

AUSTRALIAN GONOCOCCAL SURVEILLANCE PROGRAMME, 1 APRIL TO 30 JUNE 2015

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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 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.

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 (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 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 April to 30 June 2015, by state or territory

State or territory	Number of isolates tested quarter 2 2015	Decreased susceptibility		Resistance					
		Ceftriaxone		Ciprofloxacin	Azithromycin	Penicillin			
		n	%	n	%	n	%	n	%
Australian Capital Territory	23	0	0.0	1	4.3	0	0.0	11	47.8
New South Wales	439	6	1.4	133	30.3	7	1.6	112	25.5
Queensland	159	0	0.0	47	29.6	11	6.9	42	26.4
South Australia	54	0	0.0	19	35.2	0	0.0	7	13.0
Tasmania	8	0	0.0	0	0.0	0	0.0	1	12.5
Victoria	453	7	1.5	53	11.7	13	2.9	74	16.3
Northern Territory/Urban & Rural	46	0	0.0	0	0.0	0	0.0	0	0.0
Northern Territory/Remote	18	0	0.0	3	16.7	0	0.0	3	16.7
Western Australia/Urban & Rural	94	1	1.1	22	23.4	4	4.3	16	17.0
Western Australia/Remote	24	0	0.0	1	4.2	0	0.0	0	0.0
Australia	1,318	14	1.1	279	21.2	35	2.7	266	20.2

Ciprofloxacin

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

Azithromycin

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

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 2015 the only states that reported isolates with decreased susceptibility to ceftriaxone were New South Wales, Victoria and urban Western Australia. All reported a decrease in the proportion of *N. gonorrhoeae* isolates with decreased susceptibility to ceftriaxone when compared with the same quarter in 2014; and the annual data for 2014.⁴

From New South Wales there were 6 of 439 strains with decreased susceptibility to ceftriaxone. Of those, 2 (33%) were multi-drug resistant (MDR); all (100%) were from males; and 3 (50%) were isolated from extragenital sites (rectal and pharyngeal). From Victoria there were 7 of 453 strains with decreased susceptibility to ceftriaxone and of those, all (100%) were MDR; all (100%) were from males; and 4 (57%) were isolated from extragenital sites (rectal and pharyngeal). From urban Western Australia one of the 94 strains tested had decreased susceptibility to ceftriaxone. This strain was from a male, was MDR and not from an extragenital site (rectal or pharyngeal).

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 are recent reports of ceftriaxone 500 mg treatment failures in patients from Victoria and New South Wales 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 2013 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 MDR 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 decreased susceptibility as reported by the AGSP includes the MIC values 0.06–0.125 mg/L. (Table 2).

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

Table 2: Percentage of gonococcal isolates with decreased susceptibility to ceftriaxone MIC 0.06–0.125 mg/L, Australia, 2010 to 2014, 1 January to 31 March 2015, and 1 April to 30 June 2015, by state or territory

Ceftriaxone MIC mg/L	2010	2011	2012	2013	2014	2015 Q1	2015 Q2
0.06	4.6	3.2	4.1	8.2	4.8	1.6	1.1
0.125	0.1	0.1	0.3	0.6	0.6	0.1	0.0

References

1. Surveillance of antibiotic susceptibility of *Neisseria gonorrhoeae* in the WHO western Pacific region 1992–4. WHO Western Pacific Region Gonococcal Antimicrobial Surveillance Programme. *Genitourin Med* 1997;73(5):355–361.
2. Speers DJ, Fisk RE, Goire N, Mak DB. Non-culture *Neisseria gonorrhoeae* molecular penicillinase production surveillance demonstrates the long-term success of empirical dual therapy and informs gonorrhoea management guidelines in a highly endemic setting. *J Antimicrob Chemother* 2014;69(5):1243–1247.
3. Goire N, Freeman K, Tapsall JW, Lambert SB, Nissen MD, Sloots TP, et al. Enhancing gonococcal antimicrobial resistance surveillance: a real-time PCR assay for detection of penicillinase-producing *Neisseria gonorrhoeae* by use of noncultured clinical samples. *J Clin Microbiol* 2011;49(2):513–518.
4. Lahra MM. Australian Gonococcal Surveillance Programme annual report, 2013. *Commun Dis Intell* 2015;39(1):E137–E145.
5. Goire N, Lahra MM, Chen M, Donovan B, Fairley CK, Guy R, et al. Molecular approaches to enhance surveillance of gonococcal antimicrobial resistance. *Nat Rev Microbiol* 2014 Mar;12(3):223–229.
6. Chen YM, Stevens K, Tideman R, Zaia A, Tomita T, Fairley CK, et al. Failure of 500 mg of ceftriaxone to eradicate pharyngeal gonorrhoea, Australia. *J Antimicrob Chemother* 2013;68(6):1445–1447.
7. Read PJ, Limnios EA, McNulty A, Whiley D, Lahra MM. One confirmed and one suspected case of pharyngeal gonorrhoea treatment failure following 500 mg ceftriaxone in Sydney, Australia. *Sex Health* 2013;10(5):460–462.
8. Australian Sexual Health Alliance. *The Australian Sexually Transmitted Infection Management Guidelines* 2014. Available from: <http://www.sti.guidelines.org.au>