1.7-2,4 strain
- 60.0% (3/5) group Y isolates
- 33.3% (1/3) group W isolates
- 100.0% (2/2) non-groupable isolates
- 100.0% (1/1) group C isolates

Please note that isolates categorised as penicillin intermediate by CLSI (i.e. penicillin MIC of 0.12 and 0.25 mg/L) would be categorised as penicillin susceptible using the European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints.[2] Isolates with a penicillin MIC ≥0.5 mg/L would be classified as resistant using both CLSI and EUCAST breakpoints.

Penicillin non-susceptibility among New Zealand meningococci continues to increase, although fluctuations have been observed due to low case numbers. The percentage of penicillin-resistant isolates (MIC ≥0.5 mg/L) increased between 2014 and 2021, to a high of 56.0%, but decreased in 2022 to 14.0% and reduced further to 0.0% in 2023. Prior to 2020 the incidence of meningococcal disease,[3] as well as the percentage of penicillin resistant isolates, was increasing (Figure 1). This was driven by group W meningococci (Figure 2), many of which were penicillin resistant.[4,5] The B:P1.7-12.14 strain is now the dominant strain in New Zealand,[3] which is more likely to be penicillin intermediate, resulting in the overall percentage of isolates with penicillin resistance decreasing.

Figure 1. Penicillin non-susceptible *N. meningitidis* from invasive disease, 2014-2023



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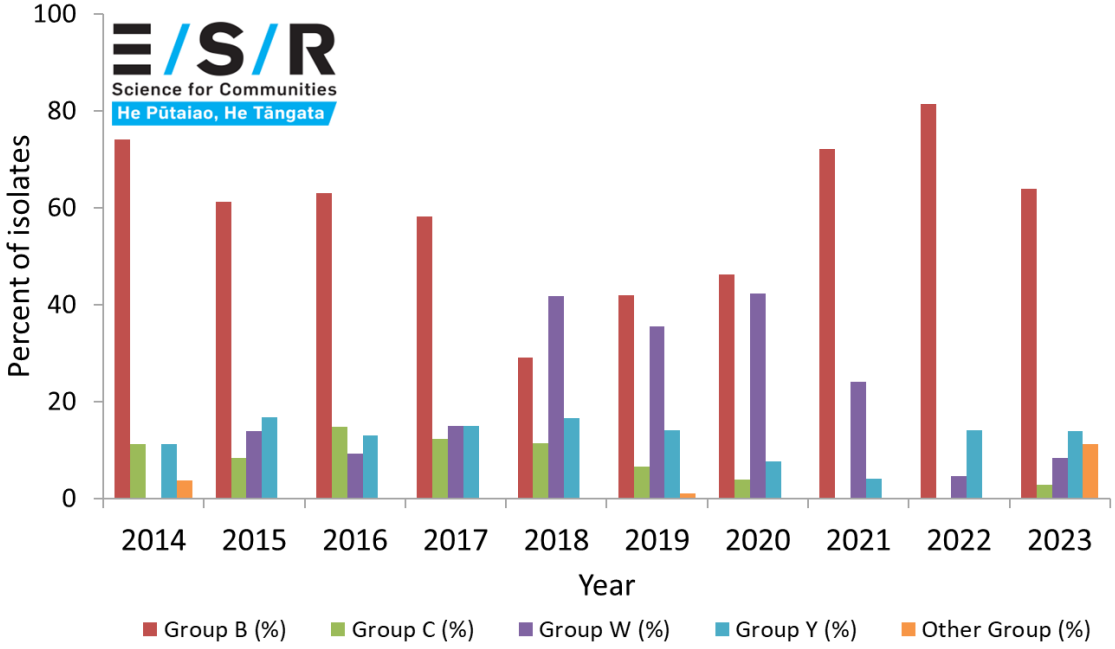
Five *penA* mutations have been shown to have a high correlation with reduced penicillin susceptibility.[6] Our data confirmed the correlation between elevated penicillin MICs and the presence of these *penA* mutations. All isolates with a penicillin MIC of 0.12 mg/L or 0.25 mg/L had a mutation in the *penA* gene, reported to confer resistance to penicillin. All isolates with wildtype *penA* had a penicillin MIC ≤ 0.06 mg/L.

Figure 2. Distribution by group for isolates of *N. meningitidis* from invasive disease, 2014-2023. Adapted from data produced by the Invasive Pathogens Laboratory, ESR[3]



In 2023 most cases of meningococcal disease were found in the North Island (25/32, 78.1%). Of the 22 penicillin intermediate isolates identified, 16 (72.7%) were from cases in the North Island and six (27.3%) were from cases in the South Island.

Rifampicin resistance is rare among meningococci from invasive disease in New Zealand. In total, seven rifampicin-resistant isolates have been identified: one group C (C:2a:P1.5-1,10-1) isolate in 2011, one group B (B:4:P1.19,15) isolate and one group C (C:2a:P1.5-1,10-8) isolate in 2009, one group B (B:4:P1.4) isolate in 2003, one group C (C:2b:P1.2) isolate in 1997, one group B (B:15:P1.7,16) isolate in 1992, and one group A isolate in 1986.

Ciprofloxacin resistance is also rare among meningococci from invasive disease in New Zealand. Four ciprofloxacin-resistant isolates have been identified: one group C isolate in 2010 (C:P1.20,23-7), 2017 (C:P1.5,2), and 2023 (C:P1.5,2), as well as a group X isolate in 2018. A mutation in the *gyrA* gene was found in the 2023 isolate, that is likely to explain the ciprofloxacin resistance found in this isolate. The USA has reported a rise

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in ciprofloxacin resistance in *N. meningitidis*,[7] highlighting the need for vigilance in New Zealand.

No resistance to ceftriaxone has ever been identified among meningococci isolated from cases of invasive disease in New Zealand.

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1 Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. 33nd ed. Wayne, USA: CLSI; 2023. CLSI supplement M100.

2 European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters. Version 13.1; 2023 June. Available from: https://www.eucast.org/

3 ESR, Invasive meningococcal disease report January – December 2023. Accessed from: www.esr.cri.nz

4 ESR, Antimicrobial susceptibility of invasive meningococcal disease, 2018. Accessed from: www.esr.cri.nz

5 ESR, Antimicrobial susceptibility of invasive meningococcal disease, 2019. Accessed from: www.esr.cri.nz.

6 Thulin S, Olcén P, Fredlund H, Unemo M. Total variation in the *penA* gene of *Neisseria meningitidis:* correlation between susceptibility to beta-lactam antibiotics and *penA* gene heterogeneity. Antimicrob Agents Chemother. 2006 Oct;50(10):3317-24.

7 Berry I, Rubis AB, Howie RL, Sharma S, Marasini D, Marjuki H, Crowe S, McNamara LA. Selection of antibiotics as prophylaxis for close contacts of patients with meningococcal disease in areas with ciprofloxacin resistance - United States, 2024. MMWR Morb Mortal Wkly Rep. 2024 Feb 8;73(5):99-103. doi: 10.15585/mmwr.mm7305a2. PMID: 38329923; PMCID: PMC10861203.

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