

AUSTRALIAN GONOCOCCAL SURVEILLANCE PROGRAMME, 1 JULY TO 30 SEPTEMBER 2014

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Introduction

The Australian National Neisseria Network (NNN) comprises reference laboratories in each state and territory that report data on sensitivity to an agreed group of antimicrobial agents for the Australian Gonococcal Surveillance Programme (AGSP). The antibiotics are penicillin, ceftriaxone, azithromycin and ciprofloxacin, which are current or potential agents used for the treatment of gonorrhoea. Azithromycin testing has been recently introduced by all states and territories as it is part of a dual therapy regimen with ceftriaxone recommended for the treatment of gonorrhoea in the majority of Australia. Because of the substantial geographic differences in susceptibility patterns in Australia, regional as well as aggregated data are presented. In certain remote regions of the Northern Territory and Western Australia gonococcal antimicrobial resistance rates are low and an oral treatment regimen comprising amoxicillin, probenecid and azithromycin is recommended for the treatment of gonorrhoea. When in vitro resistance to a recommended agent is demonstrated in 5% or more of isolates from a general population, it is usual to remove that agent from the list of recommended treatments.¹ Additional data on other antibiotics are reported in the AGSP annual report. The AGSP has a program-specific quality assurance process. The AGSP data are presented

quarterly in tabulated form, as well as in the AGSP annual report. For more information see *Commun Dis Intell* 2015;39(1):E178–E179.

Results

A summary of the proportion of isolates with decreased susceptibility to ceftriaxone, and the proportion resistant to penicillin, ciprofloxacin and azithromycin are shown in Table 1.

Penicillin

Penicillin resistant *Neisseria gonorrhoeae* (NG) are defined as those isolates with a minimum inhibitory concentration (MIC) to penicillin equal to or greater than 1.0 mg/L. Penicillin resistance includes penicillinase producing NG (PPNG), and NG that have chromosomally mediated resistance to penicillin (CMRP). In certain areas of the Northern Territory and Western Australia, which are classified as remote, a treatment regimen based on oral amoxicillin, probenecid and azithromycin is used. Due to the distance specimens must travel to a laboratory from these remote regions, low numbers of cultures are collected, and thus, by necessity, nucleic acid amplification testing (NAAT) is used. In remote Western Australia, the introduction of a targeted NAAT, developed by the NNN to detect PPNG, is in use to enhance surveillance.^{2,3}

Table 1: Gonococcal isolates showing decreased susceptibility to ceftriaxone and resistance to ciprofloxacin, azithromycin and penicillin, Australia, 1 July to 30 September 2014, by state or territory

State or territory	Number of isolates tested	Decreased susceptibility		Resistance					
		Ceftriaxone		Ciprofloxacin		Azithromycin		Penicillin	
		n	%	n	%	n	%	n	%
Australian Capital Territory	4	0	0.0	1	25.0	0	0.0	1	25.0
New South Wales	429	23	5.4	181	42.0	13	3.0	187	44.0
Queensland	143	5	3.5	39	27.0	9	6.0	34	24.0
South Australia	41	0	0.0	14	34.0	0	0.0	5	12.0
Tasmania	5	2	40.0	2	50.0	0	0.0	1	25.0
Victoria	356	19	5.3	153	43.0	8	2.2	67	20.0
Northern Territory/Urban and Rural	23	2	8.7	7	30.0	0	0.0	6	26.0
Northern Territory/Remote	30	1	3.3	1	3.3	0	0.0	0	0.0
Western Australia/Urban and Rural	104	5	4.8	22	21.0	4	3.8	21	20.0
Western Australia/Remote	27	0	0.0	0	0.0	0	0.0	0	0.0
Australia	1,162	57	4.9	420	36.0	34	2.9	322	28.0

Ciprofloxacin

Ciprofloxacin resistance includes isolates with an MIC to ciprofloxacin equal to or greater than 0.06 mg/L.

Azithromycin

Azithromycin resistance is defined as a MIC to azithromycin equal to or greater than 1.0 mg/L. In 2013, 4 gonococcal strains with azithromycin high level resistance were reported from Victoria and Queensland.⁴ There was 1 strain reported from New South Wales with high level resistance (azithromycin MIC value >256 mg/L) in this quarter of 2014.

Ceftriaxone

Ceftriaxone MIC values in the range 0.06–0.125 mg/L have been reported in the category decreased susceptibility (DS) since 2005.

In the 1st quarter of 2014 there was a decrease in the proportion of NG isolates with DS to ceftriaxone, predominantly from New South Wales and Victoria, when compared with the same quarter in 2013; and the annual data for 2013.⁴ The highest proportions of isolates with decreased susceptibility to ceftriaxone were reported from New South Wales and Victoria.

From New South Wales, there were 23 of 429 strains with DS to ceftriaxone. Of those, 16 (70%) were multi-drug resistant (MDR); 20 (87%) were from males; and 6 (26%) were isolated from extragenital sites (rectal and pharyngeal). From Victoria, there were 19 356 strains with DS to ceftriaxone and, of those, 10 (53%) were MDR; 8 (50%) were from males; and 7 (36%) were isolated from extragenital sites (rectal and pharyngeal).

From urban and rural Western Australia, there were 5 of 104 strains with DS to ceftriaxone. Of those, 3 (60%) were MDR; 5 (100%) were from males; and 3 (60%) were isolated from extragenital sites (rectal and pharyngeal). From Queensland, there were 5 of 143 strains with DS to ceftriaxone and, of those, all (100%) were MDR; 1 (20%) was from a male; and none were isolated from extragenital sites (rectal and pharyngeal). In contrast,

there were no gonococci with DS to ceftriaxone reported from Australia Capital Territory, South Australia, or remote Western Australia; and low numbers were reported from Tasmania, and urban and remote Northern Territory.

The proportion of strains with DS to ceftriaxone is of increasing concern in Australia and overseas, as this is phenotypic of the genotype with the key mutations that are the precursor to ceftriaxone resistance.⁵ There are recent reports of ceftriaxone 500 mg treatment failures in patients from Victoria and New South Wales in patients with pharyngeal gonococcal infections. In these patients the infecting gonococcal strains had ceftriaxone MIC values in the range 0.03–0.06 mg/L.^{6,7} Until 2014, there had not been an isolate reported in Australia with a ceftriaxone MIC value >0.125 mg/L.⁴ In late December 2013, there was a new multi-drug-resistant gonococcal strain (A8806) with a ceftriaxone MIC of 0.5 mg/L, the highest ever reported in Australia, which was isolated from a female traveller from Central Europe. This infection was acquired in Sydney from another traveller, also from Europe. The patient was tested in the Northern Territory, but had travelled to north-eastern Queensland before the results were available, and was treated there. To date there has been no evidence of spread of this strain.⁸

The category of ceftriaxone DS as reported by the AGSP includes the MIC values 0.06 and 0.125 mg/L. The right shift in the distribution of ceftriaxone MIC values over recent years (Table 2), is statistically significant with a sustained increase in the proportion of strains with an MIC value of 0.06 mg/L (2011–2012: [P=0.02, 95% CI: 1.04–1.62], and 2012–2013 [P<0.0001, 95% CI: 1.70–2.38]). In 2010, the proportion of strains with ceftriaxone DS was higher than that reported in 2011. This proportion has subsequently increased as shown in Table 2. The proportion of strains with a ceftriaxone MIC 0.125 mg/L has also increased from 0.1% in 2010 and 2011, to 0.3% in 2012 and to 0.6% in 2013. These differences were not significant, however this may be attributable to the low number of strains in this MIC category.⁴ In the first 2 quarters of 2014 there were lower proportions of strains with MIC values at 0.06 and 0.125 mg/L than reported in 2013. In the 3rd quarter of 2014, the proportion of strains with ceftriaxone MIC of

Table 2: Percentage of gonococcal isolates with decreased susceptibility to ceftriaxone MIC 0.06–0.125 mg/L, Australia, 2010 to 2013, and 1 July to 30 September 2014, by state or territory

Ceftriaxone MIC mg/L	2010	2011	2012	2013	2014 Q1	2014 Q2	2014 Q3
0.06	4.6%	3.2%	4.1%	8.2%	6.4%	5.4%	4.2%
0.125	0.1%	0.1%	0.3%	0.6%	0.4%	0.3%	0.7%

0.06 mg/L was lower than in the previous 2 quarters but there was an increase in the proportion of strains with an MIC of 0.125 mg/L, which will continue to be monitored.

Dual therapy of ceftriaxone plus azithromycin is the recommended treatment for gonorrhoea as a strategy to temper development of more widespread resistance.⁸ Patients with infections in extragenital sites, where the isolate has DS to ceftriaxone, are recommended to have test of cure cultures collected. Continued surveillance to monitor *N. gonorrhoeae* with elevated MIC values, coupled with sentinel site surveillance in high risk populations, remains critically important to inform therapeutic strategies, to identify incursion of resistant strains and to detect instances of treatment failure.

References

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