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Australian Gonococcal Surveillance Programme Annual Report, 2019

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Australian Gonococcal Surveillance Programme Annual Report, 2019

Monica M Lahra, Masoud Shoushtari, CR Robert George, Benjamin H Armstrong and Tiffany R Hogan for the National Neisseria Network, Australia

Abstract

The Australian Gonococcal Surveillance Programme (AGSP) has continuously monitored antimicrobial resistance in clinical isolates of *Neisseria gonorrhoeae* since 1981. In 2019, a total of 9,668 clinical isolates of gonococci from the public and private sector in all jurisdictions were tested for *in vitro* antimicrobial susceptibility by standardised methods.

The current treatment recommendation for gonorrhoea, for the majority of Australia, continues to be dual therapy with ceftriaxone and azithromycin. Decreased susceptibility (DS) to ceftriaxone (minimum inhibitory concentration [MIC] value ≥ 0.06 mg/L) was found nationally in 1.3% of isolates. Five *N. gonorrhoeae* clinical isolates were ceftriaxone-resistant (MIC value ≥ 0.25 mg/L), and therefore also resistant to penicillin; all were resistant to ciprofloxacin but susceptible to azithromycin. These isolates were reported from Victoria (3), non-remote Western Australia (1) and New South Wales (1).

Resistance to azithromycin (MIC value ≥ 1.0 mg/L) was found nationally in 4.6% of *N. gonorrhoeae* isolates, continuing a downward trend observed and reported since 2017. Isolates with high-level resistance to azithromycin (MIC value ≥ 256 mg/L) continue to be reported sporadically in Australia, with eight detected in 2019: two each from New South Wales, Queensland, and Victoria, and one each from Tasmania and non-remote Western Australia.

In 2019, in Australia, 2,136 gonococcal isolates (22.1%) were penicillin resistant; however, there remains considerable variation by jurisdiction, and in some remote settings there is little resistance and this drug is recommended empiric therapy. In 2019, in the remote Northern Territory, no penicillin resistance was reported, however in remote Western Australia six out of 85 isolates (7.1%) were penicillin resistant. There was no ciprofloxacin resistance reported from isolates tested from remote regions of the Northern Territory, and ciprofloxacin resistance rates remain comparatively low (7/85; 8.2%) in remote Western Australia.

Keywords: antimicrobial resistance; disease surveillance; gonococcal infection; *Neisseria gonorrhoeae*

Introduction

The National Neisseria Network (NNN) is a collaborative network of the jurisdictional *Neisseria* reference laboratories across Australia, established in the late 1970s, that perform testing of clinical isolates of the pathogenic *Neisseria* species: *Neisseria gonorrhoeae* (NG) and *N. meningitidis*. The Australian Gonococcal

Surveillance Programme (AGSP) is a key activity of the NNN. The AGSP has continuously monitored and reported gonococcal antimicrobial susceptibility since 1981,¹ and is the longest continually-running national surveillance system for gonococcal antimicrobial resistance (AMR). Concerns regarding AMR in NG have been the focus of national and international public health agendas, with the predicted emergence

and spread of multidrug-resistant gonorrhoea posing significant collateral health and financial costs.² Globally, the majority of settings rely on a combination of ceftriaxone and azithromycin for the treatment of gonorrhoea. A number of sporadic reports of ceftriaxone resistance have been reported, both in Australia and elsewhere, in the last two decades, although it was not until 2017 that the first evidence of sustained spread of multidrug-resistant gonorrhoea was reported.³ This was followed in 2018 by the report of the first extensively drug-resistant *N. gonorrhoeae* isolates, found in Australia and, at the same time, in the United Kingdom.^{4,5} Genomic investigations have shown that ceftriaxone resistance in these strains was associated with the *penA* allele (type 60.001) that encodes the key alterations A311V and T483S.⁴

The emergence of NG AMR in Australia has long been influenced by the introduction of multi-resistant strains from overseas.⁶ Recent work from the World Health Organization Collaborating Centre for STI and AMR (WHOCC), Sydney, investigating the emergence of resistance in ciprofloxacin (the previous first-line therapy for gonococcal infections) found that continued importation of ciprofloxacin-resistant NG isolates, rather than the expansion of a single genotype, led to ciprofloxacin resistance being established to the point that a change in therapeutic recommendations to ceftriaxone was required.⁷ The importation and spread of ceftriaxone-resistant gonococcal strains, and/or new resistance developing, remains an ongoing concern for disease control strategies and is a focus of the work of the NNN.

Whilst the background rate of strains with ceftriaxone decreased susceptibility (minimum inhibitory concentration [MIC] value ≥ 0.06 mg/L) in Australia has remained low and relatively stable since the introduction of dual therapy for gonorrhoea in 2014, vigilance in continuing culture-based surveillance to detect novel resistant strains is imperative. The increased proportion of gonococcal isolates with azithromycin resistance in recent years has also added to concerns about management strategies;

however, after an increase nationally to 9.3% in 2017, this resistance declined to 6.2% in 2018 and through the quarters of 2019.

Coincident with, but unrelated to, increasing AMR in Australia, there are recent substantive increases in gonococcal disease in this country, with an overall 80% increase in notifications in 2015–2017 in both males and females. Conversely, over the same period, reported rates of gonorrhoea decreased by 19% in the Aboriginal and Torres Strait Islander population. Disease rates in Indigenous Australians remain markedly (6.6 times) higher than in the non-Indigenous population (627.5 per 100,000 versus 95.6 per 100,000), and are highest in remote and very remote areas (1,444 per 100,000; i.e., 30 times greater than the non-Indigenous population).⁸ In contrast to non-remote Australia, NG AMR in remote regions remains low in locally-acquired infections, with the recommended therapeutic strategy based on oral penicillin.⁹

Paradoxically, the current heightened global awareness of AMR, and increasing disease notification rates reported in Australia and elsewhere,^{8,10–13} have coincided with increased use of nucleic acid amplification testing (NAAT) for gonococcal diagnosis, replacing bacterial culture and antimicrobial susceptibility testing (AST). In remote regions in Australia, NAAT is used to detect penicillin resistance^{14,15} in NAAT-positive samples for NG; this is the first documented use of routine molecular testing for NG AMR detection and surveillance, and these data continue to inform local treatment guidelines.¹⁵

Strategies for treating and controlling gonorrhoea are based on regimens effecting cure in a minimum of 95% of cases. Surveillance data of antibiotics in clinical use are critical to monitor AMR, to detect imported or novel resistance, and to inform treatment guidelines.¹⁶ The WHO has called for enhanced surveillance as a fundamental component of its Global Action Plan to control the spread and impact of gonococcal AMR.¹⁷

Methods

All confirmed cases of gonorrhoea in Australia are notifiable to the National Notifiable Diseases Surveillance System (NNDSS) under legislation. The NG isolates tested by the NNN, and reported by the AGSP, therefore represent a proportion of the total number of notified cases. The NNN laboratories test gonococcal isolates for susceptibility to ceftriaxone; azithromycin; penicillin; ciprofloxacin; spectinomycin; and variably tetracycline, using previously-described standardised methodology to determine the minimum inhibitory concentration (MIC) values.¹⁸ The MIC value is the lowest antibiotic concentration that inhibits *in vitro* growth under defined conditions. The AGSP conducts a programme-specific quality assurance program.¹⁹

Gonococcal AST data from each jurisdiction are submitted quarterly to the coordinating laboratory (the Neisseria Reference Laboratory and WHOCC Sydney) which collates the data for reporting. Where available, the AGSP collects data on the sex of the patient, country of acquisition of infection, and site of isolation of gonococcal isolates. Data collected across jurisdictions are predominantly from urban centres. Data from the Northern Territory and Western Australia are further divided into non-remote and remote regions determined at the jurisdictional level, based on antibiograms, and therapeutic recommendations consequently differ.

Results

Proportion of gonococcal infections with antimicrobial susceptibility testing

Antimicrobial susceptibility testing is able to be performed when diagnosis is made by bacterial culture. Nucleic acid amplification testing, such as polymerase chain reaction (PCR), has been widely adopted for diagnosis of gonococcal infections, and whilst molecular detection of known antimicrobial markers is possible, currently available NAATs cannot detect resistance beyond that associated with known determinants.

In 2019 there were 34,265 gonococcal infections notified in Australia; the NNN laboratories received and tested 9,668 NG isolates, representing both the highest annual total of isolates and the highest number of annual gonococcal disease notifications since records commenced in 1991 (Figure 1).²⁰ Overall, 28% of gonococcal infections notified had AST undertaken at NNN laboratories (Table 1).

There were 7,835 isolates from males (81.0%) and 1,776 from females (18.4%) tested in 2019 (Table 2). There were 57 isolates from patients where gender was not recorded. The proportion of gonococcal isolates from males and females has remained stable over recent years (2009–2017), ranging between 17% to 20% for women and 80% to 83% for men. The infected site was reported as 'other' or not specified for 85 isolates from males and 36 isolates from females (Table 2). Isolates from urine samples were regarded as genital tract isolates.

The numbers and proportions (%) of gonococcal isolates with resistance to azithromycin, penicillin and ciprofloxacin and decreased susceptibility to ceftriaxone are reported for 2019 in Table 3 by state and territory of Australia, as well as the aggregate proportions for ceftriaxone, azithromycin, ciprofloxacin and penicillin. There is demonstrated variation across jurisdictions, as well as in remote settings when compared to non-remote settings.

Ceftriaxone

Gonococcal isolates with decreased susceptibility to ceftriaxone (MIC values ≥ 0.06 mg/L) have been detected in Australia since 2001; the proportion reported increased to 4.4% in 2012, before doubling to 8.8% in 2013. From 2014, coincident with introduction of dual ceftriaxone and azithromycin therapy, the proportion of isolates with decreased susceptibility to ceftriaxone fell annually to 1.1% in 2017 before increasing slightly to 1.7% in 2018. The 2019 rate of ceftriaxone decreased susceptibility fell to

Figure 1: Number of gonococcal disease cases reported to the National Notifiable Diseases Surveillance System compared with *Neisseria gonorrhoeae* isolates available for laboratory testing by the Australian Gonococcal Surveillance Programme, Australia, 1991–2019

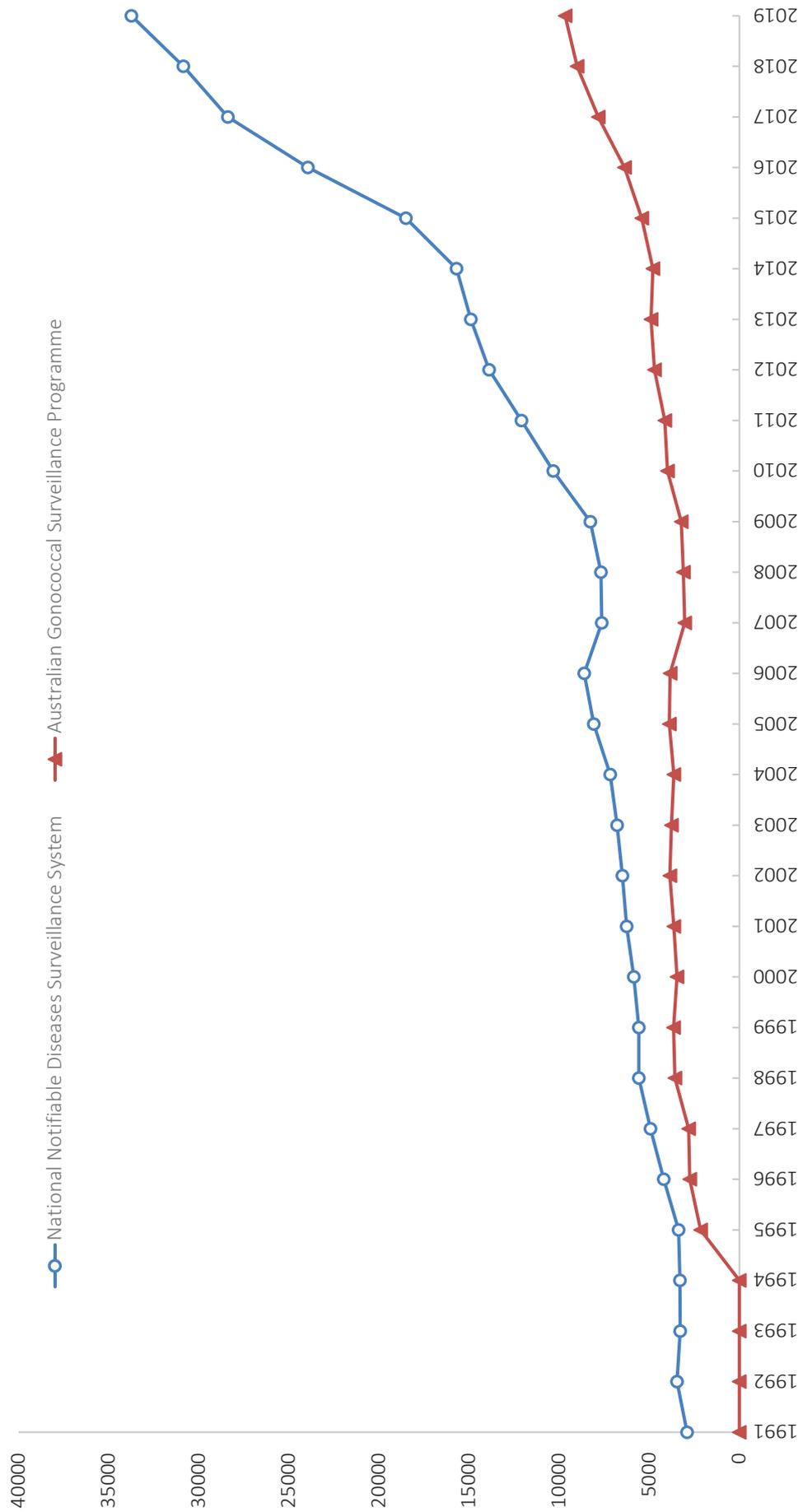


Table 1: Number of Australian Gonococcal Surveillance Programme gonococcal isolates tested as a proportion of National Notifiable Diseases Surveillance System (NNDSS) gonorrhoea notifications, Australia, 2019, by state or territory

State or territory	Number of isolates tested	NNDSS Notifications	Number of isolates tested/ Number of cases notified %
Australian Capital Territory	198	333	59
New South Wales	3,610	11,720	31
Northern Territory	126	1,327	9.5
Queensland	1,677	5,977	28
South Australia	554	2,099	26
Tasmania	49	157	31
Victoria	2,616	8,728	30
Western Australia	838	3,924	21
Australia	9,668	34,265	28

1.3%, consistent with an overall declining trend (see Table 4 and Table 5). From 2016 to 2018 the proportion of isolates with an MIC value of ≥ 0.125 mg/L for ceftriaxone remained stable in the range 0.04–0.06%, however in 2019, this increased to 0.11% (Table 5). In 2019 there were 5 NG clinical isolates with ceftriaxone MIC values ≥ 0.25 mg/L: from Victoria (3), non-remote Western Australia (1) and New South Wales (1). All had the *penA-60* allele thus were resistant to penicillin, as well as to ciprofloxacin, but all were susceptible to azithromycin.

Azithromycin

Nationally, in 2019, 4.6% of isolates exhibited azithromycin resistance (MIC value ≥ 1.0 mg/L) (Table 3), decreasing from 6.2% reported in 2018. Since 2012, rates of azithromycin resistance have increased in Australia. Compared with 2012, azithromycin resistance peaked in 2017 (an approximately sevenfold increase) with 2019 rates representing a ~ 3.5 -fold increase, as shown in Table 6. Rates of azithromycin-resistant NG were highest in the Australian Capital Territory (7.1%), Victoria (6.2%) and New South Wales (6.0%) as shown in Tables 3 and 6. In 2019, 8 isolates exhibited high-level resistance to azithromycin (MIC value ≥ 256 mg/L), two from New

South Wales, two from Queensland, two from Victoria, one from Tasmania and one from a metropolitan area of Western Australia.

Penicillin

Resistance to the penicillin group of antibiotics (penicillin, ampicillin, and amoxicillin with or without clavulanic acid) in NG results from β -lactamase production (i.e., penicillinase) and/or the aggregation of chromosomally-controlled resistance mechanisms. These are denoted, respectively, as penicillinase-producing *N. gonorrhoeae* (PPNG) and chromosomally-mediated resistant to penicillin (CMRP). Chromosomally-mediated resistance is defined as a penicillin MIC ≥ 1 mg/L.

In 2019, in Australia, 2,136 isolates (22.1%) were penicillin resistant, a proportional decrease from 2016 (32.5%), and 2017 (26.1%) but a slight increase compared to 2018 (21.1%). The proportion of penicillin-resistant isolates fluctuated in the range 22.5–44% between 2008 and 2017. In 2019, a total of 686 isolates (7.1%) had CMRP and 1,450 (15.0%) were PPNG; 67.9% of penicillin-resistant isolates were PPNG.

Table 2: Gonococcal isolates, Australia, 2019, by sex, site and jurisdiction tested

Sex	Site	ACT	NSW	NT	Qld	SA	Vic	Tas	WA	Australia
Male	Genital	59	1,614	77	738	313	1,030	21	449	4,301
	Rectal	57	880	3	298	84	837	6	109	2,274
	Pharynx	59	495	3	139	31	367	8	53	1,155
	DGI ^a	0	9	0	5	1	1	0	4	20
	Other/NS ^b	1	24	6	19	4	13	6	12	85
	Total	176	3,022	89	1,199	433	2,248	41	627	7,835
Female	Genital	11	436	34	433	117	272	7	189	1,499
	Rectal	3	15	0	7	3	13	0	6	47
	Pharynx	6	101	0	23	1	42	1	9	183
	DGI	0	0	3	3	0	2	0	3	11
	Other/NS	1	10	0	12	0	9	0	4	36
	Total	21	562	37	478	121	338	8	211	1,776
Unknown	Total	1	26	0	0	0	30	0	0	57
Total	198	3,610	126	1,677	554	2,616	49	838	9,668	

a DGI: Disseminated Gonococcal Infection.

b NS: not specified.

Table 3: Number and proportion (%) of gonococcal isolates with resistance to azithromycin, penicillin and ciprofloxacin and decreased susceptibility to ceftriaxone reported, Australia, 2019, by state or territory

State or territory	Number of isolates tested		Decreased susceptibility				Resistance					
	2019		Ceftriaxone		Azithromycin		Penicillin		Ciprofloxacin			
	n	%	n	%	n	%	n	%	n	%		
Australian Capital Territory	198	1	0.5	14	7.1	19	9.6	44	22.2			
New South Wales	3,610	44	1.2	215	6.0	967	26.8	1,156	32.0			
Queensland	1,677	16	1.0	32	1.9	344	20.5	388	23.1			
South Australia	554	9	1.6	11	2.0	75	13.5	148	26.7			
Tasmania	49	1	2.0	1	2.0	19	38.8	7	14.3			
Victoria	2,616	42	1.6	161	6.2	522	20.0	780	29.8			
Northern Territory non-remote	55	0	0	1	1.8	10	18.2	9	16.4			
Northern Territory remote	71	0	0	0	0.0	0	0.0	0	0.0			
Western Australia non-remote	753	11	1.5	12	1.6	174	23.1	204	27.1			
Western Australia remote	85	2	2.4	1	1.2	6	7.1	7	8.2			
Australia	9,668	126	1.30	448	4.6	2,136	22.1	2,743	28.4			

Table 4: Number and proportion (%) of gonococcal isolates with decreased susceptibility to ceftriaxone (MIC $\geq 0.06\text{mg/L}$), Australia, 2013 to 2019, by state or territory.

State or territory	Decreased susceptibility to ceftriaxone																	
	2013		2014		2015		2016		2017		2018		2019					
	n	%	n	%	n	%	n	%	n	%	n	%	n	%				
Australian Capital Territory	0	0	2	2.7	0	0.0	1	0.9	0	0	4	1.9	1	0.5				
New South Wales	183	11.8	119	7.1	52	2.7	45	2.0	13	0.5	30	0.8	44	1.2				
Queensland	33	4.9	21	3.2	7	1.0	32	3.7	11	0.9	18	1.3	16	1.0				
South Australia	4	1.9	2	1.0	9	3.6	2	0.6	2	0.6	3	1.3	9	1.6				
Tasmania	11	24.4	0	0	0	0	1	3.6	0	0	4	7.3	1	2.1				
Victoria	181	11.8	95	6.6	25	1.5	19	1.1	48	2.1	83	3.2	42	1.6				
Northern Territory non-remote	2	1.9	3	3.0	0	0	0	0	0	0	0	0	0	0				
Northern Territory Remote	2	0.8	1	0.8	0	0	0	0	0	0	0	0	0	0				
Western Australia non-remote	13	2.7	14	3.6	5	1.3	9	1.3	9	1.4	14	2.1	11	1.5				
Western Australia Remote	0	0	1	0.9	0	0	0	0	0	0	0	0	2	2.4				
Australia	429	8.8	258	5.4	98	1.8	109	1.7	83	1.1	156	1.7	127	1.3				

Table 5: Proportion (%) of gonococcal isolates tested in Australia with ceftriaxone MIC values at 0.06 mg/L and \geq 0.125 mg/L, 2010–2019

Ceftriaxone MIC mg/L	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
0.06	4.80%	3.20%	4.10%	8.20%	4.80%	1.70%	1.65%	1.02%	1.67%	1.19%
\geq 0.125	0.10%	0.10%	0.30%	0.60%	0.60%	0.10%	0.05%	0.04%	0.06%	0.11%

Penicillin resistance in remote Australia

In 2019, there were 126 isolates tested from the Northern Territory, with 71 derived from remote areas (including Alice Springs, Katherine, Tennant Creek, and Arnhem Land region) and 55 from Darwin and surrounding urban areas (non-remote). In 2019, there were 838 isolates tested from Western Australia, with 85 obtained from remote regions and 753 from urban and suburban Perth (non-remote).

Of the 71 isolates from the remote Northern Territory, none was penicillin-resistant; 10 isolates (18.2%) from Darwin and surrounding urban areas were penicillin-resistant, all of which were PPNG (Table 3). Of the 85 isolates from remote Western Australia, six (7.1%) were penicillin-resistant with 5 being PPNG. While no isolate from the remote Northern Territory demonstrated decreased susceptibility to ceftriaxone, one isolate from remote Western Australia had a ceftriaxone MIC of 0.125 mg/L and one isolate from non-remote Western Australia had a ceftriaxone MIC of 0.5 mg/L.

Ciprofloxacin

Ciprofloxacin resistance is defined as MIC \geq 1 mg/L. In 2019, there were 2,743 ciprofloxacin-resistant isolates (28.4%) (Table 3). The rate of ciprofloxacin resistance has progressively declined in Australia since 2008, when 54% of isolates tested resistant.

Tetracyclines

To facilitate accurate reporting of NG tetracycline resistance in Australia, the NNN reference laboratories have, from 2018, performed tetracycline

MIC testing where possible. This replaces historical testing for high-level tetracycline resistance which was reported by the NNN, since inception, as an epidemiological marker for plasmid-mediated resistance. Tetracycline resistance is defined as an MIC \geq 2 mg/L and utilises various mechanisms including plasmid-mediated resistance. The previously-employed methods only detected high-level plasmid-mediated tetracycline-resistant *N. gonorrhoeae* (TRNG) (MIC value \geq 16mg/L). Whilst tetracyclines are not a recommended treatment for gonorrhoea, and are rarely, if ever, used for treatment of gonorrhoea in Australia, there has been recent interest in the proportion of tetracycline resistance. Nationally, 3,682 isolates were tested (representing 38.1% of isolates received by the NNN) and 27% (994/3,682) were tetracycline-resistant. Tetracycline resistance data are presented by jurisdiction and aggregated for Australia as shown in Table 7.

Spectinomycin

In 2019, all isolates tested (n = 9,668) were susceptible to spectinomycin.

Discussion

The World Health Organization recommends that treatment regimens for gonorrhoea are based on epidemiological surveillance of the distribution and extent of AMR, and that a resistance rate of 5% or more is the nominal threshold for change of treatment recommendations.¹⁶ The AGSP has continuously monitored gonococcal AMR in Australia since 1981, providing data to inform treatment and public health strategies. Further, the WHOCC Sydney has established and coordinated quality assurance, and quality

Table 6: Number and proportion (%) of gonococcal isolates with resistance to azithromycin (MIC ≥ 1.0 mg/L), Australia, 2012–2019, by state or territory

State or Territory	Azithromycin resistance																	
	2012		2013		2014		2015		2016		2017		2018		2019			
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%		
ACT	0	0	1	2.2	7	9.3	0	0	8	7.1	3	2.1	18	8.7	14	7.1		
NSW	9	0.5	14	0.9	33	2.0	43	2.3	82	3.6	261	9.3	230	6.5	215	6.0		
Qld	15	2.1	38	5.7	23	3.5	42	5.8	10	1.2	61	4.9	68	4.9	32	1.9		
SA	1	0.7	6	2.8	1	0.5	7	2.8	68	19.5	46	12.8	7	3.0	11	2.0		
Tas	0	0	0	0	1	3.3	1	4.3	4	14.3	5	9	3	6	1	2.0		
Vic	34	2.7	35	2.3	33	2.3	30	1.8	93	5.4	304	13.5	217	8.3	161	6.2		
NT non-remote	0	0	1	1.0	0	0	0	0	1	1.9	1	1.7	1	1.5	1	1.8		
NT remote	0	0	0	0	0	0	0	0	0	0	1	0.6	0	0.0	0	0.0		
WA non-remote	3	0.6	9	1.9	21	5.3	15	3.8	51	7.6	40	6.4	16	2.5	12	1.6		
WA remote	0	0	0	0	0	0	0	0	1	0.8	4	3.4	1	0.9	1	1.2		
Australia	62	1.3	104	2.1	119	2.5	138	2.6	318	5.0	726	9.3	561	6.2	448	4.6		

Table 7; Number and proportion (%) of gonococcal isolates with resistance to tetracycline (MIC \geq 2 mg/L), Australia, 2019, by state or territory

State or Territory	Number of isolates tested	Resistance MIC \geq 2 mg/L	
	2019	Tetracycline	
		n	%
Australian Capital Territory	175	19	10.9
New South Wales	0	0	0
Queensland	0	0	0
South Australia	0	0	0
Tasmania	47	8	17.0
Victoria	2,585	743	28.7
Northern Territory Non Remote	16	0	0.0
Northern Territory Remote	27	0	0.0
Western Australia Non Remote	747	212	28.4
Western Australia Remote	85	12	14.1
Australia	3,682	994	27.0

control, for gonococcal AMR testing with the AGSP External Quality Assurance Program and with the development of the WHO NG reference strains, thus ensuring the quality of the AGSP data.^{19,21}

In 2019 the NNN examined 9,668 clinical isolates for susceptibility testing to ceftriaxone, azithromycin, ciprofloxacin, penicillin and high-level resistance to tetracycline. These isolates were from urban and remote settings, in the public and private health sectors, constituting a comprehensive sample of about one-third of all notifications nationally. Coincident with increasing NG disease rates in Australia,⁸ there has been an increase in the numbers of gonococcal isolates tested for AST. However, the proportion nationally remains relatively unchanged at approximately 30%.

Remote populations of Western Australia and the Northern Territory, which have high proportions of Aboriginal and Torres Strait Islander peoples, report high rates of gonococcal disease, but low rates of culture (n = 156), as a function of laboratory access. Possibly secondary to their isolation, these communities have low rates of AMR in NG. Consequently, these regions require continued vigilance with monitoring of AMR in NG using culture- and molecular-based surveillance strategies.

For the majority of gonococcal surveillance programmes around the world, the monitoring of ceftriaxone and azithromycin MIC values is the primary focus. For the AGSP, ceftriaxone MIC values of \geq 0.06 mg/L have been reported historically to have decreased susceptibility. In Australia, the proportion of isolates with decreased susceptibility to ceftriaxone has

steadily and substantially declined since 2013 from 8.8% to 1.3% in 2019 (Table 4). However, as noted, little reassurance should be taken from this, as multidrug- and extensively-resistant strains have been reported from Asia, Europe and Australia in recent years.^{22–25} It has been shown that continued importation of resistant strains is the first step to establishment of resistance.⁷ It is thus a realistic concern that more frequent reports of ceftriaxone-resistant strains foreshadow establishment of these strains in Australia and elsewhere, and that such reports herald a clear warning that needs to be heeded with disease prevention strategies. Further, lessons learned from the extensively-drug-resistant gonococcal infections include the need for carbapenem therapy, which will not be possible in all settings.²⁶

In 2013, high-level resistance (HLR; MIC value ≥ 256 mg/L) to azithromycin in gonococci was reported for the first time in Australia in four strains, two with suspected contact in China.²⁷ Since then there have been only sporadic reports of HLR to azithromycin in Australia annually; there were eight such isolates in 2019. The proportion of azithromycin-resistant isolates that were also resistant to penicillin and ciprofloxacin was 6.0%. Continued close observation is needed, as evidence of co-evolving cephalosporin and azithromycin resistance is being observed outside Australia and is of significant concern.²⁸ Azithromycin resistance has been monitored since the inception of the AGSP. Following the introduction of dual therapy in 2014, we have seen lability in the proportions of isolates with resistance to azithromycin in all jurisdictions of Australia (Table 6). Rising from 2015 and peaking at 9.3% in 2017, proportional resistance to azithromycin fell to 4.6% in 2019 nationally (Table 6). Importantly, following a proportional rise of over 23% (2.8% in 2015 to 26% in 2016) in South Australia, azithromycin resistance rates in that state have now fallen and stabilised at $< 5\%$ (2% in 2019) (Table 6).²³ In 2019, azithromycin resistance was highest in the Australian Capital Territory (7.1%), Victoria (6.2%) and New South Wales (6.0%). Globally there have been increasing reports of azithromycin resistance.²⁹

The recent reports of international spread of NG with resistance to ceftriaxone,⁵ and the emergence of azithromycin resistance, heighten concerns about the future treatment strategies for NG AMR.²⁶ As developed nations continue to transition to widespread pharmacological prevention of HIV infection (e.g. pre-exposure prophylaxis, treatment as prevention) in high-risk populations, a return to, and reinvigoration of public health strategies promoting primary prevention (e.g. condoms) of gonorrhoea and other sexually transmissible infections is urgently required. Additionally, NG vaccine development is a research priority and may be key in the control of this disease. As Australian clinicians become increasingly dependent on NAAT for diagnosis of NG (with 71% of diagnoses in 2019 made with NAAT alone), health care provider education regarding the continued importance of bacterial culture and AST is paramount. Whilst advances in molecular detection of AMR has great promise, this report underscores the ongoing importance of bacterial culture and AST of NG for clinical management, detection of resistance and novel resistant strains, AMR surveillance, and test of cure. Given its strong history and association with NG AMR in Australia, treating clinicians should pay particular note to patient travel history, since for imported cases of NG, the benefit of bacterial culture and susceptibility testing is critical.

The WHO Global Action Plan states that disease control strategies and the understanding of the global scope of AMR need to continue to be informed by surveillance programs of AMR, nationally and internationally.¹⁷ The ongoing need for close and enhanced monitoring of gonococcal AMR can be supported, but not replaced, by molecular-based assays, and strain specific assays can be used for routine and sentinel site surveillance in high-risk populations. The data are critically important to inform therapeutic strategies, to monitor for the presence and spread of resistance and to detect instances of treatment failure.

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