Science for Communities
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Antimicrobial susceptibility of invasive *Neisseria meningitidis,* 2021

The antimicrobial susceptibility of 25 viable meningococcal isolates received at ESR from cases of invasive disease in 2021 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.

All meningococcal isolates were characterised using whole genome sequencing (WGS). Genomic DNA was extracted using the Roche High Pure PCR template preparation kit, the DNA library was created using the Nextera XT DNA preparation kit (Illumina), and sequencing was performed using Illumina technology. WGS data was analysed using an in-house developed pipeline linking together open-source established packages and in-house scripts. AMRFinderPlus (v 3.10.24) was used to identify acquired genes and point mutations that may confer antimicrobial resistance from genomic assemblies generated using SKESA (v2.3.0).

The 25 meningococcal isolates tested for susceptibility included 18 group B isolates (including five NZ B:P1.7-2,4 epidemic strain), 6 group W isolates and 1 group Y isolate.

56.0% (14/25) of isolates were categorised as penicillin resistant (ie, MICs ≥0.5 mg/L) (Table 1). The prevalence of penicillin resistance in each of the meningococcal groups was:

- 44.4% (8/18) group B isolates, of which none belonged to the NZ B:P1.4 epidemic strain
- 83.3% (5/6) group W isolates
- 100.0% (1/1) group Y isolates

76.0% (19/25) of isolates were penicillin non-susceptible (i.e. penicillin intermediate or resistant, with MICs ≥0.12 mg/L). The prevalence of penicillin non-susceptibility in each of the meningococcal groups was:

- 72.2% (13/18) group B isolates, of which one belonged to the NZ B:P1.4 epidemic strain
- 83.3% (5/6) group W isolates
- 100.0% (1/1) group Y isolates

All isolates with a penicillin MIC >0.12 mg/L had at least one of the five *penA* mutations that have a high correlation with reduced penicillin susceptibility.[2] Three isolates with a penicillin MIC = 0.12 mg/L also had at least one of these *penA* mutations, although one

further isolate with this MIC did not have any *penA* mutations. No isolates with an MIC <0.12 mg/L had any mutations associated with reduced penicillin susceptibility.

In 2021 most cases of meningococcal disease were found in the North Island (16/25, 64.0%). Of the 14 penicillin resistant isolates identified in New Zealand in 2021, 12 were from cases in the North Island and two were from cases in the South Island. Of the 19 penicillin non-susceptible isolates, 15 were from cases in the North Island. There was one death, in the case with a group Y meningococcus.

All 2021 isolates were susceptible to ciprofloxacin, ceftriaxone and rifampicin (Table 1).

Table 1. Antimicrobial susceptibility, MIC range and MIC_{90} of *N. meningitidis* from invasive disease cases, 2021

Antimicrobial	Percent (number)			MIC range (mg/L)	MIC_{90} (mg/L)
	Susceptible	Intermediate	Resistant		
penicillin[1]	24.0 (6)	20.0 (5)	56.0 (14)	0.06-0.5	0.5
ceftriaxone	100 (25)	-[2]	0.0 (0)	<0.002-0.004	0.002
rifampicin	100 (25)	0.0 (0)	0.0 (0)	0.008-0.25	0.25
ciprofloxacin	100 (25)	0.0 (0)	0.0 (0)	0.004-0.008	0.008

[1] penicillin susceptible, MIC ≤0.06 mg/L; intermediate, MIC 0.12-0.25 mg/L; resistant, MIC ≥0.5 mg/L

[2] there is no intermediate or resistant category for ceftriaxone

Over the last 10 years the proportion of isolates non-susceptible to penicillin has been increasing, except during 2020 where the proportion of penicillin non-susceptible isolates decreased (Figure 1). However, in 2020 there were also fewer cases, likely an effect of the public health response to the SARS-CoV-2 pandemic. The proportion of penicillin resistant isolates (MIC ≥0.5 mg/L) continued to increase in both 2020 and 2021.

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. In total three ciprofloxacin-resistant isolates have been identified: group C meningococci in 2010 (C:ns:P1.20,23-7) and 2017 (C:P1.5,2) as well as a group X meningococcus in 2018.

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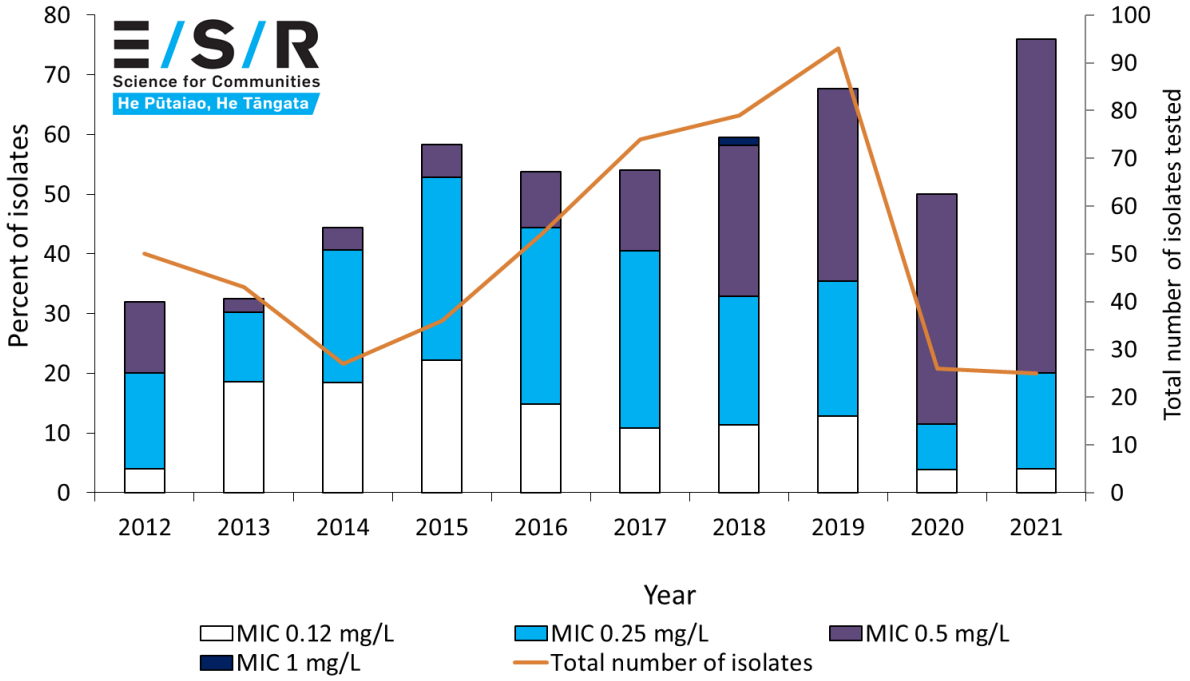
No resistance to ceftriaxone has ever been identified among meningococci isolated from cases of invasive disease in New Zealand.

Figure 1. Penicillin-non-susceptible *N. meningitidis* from invasive disease, 2012-2021



[1] Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. 31st ed. Wayne, USA: CLSI; 2021. CLSI supplement M100.

[2] 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.

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