



Australian Government
Department of Health

COMMUNICABLE DISEASES INTELLIGENCE

2019 Volume 43
<https://doi.org/10.33321/cdi.2019.43.13>

Australian Gonococcal Surveillance Programme Annual Report, 2017

Monica M Lahra, Rodney Enriquez and C R Robert George
for the National Neisseria Network, Australia.

Communicable Diseases Intelligence

ISSN: 2209-6051 Online

This journal is indexed by Index Medicus and Medline.

Creative Commons Licence - Attribution-NonCommercial-NoDerivatives CC BY-NC-ND

© 2019 Commonwealth of Australia as represented by the Department of Health

This publication is licensed under a Creative Commons Attribution-Non-Commercial NoDerivatives 4.0 International Licence from <https://creativecommons.org/licenses/by-nc-nd/4.0/legalcode> (Licence). You must read and understand the Licence before using any material from this publication.

Restrictions

The Licence does not cover, and there is no permission given for, use of any of the following material found in this publication (if any):

- the Commonwealth Coat of Arms (by way of information, the terms under which the Coat of Arms may be used can be found at www.itsanhonour.gov.au);
- any logos (including the Department of Health's logo) and trademarks;
- any photographs and images;
- any signatures; and
- any material belonging to third parties.

Disclaimer

Opinions expressed in Communicable Diseases Intelligence are those of the authors and not necessarily those of the Australian Government Department of Health or the Communicable Diseases Network Australia. Data may be subject to revision.

Enquiries

Enquiries regarding any other use of this publication should be addressed to the Communication Branch, Department of Health, GPO Box 9848, Canberra ACT 2601, or via e-mail to: copyright@health.gov.au

Communicable Diseases Network Australia

Communicable Diseases Intelligence contributes to the work of the Communicable Diseases Network Australia.
<http://www.health.gov.au/cdna>



Communicable Diseases Intelligence (CDI) is a peer-reviewed scientific journal published by the Office of Health Protection, Department of Health. The journal aims to disseminate information on the epidemiology, surveillance, prevention and control of communicable diseases of relevance to Australia.

Editor

Cindy Toms

Deputy Editors

Phil Wright and Simon Petrie

Editorial and Production Staff

Leroy Trapani and Kasra Yousefi

Editorial Advisory Board

David Durrheim,
Mark Ferson, John Kaldor,
Martyn Kirk and Linda Selvey

Website

<http://www.health.gov.au/cdi>

Contacts

Communicable Diseases Intelligence is produced by:
Health Protection Policy Branch
Office of Health Protection
Australian Government
Department of Health
GPO Box 9848, (MDP 6)
CANBERRA ACT 2601

Email:

cdi.editor@health.gov.au

Submit an Article

You are invited to submit your next communicable disease related article to the Communicable Diseases Intelligence (CDI) for consideration. More information regarding CDI can be found at:
<http://health.gov.au/cdi>.

Further enquiries should be directed to:

cdi.editor@health.gov.au

Australian Gonococcal Surveillance Programme Annual Report, 2017

Monica M Lahra, Rodney Enriquez and C. R. 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 2017, there were 7,835 clinical isolates of gonococci from public and private sector sources tested for *in vitro* antimicrobial susceptibility by standardised methods. Current treatment recommendations for gonorrhoea for the majority of Australia, is a dual therapeutic strategy of ceftriaxone and azithromycin. Decreased susceptibility to ceftriaxone (Minimum Inhibitory Concentration or MIC value 0.06-0.125 mg/L) was found nationally in 1.06% of isolates, which is lower than that reported in the AGSP Annual Report 2016 (1.7%). The highest proportions were reported from Victoria and Western Australia (urban and rural) (2.1% and 1.4% respectively). Resistance to azithromycin (MIC value ≥ 1.0 mg/L) was found nationally in 9.3% of isolates, which is approximately double the proportion reported in 2016 (5.0%) and more than three times the proportion reported in 2015 (2.6%). The highest proportions were reported from Victoria (13.5%), South Australia (12.8%) and New South Wales (9.3%). High level resistance to azithromycin (MIC value ≥ 256 mg/L) was reported in 4 strains nationally in 2017, 2 from Victoria, one from New South Wales, and one from Queensland.

The proportion of strains resistant to penicillin in non-remote Australia ranged from 10.3% in non-remote Northern Territory to 44.1% in Tasmania. In remote Northern Territory, penicillin resistance rates remain low (2.5%). In remote Western Australia, penicillin resistance rates continue to increase (6.7%) compared to the previous years, however, there were relatively low numbers of strains available for isolate based testing (n=12). To address this and to monitor resistance and inform treatment guidelines, widespread molecular testing for penicillin resistance in Western Australia is in place, and these data are included in the AGSP.

The proportion of strains resistant to ciprofloxacin in non-remote Australia ranged from 17.2% in non-remote Northern Territory to 61% in Tasmania. Ciprofloxacin resistance rates remain comparatively low in remote Northern Territory (1.3%) and remote Western Australia (5.0%).

Keywords: *antimicrobial resistance; disease surveillance; gonococcal infection; Neisseria gonorrhoeae*

Introduction

Antimicrobial resistance (AMR) in *Neisseria gonorrhoeae* (NG) is a threat to global health security, and the emergence and spread of multi-drug resistant (MDR) gonorrhoea is predicted to pose significant collateral health and financial

costs.¹ Ceftriaxone and azithromycin dual therapy is widely recommended for treatment for gonorrhoea.

The key concerns regarding NG in Australia are increasing disease rates,² increasing azithromycin resistance, new reports of novel ceftriaxone resistant strains with international spread,³ in

the context of uncertainty regarding the future direction of gonococcal treatment as an ideal alternative to the current regimen has yet to be decided.

In Australia, gonococcal disease notification rates have increased by 63% (62 to 101 per 100 000) in the last 5 years (2012 to 2016). Increases have been reported in both males (72%) and females (43%), and the notification rates in 2016 remains higher in males (146 per 100,000) than in females (56 per 100,000).² Over this same period, in the Aboriginal and Torres Strait Islander population, gonorrhoea annual notification rates decreased by 17%, however notifications in this population remain disproportionately high at 6.9 times that of the non indigenous population (582 per 100,000 compared to 84 per 100 000); and were highest in remote and very remote areas (1,444 per 100,000) - 30 times as high as the non-indigenous population in 2016.² However, gonococcal AMR in these remote regions remains paradoxically low in infections acquired locally, and oral penicillin based therapeutic strategy remains recommended for use.⁴

Since 2014, when ceftriaxone and azithromycin dual therapy was introduced in Australia for the treatment of NG in an attempt to forestall resistance to ceftriaxone,⁵ there has been a steady decline in the proportion of strains with raised MIC values to ceftriaxone. However, there has been a coincident and marked increase in the proportion of NG strains resistant to azithromycin following rapid emergence of azithromycin resistance in South Australia in early 2016.⁶

Coincident with the current heightened global awareness of AMR, and increasing disease notification rates reported in Australia and elsewhere,^{2,7-10} has been the wide spread adoption of nucleic acid amplification testings (NAATs) in place of bacterial culture and antimicrobial susceptibility testing (AST) is not currently possible with NAATs. However, there are NAAT assays in use in remote regions in Australia to detect penicillin resistance^{11,12} – this was the first documented use of routine molecular

testing for gonococcal AMR detection and surveillance, and these continue to inform local treatment guidelines.¹²

The World Health Organization (WHO) estimates there are 106 million new NG infections reported in those aged 15-49 years, annually worldwide, with almost two thirds occurring in the Asia Pacific.¹³ In addition to the high burden of disease in the region, the WHO Gonococcal Antimicrobial Surveillance Programme data from the Asia Pacific indicates that there are high levels of gonococcal AMR but there are significant gaps in surveillance. Compounding this is unregulated antimicrobial use in these regions providing ideal conditions for the development of AMR.¹⁴ The emergence of new AMR in NG 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 resistance developing under selection pressure 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 is critical to monitor AMR, detect imported or novel resistance and to inform treatment guidelines.¹⁶ The WHO has called for enhanced surveillance as a fundamental component of their Global Action Plan to control the spread and impact of gonococcal AMR.¹⁷

The National Neisseria Network (NNN) is a collaboration of *Neisseria* reference laboratories in each state and territory that perform phenotypic and genotypic testing of clinical isolates of pathogenic *Neisseria* species. Clinical isolates are referred to the jurisdictional NNN laboratories from both public and private sector laboratories representing as wide a section of the community as possible, for determination of phenotypic and genotypic characteristics, including antimicrobial resistance, and additional investigations where required. The Australian Gonococcal Surveillance Programme (AGSP) is a key activity of the NNN and has continuously monitored

the susceptibility of NG since 1981, making it the longest, continually running, national surveillance system for gonococcal AMR. Here follows the 2017 AGSP Annual Report.

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 (representing this group of antibiotics); ceftriaxone (representing later generation cephalosporin antibiotics); ciprofloxacin (representing quinolone antibiotics); azithromycin; spectinomycin; and for high level plasmid mediated resistance to tetracycline using previously described standardised methodology to determine the MIC values.¹⁸ The MIC value is the least concentration of an antibiotic that inhibits *in vitro* growth under defined conditions. The AGSP conducts a program-specific quality assurance program.¹⁹

Antibiotic susceptibility data from each jurisdiction are submitted quarterly to the coordinating laboratory (the Neisseria Reference Laboratory and WHO Collaborating Centre for Sexually Transmitted Diseases, 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 strains. Data from isolates from all jurisdictions are predominantly from urban centres. Data from the Northern Territory and Western Australia are further divided into urban versus rural and remote as therapeutic recommendations differ.

Statistics

Statistical analyses were performed using Prism version 5.0d. Results were compared using Fisher's exact test for differences in proportions.

Results

Numbers of isolates

There were 7,835 gonococcal isolates tested in NNN laboratories in 2017, representing 28% of the 28,399 cases of gonococcal infection notified to the NNDSS in 2017 (Table 1).²⁰ This is the same as the proportion tested in 2015 and 2016 and lower than the range of 31%-42% referred between 2008 and 2014, and coincident with widespread uptake of NAAT diagnosis in Australia.

Source of isolates

There were 6,404 isolates from males (81.7%) and 1,395 (17.8%) from females (Table 2). 36 isolates were from patients where gender was not recorded. The proportion of gonococcal isolates from males and females tested by the AGSP has remained stable over recent years (2009-14); ranging between 17 and 20% for women and 80 and 83% for men. The infected site was reported as 'other' or not specified for 86 isolates from males and 32 isolates from females (Table 2). Isolates from urine samples were regarded as genital tract isolates.

Antibiotic susceptibility patterns

As in past years, the patterns of gonococcal antibiotic susceptibility differed between the various states and territories. The data are presented by region as well as aggregated for Australia (Table 3).

Ceftriaxone

From 2001 onwards, gonococcal isolates categorised as having decreased susceptibility to ceftriaxone by the AGSP criteria (MIC values ≥ 0.06 mg/L) have been reported in Australia.

Table 1: Number of Australian Gonococcal Surveillance Programme gonococcal isolates tested as a proportion of National Notifiable Diseases Surveillance System gonorrhoea notifications, Australia, 2017, by state or territory

State or territory	Number of isolates tested	Number of cases notified	Number of isolates tested/ Number of cases notified %
Australian Capital Territory	145	251	58
New South Wales	2,806	9,219	30
Northern Territory	216	1,788	12
Queensland	1,249	5,058	25
South Australia	359	1,272	28
Tasmania	59	117	50
Victoria	2,258	7,355	31
Western Australia	743	3,339	22
Australia	7,835	28,399	28

Table 2: Gonococcal isolates, Australia, 2017, by sex, site and jurisdiction tested.

Sex	Site	NSW	NT	Qld	SA	Vic	WA	ACT	Tas	AUSTRALIA
Male	Genital	1,226	115	555	141	923	390	43	29	3,422
	Rectal	727	5	251	66	599	67	38	7	1,760
	Pharynx	439	4	112	43	413	41	40	9	1,101
	DGI	9	3	7	1	5	9	1	0	35
	Other/NS	23	1	19	10	20	6	0	7	86
	Total	2,424	128	944	261	1,960	513	122	52	6,404
Female	Genital	287	83	273	79	228	212	19	7	1,188
	Rectal	16	0	9	6	4	4	0	0	39
	Pharynx	51	0	14	6	46	9	1	0	127
	DGI	3	1	1	0	1	3	0	0	9
	Other/NS	8	3	8	5	6	2	0	0	32
	Total	365	87	305	96	285	230	20	7	1,395
Unknown	Total	17	1	0	2	13	0	3	0	36
Total		2,806	216	1,249	359	2,258	743	145	59	7,835

*DGI: Disseminated Gonococcal Infection; **NS: not specified

Table 3: Proportion of gonococcal isolates with resistance to azithromycin, penicillin and ciprofloxacin and decreased susceptibility to ceftriaxone reported, Australia, 2017, by state or territory

State or Territory	Number of isolates tested 2017	Decreased Susceptibility		Resistance					
		Ceftriaxone		Azithromycin		Penicillin		Ciprofloxacin	
		n	%	n	%	n	%	n	%
Australian Capital Territory	145	0	0	3	2.1	25	17.2	36	24.8
New South Wales	2,806	13	0.5	261	9.3	709	25.3	857	30.5
Queensland	1,249	11	0.9	61	4.9	325	26.0	265	21.2
South Australia	359	2	0.6	46	12.8	149	41.5	136	37.9
Tasmania	59	0	0	5	8.5	26	44.1	36	61.0
Victoria	2,258	48	2.1	304	13.5	668	29.6	691	30.6
Northern Territory (non-remote)	58	0	0	1	1.7	6	10.3	10	17.2
Northern Territory (remote)	158	0	0	1	0.6	4	2.5	2	1.3
Western Australia (non-remote)	624	9	1.4	40	6.4	125	20.0	115	18.4
Western Australia (remote)	119	0	0	4	3.4	8	6.7	6	5.0
AUSTRALIA	7,835	83	1.06	726	9.3	2,045	26.1	2,154	27.5

The proportion of gonococci with decreased susceptibility to ceftriaxone nationally increased incrementally from 0.6% in 2006, to 4.4% in 2012, then in 2013 doubled to 8.8%. In 2014, the proportion decreased to 5.4% and decreased 1.8% in 2015 and 1.7% in 2016. In 2017, the proportion has again decreased to 1.06%. (Table 4).

The significant right shift in the distribution of ceftriaxone MIC values over 2011-2013 (Table 5), with the sustained increase in proportion of strains with an MIC value of 0.06 mg/L (2011-2012: [p=0.02, 95% CI: 1.04-.62], and 2012-2013 [p<0.0001, 95% CI: 1.70-2.38]) declining steadily in the following years. In 2015, the proportion of strains with an MIC value of ≥ 0.125 mg/L decreased to 0.1%, and further decreased to 0.04% in 2017 (Table 5). However, in 2017, there were two NG isolates with a ceftriaxone MIC value of 0.5 mg/L reported, the highest MIC value obtained in Australia since the A8806 isolate reported in 2013.²¹ These ceftriaxone resistant isolates were resistant to ciprofloxacin (MIC >32 mg/L); susceptible to spectinomycin (MIC 8 mg/L) and azithromycin (MIC 0.25 mg/L); and, unlike all previously described ceftriaxone-resistant strains, were penicillinase-producing NG (PPNG; MIC ≥ 32 mg/L).

Azithromycin

Nationally, the proportion of isolates exhibiting resistance (MIC value ≥ 1.0 mg/L) was 9.3% (Table 3), greater than an eight-fold increase from that reported in 2012 (1.3%) (Table 6). The proportion of isolates exhibiting resistance was highest in Victoria (13.5% in 2017, compared with 5.4% in 2016) (Table 6). Increases in the number and proportion of isolates exhibiting resistance compared with previous years were also seen in New South Wales (NSW), Queensland and remote Western Australia (Table 6). In 2017, there were 4 isolates that exhibited high level resistance to azithromycin (MIC value ≥ 256 mg/L), two from Victoria and one from Queensland and one from NSW.

Penicillin

Resistance to the penicillin group of antibiotics (penicillin, ampicillin and amoxycillin with or without clavulanic acid) in gonococci is a result of the production of a specific β -lactamase: penicillinase; and/or by the aggregation of chromosomally-controlled resistance mechanisms. These are denoted respectively, as penicillinase-producing *N. gonorrhoeae* (PPNG); and chromosomally mediated resistant to penicillin (CMRP). Chromosomal resistance is defined as an MIC to penicillin of 1 mg/L or more.

In 2017, in Australia, 2,045 (26.1%) of isolates were penicillin resistant, a proportional decrease from 2016 (32.5%). The proportion of penicillin resistant strains has continued to fluctuate in the range 22.5-44% over the period 2008 – 2017. In 2017, there were 1,052 (13.4%) isolates with CMRP; and 993 (12.7%) with PPNG.

Penicillin resistance in the Northern Territory

In 2017, there were 216 isolates tested from the Northern Territory. There were 58 from Darwin (non-remote), and 158 from remote areas of Northern Territory (NT) (including Alice Springs, Katherine, Tennant Creek, and Arnhem Land region).

Of the isolates tested from the NT, six (10.3%) from the city of Darwin and surrounding urban areas were penicillin resistant: (4/6 PPNG) (Table 3: Northern Territory non-remote). From the remote regions of the NT, four (2.5%) strains tested were penicillin resistant (2 PPNG). No strains from the NT had decreased susceptibility to ceftriaxone. In 2017, there were 743 isolates tested from Western Australia (WA), with 119 of these from remote regions, and 624 from non-remote regions. Of the isolates tested from non-remote regions, 20% were reported as resistant, whereas of the 119 isolates tested from remote regions, there were 8 isolates (6.7%) that were penicillin resistant (all PPNG).

Table 4: Number (%) of gonococcal isolates with decreased susceptibility to ceftriaxone (MIC ≥ 0.06 mg/L), Australia, 2010 to 2017, by state or territory. Remote Western Australian data is de-aggregated from 2014.

State or territory	Decreased susceptibility to ceftriaxone															
	2010		2011		2012		2013		2014		2015		2016		2017	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Australian Capital Territory	3	6.7	2	3.1	2	3.6	0	0	2	2.7	0	0.0	1	0.9	0	0
New South Wales	74	5.6	58	4.4	76	4.5	183	11.8	119	7.1	52	2.7	45	2.0	13	0.5
Northern Territory (non-remote)	1	0.2	2	0.4	0	0	2	1.9	3	3.0	0	0	0	0	0	0
Northern Territory (remote)	0	0	0	0	0	0	2	0.8	1	0.8	0	0	0	0	0	0
Queensland	17	3.2	18	2.3	17	2.4	33	4.9	21	3.2	7	1.0	32	3.7	11	0.9
South Australia	12	11.6	1	0.7	1	0.7	4	1.9	2	1.0	9	3.6	2	0.6	2	0.6
Tasmania	0	0	0	0	0	0	11	24.4	0	0	0	0	1	3.6	0	0
Victoria	52	5.7	50	5.3	105	8.4	181	11.8	95	6.6	25	1.5	19	1.1	48	2.1
Western Australia	17	5.2	3	0.7	6	1.2	13	2.7								
Western Australia (non-remote)									14	3.6	5	1.3	9	1.3	9	1.4
Western Australia (remote)									1	0.9	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

Quinolone antibiotics

The AGSP uses ciprofloxacin as the representative quinolone. Ciprofloxacin resistance is defined as MIC \geq 1 mg/L. In 2017, there were 2,154 isolates (27.5%) that were resistant to ciprofloxacin (Table 3). Overall there has been a trend of decreasing proportions since 2008, when 54% isolates were reported as ciprofloxacin resistant.

High-level tetracycline resistance

High-level tetracycline resistant NG (TRNG) (MIC value \geq 16mg/L) is used as an epidemiological marker, even though tetracyclines are not a recommended treatment for gonorrhoea and are rarely, if ever used for treatment of gon-

orrhoea in Australia. The proportion of TRNG detected nationally between 2006 and 2016 has ranged from 12% to 21%. In 2017, the proportion of TRNG was 10.2% TRNG were present in all jurisdictions.

Spectinomycin

In 2017, 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

Table 5: Proportion (%) of gonococcal isolates tested in Australia with MIC values at 0.06 mg/L and \geq 0.125 mg/L 2010 - 2017.

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

Table 6: Number (%) of gonococcal isolates with resistance to azithromycin (MIC \geq 1.0mg/L), Australia, 2012 to 2017, by state or territory.

State or territory	Azithromycin Resistance											
	2012		2013		2014		2015		2016		2017	
	n	%	n	%	n	%	n	%	n	%	n	%
Australian Capital Territory	0	0	1	2.2	7	9.3	0	0	8	7.1	3	2.1
New South Wales	9	0.5	14	0.9	33	2.0	43	2.3	82	3.6	261	9.3
Northern Territory (non-remote)	0	0	1	1.0	0	0	0	0	1	1.9	1	1.7
Northern Territory (remote)	0	0	0	0	0	0	0	0	0	0	1	0.6
Queensland	15	2.1	38	5.7	23	3.5	42	5.8	10	1.2	61	4.9
South Australia	1	0.7	6	2.8	1	0.5	7	2.8	68	19.5	46	12.8
Tasmania	0	0	0	0	1	3.3	1	4.3	4	14.3	5	8.5
Victoria	34	2.7	35	2.3	33	2.3	30	1.8	93	5.4	304	13.5
Western Australia (non-remote)	3	0.6	9	1.9	21	5.3	15	3.8	51	7.6	40	6.4
Western Australia (remote)	0	0	0	0	0	0	0	0	1	0.8	4	3.4
Australia	62	1.3	104	2.1	119	2.5	138	2.6	318	5.0	726	9.3

is the nominal threshold for change of treatment recommendations.¹⁶ The AGSP has continuously monitored AMR in Australia since 1981, and has established quality assurance and quality control for gonococcal AMR testing with the AGSP External Quality Assurance Program, and WHO NG reference strains, thus ensuring the quality of the AGSP data.^{19, 22}

In 2017, the NNN examined 7,835 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 nearly one-third of all notifications nationally.

For the majority of Australia, and in most countries, the monitoring of ceftriaxone and azithromycin MIC values is the primary focus of surveillance for gonococcal AMR. With regard to ceftriaxone, MIC values in the range 0.06-0.125 mg/L are reported to have decreased susceptibility. The proportion of strains with decreased susceptibility to ceftriaxone has steadily and substantially declined since 2013 from 8.8% to 1.1% in 2017 (Table 4). However, little reassurance should be taken from this, as fluctuation of circulating clones of NG within a population is to be expected and multidrug resistant strains with high level resistance to ceftriaxone have been reported from Asia, Europe and Australia in recent years.²³⁻²⁶

In 2017, we identified 2 new multidrug resistant NG strains isolated in Australia from heterosexual males visiting from Asia. These strains were phenotypically similar to ceftriaxone resistant strain first reported in Japan in 2015 (FC428), and similar strains in Denmark (GK124) and Canada (47,707). As part of a WHO collaboration we investigated the possible spread of the FC428 using bioinformatic analyses including core single-nucleotide variation phylogeny and *in silico* molecular typing. Phylogenetic analyses showed genetic relatedness amongst these 5 isolates providing further evidence of international transmission of ceftriaxone-resistant NG.³

In contrast, the 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 4 strains, 2 with suspected contact in China.²⁷ Since then there have been only sporadic reports of HLR to azithromycin and there were 4 such strains in 2017. Continued close observation is ongoing as evidence of coevolving cephalosporin and azithromycin resistance is being observed outside Australia and is of significant concern.²⁸

Another important and concerning finding by the AGSP in 2017, 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 Western Australia (WA) there were 4 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 2016.²⁹ 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 1 treatment failure was reported in a patient treated with azithromycin single agent therapy.³⁰ A review and change of the South Australian gonococcal treatment guidelines followed.³⁰ In 2017, azithromycin resistance was highest in Victoria (13.5%); South Australia (12.8%) and NSW (9.3%) and Tasmania (8.5%). Globally there have been increasing reports of azithromycin resistance.³¹

The recent reports of international spread of NG with resistance to ceftriaxone, 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, monitor for the presence and spread of resistance and to detect instances of treatment failure.

Acknowledgements

The NNN is supported by the Commonwealth Department of Health to provide the AGSP. We thank the many laboratories, private and public, throughout Australia for referral of isolates for testing, and Dr David Speers for the communication regarding the PPNG assay data from WA.

Members of the NNN in 2017 (and to whom isolates should be referred) were: John Bates and Vicki Hicks (Queensland Public Health Microbiology, Forensic and Scientific Services, Coopers Plains, Queensland); Athena Limnios, Tiffany Hogan, Ratan Kundu, Rodney Enriquez, Jasmin El-Nasser and Monica M. Lahra (New South Wales Health Pathology Department of Microbiology, The Prince of Wales Hospital,

Randwick, New South Wales and School of Medical Sciences, Faculty of Medicine, the University of New South Wales, Kensington, NSW Australia); Kerrie Stevens, Samantha Tawil, and Benjamin P. Howden (The Microbiological Diagnostic Unit (PHL), Department of Microbiology and Immunology, Peter Doherty Institute for Infection and Immunity, The University of Melbourne, Parkville, Victoria); Andrew Lawrence and Judith Holds (SA Pathology); Julie Pearson; Jane Bew and David Speers (Department of Microbiology and Infectious Diseases, PathWest Laboratory Medicine, Fiona Stanley Hospital, Western Australia); Belinda McEwan (Department of Microbiology and Infectious Diseases, Royal Hobart Hospital, Hobart, Tasmania) Kevin Freeman and Microbiology Staff, (Microbiology Laboratory, Territory Pathology, Royal Darwin Hospital, Tiwi, Northern Territory) Susan Bradbury and Peter Collignon (Microbiology Department, The Canberra Hospital, Garran, Australian Capital Territory).

Author details

Monica M Lahra^{1,2} Rodney Enriquez¹
C. R. Robert George¹

1. Neisseria Reference Laboratory and World Health Organisation Collaborating Centre for STI and AMR, Sydney. New South Wales Health Pathology, Microbiology, The Prince of Wales Hospital, Randwick, NSW Australia.
2. School of Medical Sciences, Faculty of Medicine, The University of New South Wales, 2053 Australia

Corresponding author: Professor Monica M Lahra, World Health Organization Collaborating Centre for STI and AMR, Sydney and, Neisseria Reference Laboratory, Microbiology Department, SEALS, The Prince of Wales Hospital, Randwick, NSW, 2031. School of Medical Sciences, Faculty of Medicine, the University of New South Wales,

NSW 2050 Australia. Telephone: +61 2 9382 9050. Facsimile: +61 2 9382 9210. Email: monica.lahra@health.nsw.gov.au

References

1. Centers for Disease Control and Prevention. Antibiotic Resistance Threats in the United States, 2013. 2013.
2. The Kirby Institute. HIV, viral hepatitis and sexually transmissible infections in Australia: Annual Surveillance Report 2017/2017. Available from: https://kirby.unsw.edu.au/sites/default/files/kirby/report/SERP_Annual-Surveillance-Report-2017_compressed.pdf.
3. Lahra MM, Martin I, Demczuk W, Jennison AV, Lee KI, Nakayama SI, et al. Cooperative Recognition of Internationally Disseminated Ceftriaxone-Resistant *Neisseria gonorrhoeae* Strain. *Emerg Infect Dis*. 2018;24(4).
4. Lahra MM, Enriquez RP. Australian Gonococcal Surveillance Programme. Annual Report 2016. *Commun Dis Intell*. In press.
5. Australian Sexual Health Alliance. Australian STI management guidelines for use in primary care 2018 [Available from: <http://www.sti.guidelines.org.au/sexually-transmissible-infections/gonorrhoea>].
6. Lahra MM, Ward A, Trembizki E, Hermanson J, Clements E, Lawrence A, et al. Treatment guidelines after an outbreak of azithromycin-resistant *Neisseria gonorrhoeae* in South Australia. *The Lancet Infectious Diseases*. 2017;17(2):133-4.
7. Family Planning Association. Sexually transmitted infections factsheet 2016 [Available from: <https://www.fpa.org.uk/factsheets/sexually-transmitted-infections>].
8. Centers for Disease Control and Prevention. 2016 Sexually Transmitted Diseases Surveillance. Atlanta: U.S. Department of Health and Human Services; 2017.
9. European Centre for Disease Prevention and Control. Annual Epidemiological Report 2016 – Gonorrhoea. Stockholm: European Centre for Disease Prevention and Control; 2016.
10. Government of Canada. Gonorrhoea 2017 [Available from: <https://www.canada.ca/en/public-health/services/diseases/gonorrhoea.html>].
11. 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. *Journal of Clinical Microbiology*. 2011;49(2):513-8.
12. 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. *The Journal of antimicrobial chemotherapy*. 2014;69(5):1243-7.
13. WHO/UNAIDS. Progress Report Global HIV/AIDS response: Epidemic update and health sector progress towards universal access 2011.
14. Lahra MM, Lo YR, Whiley DM. Gonococcal antimicrobial resistance in the Western Pacific Region. *Sexually Transmitted Infections*. 2013;89 Suppl 4:19-23.
15. Tapsall JW, Limnios EA, Murphy DM. An analysis of trends in antimicrobial resistance in *Neisseria gonorrhoeae* isolated in Australia, 1997 – 2006. *The Journal of antimicrobial chemotherapy*. 2008;61 150-5.
16. Tapsall J. Antimicrobial resistance in *Neisseria gonorrhoeae*. Switzerland: World Health Organization; 2001.

17. WHO. Global action plan to control the spread and impact of antimicrobial resistance in *Neisseria gonorrhoeae*: WHO Department of Reproductive Health and Research; 2012.
18. Bell SM, Pham JN, Rafferty DL, Allerton JK. Antibiotic susceptibility testing by the CDS method: A manual for medical and veterinary laboratories. 8th ed. Kogarah NSW: South Eastern Area Laboratory Services; 2016.
19. Australian Gonococcal Surveillance Programme. Use of a quality assurance scheme in a long-term multicentric study of antibiotic susceptibility of *Neisseria gonorrhoeae*. Genitourin Med. 1990;66:437-44.
20. Australian Government Department of Health. National Notifiable Diseases Surveillance System 2018 Accessed 16 Apr 2018. Available from: <http://www9.health.gov.au/cda/source/cda-index.cfm>.
21. Lahra MM, Ryder N, Whiley DM. A new multidrug-resistant strain of *Neisseria gonorrhoeae* in Australia. N Engl J Med. 2014;371(19):1850-1.
22. Unemo M, Fasth O, Fredlund H, Limnios A, Tapsall J. Phenotypic and genetic characterization of the 2008 WHO *Neisseria gonorrhoeae* reference strain panel intended for global quality assurance and quality control of gonococcal antimicrobial resistance (AMR) surveillance for public health purposes. The Journal of antimicrobial chemotherapy. 2009;63 (6):1142-51.
23. Ohnishi M, Golparian D, Shimuta K, Saika T, Hoshina S, Iwasaku K, et al. Is *Neisseria gonorrhoeae* Initiating a future era of untreatable gonorrhoea?: Detailed characterization of the first strain with high-level resistance to ceftriaxone. Antimicrob Agents Chemother. 2011;55:3538-45.
24. Unemo M, Golparian D, Nicholas R, Ohnishi M, Gallay A, Sednaoui P. High-level cefixime- and ceftriaxone-resistant *Neisseria gonorrhoeae* in France: Novel penA mosaic allele in a successful international clone causes treatment failure. Antimicrob Agents Chemother. 2012;56:1273-80.
25. Cámara J, Serra J, Ayats J, Bastida T, Carnicer-Pont D, Andreu A, et al. Molecular characterization of two high-level ceftriaxone-resistant *Neisseria gonorrhoeae* isolates detected in Catalonia, Spain. J Antimicrob Chemother 2012 67:1858-60.
26. Lahra MM, Ryder N, Whiley DM. A New Multidrug-Resistant Strain of *Neisseria gonorrhoeae* in Australia. New England Journal of Medicine. 2014;371(19):1850-1.
27. Stevens K, Zaia A, Tawil S, Bates J, Hicks V, Whiley D, et al. *Neisseria gonorrhoeae* isolates with high-level resistance to azithromycin in Australia. The Journal of antimicrobial chemotherapy. 2015;70(4):1267-8.
28. Whiley DM, Lahra MM, Unemo M. Prospects of untreatable gonorrhoea and ways forward. Future microbiology. 2015;10:313-6.
29. Lahra MM, Enriquez RP. Australian Gonococcal Surveillance Programme, 1 July to 30 September 2016. Communicable diseases intelligence quarterly report. 2017;41(1):E109-e10.
30. Lahra MM, Ward A, Trembizki E, Hermanson J, Clements E, Lawrence A, et al. Treatment guidelines after an outbreak of azithromycin-resistant *Neisseria gonorrhoeae* in South Australia. The Lancet Infectious diseases. 2017;17(2):133-4.
31. Unemo M. Current and future antimicrobial treatment of gonorrhoea - the rapidly evolving *Neisseria gonorrhoeae* continues to challenge. BMC infectious diseases. 2015;15:364.