Australian Gonococcal Surveillance Programme annual report, 2014

Monica M Lahra for the Australian Gonococcal Surveillance Programme

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 2014, 4,804 clinical isolates of gonococci from public and private sector sources were tested for *in vitro* antimicrobial susceptibility by standardised methods. Decreased susceptibility to ceftriaxone (MIC value 0.06–0.125 mg/L) was found nationally in 5.4% of isolates, a lower proportion than that reported in the AGSP 2013 annual report (8.8%). The highest proportions were reported from New South Wales and Victoria (7.1% and 6.6% respectively). The proportion of strains resistant to penicillin in urban and rural Australia ranged from 11% in South Australia to 43% in New South Wales. In rural and remote Northern Territory penicillin resistance rates remained low (1.5%). In remote Western Australia relatively low numbers of strains are available for testing, however there is now widespread molecular testing for penicillin resistance in Western Australia to monitor resistance and inform guidelines and, for first time, these data are included in the AGSP annual report. Quinolone resistance ranged from 27% in the urban and rural areas of the Northern Territory, to 44% in the Australian Capital Territory, and quinolone resistance rates remain comparatively low in remote areas of the Northern Territory (3.1%) and remote areas of Western Australia (5.6%). Azithromycin resistance ranged from 0.5% in South Australia to 5.3% in rural and urban Western Australia. High rates were also reported from the Australian Capital Territory but relatively low numbers were tested. High level resistance to azithromycin (MIC value ≥256 mg/L) was again reported in 2014, in 2 strains from New South Wales. No resistance was reported from the Northern Territory, or remote Western Australia. *Commun Dis Intell* 2015;39(3):E347–E354.

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

Introduction

Gonococcal antimicrobial resistance (AMR) was identified as an urgent public health threat by the United States Centers for Disease Control and Prevention in 2013,[1] and the emergence and spread of multidrug-resistant gonorrhoea is predicted to impose significant collateral health and financial costs.[1] For the majority of Australia, and internationally, there is reliance on a dual treatment protocol for gonorrhoea of ceftriaxone and azithromycin, with uncertainty regarding the future direction of gonococcal treatment as the ideal alternative strategy is yet to be identified.[2] In recent years in Australia, there has been a significant increase in rates of gonococcal disease observed in both males and females in the eastern states (Victoria, New South Wales and Queensland), and males in the Australian Capital Territory.[3] In contrast, in Indigenous populations in remote regions of the Northern Territory and Western Australia, gonococcal disease notifications rates are significantly higher but remain relatively stable.[3] The overall Australian age standardised gonorrhoea notification rates in 2012 for Indigenous compared with non-Indigenous Australians were 933 per 100,000 population and 38.5 per 100,000 population, respectively.[3] In these remote areas where disease rates are high, antimicrobial resistance is paradoxically low, and gonorrhoea acquired locally or in an endemic region can still be effectively treated with an oral antibiotics regimen (amoxycillin 3 g, probenecid 1 g and azithromycin 1 g).[4] Importantly though, the remoteness of these regions poses limits in terms of access to diagnostic services. For this reason nucleic acid amplification tests are relied on for diagnosis, and relatively few isolates are available for antimicrobial resistance testing in these regions where monitoring antimicrobial resistance is critical. The development and implementation of an assay to detect penicillinase production[5,6] (the primary cause of penicillin resistance in remote regions) is the first documented use of molecular testing for gonococcal antimicrobial resistance detection and surveillance to monitor AMR and inform local treatment guidelines.[6]

The Australian gonococcal AMR data for 2013 were cause for considerable concern as the proportion of strains with decreased susceptibility to ceftriaxone was reported to be 8.8%, double that of 2012 (4.4%). The highest proportions (11.8%) were reported from New South Wales and Victoria where the greatest increases in gonococcal disease notifications occurred.[7] High level resistance to azithromycin (MIC value >256 mg/L) was also reported in 2013, in 2 strains from Victoria and 2 strains from Queensland.[8] In addition, an

imported multi-drug resistant gonococcal strain, known as the A8806 strain, with a ceftriaxone MIC of 0.5 mg/L, the highest ever reported in Australia, was identified in Australia in 2013.[9] Molecular investigations of this strain showed key genetic similarities to the ceftriaxone-resistant strain H041, which was observed in only a single case in Japan.[9] Enhanced surveillance in the Northern Territory and Queensland has not detected further evidence of the A8806 strain in 2014 (unpublished data from the NNN).

Almost two-thirds of the World Health Organization (WHO) estimated 106 million new *Neisseria gonorrhoeae* infections reported in those aged 15–49 years worldwide each year occur in the Asia–Pacific Region.[10] The WHO gonococcal antimicrobial surveillance data from the Asia–Pacific indicate that there are high levels of gonococcal AMR in the Region, which is densely populated with a disproportionate burden of gonococcal disease. In many countries there is uncontrolled antimicrobial use providing ideal conditions for the development of AMR.[11] This is of continuing concern to Australia where, in urban centres, AMR in *N. gonorrhoeae* has long been influenced by the introduction of multi-resistant strains from overseas.[12] Importation and spread of resistant gonococcal strains and/or resistance developing under selection pressure is an ongoing concern.

Strategies for treating and controlling gonorrhoea are based on regimens effecting cure in a minimum of 95% of cases. Surveillance data derived from continuous monitoring of resistance to the antibiotics in clinical use is therefore critical to monitor AMR, detect imported or novel resistance and to inform treatment guidelines.[13] The WHO has called for enhanced surveillance as a fundamental component of the Global Action Plan to control the spread and impact of gonococcal AMR.[14]

In Australia, the National Neisseria Network (NNN) is a collaboration of reference laboratories in each state and territory that monitors clinical isolates of pathogenic *Neisseria* species nationally from public and private sector laboratories representing as wide a section of the community as possible, for phenotypic and genotypic characteristics, including antimicrobial resistance. The Australian Gonococcal Surveillance Programme (AGSP) is a key activity of the NNN and has continuously monitored the susceptibility of *N. gonorrhoeae* since 1981, making it the longest continually running national surveillance system for gonococcal AMR. In this annual report, for the first time, we provide molecular surveillance data from Western Australia to supplement the AGSP data. This is amid increasing concerns nationally of the status of gonococcal AMR in Australia.

Methods

The NNN AMR data for gonococcal isolates are collated for the AGSP quarterly and annual reports. Gonococcal infection is a notifiable disease in Australia and each confirmed case is notified 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 number of cases reported to the NNDSS. The NNN tests approximately one-third of the number of notified cases in Australia.

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 minimum inhibitory concentration (MIC) values.[15, 16] 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.[17]

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 results for reporting. Where available, the AGSP collects data on the gender of the patient, country of acquisition, and site of isolation of gonococcal strains. Data from isolates from all jurisdictions is 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 analysis was performed using Prism % version 5.0d. Results were compared using Fisher's exact test for proportional differences.

Results

Number of isolates

There were 4,804 gonococcal isolates tested in NNN laboratories in 2014, representing 31% of the 15,728 cases of gonococcal infection notified to the NNDSS in 2014 (Table 1).[18] This was slightly lower than the proportion tested in 2013 (33%) and lower than the 35%–42% referred between 2008 and 2012.

Table 1: Number of Australian Gonococcal Surveillance Programme gonococcal isolates tested as a proportion of National Notifiable Diseases Surveillance System gonorrhoea notifications, Australia, 2014, 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	75	120	63
New South Wales	1,672	4,862	34
Northern Territory	229	1,759	13
Queensland	650	2,723	24
South Australia	207	765	27
Tasmania	30	65	46
Victoria	1,440	3,240	44
Western Australia	501	2,194	23
Australia	4,804	15,728	31

Source of isolates

There were 4,009 isolates from men (83%) and 791 (17%) from women (Table 2). Four isolates were from patients of unknown gender. The proportion of gonococcal isolates from males and females tested by the AGSP has remained stable over recent years (2009–2012); ranging between 18% and 20% for women and 80% and 82% for men. The infected site was reported as 'other' or not specified for 58 isolates from males and 25 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).

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 beta lactamase: penicillinase; and/ or by the aggregation of chromosomally-controlled resistance mechanisms. These are denoted respectively, as penicillinase-producing *N. gonorrhoeae* (PPNG); and chromo-

Table 2: Gonococcal isolates tested, Australia, 2014, by sex, site and state or territory

Sex	Site	ACT	NSW	NT	Qld	SA	Tas.	Vic.	WA	Aust.
Male	Genital	21	823	141	354	109	20	620	290	2,378
	Rectal	21	328	1	93	41	3	384	74	945
	Pharynx	22	277	1	40	22	1	210	39	612
	DGI	0	1	3	10	0	0	0	2	16
	Other/NS	1	21	1	2	0	1	30	2	58
	Total	65	1,450	147	499	172	25	1,244	407	4,009
Female	Genital	8	169	73	130	29	2	167	74	652
	Rectal	0	6	1	3	3	0	3	5	21
	Pharynx	0	39	1	6	3	0	13	9	71
	DGI	0	1	5	9	0	0	0	6	21
	Other/NS	2	4	1	3	0	3	13	0	26
	Total	10	219	81	151	35	5	196	94	791
Unknown	Total	0	3	1	0	0	0	0	0	4
Total		75	1,672	229	650	207	30	1,440	501	4,804

DGI: Disseminated Gonococcal Infection; NS: not specified

Table 3: Proportion of gonococcal isolates with resistance to penicillin, ciprofloxacin and azithromycin and decreased susceptibility to ceftriaxone reported, Australia, 2014, by state or territory

State or territory	Number of isolates tested	Decreased susceptibility Ceftriaxone		Resistance Ciprofloxacin		Azithromycin		Penicillin	
		n	%	n	%	n	%	n	%
Australian Capital Territory	75	2	2.7	33	44.0	7	9.3	9	12.0
New South Wales	1,672	119	7.1	726	43.0	33	2.0	725	43.0
Queensland	650	21	3.2	184	28.0	23	3.5	153	24.0
South Australia	207	2	1.0	86	42.0	1	0.5	22	11.0
Tasmania	30	0	0.0	8	27.0	1	3.3	7	23.0
Victoria	1,440	95	6.6	559	39.0	33	2.3	322	22.0
Northern Territory/Urban	99	3	3.0	27	27.0	0	0.0	21	21.0
Northern Territory/Remote & Rural	130	1	0.8	4	3.1	0	0.0	2	1.5
Western Australia/Urban & Rural	393	14	3.6	117	30.0	21	5.3	104	26.0
Western Australia/Remote	108	1	0.9	6	5.6	0	0.0	5	4.6
Australia	4,804	258	5.4	1,750	36.0	119	2.5	1,370	29.0

somally mediated resistant to penicillin (CMRP). Chromosomal resistance is defined as an MIC to penicillin of 1 mg/L or more.

In 2014, 1,370 (29%) isolates were penicillin resistant, which was a proportional decrease from 2012–2013 (3%2–35%); similar to that reported in 2010–2011 (25%–29%); but lower than 2008–2009 (36%–44%). In 2014, there were 652 (14%) isolates with CMRP; and 718 (15%) with PPNG. In comparison in 2013, the proportion of isolates with CMRP was 20%, and 15% were PPNG. Thus the decrease in penicillin resistance nationally in 2014 was due to a decrease in the proportion of isolates with CMRP.

Penicillin resistance in the Northern Territory

In 2014 there were 229 isolates tested from the Northern Territory. Of these, 99 were from Darwin, and 130 were from rural and remote Northern Territory comprising 117 from Alice Springs, 5 isolates from Katherine and 8 isolates from other areas.

Of the isolates tested from the Northern Territory, 21 (21%) from the city of Darwin were penicillin resistant: (3 CMRP and 18 PPNG) (Table 3). Of these, two also had decreased susceptibility to ceftriaxone. In contrast, from the remote regions of the Northern Territory, 2 (1.5%) strains tested were penicillin resistant (both PPNG).

Penicillin resistance in Western Australia

In 2014, there were 501 isolates tested from Western Australia; 108 from remote regions and 393 from rural and urban regions. Of the isolates tested from rural and urban regions, 26% were reported as resistant, whereas of the 108 from remote regions there were 5 isolates (4.6%) that were penicillin resistant (3 PPNG and 2 CMRP).

In addition to the isolate based surveillance for penicillin, specimens that were *N. gonorrhoeae* positive by a nucleic acid amplification test (NAAT) in Western Australia were tested using a PPNG assay now routinely in use at PathWest.[5,6] There were 1,158 gonococcal diagnoses by NAATs at PathWest from across Western Australia and of those, 1,011 (87%) were able to be tested for PPNG. There were high rates of PPNG in Perth (17%); Wheatbelt (14%); Great Southern (33%) and SouthWest (25%). Conversely, the remote regions continue to have lower rates of PPNG positive *N. gonorrhoeae*. There were 4/120 (3%) from the Pilbara and 0/475 (0%) from the Kimberley region. Lower rates of PPNG were also reported from the Midwest and Goldfields (7% and 11% respectively), but these rates are considered less reliable as lower numbers were tested in these regions (58 and 35 respectively). These data support and enhance the isolate based surveillance findings of the AGSP, that PPNG rates remain low in the remote regions of Western Australia. All PPNG positive *N. gonorrhoeae* from remote regions were determined to be in non-local workers or residents in the major regional centres and there was no PPNG positive

N. gonorrhoeae detected from remote Indigenous communities (personal communication, Dr David Speers, PathWest).

Ceftriaxone

From 2001 onwards, gonococcal isolates categorised as having decreased susceptibility to ceftriaxone, by the AGSP criteria (MIC values 0.06–0.125 mg/L), have been reported in Australia. The proportion increased incrementally from 0.6% in 2006, to 4.4% in 2012, then in 2013 doubled to 8.8%. In 2014, the proportion of gonococci with decreased susceptibility to ceftriaxone nationally decreased to 5.4% (Table 4).

Ceftriaxone decreased susceptibility 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 5), 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–.62], and 2012–2013 [P<0.0001, 95% CI: 1.70–2.38]). In 2014, the proportion of strains with an MIC value of 0.06 mg/L decreased to 4.8%.

The proportion of strains with a ceftriaxone MIC 0.125 mg/L also increased from 0.1% in 2010 and 2011, to 0.3% in 2012 to 0.6% in 2013, but was unchanged in 2014 (Table 5). These differences were not significant, which may be attributable to the low number of strains in this MIC category. No isolates of *N. gonorrhoeae* with an MIC value greater than 0.125 mg/L were reported from Australia in 2014.

Azithromycin

Nationally, the proportion of isolates exhibiting any resistance to azithromycin (2.4%) was higher than that reported in 2011–2012 (1.1%–1.3%), and slightly higher than the previous year (2.1%) (Table 3). There were marked increases in the proportion of strains with resistance to azithromycin between 2012 and 2013 from the Australian Capital Territory (from 2.2% to 9.3%) but the number of isolates tested was relatively low; and in Western Australia (from 1.9% to 4.2%); and also New South Wales (from 1.0% to 2.0%). In 2014, there were 2 isolates, both from New South Wales, that exhibited high level resistance to azithromycin (MIC value > 256 mg/L).

Quinolone antibiotics

The AGSP uses ciprofloxacin as the representative quinolone. Quinolone resistant *N. gonorrhoeae* are defined as MICs ≥ 1 mg/L. The resistance mechanism in *N. gonorrhoea* has thus far been mediated only by chromosomal mechanisms so that incremental changes in MIC values are observed.

Table 4: Number and percentage of gonococcal isolates with decreased susceptibility to ceftriaxone (MIC 0.06–0.125 mg/L), Australia, 2010 to 2014, by state or territory

State or territory	Decreased susceptibility to ceftriaxone									
	2010		2011		2012		2013		2014	
	n	%	n	%	n	%	n	%	n	%
Australian Capital Territory	2	6.7	2	3.1	2	3.6	0	0.0	2	2.7
New South Wales	74	5.6	58	4.4	76	4.5	183	11.8	119	7.1
Northern Territory	1	0.2	2	0.4	0	0.0	4	1.5	4	1.7
Queensland	26	3.2	18	2.3	17	2.4	33	4.9	21	3.2
South Australia	19	11.6	1	0.7	1	0.7	4	1.9	2	1.0
Tasmania	0	0.0	0	0.0	0	0.0	11	24.4	0	0.0
Victoria	52	5.7	50	5.3	105	8.4	181	11.8	95	6.6
Western Australia	17	5.2	3	0.7	6	1.2	13	2.7	15	3.0
Australia	191	4.8	134	3.2	207	4.4	429	8.8	258	5.4

Table 5: Proportion of gonococcal isolates tested with MIC values at 0.06 mg/L and 0.125 mg/L, Australia, 2010 to 2014

Ceftriaxone MIC mg/L	2010	2011	2012	2013	2014
0.06	4.8%	3.2%	4.1%	8.2%	4.8%
0.125	0.1%	0.1%	0.3%	0.6%	0.6%

In 2014, 1,750 of the 4,800 gonococci examined (36%) were resistant to ciprofloxacin (Table 3). The proportion reported by the AGSP in 2012 (30%) and 2013 (34%) was lower, however 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 *N. gonorrhoeae* (TRNG) 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 gonorrhoea in Australia. The proportion of TRNG detected nationally increased between 2006 and 2011 from 12% to 21% and decreased to 14% in 2012, and was again reported as 14% in 2013. In 2014 the proportion of TRNG was 19%.

TRNG were present in all jurisdictions in 2014, with the highest proportions in remote Northern Territory (44%), New South Wales (26%), and remote Western Australia (23%).

Spectinomycin

In 2014, all isolates from jurisdictions testing (Western Australia; Victoria; South Australia; Queensland; Tasmania) 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 is the nominal threshold for change of treatment recommendations.[13] The AGSP has continuously monitored antimicrobial resistance in Australia since 1981, and has established quality assurance and quality control of gonococcal AMR data with the AGSP External Quality Assurance Program and WHO *N. gonorrhoeae* reference strains.[17,19]

The overall number of gonococcal strains examined by the AGSP in 2014 was higher in number but proportionally the same as 2013. The clinical isolates were from both the public and private health sectors, constituting a comprehensive sample of 31% of all notifications nationally. The increasing use of NAATs for diagnosis, both in urban setting and remote settings is of increasing concern for gonococcal AMR surveillance programs worldwide because of the impact on the number of strains for AMR testing, and therefore antimicrobial resistance surveillance data. Whilst NAATs have an advantage over culture in terms of sensitivity, and are more robust and reliable for remote settings where cultures may not survive, the distinct disadvantage is that they cannot test broadly for AMR. However, molecular AMR testing strategies can give targeted and specific information, which is clinically and epidemiologically important.[2] At this stage, however, NAATs are unable to provide definitive data for predicting AMR, thus the continued commitment to the support of surveillance programs such as the AGSP is vital to monitor and detect new resistant strains. However, directed and specific NAATs such as the PPNG assay can contribute to surveillance programs and can be used to inform treatment guidelines.[6] This AGSP report includes for the first time, the PPNG NAAT data from Western Australia, which provides important additional situational data for the AGSP in a region where penicillin based treatment strategies are still in place. Introduction of this assay is planned for the Northern Territory, where penicillin based treatment strategies are also in use, to provide enhanced surveillance data for 2015.

The primary focus for surveillance for the majority of Australia, and in most countries, is the monitoring of ceftriaxone MIC values. Gonococci with decreased susceptibility to ceftriaxone (MIC value in the range 0.06–0.125 mg/L) have been reported in increasing proportions in Australia, with the rate doubling over the period 2012 to 2013, from 4.4% to 8.8%.[7] In 2014, there was a decrease in the proportion of isolates with decreased susceptibility to ceftriaxone in New South Wales, Victoria, South Australia and Queensland, whereas proportions were essentially unchanged in Western Australia and the Northern Territory. Low numbers of isolates were tested in Tasmania and the Australian Capital Territory. There was no evidence of spread of the A8806 strain reported in 2013. Decreased susceptibility to the cephalosporin antibiotics has been accompanied by increasing numbers of reports of treatment failures; and multi-drug resistant strains with high level resistance to ceftriaxone have been reported from Japan, France, Spain and now Australia.[9,20–22] All of these strains with high level resistance to ceftriaxone have been shown to have a mosaic penicillin binding protein 2 (PBP2) encoded by a mosaic *PenA* gene, with as little as a single additional amino acid substitution required to confer resistance.[23]

Of significant concern is that molecular studies have shown that strains harbouring the mosaic PBP2 are present in a significant proportion of circulating strains globally; are critically only one mutation from high level resistance, and are under constant selection pressure. Paradoxically, these strains with a mosaic PBP2 may not have an elevated ceftriaxone MIC value (i.e. decreased susceptibility) so would not be included in phenotypic

surveillance. Given these considerations, the level of concern about the development of ceftriaxone resistance is growing globally.[23]

International surveillance programs define decreased susceptibility to ceftriaxone differently. The absence of an international standard definition of decreased susceptibility to ceftriaxone, and non-uniform methods of AMR testing confound comparison of surveillance data. However in 2012, the WHO Global Action Plan nominated the criteria for decreased susceptibility to ceftriaxone as an MIC value ≥0.125 mg/L.[14] The proportion of strains tested by the AGSP with a ceftriaxone MIC value of 0.125 mg/L also doubled from 0.3% in 2012 to 0.6% in 2013 but was unchanged in 2014.

A dual therapy strategy of ceftriaxone with oral azithromycin for uncomplicated gonococcal infection is recommended in Australia.[4] In 2013, high level resistance to azithromycin in gonococci was reported for the first time in Australia.[8] There were 4 strains reported; two from Victoria and two from Queensland, and of these, two were likely to have been acquired from China).[8] In 2014, there were 2 further strains reported with high level azithromycin resistance in New South Wales. Evidence of coevolving cephalosporin and azithromycin resistance is being observed outside Australia and is of significant concern.[23]

The proportion of gonococci with high-level tetracycline resistance in Australia increased from 2006 to 2008 and stabilised at 21% in 2009 to 2010. The proportion of TRNG decreased to 18% in 2011, then to 14% in 2012 and remained unchanged (14%) in 2013. In 2014, there was an increase to 19%. Outside of the remote regions of Western Australia and the Northern Territory penicillin and ciprofloxacin resistance rates remain high. There was no resistance to spectinomycin reported in the jurisdictions testing for this antibiotic.

The continued emergence and spread of AMR in *N. gonorrhoeae* is widely recognised as a global public health threat. Broad based disease control strategies including the rational use of antibiotics have been called for. 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.[14] The need for close and enhanced monitoring of gonococcal AMR is patently clear. NAATs can play a role in this; however, isolate based 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 and to detect instances of treatment failure. Sentinel site surveillance programs involve patient follow up and test of cure cultures after treatment of *N. gonorrhoeae* infections, in particular those in oropharyngeal sites. This is currently conducted in a very limited number of settings in Australia, and needs to be expanded throughout all jurisdictions as a matter of priority.

In summary, gonococcal disease rates and AMR rates are increasing. In 2013, the proportion of strains with elevated ceftriaxone MIC values doubled from that reported in 2012. In 2014 this declined to 5.4% but there is little reassurance in this. For the second consecutive year in Australia, high level resistance to azithromycin has been reported. The next direction for treatment is uncertain, but what is clear is that additional and renewed efforts for disease prevention and disease control are urgently called for, and that continued monitoring of AMR to inform treatment and monitor interventions is paramount.

Acknowledgements

The National Neisseria Network is supported by the Australian Government Department of Health. We thank the many laboratories, private and public, throughout Australia for submission of isolates for testing.

Members of the Australian Gonococcal Surveillance Programme in 2014 (and to whom isolates should be referred) were: John Bates and Vicki Hicks (Queensland Health Scientific Services, Coopers Plains, Queensland); Athena Limnios, Tiffany Hogan, Ratan Kundu, Rodney Enriquez and Monica M. Lahra (Department of Microbiology, The Prince of Wales Hospital, Randwick, New South Wales); Kerrie Stevens, Samantha Tawil, Mark Bek, 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 Jan Bell (SA Pathology at Women's and Children's Hospital, Adelaide, South Australia); Julie Pearson; Hui leen Tan 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, Royal Darwin Hospital, Casuarina, Northern Territory) Susan Bradbury, Angelique Clyde-Smith and Peter Collignon (Microbiology Department, The Canberra Hospital, Garran, Australian Capital Territory).

Author details

Corresponding author: Associate Professor Monica M Lahra, World Health Organization Collaborating Centre for STD, Sydney and, Neisseria Reference Laboratory, Microbiology Department, SEALS, The Prince of Wales Hospital, Randwick, NSW, 2031. Telephone: +61 2 9382 9054. Facsimile: +61 2 9382 9210. Email: monica.lahra@sesiahs.health.nsw.gov.au

References

1. Centers for Disease Control and Prevention. Antibiotic Resistance Threats in the United States. In: *Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Disease*. Atlanta: Centers for Disease Control and Prevention; 2013.
2. 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;12(3):223–229.
3. Roberts-Witteveen A, Pennington K, Higgins N, Lang C, Lahra M, Waddell R, et al. Epidemiology of gonorrhoea notifications in Australia, 2007–12. *Sex Health* 2014;11(4):324–331.
4. Australasian Sexual Health Alliance. Australian STI Management Guidelines. 2014. Available from: http://www.sti.guidelines.org.au/about-asha
5. 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.
6. 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.
7. Lahra MM, Australian Gonococcal Surveillance Programme. Australian Gonococcal Surveillance Programme annual report, 2013. *Commun Dis Intell* 2015;39(1):E137–E145.
8. 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. *J Antimicrob Chemother* 2015;70(4):1267–1268.
9. Lahra MM, Ryder N, Whiley DM. A new multidrug-resistant strain of *Neisseria gonorrhoeae* in Australia. *N Engl J Med* 2014;371(19):1850–1851.
10. World Health Organization, UNAIDS, Unicef. Progress report 2011: Global HIV/AIDS response. 2011. Available from: http://www.who.int/hiv/pub/progress_report2011/en/
11. Lahra MM, Lo YR, Whiley DM. Gonococcal antimicrobial resistance in the Western Pacific Region. *Sex Transm Infect* 2013;89 Suppl 4:iv19–23.
12. Tapsall JW, Limnios EA, Murphy D. Analysis of trends in antimicrobial resistance in *Neisseria gonorrhoeae* isolated in Australia, 1997–2006. *J Antimicrob Chemother* 2008;61(1):150–155.
13. Tapsall J. Antimicrobial resistance in *Neisseria gonorrhoeae*. 2001. Available from: http://www.who.int/drugresistance/Antimicrobial_resistance_in_Neisseria_gonorrhoeae.pdf
14. World Health Organization. *Global action plan to control the spread and impact of antimicrobial resistance in Neisseria gonorrhoeae*. Geneva: World Health Organization, Department of Reproductive Health and Research; 2012.
15. Tapsall J. Penicillin sensitivity of gonococci in Australia: the development of an Australian gonococcal surveillance programme. *Br J Vener Dis* 1984;60:226–230.
16. Tapsall J, editor. *Antimicrobial testing and applications in the pathogenic Neisseria*. Sydney: Australian Society for Microbiology; 2004.
17. Tapsall JW. Use of a quality assurance scheme in a long-term multicentric study of antibiotic susceptibility of *Neisseria gonorrhoeae*. *Genitourin Med* 1990;66(1):8–13.
18. Communicable Diseases Network Australia. National Notifiable Diseases Surveillance System. 2013. Available from: www.health.gov.au/nndssdata
19. 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 surveillance for public health purposes. *J Antimicrob Chemother* 2009;63(6):1142–1151.
20. Ohnishi M, Golparian D, Shimuta K, Saika T, Hoshina S, Iwasaku K, et al. Is *Neisseria gonorrhoeae* Initiating a future era of untreatable gonorrhea?: Detailed characterization of the first strain with high-level resistance to ceftriaxone. *Antimicrob Agents Chemother* 2011;55(7):3538–3545.
21. 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(3):1273–1280.
22. Camara 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(8):1858–1860.
23. Whiley DM, Lahra MM, Unemo M. Prospects of untreatable gonorrhea and ways forward. *Future Microbiol* 2015;10(3):313–316.