Australian Gonococcal Surveillance Programme, 1 April to 30 June 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 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] 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, which includes additional data on other antibiotics. For more information see *Commun Dis Intell* 2014;38(1):E94–E95.

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* 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 *N. gonorrhoeae* (PPNG), and *N. gonorrhoeae* that have chromosomally mediated resistance to penicillin. In certain areas, classified as remote in the Northern Territory and Western Australia, a treatment regimen based on oral amoxycillin, probenecid and azithromycin is used. Low numbers of cultures are collected in these remote regions due to the distance specimens must travel to a laboratory, and thus by necessity use nucleic acid amplification testing (NAAT). In remote Western

Table 1: Gonococcal isolates showing decreased susceptibility to ceftriaxone and resistance to ciprofloxacin, azithromycin and penicillin, Australia, 1 April to 30 June 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	15	0	0.0	8	53.0	0	0.0	2	13.0
New South Wales	370	16	4.3	189	51.0	3	0.8	174	47.0
Queensland	172	2	1.0	58	34.0	5	3.0	40	23.0
South Australia	49	1	2.0	23	47.0	0	0.0	3	6.1
Tasmania	4	1	25.0	2	50.0	0	0.0	1	25.0
Victoria	339	37	10.9	135	40.0	7	2.1	69	20.0
Northern Territory/Urban and Rural	17	0	0.0	3	18.0	0	0.0	2	12.0
Northern Territory/Remote	34	0	0.0	2	5.9	0	0.0	3	8.8
Western Australia/Urban and Rural	86	6	7.0	27	31.0	4	4.8	22	26.0
Western Australia/Remote	31	0	0.0	2	6.5	0	0.0	1	3.2
Australia	1,117	63	5.6	449	40.0	19	1.7	317	28.0

Australia the introduction of a targeted NAAT, developed by the NNN to detect PPNG, is in use to enhance surveillance.[2,3]

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 were no isolates reported in Australia with high level resistance (azithromycin MIC value >256 mg/L) in this quarter, 2014.

Ceftriaxone

Ceftriaxone 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 2014 there was a decrease in the proportion of *N. gonorrhoeae* isolates with decreased susceptibility to ceftriaxone, when compared with the same quarter in 2013; and the annual data for 2013.[4] There were predominantly from New South Wales and Victoria. When compared to the 1st quarter of 2013, there was a decrease from 6.8% to 5.6% in the proportion of *N. gonorrhoeae* isolates with decreased susceptibility to ceftriaxone nationally; however this proportion is more than double that reported in the 2nd quarters of 2011 and 2012 (2.7%–3.5%).

The highest proportions of isolates with decreased susceptibility to ceftriaxone were reported from Victoria, New South Wales and Western Australia. From Victoria there were 37 strains with decreased susceptibility to ceftriaxone and of those, 20 (45%) were multi-drug resistant (MDR); 34 (92%) were from males; and 24 (%) were isolated from extragenital sites (rectal and pharyngeal). From New South Wales, there were 16 strains with decreased susceptibility to ceftriaxone and of those, 10 (62%) were (MDR; 16 (100%) were from males; and 9 (56%) were isolated from extragenital sites (rectal and pharyngeal). From Western Australia there were 6 strains with decreased susceptibility to ceftriaxone and, of those, 5 (83%) were MDR; 6 (100%) were from males; and 3 (50%) were isolated from extragenital sites (rectal and pharyngeal). In contrast, there were no gonococci with decreased susceptibility to ceftriaxone reported from the Australian Capital Territory, the Northern Territory or remote Western Australia and low numbers were reported from Queensland and South Australia. From Tasmania there was 1 strain with decreased susceptibility to ceftriaxone of the 4 strain tested.

The proportion of strains with decreased susceptibility 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 were 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, a MDR gonococcal strain with a ceftriaxone MIC of 0.5 mg/L, the highest ever reported in Australia, was isolated (unpublished data from the NNN). To date, there has been no evidence of spread of this strain in the first 2 quarters of 2014.

The category of ceftriaxone decreased susceptibility 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 decreased susceptibility was higher than that reported in 2011. This proportion has subsequently increased as described. 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, which may be attributable to the low

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

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

number of strains in this MIC category.[4] In the first 2 quarters of 2014, there are lower proportions of strains at both 0.06 and 0.125 mg/L than reported in 2013.

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 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 critically important to inform therapeutic strategies, to identify incursion of resistant strains and to detect instances of treatment failure.

References

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