Australian Gonococcal Surveillance Programme, 1 January to 31 March 2016

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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 combined with ceftriaxone is the recommended treatment regimen for gonorrhoea in the majority of Australia. However, there are substantial geographic differences in susceptibility patterns in Australia and in certain remote regions of the Northern Territory and Western Australia gonococcal antimicrobial resistance rates are low, and an oral treatment regimen comprising amoxycillin, 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.

Results

A summary of the proportion of isolates with decreased susceptibility to ceftriaxone, and the proportion resistant to azithromycin, penicillin, and ciprofloxacin for the 1st quarter of 2016 are shown in Table 1.

Ceftriaxone

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

In the 1st quarter of 2016 the states that reported isolates with decreased susceptibility to ceftriaxone were New South Wales, Victoria, Queensland, urban/rural Western Australia and the Australian Capital Territory. No decreased susceptibility to ceftriaxone was reported in South Australia, the remote regions of Western Australia, the Northern Territory or Tasmania. New South Wales and Victoria reported a decrease in the proportion of *Neisseria gonorrhoeae* isolates with decreased susceptibility to ceftriaxone when compared with the same quarter in 2015. Compared with the annual data for 2015, New South Wales, Victoria, and

Table 1: Gonococcal isolates showing decreased susceptibility to ceftriaxone and resistance to azithromycin, penicillin, and ciprofloxacin, Australia, 1 January to 31 March 2016, by state or territory

State or territory	Number of isolates tested	Decreased susceptibility		Resistance					
		Ceftriaxone		Azithromycin		Penicillin		Ciprofloxacin	
		n	%	n	%	n	%	n	%
Australian Capital Territory	22	1	4.5	2	9.1	2	9.1	6	27.3
New South Wales	590	14	2.4	5	0.8	205	34.7	206	34.9
Queensland	166	2	1.2	4	2.4	43	25.9	37	22.3
South Australia	88	0	0.0	26	29.5	37	42.0	24	27.3
Tasmania	7	0	0.0	0	0.0	3	42.9	2	28.6
Victoria	445	3	0.7	7	1.6	111	24.9	157	9.4
Northern Territory Urban & Rural	14	0	0.0	0	0.0	4	28.6	3	21.4
Northern Territory Remote	63	0	0.0	0	0.0	2	3.2	4	6.3
Western Australia Urban & Rural	152	3	2.0	6	3.9	29	19.1	35	23.0
Western Australia Remote	25	0	0.0	0	0.0	1	4.0	0	0.0
Australia	1,572	23	1.5	50	3.2	437	27.8	474	30.2

South Australia reported a decrease in the proportion of *N. gonorrhoeae* isolates with decreased susceptibility to ceftriaxone. Queensland and urban/rural Western Australia reported an increase in the proportion of *N. gonorrhoeae* isolates with decreased susceptibility to ceftriaxone, while the other states reported similar results.[2]

From New South Wales there were 14 of 590 strains with decreased susceptibility to ceftriaxone. Of those, all were multidrug-resistant (MDR); 12 (86%) were from males; and 6 (43%) were isolated from extragenital sites (rectal and pharyngeal). From Victoria, 3 of 445 strains had decreased susceptibility to ceftriaxone. All were MDR and from males; and 2 (67%) were isolated from extragenital sites. From Queensland, 2 of 166 strains had decreased susceptibility to ceftriaxone and of those, 1 (50%) was MDR, 1 (50%) was from a male, and 1 (50%) was from an extragenital site. From urban/rural Western Australia there were 3 of 152 strains with decreased susceptibility to ceftriaxone; all of which were MDR, from males, and from extragenital sites. From the Australian Capital Territory there was 1 of 22 strains with decreased susceptibility to ceftriaxone, it was MDR, from a male, but not from an extragenital site.

In recent years the proportion of strains with decreased susceptibility to ceftriaxone has been 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.[3] 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.[4,5] Until 2013 there had not been an isolate reported in Australia with a ceftriaxone MIC value >0.125 mg/L.[2] In late December 2013 there was a new multidrug-resistant gonococcal strain (A8806) with a ceftriaxone MIC of 0.5 mg/L, the highest ever reported in Australia that 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.[6]

The category of ceftriaxone decreased susceptibility as reported by the AGSP includes the MIC values 0.06 and 0.125 mg/L (Table 2).

Azithromycin

Azithromycin resistance is defined as a MIC to azithromycin equal to or greater than 1.0 mg/L.

In the 1st quarter of 2016, all states reported isolates with resistance to azithromycin, with the exception of Tasmania, the Northern Territory and remote Western Australia. Notably the reported proportion of *N. gonorrhoeae* isolates with resistance to azithromycin in South Australia was 26/88 (29.5%) in the 1st quarter of 2016, compared with none in the same quarter in 2015. None of these strains had high level resistance, all were resistant to penicillin (beta-lactamase producing); and sensitive to ceftriaxone and ciprofloxacin. Enhanced surveillance, case reviews, and genotypic investigations are in process in South Australia with further results to follow.

In the Australian Capital Territory there were 2/22 (9.1%) isolates from the 1st quarter of 2016 that were resistant to ceftriaxone compared with none in the same quarter in 2015. The states that reported a decrease in the proportion of *N. gonorrhoeae* isolates with resistance to azithromycin when compared with the same quarter in 2015 were New South Wales, Queensland, Tasmania, and urban/rural Western Australia. The other states reported similar results from the same quarter of 2015.

Penicillin

Penicillin resistant *N. gonorrhoeae* are defined as those isolates with a MIC to penicillin equal to or greater than 1.0 mg/L. Penicillin resistance includes penicillinase producing *N. gonorrhoeae* (PPNG), and *N. gonorrhoeae* 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 in these remote regions to a laboratory, low numbers of cultures are collected, and thus, by necessity, nucleic acid amplification testing (NAAT) is used. In remote

Table 2: Percentage of gonococcal isolates with decreased susceptibility to ceftriaxone MIC 0.06–0.125 mg/L, Australia, 2011 to 2015, and 1 January to 31 March 2016

Ceftriaxone MIC mg/L	2011	2012	2013	2014	2015	2016 Q1
0.06 (%)	3.2	4.1	8.2	4.8	1.7	1.5
0.125 (%)	0.1	0.3	0.6	0.6	0.1	0.0

Western Australia the introduction of a targeted NAAT, developed by the NNN to detect PPNG, is in use to enhance surveillance.[7,8]

Ciprofloxacin

Ciprofloxacin resistance includes isolates with an MIC to ciprofloxacin equal to or greater than 1.0 mg/L.

Dual therapy of ceftriaxone plus azithromycin is the recommended treatment for gonorrhoea as a strategy to temper development of more widespread resistance.[6] Patients with infections in extragenital sites, where the isolate has decreased susceptibility 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 important to inform therapeutic strategies, to identify incursion of resistant strains, and to detect instances of treatment failure.

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