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Australian Gonococcal Surveillance Programme Annual Report, 2018

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Annual report

Australian Gonococcal Surveillance Programme Annual Report, 2018

Monica M Lahra, Rodney Enriquez and CR Robert George for the National Neisseria Network, Australia

Abstract

The Australian Gonococcal Surveillance Programme (AGSP) has continuously monitored antimicrobial resistance in clinical isolates of *Neisseria gonorrhoeae* from all states and territories since 1981. In 2018, there were 9,006 clinical isolates of gonococci from public and private sector sources tested for *in vitro* antimicrobial susceptibility by standardised methods. This was the highest annual total of isolates tested since the inception of the AGSP. The current treatment recommendation for gonorrhoea, for the majority of Australia, remains dual therapy with ceftriaxone and azithromycin. Decreased susceptibility to ceftriaxone (minimum inhibitory concentration (MIC) value ≥0.06 mg/L) was found nationally in 1.73% of isolates. The highest proportions were reported from Tasmania and non-remote Western Australia (7.3% and 2.1% respectively). In 2018 two extensively drug-resistant isolates were reported from Queensland patients. These two isolates, with ceftriaxone MIC values of 0.50 mg/L, high-level resistance to azithromycin (MIC ≥ 256 mg/L), and resistance to penicillin and ciprofloxacin were identified and reported to the World Health Organization as isolates of international significance. Resistance to azithromycin (MIC value ≥1.0 mg/L) was found nationally in 6.2% of isolates, lower than the 9.3% reported in 2017, but more than double the proportion reported in 2015 (2.6%). The highest proportions were reported from the Australian Capital Territory (8.7%), Victoria (8.3%), and New South Wales (6.5%). High-level resistance to azithromycin (MIC value ≥256 mg/L) was reported in nine isolates nationally in 2018: four from New South Wales, three from Victoria, and two from Queensland.

The proportion of isolates resistant to penicillin in non-remote Australia ranged from 8.8% in non-remote Northern Territory to 44.1% in South Australia. In remote Northern Territory penicillin resistance rates remain low (1.9%), and higher in remote Western Australia (6.5%).

The proportion of isolates resistant to ciprofloxacin in non-remote Australia ranged from 10.3% in non-remote Northern Territory to 48.3% in South Australia. Ciprofloxacin resistance rates remain comparatively low in remote Northern Territory (1.9%) and remote Western Australia (4.6%).

Keywords: antimicrobial resistance, disease surveillance, gonococcal infection, Neisseria gonorrhoeae

Introduction

Antimicrobial resistance (AMR) in *Neisseria gonorrhoeae* (NG) is a threat to global health security, with the emergence and spread of multidrug-resistant gonorrhoea predicted to pose significant collateral health and financial costs.[1] In Australia, increasing gonococcal infection rates,[2] the emergence of azithromycin resistance, and new reports of novel ceftriaxone-resistant strains with international spread,[3] are key concerns and remain the focus of the National Neisseria Network (NNN). The NNN is a collaborative network of jurisdictional *Neisseria* reference laboratories that performs phenotypic and genotypic testing of clinical isolates of

pathogenic *Neisseria*. Clinical isolates referred to NNN laboratories from public and private sector laboratories represent as wide a section of the community as possible. The Australian Gonococcal Surveillance Programme (AGSP) is a key activity of the NNN which has continuously monitored NG AMR susceptibility since 1981; it is the longest, continually running, national surveillance system for gonococcal AMR.

In Australia, gonorrhoea notifications increased by 80% (from 65.5 to 118.0 per 100,000) in the five years 2013 to 2017. Increases were greater in males (91%) than in females (56%), with notification rates in 2016 remaining higher in males (174.2 per 100,000) than in females (61.8 per 100,000).[2]

In the five years 2013 to 2017, gonorrhoea annual notification rates in the Aboriginal and Torres Strait Islander (ATSI) population decreased by 19%; the 2017 gonorrhoea notification rate in the ATSI population remains markedly higher (6.6 times) than in the non-Indigenous population (627.5 per 100,000 versus 95.6 per 100,000) and is highest in remote and very remote areas (1,444 per 100,000; i.e., 30 times greater than the nonIndigenous population).[2] 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.[4]

Ceftriaxone and azithromycin dual therapy is recommended in Australia,[5] having been introduced in 2014 in an attempt to forestall resistance to ceftriaxone; this was followed by both a steady decline in the proportion of isolates with raised MIC values to ceftriaxone, but also an increase in the proportion of isolates resistant to azithromycin, following rapid emergence of azithromycin resistance in South Australia in early 2016.[6]

Paradoxically, the current heightened global awareness of AMR, and increasing disease notification rates reported in Australia and elsewhere,[2,7–10] have coincided with increased use of nucleic acid amplification testing (NAAT) for diagnosis, replacing bacterial culture and antimicrobial susceptibility testing (AST). In remote regions in Australia, NAAT is used to detect penicillin resistance[11,12] 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.[12]

The World Health Organization (WHO) 2018 Report on Global STI Surveillance estimates 87 million new NG infections annually worldwide in those aged 15–49 years, with the highest burden occurring in the Asia Pacific regions.[13] Additional to this high disease burden in the Asia Pacific, the WHO Gonococcal Antimicrobial Surveillance Programme data indicate high levels of gonococcal AMR with significant gaps in surveillance. Furthermore, unregulated antimicrobial use in these regions provides ideal conditions for the development of AMR.[14] The emergence of NG AMR in Australia has long been influenced by the introduction of multi-resistant strains from overseas.[15] The importation and spread of resistant gonococcal strains, and/or new resistance developing, remains an ongoing concern.

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

The NNN AMR data for gonococcal isolates are collated for the AGSP quarterly and annual reports. All confirmed cases of gonorrhoea in Australia are notifiable to the National Notifiable Diseases Surveillance System (NNDSS). The number of isolates tested by the NNN and reported by the AGSP represents a proportion

of the total number of cases reported to the NNDSS. The NNN laboratories test gonococcal isolates for susceptibility to penicillin; ceftriaxone; ciprofloxacin; azithromycin; spectinomycin and tetracycline, using previously-described standardised methodology to determine the MIC values.[18] The MIC value is the lowest antibiotic concentration that inhibits *in vitro* growth under defined conditions. The AGSP conducts a program-specific quality assurance program.[19]

Gonococcal AST data from each jurisdiction are submitted quarterly to the coordinating laboratory (the Neisseria Reference Laboratory and WHO Collaborating Centre for Sexually Transmitted Infections and Antimicrobial Resistance, Sydney) which collates the data for reporting. Where available, the AGSP collects data on the sex of the patient, country of acquisition, 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 and coincident with antibiograms and consequent therapeutic recommendations.

Results

Number of gonococcal isolates and infections

NNN laboratories tested 9,006 NG isolates in 2018, representing the highest annual total of isolates ever assessed by the AGSP. There were 30,858 gonococcal infections notified to the NNDSS in 2018, similarly representing the highest number of annual gonococcal disease notifications since records commenced in 1991 (Figure 1).[20] Isolates from 29% of all cases of gonorrhoea notified to the NNDSS were tested by the NNN laboratories (Table 1); this rate equals the proportion tested in 2015–2017 but is lower than the rate from 2008–2014 (31% – 42%). The reduced referral rate reflects decreasing reliance on culture in Australia for NG diagnosis given the widespread uptake of NAAT.

Referred Isolates

There were 7,415 isolates from males (82.3%) and 1,547 (17.2%) from females (Table 2). 44 isolates were 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 and 20% for women and 80 and 83% for men. The infected site was reported as 'other' or not specified for 83 isolates from males and 42 isolates from females (Table 2). Isolates from urine samples were regarded as genital tract isolates.

Antibiotic susceptibility patterns

As in previous years, gonococcal AMR patterns differed by state and territory (Table 3).

Ceftriaxone

Gonococcal isolates with decreased susceptibility to ceftriaxone (MIC values ≥0.06 mg/L) have been detected in Australia since 2001; the proportion increased to 4.4% in 2012, before doubling to 8.8% in 2013. From 2014, coincident with the introduction of dual ceftriaxone and azithromycin therapy, the proportion of isolates with decreased susceptibility to ceftriaxone fell annually to 1.06% in 2017 before increasing slightly to 1.73% in 2018 (see Table 4 and Table 5). From 2010, the proportion of isolates with an MIC value of ≥0.125 mg/L increased from 0.1% to 0.6% in 2013–2014 and then decreased to 0.04% in 2017. In 2018, an increase to 0.06% was observed as shown in Table 5. Gonococcal isolates from two patients from Queensland, not determined to be contacts, were found to be extensively drug-resistant (XDR) with ceftriaxone MIC values of 0.50 mg/L, high-level resistance to azithromycin (MIC ≥ 256 mg/L) and resistance to penicillin and ciprofloxacin. One had a history of travel to South East Asia.

Azithromycin

Nationally, in 2018, 6.2% of isolates exhibited azithromycin resistance (MIC ≥1.0 mg/L) (Table 3), decreasing from 9.3% reported in 2017.

Figure 1: Number of gonococcal disease cases reported to the National Notifiable Diseases Surveillance System compared with *N. gonorrhoeae* isolates available for laboratory testing by the Australian Gonococcal Surveillance Programme, Australia, 1991–2018

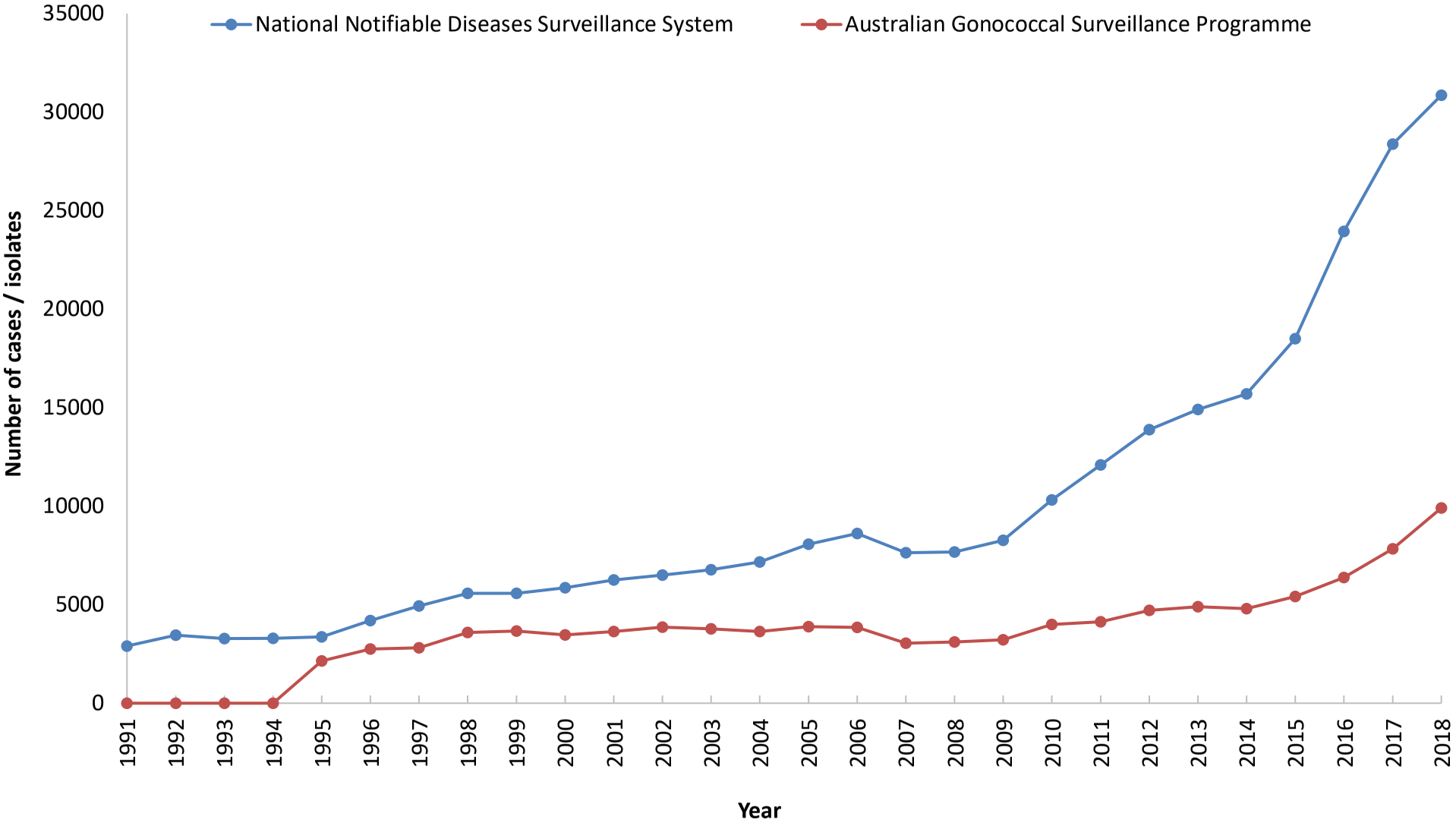

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Table 1: Number of Australian Gonococcal Surveillance Programme gonococcal isolates tested as a proportion of National Notifiable Diseases Surveillance System gonorrhoea notifications, Australia, 2018, by state or territory

State or territory	Number of isolates tested	Number of cases notified	Isolates Tested/Notifications (%)
Australian Capital Territory	206	330	62
New South Wales	3,535	10,559	33
Northern Territory	225	2,124	11
Queensland	1,375	4,906	28
South Australia	231	1,288	18
Tasmania	55	149	37
Victoria	2,619	8,091	32
Western Australia	760	3,411	22
Australia	**9,006**	**30,858**	**29**

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Table 2: Gonococcal isolates, Australia, 2018, by sex, site and jurisdiction tested.

Sex	Site	ACT	NSW	NT	Qld	SA	Vic	Tas	WA	AUSTRALIA
Male	Genital	65	1,614	167	628	106	1,111	20	405	**4,116**
	Rectal	51	854	2	270	50	659	11	99	**1,996**
	Pharynx	71	500	0	131	10	426	10	58	**1,206**
	DGI[a]	0	4	0	6	0	2	0	2	**14**
	Other/NS[b]	0	29	3	10	10	14	8	9	**83**
	Total	**187**	**3,001**	**172**	**1,045**	**176**	**2,212**	**49**	**573**	**7,415**
Female	Genital	11	378	52	302	43	299	3	179	**1,267**
	Rectal	0	14	0	7	3	7	0	1	**32**
	Pharynx	8	105	0	10	1	72	2	2	**200**
	DGI[a]	0	2	0	2	0	0	0	2	**6**
	Other/NS[b]	0	16	1	8	8	5	1	3	**42**
	Total	**19**	**515**	**53**	**329**	**55**	**383**	**6**	**187**	**1,547**
Unknown	Total	0	19	0	1	0	24	0	0	**44**
Total		**206**	**3,535**	**225**	**1,375**	**231**	**2,619**	**55**	**760**	**9,006**

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, 2018, by state or territory

Jurisdiction	Number of isolates tested 2018	Decreased susceptibility		Resistance					
		Ceftriaxone		Azithromycin		Penicillin		Ciprofloxacin	
		n	%	n	%	n	%	n	%
Australian Capital Territory	206	4	1.9	18	8.7	24	11.7	26	12.6
New South Wales	3,535	30	0.8	230	6.5	823	23.3	1,023	28.9
Queensland	1,375	18	1.3	68	4.9	284	20.7	379	27.6
South Australia[a]	231	3	1.3	7	3.0	52	44.1	57	48.3
Tasmania	55	4	7.3	3	5.5	14	25.5	20	36.4
Victoria	2,619	83	3.2	217	8.3	529	20.2	610	23.3
Northern Territory non-remote	68	0	0	1	1.5	6	8.8	7	10.3
Northern Territory remote	157	0	0	0	0	3	1.9	3	1.9
Western Australia non-remote	652	14	2.1	16	2.5	155	23.8	173	26.5
Western Australia remote	108	0	0	1	0.9	7	6.5	5	4.6
Australia	**9,006**	**156**	**1.73**	**561**	**6.2**	**1,897**	**21.1**	**2,303**	**25.6**

a Number of isolates resistant to both penicillin and ciprofloxacin = 120

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Table 4: Number and proportion (%) of gonococcal isolates with decreased susceptibility to ceftriaxone (MIC ≥0.06 mg/L), Australia, 2010 to 2018, by state or territory. Remote Western Australian data was de-aggregated from 2014.

Jurisdiction	Decreased susceptibility to ceftriaxone																	
	2010		2011		2012		2013		2014		2015		2016		2017		2018	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
ACT	3	**6.7**	2	**3.1**	2	**3.6**	0	**0**	2	**2.7**	0	**0.0**	1	**0.9**	0	**0**	4	**1.9**
NSW	74	**5.6**	58	**4.4**	76	**4.5**	183	**11.8**	119	**7.1**	52	**2.7**	45	**2.0**	13	**0.5**	30	**0.8**
Qld	17	**3.2**	18	**2.3**	17	**2.4**	33	**4.9**	21	**3.2**	7	**1.0**	32	**3.7**	11	**0.9**	18	**1.3**
SA	12	**11.6**	1	**0.7**	1	**0.7**	4	**1.9**	2	**1.0**	9	**3.6**	2	**0.6**	2	**0.6**	3	**1.3**
Tas	0	**0**	0	**0**	0	**0**	11	**24.4**	0	**0**	0	**0**	1	**3.6**	0	**0**	4	**7.3**
Vic	52	**5.7**	50	**5.3**	105	**8.4**	181	**11.8**	95	**6.6**	25	**1.5**	19	**1.1**	48	**2.1**	83	**3.2**
NT non-Remote	1	**0.2**	2	**0.4**	0	**0**	2	**1.9**	3	**3.0**	0	**0**	0	**0**	0	**0**	0	**0**
NT Remote	0	**0**	0	**0**	0	**0**	2	**0.8**	1	**0.8**	0	**0**	0	**0**	0	**0**	0	**0**
WA	17	**5.2**	3	**0.7**	6	**1.2**	13	**2.7**										
WA Urban/Rural									14	**3.6**	5	**1.3**	9	**1.3**	9	**1.4**	14	**2.1**
WA Remote									1	**0.9**	0	**0**	0	**0**	0	**0**	0	**0**
Australia	**191**	**4.8**	**134**	**3.2**	**207**	**4.4**	**429**	**8.8**	**258**	**5.4**	**98**	**1.8**	**109**	**1.7**	**83**	**1.1**	**156**	**1.7**

Table 5: Proportion (%) of gonococcal isolates tested in Australia with ceftriaxone MIC values at 0.06 mg/L and ≥0.125 mg/L, 2010–2018.

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

Since 2012 the rate of azithromycin resistance in Australian NG isolates increased almost five-fold, as shown in Table 6. Rates of azithromycin-resistant NG were highest in the Australian Capital Territory (8.7%), Victoria (8.3%) and New South Wales (6.5%) as shown in Tables 3 and 6. In 2018, 9 isolates exhibited high level resistance to azithromycin (MIC value ≥ 256 mg/L), four from New South Wales, three from Victoria and two from Queensland. As noted above, the two isolates from Queensland were extensively drug-resistant (XDR) strains with high ceftriaxone MIC values. An additional 21 isolates were detected with resistance to azithromycin, penicillin and ciprofloxacin. 4.1% of azithromycin-resistant isolates demonstrated penicillin and ciprofloxacin resistance.

Penicillin

Resistance to the penicillin group of antibiotics (penicillin, ampicillin and amoxycillin with or without clavulanic acid) in NG results from ß-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 resistance to penicillin (CMRP). Chromosomal resistance is defined as a penicillin MIC value ≥1 mg/L.

In 2018, in Australia, 1,897 (21.1%) isolates were penicillin resistant, a proportional decrease from 2016 (32.5%), and 2017 (26.1%). The proportion of penicillin-resistant isolates fluctuated in the range 22.5 to 44% between 2008 and 2017. In 2018, a total of 1,004 (11.3%) isolates had CMRP and 893 (10.0%) were PPNG; 47.1% of penicillin-resistant isolates were PPNG.

Penicillin resistance in remote Australia

In 2018, there were 225 isolates tested from the Northern Territory with 157 derived from remote areas of NT (including Alice Springs, Katherine, Tennant Creek, and Arnhem Land region) and 68 from Darwin and surrounding urban areas (non-remote). In 2018, a total of 760 isolates were tested from Western Australia, with 108 obtained from remote regions and 652 from urban and suburban Perth (non-remote).

Of the 157 isolates from remote NT, only 3 (1.9%) were penicillin resistant (1 was PPNG). 6 isolates (8.8%) from Darwin and surrounding urban areas were penicillin resistant (4 were PPNG) (Table 3). Of the 108 isolates from remote Western Australia, 7 (6.5%) were penicillin resistant, with 6 being PPNG. No isolate from remote NT or WA demonstrated decreased susceptibility to ceftriaxone.

Quinolones

The AGSP uses ciprofloxacin as the representative quinolone. Ciprofloxacin resistance is defined as MIC ≥1 mg/L. In 2018, there were 2,303 ciprofloxacin resistant isolates (25.6%) (Table 3). Since 2008, when 54% of isolates tested ciprofloxacin resistant, the resistance rate has progressively declined.

Tetracyclines

To facilitate accurate reporting of NG tetracycline resistance in Australia, from 2018 NNN reference laboratories have performed tetracycline MIC testing where possible. This replaces historical testing for high level tetracycline testing which was reported by the NNN as an epidemiological marker for plasmid mediated resistance since inception. Tetracycline resistance is defined as an MIC value ≥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 ≥16 mg/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, 2,493 isolates were tested and 32% (797/2,493) were tetracycline resistant. Tetracycline resistance data are presented by jurisdiction and aggregated for Australia as shown in Table 7.

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Table 6: Number and proportion (%) of gonococcal isolates with resistance to azithromycin (MIC ≥1.0 mg/L), Australia, 2012 to 2018, by state or territory.

State or territory	Azithromycin resistance													
	2012		2013		2014		2015		2016		2017		2018	
	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**
NSW	9	**0.5**	14	**0.9**	33	**2.0**	43	**2.3**	82	**3.6**	261	**9.3**	230	**6.5**
Qld	15	**2.1**	38	**5.7**	23	**3.5**	42	**5.8**	10	**1.2**	61	**4.9**	68	**4.9**
SA	1	**0.7**	6	**2.8**	1	**0.5**	7	**2.8**	68	**19.5**	46	**12.8**	7	**3.0**
Tas	0	**0**	0	**0**	1	**3.3**	1	**4.3**	4	**14.3**	5	**9**	3	**6**
Vic	34	**2.7**	35	**2.3**	33	**2.3**	30	**1.8**	93	**5.4**	304	**13.5**	217	**8.3**
NT Urban & Rural	0	**0**	1	**1.0**	0	**0**	0	**0**	1	**1.9**	1	**1.7**	1	**1.5**
NT Remote	0	**0**	0	**0**	0	**0**	0	**0**	0	**0**	1	**0.6**	0	**0.0**
WA Urban and Rural	3	**0.6**	9	**1.9**	21	**5.3**	15	**3.8**	51	**7.6**	40	**6.4**	16	**2.5**
WA Remote	0	**0**	0	**0**	0	**0**	0	**0**	1	**0.8**	4	**3.4**	1	**0.9**
Australia	**62**	**1.3**	**104**	**2.1**	**119**	**2.5**	**138**	**2.6**	**318**	**5.0**	726	**9.3**	561	**6.2**

Spectinomycin

In 2018, all isolates tested were susceptible to spectinomycin.

Discussion

The WHO 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, and has established and coordinated quality assurance, and quality control, for gonococcal AMR testing with the AGSP External Quality Assurance Program, and the development of the WHO NG reference strains, thus ensuring the quality of the AGSP data.[19,21] In 2018 the NNN examined 9,006 clinical isolates for susceptibility testing to ceftriaxone, azithromycin, ciprofloxacin, penicillin and high-level resistance to tetracycline. These isolates were referred from both the public and private health sectors, constituting a comprehensive sample of about one-third of all notifications nationally. Coincident with the increases in NG disease rates in Australia,[2] there has been an increase in the numbers of gonococcal isolates tested for AMR. However, the proportion remains relatively unchanged at about 30%.

Both in Australia and internationally, the monitoring of ceftriaxone and azithromycin MIC values is the primary focus of surveillance for gonococcal AMR. With regard to ceftriaxone, MIC values ≥0.06 mg/L are reported to have decreased susceptibility. The AGSP proportion of isolates with decreased susceptibility to ceftriaxone has steadily and substantially declined since 2013 from 8.8% to 1.7% in 2018 (Table 4). However little reassurance should be taken from this, as multidrug-resistant strains with high-level resistance to ceftriaxone have been reported from Asia, Europe and Australia in recent years.[22–25]

In 2017 the AGSP identified two new multidrug-resistant NG isolates in Australia. These strains were phenotypically similar to the ceftriaxone-resistant strain first reported in Japan in 2015 (FC428), and similar strains in Denmark (GK124) and Canada (47,707).[3] Further investigations, in collaboration by the NNN with international colleagues, found that, on bioinformatic analysis, there was close genetic relatedness amongst other phenotypically similar isolates from Japan and Canada providing further evidence of international transmission of this ceftriaxone-resistant *N. gonorrhoeae* strain.[3]

In 2018 two isolates of global concern were detected by the AGSP and reported by the Australian Government to the World Health Organization due to their international significance. These two isolates, with ceftriaxone MIC values of 0.50 mg/L, high-level resistance to azithromycin (MIC value ≥ 256 mg/L), and resistance to penicillin and ciprofloxacin were isolated from patients, not determined to be contacts, from Queensland. One had a history of travel to South East Asia. At the same time an isolate with a similar phenotype was identified in England, also with a history of travel to South East Asia.[26] Again, the NNN, through international collaboration, this time with UK colleagues through the WHO Collaborating Centre Network, worked to investigate the genotypic analysis of these three isolates and determined that they represent a single gonococcal clone, the A2543 clone.[27] In all likelihood this A2543 clone is circulating, but undetected due to gaps in NG AMR surveillance internationally.[27]

Remote populations of Australia, which are predominantly Aboriginal and Torres Strait Islander, have low rates of AMR despite very high rates of disease, but require continued vigilance with monitoring of AMR in NG using molecular and culture-based surveillance strategies.

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.[28] Since then there have been only sporadic reports

Table 7: Number and proportion (%) of gonococcal isolates with resistance to tetracycline (MIC ≥2 mg/L), Australia, 2018, by state or territory

State or Territory	Number of isolates tested	Resistance MIC ≥2 mg/L	
	2018	Tetracycline	
		n	%
Australian Capital Territory	190	16	8.4
New South Wales	88	59	67.0
Queensland	3	2	66.7
South Australia	2	1	50
Tasmania	53	9	17.0
Victoria	1,320	519	39.3
Northern Territory (non-remote)	17	3	17.6
Northern Territory (remote)	65	5	7.7
Western Australia (non-remote)	648	173	26.7
Western Australia (remote)	107	10	9.3
AUSTRALIA	**2,493**	**797**	**32.0**

of HLR to azithromycin; however, there were nine such strains in 2018. Additionally, there were 23 isolates (including the XDR strains described above) that were resistant to azithromycin, penicillin and ciprofloxacin. The proportion of azithromycin resistant isolates that were also resistant to penicillin and ciprofloxacin was 4.1%. Continued close observation is ongoing as evidence of coevolving cephalosporin and azithromycin resistance is being observed outside Australia and is of significant concern.[29]

Another important and concerning finding by the AGSP in 2018 is the increase in isolates with low level resistance to azithromycin in all jurisdictions of Australia, excepting the ACT and Northern Territory (Table 6). In remote WA there were four azithromycin resistant strains reported. Until recently azithromycin resistance in Australia in NG has remained relatively low at 1.3–2.6% over the years 2012–2015 but has then increased from 5% in 2016 to 9.3% in 2017 (Table 6). In South Australia in 2016, azithromycin resistance in NG significantly increased (p<0.0001) from less than 5% in the latter half of 2015 to 26% in the first half of 2016.[30] Overall in 2016, there were 68/349 (19.5%) strains in South Australia that were azithromycin resistant with MIC values in the range 1.0 mg/L to 8.0 mg/L. Enhanced surveillance was conducted, and one treatment failure was reported in a patient treated with azithromycin single agent therapy.[6] A review and change of the South Australian gonococcal treatment guidelines followed.[6] In 2018 azithromycin resistance was highest in the Australian Capital Territory (8.7%), Victoria (8.3%) and New South Wales 6.5%). Globally there have been increasing reports of azithromycin resistance.[31]

The recent reports of international spread of NG with resistance to ceftriaxone,[26] and the emergence of azithromycin resistance, heighten concerns about the future treatment strategies

for NG AMR. Public health strategies promoting primary prevention of gonorrhoea and other sexually transmissible infections are urgently required, and NG vaccine development is a research priority to control this disease. This report underscores the importance of bacterial culture and antimicrobial susceptibility testing of NG for clinical management, detection of resistance and novel resistant strains, AMR surveillance, and test of cure. Clinicians should note and consider travel history given the association with NG AMR.

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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