Annual report of the Australian Gonococcal Surveillance Programme, 2000

The Australian Gonococcal Surveillance Programme

Abstract

The Australian Gonococcal Surveillance Programme (AGSP) monitors the antibiotic susceptibility of *Neisseria gonorrhoeae* isolated in all States and Territories. In 2000 the *in vitro* susceptibility of 3,468 isolates of gonococci was determined by standardised methods. Antibiotic susceptibility patterns varied considerably between regions. Resistance to the penicillins was highest in larger urban centres and warrants close attention in those rural centres where treatment with the penicillins continues. Quinolone resistance in gonococci became more widespread in Australia in 2000. Endemic cycles of transmission of quinolone-resistant gonococci (QRNG) in homosexually active men continued in Victoria but declined in New South Wales. Heterosexual endemic transmission of QRNG increased substantially in New South Wales and the proportion of all gonococci represented by QRNG also increased markedly in Queensland and Western and South Australia. All isolates remained sensitive to spectinomycin, but a small number of isolates in a number of jurisdictions showed some decreased susceptibility to ceftriaxone. Strains examined in South Australia, New South Wales and Victoria were predominantly from male patients and rectal and pharyngeal isolates were common. In other centres the male to female ratio of cases was lower, and most isolates were from the genital tract. *Commun Dis Intell* 2001;25:59-63.

Keywords: surveillance, Neisseria gonorrhoeae*, antimicrobial resistance, gonorrhoea, antibiotics, quinolones, penicillins, spectinomycin, cephalosporins*

Introduction

Gonorrhoea is essentially the only bacterial STI found in Australia where antibiotic resistance materially affects both individual management and public health control. *Neisseria gonorrhoeae* has developed some form of resistance to all agents used in the treatment of gonococcal disease. This resistance has led to the abandonment or modification of some antibiotic treatment regimens and hindered efforts aimed at disease control. The Australian Gonococcal Surveillance Programme (AGSP) was established to monitor the susceptibility to antibiotics of gonococci isolated throughout the country. The AGSP is a long-term collaborative programme of surveillance conducted by reference laboratories in each State and Territory. Data from this programme were published each quarter in *Communicable Diseases Intelligence* from 1981 and annual reports have been produced since 1996.

Methods

The AGSP comprises participating laboratories in each State and Territory (see acknowledgments). It is a collaborative network of laboratories which obtains isolates for examination from as wide a section of the community as possible. Both public and private sector laboratories refer isolates to regional testing centres. The sources of isolates remained relatively unchanged in 2000. However, the increasing use of non-culture based methods of diagnosis has the potential to reduce the number of cultures available for susceptibility testing.

Gonococci isolated in and referred to the participating laboratories were examined for antibiotic susceptibility to the penicillins, quinolones, spectinomycin and third generation cephalosporins and for high level resistance to the tetracyclines by a standardised methodology.[1] In 2000, the AGSP also conducted a programme-specific quality assurance (QA) programme.[2] Antibiotic sensitivity data were submitted quarterly to a coordinating laboratory which collated the results and also conducted the QA programme. Additionally, the AGSP received data on the sex of the patient and site of isolation of gonococcal strains. The geographic source of acquisition of resistant strains was ascertained whenever possible.

Results

Numbers of isolates

There were 3,547 gonococcal isolates referred to or else isolated in AGSP laboratories in 2000 and the distribution and site of infection of these isolates are shown in the Table. Of these, 3,468 (97.8%) remained viable for susceptibility testing in 2000. One-thousand, two-hundred and fifty-five gonococci (35% of the Australian total) were isolated in New South Wales, 802 (22.6%) in Victoria, 620 (17.5%) in Queensland, 445 (12.5%) in the Northern Territory, 317 (9%) in Western Australia, and 93 (2.6%) in South Australia with small numbers in Tasmania and the Australian Capital Territory. The site of isolation and sex of some infected patients was not known.

Corresponding author: Associate Professor John Tapsall, The Prince of Wales Hospital Randwick NSW Australia 2031. Telephone: +61 2 9382 9079. Facsimile: +61 2 9398 4275. E-mail: j.tapsall@unsw.edu.au

Table. Gonococcal isolates, Australia, 2000, by sex, site and region (excluding those from the Australian Capital Territory and Tasmania)

	Site	NSW	Vic	Qld	SA	WA	NT	Aust
Male	Urethra	892	620	413	62	224	128	2,352
	Rectal	182	91	16	12	7	0	308
	Pharynx	91	44	8	5	2	1	152
	Other/NS	22	8	22	4	20	127	203
	Total	1,187	763	459	83	253	256	3,015
Female	Cervix	57	33	151	3	55	147	447
	Other/NS	8	6	10	7	9	42	82
	Total	65	39	161	10	64	189	529
Total		1,255	802	620	93	317	445	3,547

Compared with data from the same sources in recent years, there were continuing increases in the number of isolates in Victoria (from 362 in 1997, 565 in 1998 and 744 in 1999 to 802) and Queensland (from 516 in 1998 and 589 in 1999). The number of isolates available from the Northern Territory, Western Australia and South Australia was stable. In New South Wales the number of isolates decreased for the first time in many years (from 902 in 1997, 1,386 in 1998 and 1,528 in 1999). Numbers in other centres were low.

Source of isolates

For the 3,544 cases isolated for whom data on gender were available, there were 3,015 strains from men and 529 from women, with a male:female ratio of 5.7:1. The number of strains from men decreased slightly from the 3,111 examined in 1999 but was still higher than the 2,233 in 1997 and 2,886 in 1998. Strains from women decreased further from 628 in 1999 and 697 in 1998 and the total was below the 1997 figure of 597. The male:female ratio was 3.7:1 in 1997, 4.1 in 1998 and 5.1 in 1999. The male:female ratio remained highest in Victoria (19.5:1) and New South Wales (18.3:1) where strains were obtained more from urban populations, but lower in South Australia (8.3:1). The lower ratios in Western Australia (3.9:1), Queensland (2.8:1) and the Northern Territory (1.4:1) reflected the large non-urban component of gonococcal disease in those regions. Male rectal and pharyngeal isolates were most frequently found in New South Wales (23% of isolates from men) and Victoria (17.6%). This pattern is similar to that noted in recent years. About 8 per cent of isolates are shown as being isolated from 'other' sites. These included 13 cases of disseminated gonococcal infection, 11 in men and 2 in women. Not all infected sites were identified. Isolates from urine samples were regarded as genital tract isolates. Although most of the other isolates were probably from this source, they were not so specified. There were a small number of isolates from the eyes of both newborn and older infants.

Antibiotic susceptibility patterns

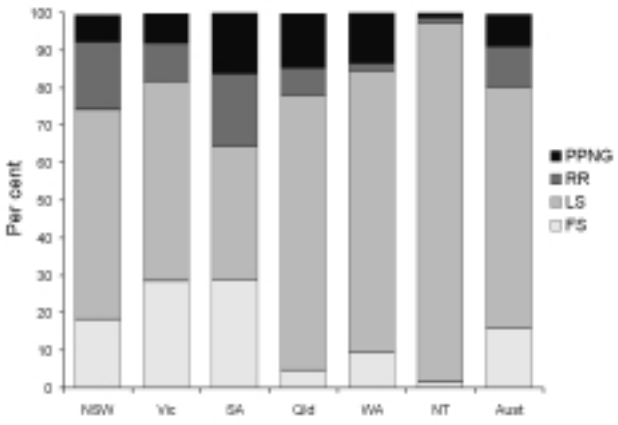
In 2000 the AGSP reference laboratories examined 3,468 gonococcal isolates for sensitivity to penicillin (representing this group of antibiotics), ceftriaxone (representing later generation cephalosporins), ciprofloxacin (representing quinolone antibiotics) and spectinomycin and for high level resistance to tetracycline (TRNG). As in past years the patterns of gonococcal antibiotic susceptibility differed greatly between the various States and Territories. For this reason data are presented by region as well as aggregated for Australia as a whole.

Penicillins

Resistance to the penicillin group (penicillin, ampicillin, amoxycillin) may be mediated by the production of beta-lactamase (penicillinase-producing *N. gonorrhoeae* - PPNG) or by chromosomally-controlled mechanisms (CMRNG).

Chromosomal resistance is expressed as the minimal inhibitory concentration in mg/L (MIC) which is the least amount of antibiotic which inhibits *in vitro* growth under defined conditions. The categorisation of strains in Australia in 2000 by penicillin MIC is shown in Figure 1. The MIC reflects the expression of multiple and different chromosomal changes present in an organism. These multiple changes result in incremental increases in the MIC. Strains are classified as fully sensitive (FS, MIC 0.03 mg/L), less sensitive (LS, MIC 0.06 - 0.5 mg/L) or relatively resistant (RR, MIC 1 mg/L). PPNG are a separate (resistant)

Figure 1. Penicillin resistance of gonococcal isolates, Australia, 2000, by region, (excluding those from the Australian Capital Territory and Tasmania)



FS fully sensitive to penicillin, MIC 0.03 mg/L
LS less sensitive to penicillin, MIC 0.06 – 0.5 mg/L
RR relatively resistant to penicillin, MIC 1 mg/L
PPNG penicillinase producing *N. gonorrhoeae*

category. Infections with strains in the less sensitive or fully sensitive categories usually respond to therapy with standard treatment regimens with the penicillins. Infections caused by strains which are PPNG or in the relatively resistant category (CMRNG) usually fail to respond to treatment with the penicillins.

In 2000, there were 377 isolates found to be resistant to penicillin (10.6%) by chromosomal mechanisms. This was lower than the 782 (21.8%) recorded in 1998 and the 525 (14.3%) in 1999. Strains of this type were concentrated in New South Wales (224 CMRNG, 18% of all isolates), Victoria (81 CMRNG, 10% of all isolates), South Australia (18 CMRNG, 19%) and Queensland (42 CMRNG, 7.2%). In contrast there were 6 (2%) CMRNG amongst Western Australian isolates and 6 (1.4%) in the Northern Territory strains.

PPNG again increased in 2000 both numerically (to 302 from 269 in 1999 and 206 in 1998), and as a proportion of all isolates (to 8.7% from 7.4% and 5.3% in 1999 and 1998 respectively). Again the distribution of PPNG differed significantly by region. New South Wales had the highest number, 92 (7.4%) of PPNG but the highest proportions were in South Australia (15 strains, 16%); Queensland (85, 14.6%) and Western Australia (41, 13.4%). The 62 PPNG in Victoria represented 7.8 per cent of strains. Five PPNG were found in the Northern Territory (1.1%) and there were 2 PPNG strains in Tasmania. Indonesia, the Philippines, Thailand, Vietnam and China were the most frequently nominated countries of PPNG acquisition. PPNG acquisition was also reported from contact in Korea, Singapore, Hong Kong, Brazil, Malaysia, Cambodia and Taiwan.

Ceftriaxone

A small number of strains in a number of states and territories showed a small increase in ceftriaxone MICs. This phenomenon requires continued monitoring.

Spectinomycin

All isolates of *N. gonorrhoeae* were susceptible to spectinomycin in 2000.

Quinolone antibiotics

Resistance to the quinolone antibiotics is mediated only by chromosomal mechanisms so that incremental increases in MICs are observed. The AGSP uses ciprofloxacin as the representative quinolone and defines altered resistance as an MIC of 0.06 mg/L or more. Treatment with currently recommended doses of 500 mg of ciprofloxacin is effective for strains with this less developed resistance in about 90 per cent of cases, but lower doses of the antibiotic will more often result in treatment failure. The proportion of treatment failures increases exponentially as MICs rise. Treatment failure occurs in about 60 per cent of infections with strains with MICs of 1 mg/L or more, even when higher doses are used. Currently gonococci with MICs up to 16 and 32 mg/L are being seen in Australia. Newly released quinolone agents would not be expected to offer any significant advantage over ciprofloxacin for the treatment of gonorrhoea.

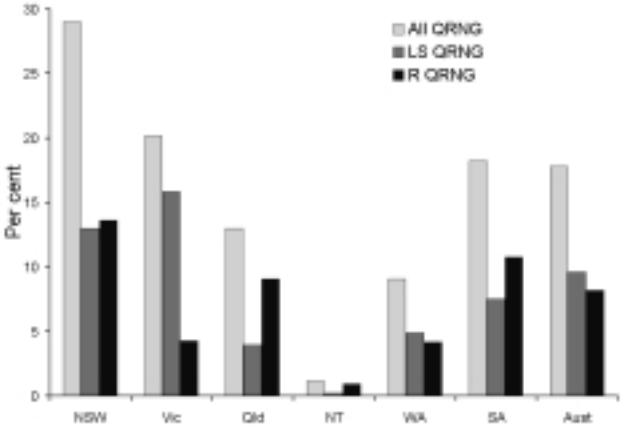
In 2000 a total of 619 gonococci (17.8%) displayed altered sensitivity to the quinolones (QRNG). This is about the same number and proportion of QRNG seen in 1999 (628, 17.2%) but more than the three times the number of QRNG seen in 1998 (186, 5.2%). The distribution of QRNG changed significantly in 2000, with larger numbers found in more states and territories, apart from a slight decline which occurred in the two larger States. In 1999 the high rate of QRNG mainly resulted from their distribution in homosexually active men (HAM) in New South Wales and Victoria. This high rate of QRNG in HAM in Victoria was maintained, but declined in New South Wales in 2000. The QRNG in HAM in these states were in the lower MIC range, namely, 0.06 – 0.5 mg/L.

Although the proportion of QRNG in HAM declined in New South Wales throughout 2000, an increasing proportion of isolates from that State were higher level QRNG (MIC 1mg/l or more). These QRNG were seen in infections in the male clients of female commercial sex workers. Rates of QRNG have been high in New South Wales since an increase in the number and proportion of QRNG in heterosexuals was noted in New South Wales in the December quarter of 1996. This rate of isolation was sustained throughout 1997 and the early part of 1998, but declined in the latter part of that year. The 332 QRNG in New South Wales represented 26.6 per cent of all isolates and similar numbers of low and higher level QRNG were noted.

In Victoria 160 QRNG accounted for 20 per cent of all isolates but 126 nearly (80%) were in the less sensitive range. The proportion of QRNG in Victoria in 1999 was 24 per cent.

About 80 per cent of all QRNG identified in Australia in 2000 were found in Victoria or New South Wales (Figure 2). QRNG were found in all centres except the Australian Capital Territory. Numbers of QRNG increased in all other states and territories. Queensland had 76 (13%) QRNG, almost twice the proportion in 1999. In South Australia there were 17 QRNG, also a substantial increase over 1999. In Western Australia there were 28 QRNG (8.8%), up from 9 (3%) in 1999. The Northern Territory recorded 5 QRNG (1.1%). The spread of QRNG in Sydney and Melbourne was mainly by local as opposed to overseas contact, but in most other centres cases were imported from overseas contact

Figure 2. Quinolone-resistant *N. gonorrhoeae*, Australia, 2000, by region, (excluding those from Tasmania)



LS QRNG Ciprofloxacin MICs 0.06 – 0.5 mg/L
R QRNG Ciprofloxacin MICs 1 mg/L

from sources similar to those described for PPNG acquisition.

High level tetracycline resistance

Three hundred and eighteen high level tetracycline resistant *N. gonorrhoeae* (TRNG, 9.1 % of isolates) were detected throughout Australia in 2000, continuing a slight upward trend (288, 7.9% in 1999). Most TRNG were found in Queensland (115, 19.8%) with a high proportion also recorded in Western Australia (38, 12.4%). There were 91 (7.3%) TRNG in New South Wales, 56 (7%) in Victoria, 9 (9.6%) in South Australia, and 7 (1.6%) in the Northern Territory. Infections with TRNG were mainly acquired overseas in Indonesia, Thailand and Singapore.

Discussion

The World Health Organization guidelines suggest that a rate of gonococcal resistance to an antibiotic of 5 per cent or more is an indication to change treatment schedules. The AGSP data has noted considerable regional variation in susceptibility patterns over many years and this was again present in 2000. This suggests that treatment regimens suited to local patterns of resistance should be adopted.

A high proportion of the gonococci isolated in urban centres has been resistant to the penicillins for many years and this trend was maintained in 2000. Rates of penicillin resistance in New South Wales, Victoria, South Australia, Queensland and Western Australia ranged between 15 and 35 per cent. Most of this resistance was chromosomally mediated and in locally acquired strains in New South Wales and Victoria, but in Western Australia and Queensland PPNG were more important. While PPNG rates had declined for a number of years prior to 1999, PPNG are now being seen in widely dispersed areas of rural Australia and the proportion of PPNG is again increasing. Although the proportion of CMRNG in the Northern Territory and Western Australia remains low, there has been a continuing shift upwards in MICs to the point where close surveillance needs to be maintained if penicillins are to remain the preferred treatment option.

There has also been considerable volatility in the proportion of QRNG seen in Australia over recent years and this continued in 2000. The pattern of a high proportion of strains less sensitive to the quinolones was maintained in Victoria. In New South Wales the less sensitive strains in HAM declined but higher level resistance was seen in another sub-population. The continuing high levels of endemic transmission of QRNG observed in these two centres indicate that use of quinolones should be discontinued. The proportion of QRNG in other centres increased significantly in 2000 suggesting that use of these agents in the treatment of gonorrhoea should also be reconsidered in these jurisdictions.

Most gonococcal isolates were fully susceptible to the third generation cephalosporin ceftriaxone, although a few strains showed a ‘shift to the right’ in terms of slightly increased MICs. All gonococci tested in Australia were susceptible to spectinomycin.

The number of TRNG increased only slightly in 2000 after several years of substantial rises. Sustained domestic transmission of TRNG was evident especially in Sydney. The spread of TRNG is examined as an epidemiological marker and tetracyclines are not a recommended treatment for gonorrhoea.

The sample of available isolates in 2000 declined slightly, but was sufficient for the purpose of susceptibility surveillance. AGSP has until now been able to confirm other findings on rates of gonococcal disease in Australia by comparing data from its sample of isolates obtained from relatively unchanging sources. Additionally, AGSP data record site of isolation that was not always available in other data sets. This had allowed the AGSP to comment on trends in gonococcal disease in Australia as a by-product of its prime role in antibiotic susceptibility surveillance. This situation has been irrevocably altered by the increasing use of non-culture based methods of diagnosis. It is not possible to determine the number of diagnoses made by nucleic acid amplification testing methods or if these were additional diagnoses made in outreach settings or simply a replacement of traditionally derived diagnoses. For these reasons no comment is made on the significance of altered numbers in the AGSP sample.

Gonorrhoea remains an important disease globally. Mucosal infection has a well documented complication and morbidity rate and deleterious consequences include decreased fertility through early trimester abortion and pelvic inflammatory disease. Neonatal and, in Australia, childhood ophthalmia, is also well recognised. Gonorrhoea also is known to significantly amplify the rate of transmission of HIV. Rates of gonorrhoea are again increasing in a number developed countries and this increase has also been reported in parts of Australia. Control of gonorrhoea is therefore essential but is a complex issue requiring a concerted and continuing effort on many fronts. One essential component of this integrated approach to control is the availability of simple but effective antibiotic treatments for the disease. However treatment is becoming more difficult as the choice of suitable therapy is increasingly restricted by antibiotic resistance. Continued monitoring of resistance patterns is therefore required to optimise treatment regimens, individual case management and disease control.

Acknowledgements

Participating laboratories in the AGSP (to whom isolates should be referred):

John Bates, Denise Murphy and Vicki Hicks. Queensland Health Scientific Services, Coopers Plains, Queensland.

Athena Limnios, Tiffany Shultz and John Tapsall. Department of Microbiology, The Prince of Wales Hospital, Randwick, New South Wales.

Julia Griffith, Mark Veitch, Vesna De Petra and Geoff Hogg. The Microbiological Diagnostic Unit, Department of Microbiology and Immunology, University of Melbourne, Parkville, Victoria.

Lance Mickan, Rachael Pratt, Ingrid Lusis, Infectious Diseases Laboratories, Institute of Medical and Veterinary Science, Adelaide, South Australia.

Julie Pearson and John Pearman. Microbiology Department, Royal Perth Hospital, Perth, Western Australia.

Mark Gardam and Alistair Macgregor. Department of Microbiology and Infectious Diseases, Royal Hobart Hospital, Hobart, Tasmania.

Gary Lum and Microbiology Staff. Microbiology Laboratory, Royal Darwin Hospital, Casuarina, Northern Territory.

Paul Southwell and Peter Collignon. Microbiology Department, Canberra Hospital, Woden, Australian Capital Territory.

References

1. Australian Gonococcal Surveillance Programme. Penicillin sensitivity of gonococci in Australia: the development of an Australian gonococcal surveillance programme. *Br J Vener Dis* 1984,60:226-230.
2. Australian Gonococcal Surveillance Programme. Use of a quality assurance scheme in a long-term multicentric study of antibiotic susceptibility of *Neisseria gonorrhoeae*. *Genitourin Med* 1990,66:437-444.