Annual report of the Australian Gonococcal Surveillance Programme, 1997

The Australian Gonococcal Surveillance Programme[1]

Abstract

The Australian Gonococcal Surveillance Programme (AGSP) examined 2,817 isolates of *Neisseria gonorrhoeae* in the period 1 January to 31 December 1997, a number similar to that reported in 1996. The biggest change in incidence of gonococcal disease occurred in New South Wales and Queensland where a 20% rise in the number of isolates was noted. In the latter case this was due to improved surveillance, but in the former represented a real increase. The sites of infection and antibiotic susceptibility patterns varied considerably between regions reflecting considerable differences between rural and urban gonorrhoea in Australia. 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 was lower and most isolates were from the genital tract. Resistance to the penicillin and quinolone groups of antibiotics were also highest in urban centres, but penicillins remained suitable for use in many parts of rural Australia. Quinolone resistance in gonococci continued to increase. This was particularly so in Sydney where quinolone resistant *N. gonorrhoeae* (QRNG) accounted for about 15% of all isolates and spread of QRNG was predominantly by local contact. QRNG in other centres continued to be isolated at a lower frequency, mostly from overseas travellers. All isolates remained sensitive to spectinomycin and ceftriaxone. ***Commun Dis Itell*** **1998;22:212-216.**

Introduction

There is renewed interest in rates of gonococcal disease and control of gonorrhoea following converging epidemiological and biological studies showing the significant role of this disease as an amplification factor in the spread of HIV. [1-4] The gonococcus has a well demonstrated capacity to develop antibiotic resistance by numerous chromosomal and extrachromsomal mechanisms. Continuing and long term surveillance is required to monitor and respond to changes in resistance which can occur in a short space of time.[5]

The Australian Gonococcal Surveillance Programme (AGSP) is a collaborative programme conducted by reference laboratories in each State and Territory. The primary aim of the programme is to monitor antibiotic susceptibility of Australian isolates of *Neisseria gonorrhoeae*, to assist in the formulation of treatment regimens appropriate to proper management of gonorrhoea. Management of gonorrhoea is based on single dose antibiotic therapy at first diagnosis, a strategy that assists patient compliance. There is a close correlation between the likely outcome of treatment and the *in vitro* susceptibility of the causative organism. However treatment is usually provided before results of susceptibility tests on individual isolates can be performed. Treatment regimens are therefore formulated using knowledge of the *in vitro* sensitivity of prevalent gonococci.[5] That is, the overall pattern of susceptibility of prevalent gonococci is the critical determinant of appropriate antibiotic therapy rather than individual strain susceptibility identified on a case by case basis.[6]

Quarterly reports have been provided to *CDI* since antibiotic sensitivity data were first produced by the AGSP in 1981.[7-10] Initially only data on penicillin resistance were reported and the AGSP documented the appearance and spread of penicillinase producing gonococci (PPNG) in Australia.[11] Monitoring of resistance to other antibiotics was added as newer therapeutic agents became available. Currently the emergence and spread of gonococci resistant to the quinolone antibiotics, agents widely used in Australia, is of particular concern. This is the second annual summary of AGSP data in *CDI* and provides information on trends in disease as well as antibiotic sensitivity data.

Methods

The AGSP comprises participating laboratories in each State and Territory (see acknowledgements). It is a network of collaborating centres which seeks to obtain isolates for examination from as wide a section of the community as possible. For example, strains from the Northern Territory are isolated in Alice Springs, Katherine and Darwin and in the laboratories of Western Diagnostic Pathology and Queensland Medical Laboratory in the Northern Territory and further tested in AGSP centres in Perth, Adelaide and Sydney. The sources of isolates remained relatively unchanged between 1996 and 1997. Gonococci isolated in and referred to the participating laboratories were examined for antibiotic susceptibility by a standardised methodology[11] and the AGSP conducted a programme-specific quality assurance programme.[12] Antibiotic sensitivity data were submitted quarterly to the co-ordinating laboratory which collated the results and also conducted the QA programme. Additionally the AGSP received data on the sex and site of isolation of

1. Corresponding author, J. W. Tapsall, Department of Microbiology, The Prince of Wales Hospital Randwick NSW 2031

gonococcal strains. The geographic source of acquisition of resistant strains was ascertained whenever possible.

Results

Number of isolates

There were 2817 isolates examined in 1997 (Table 1) . Nine hundred and two gonococci (32% of the Australian total) were isolated in New South Wales, 595 (21%) in Queensland, 445 (16%) in Western Australia, 393 (14%) in the Northern Territory, 362 (13%) in Victoria, and 107 (4%) in South Australia, with small numbers in Tasmania and the Australian Capital Territory. Compared with data from the same sources in 1996, the greatest changes in the number and percentage of isolates were the increases in New South Wales (from 723) and Queensland (from 504) and the decrease in Western Australia (from 578). In New South Wales, where the sources of referral have been stable, the increase in the number of isolates continues a trend evident since 1994 (Figure 1). In Queensland, improved retrieval and referral of isolates to the AGSP contributed to the increase.

Figure 1. The number of gonococcal isolates from similar sources, New South Wales, 1994 - 1997

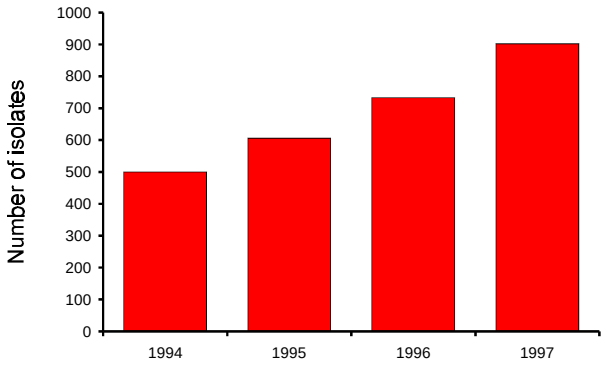


Table 1. Gonococcal isolates, Australia, 1997, by sex, site and region

Sex	Site	Region NSW	Vic	Qld	SA	WA	NT	Australia
Male	Urethra	707	255	346	65	300	95	1,778
	Rectal	73	50	16	19	5	0	164
	Pharynx	51	18	8	10	1	1	89
	Other/NS	3	3	18	0	20	148	192
	Total	834	326	388	94	326	244	2,223
Female	Cervix	62	30	196	13	108	95	505
	Other/NS	6	6	11	0	11	54	89
	Total	68	36	207	13	119	149	594
TOTAL	All sites	902	362	595	107	445	393	2,817

Source of isolates

There were 2,223 strains from men and 594 from women, giving a male : female (M:F) ratio of 3.7:1. This is higher than the 1996 ratio of 2.8:1 because of a concurrent increase in the number of strains from men (up from the 2,033) and decrease in the number from women (down from 720).

The M:F ratio was higher in South Australia (7.2), New South Wales (12.2) and Victoria (9.0) where strains were obtained more from urban populations (which have a higher rate of homosexual transmission), but lower in Western Australia (2.7), Queensland (1.9) and the Northern Territory (1.6), reflecting the large non-urban component of gonococcal disease (mainly heterosexual transmission) in those regions. Male rectal and pharyngeal isolates were most frequently found in New South Wales (together accounting for 14.9% of male isolates there), South Australia (30.9%) and Victoria (20.8%). This pattern is similar to that noted in 1996. Just under 10% of isolates were from ‘other’ sites. These included 9 cases of disseminated gonococcal infection, 7 in men and 2 in women. Many of the remaining isolates were from urine samples collected in northern Australia, and can best be regarded as genital tract isolates. There were also ophthalmic isolates from this region from young children and a small number of isolates from the eyes of newborn infants.

Antibiotic susceptibility patterns

In 1997, the AGSP reference laboratories examined 2,817 gonococcal isolates for sensitivity to the penicillins, ceftriaxone, ciprofloxacin and spectinomycin and for high level resistance to tetracycline (TRNG). However the patterns of gonococcal antibiotic susceptibility differed between the various States and Territories. For this reason data are presented by region as well as aggregated for Australia.

Penicillins

The categorisation of strains in Australia in 1997 by penicillin MIC is shown in Figure 2. Resistance to the penicillin group (penicillin, ampicillin, amoxycillin) may be mediated by the production of beta-lactamase

Figure 2. Penicillin resistance of gonococcal isolates, Australia, 1997, by region

FS Fully sensitive to penicillin, MIC ≤ 0.03mg/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 *Neisseria gonorrhoeae*

(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 MIC reflects the expression of multiple and different chromosomal changes present in an organism. These multiple changes result in incremental increases in the MIC and 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 category. Infections with strains in the LS or FS categories usually respond to therapy with standard treatment regimens with the penicillins. Infections with strains which are PPNG or in the RR category usually fail to respond to the penicillins.

There were 361 (12.8%) isolates with resistance to penicillin mediated by chromosomal mechanisms (CMRNG). Strains of this type were concentrated in Victoria (52 CMRNG, 14.6% of all isolates), New South Wales (246 CMRNG, 27.3% of all isolates) and South Australia (38 CMRNG, 35.5%). In contrast there were no CMRNG amongst Northern Territory isolates and only 3 (0.7%) in Western Australian strains. The 21 CMRNG in Queensland represented 3.5% of all isolates there.

The number (180), and proportion (6.4%), of PPNG rose slightly in 1997. Again the distribution of PPNG differed by region. While New South Wales had the highest number of PPNG (62), Victoria had the highest proportion (10.7%). PPNG were an important mechanism of resistance in Perth where the 33 strains accounted for 7.4% of isolates. The Australian Capital Territory was the only State or Territory where PPNG were not isolated in 1997. Most isolates were from patients infected overseas. Isolates which were fully sensitive to the penicillin group remained prominent in Victoria.

Ceftriaxone and Spectinomycin

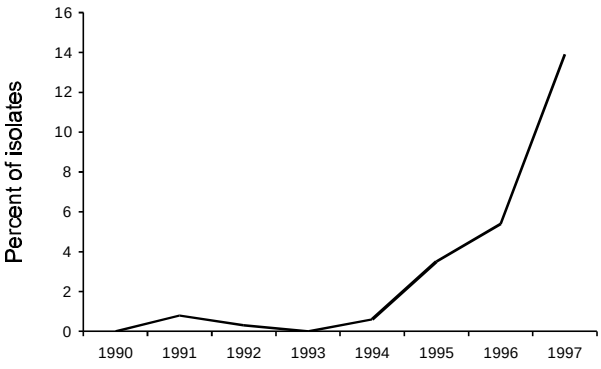
All strains from all parts of Australia were sensitive to these injectable agents.

Quinolone antibiotics

Resistance to the quinolone antibiotics is mediated only by chromosomal mechanisms and is thus incremental. The AGSP uses ciprofloxacin as the representative quinolone and defines altered resistance as a MIC ≥ 0.06 mg/l. Treatment with the currently recommended dose (500 mg) of ciprofloxacin is usually effective for strains with this less developed resistance, but lower doses of the antibiotic will often result in treatment failure. Treatment failure is also likely with high doses in infections with strains with MICs of 1 mg/l or more. Currently, gonococci with MICs up to 16 and 32 mg/l are being seen in Australia.

In 1997, a total of 204 (7.2%) of gonococcal isolates displayed altered sensitivity to the quinolones (QRNG). This is a large increase on the 108 (4%) QRNG seen in the previous year. QRNG were found in all States and Territories except Tasmania and the Australian Capital Territory. Victoria had 21 (5.8%) QRNG, Queensland 18 (3%), and Western Australia 13 (2.9%), with smaller numbers in South Australia and the Northern Territory. The biggest change in 1997 occurred in New South Wales where 144 (16%) of all isolates showed altered sensitivity to quinolones and 14% showed high level quinolone resistance. An increase in the number and proportion of high level QRNG had been noted in New South Wales in the December quarter of 1996 and this rate of isolation was sustained throughout 1997 (Figure 3). Another disturbing feature of the QRNG isolated in Sydney was their spread by local contact so that there is now sustained domestic transmission of these antibiotic resistant strains in that city. While most other centres showed a slight change in the number and percentage of QRNG isolated, the pattern of acquisition outside New South Wales is still mainly through overseas contact.

Figure 3. High level quinolone resistance (MIC≥ 1 mg/l) in gonococci, New South Wales, 1990 - 1997



High level tetracycline resistance (TRNG)

One hundred and sixty two TRNG (5.8% of isolates) were detected throughout Australia in 1997, a slight increase over the 1996 numbers. Approximately equal numbers

were found in Western Australia (40), Queensland (44) and New South Wales (47), corresponding to 9%, 7.4% and 5.2% of their isolates respectively. TRNG were also seen in Victoria, with 15 isolates (4%), and the Northern Territory, with 11 isolates (2.8%). The Australian Capital Territory was the only centre not reporting TRNG in 1997. Infections with TRNG were mainly acquired overseas in Indonesia, Thailand and Singapore. However an increasing number of isolates were acquired through local contact.

Discussion

Until 1996, the AGSP reported data on the basis of financial rather than calendar years. Also, while there have been stable sources of isolates in some regions, such as New South Wales, additional numbers of strains from Western Australia, the Northern Territory and Queensland have become available for examination in the Programme. Therefore, historical comparisons are restricted to 1996 data in this report.

A number of significant changes have been identified or confirmed in the 1997 AGSP data. The number of isolates examined increased only slightly overall (from 2,753 to 2,817), but decreased in some centres and increased in others. The most notable increase in the number of isolates was in New South Wales and Queensland where the number of strains rose by about 20% when compared with 1996 data. In New South Wales this further accelerated a trend noted since 1994 (Figure 1).

Although all participating centres have an urban and non-urban component in their mix of isolates, the relative contributions of each differs. The greater urban impact is reflected in the high male to female ratio and rate of extra-genital infection in New South Wales, Victoria and South Australia. The different pattern of gonococcal disease in northern Australia is shown in the lower male to female ratio and high rate of genital tract isolates in data from Queensland, Western Australia and the Northern Territory.

The differing urban and non-urban components of gonococcal disease are also seen in the regional differences in antibiotic susceptibility profiles of gonococci examined in different centres. In general most resistance is present in isolates from the more populous urban centres. For this reason the regional sensitivity patterns provide a more precise guide to suitable treatment than aggregated Australian data. However trends towards resistance noted in the large urban centres have in the past been indicative of subsequent directions in resistance in other regions.

The major trends in antibiotic resistance in 1997 related to the penicillins and the quinolones. Penicillin resistance in the larger centres, especially Melbourne and Sydney, has been high for many years. In these cities and in Adelaide, chromosomal resistance has been of greater importance than PPNG for a number of years and this trend was maintained or increased in 1997. In the other centres, PPNG were the main vehicle of resistance to the penicillins, but in rural areas these strains are not yet endemic and the penicillin group of drugs remains a suitable standard treatment.

The quinolone group of antibiotics is important as it is essentially the only currently available oral alternative to the penicillins in Australia. The patterns of resistance noted in 1997 are therefore cause for concern although they are as yet limited principally to Sydney. There has been a slow but progressive increase in both the number of QRNG isolated in Australia and in the MICs of the these QRNG for a number of years. It is not surprising, given the high incidence of QRNG in countries close to Australia, that QRNG have been repeatedly isolated from infected travellers entering or returning to Australia. The significant difference noted in Sydney in 1997 was not only the continuing high proportion of QRNG in that city, but their spread by local as opposed to overseas contact. It has been suggested that treatment regimens should be altered when resistance to an agent is found in 5% of isolates. The number of QRNG in Sydney in 1997 exceeds this level several fold.

The global decline in incidence of gonococcal disease in more developed countries has now been arrested and, in parts of Australia at least, the number of cases is again increasing. The choice of suitable treatment for gonorrhoea in Australia is becoming increasingly restricted, especially in the larger cities. Continued monitoring of resistance patterns is required to optimise treatment regimens.

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

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

Julia Griffith and Geoff Hogg. The Microbiological Diagnostic Unit, University of Melbourne, Parkville, Victoria

Greg Handke and Rosemary Perrie. Infectious Diseases Laboratories, Institute of Medical and Veterinary Science, Adelaide, South Australia

Cheryll McCullough. Microbiology Department, Royal Perth Hospital, Perth, Western Australia

Mark Gardam and Keith Ott. Department of Microbiology and Infectious Diseases, Royal Hobart Hospital, Hobart, Tasmania

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

Linda Halliday and Peter Collignon. Microbiology Department, Royal Canberra Hospital, Woden, Australian Capital Territory

References

1. Cohen MS, Hoffman IF, Royce RA, et al. Reduction of concentration of HIV-1 in semen after treatment of urethritis: implications for prevention of sexual transmission of HIV-1. *Lancet* 1997;349:1868-1873.
2. Ghys PD, Fransen K, Diablo MO, et al. The association between cervicovaginal HIV shedding, sexually transmitted diseases and immunosupression in female sex workers in Abidjan, Cote d'Ivoire. *AIDS* 1997;11:F85-F93.

3. Grosskurth H, Mosha F, Todd J, et al. Impact of improved treatment of sexually transmitted diseases on HIV infection in rural Tanzania: randomised controlled trial. *Lancet* 1995;346:530-536.
4. Page-Shafer K, Veuglers PJ, Moss AR, et al. Sexual risk behaviour and risk factors for HIV-1 seroconversion in homosexual men participating in the tricontinental seroconverter study, 1982 - 1994. *American Journal of Epidemiology* 1997;146;531-542.
5. Tapsall JW. Surveillance of antibiotic resistance in *Neisseria gonorrhoeae* and implications for the therapy of gonorrhoea. *Int J STD & AIDS* 1995;6:233-236.
6. Philpot CR and Tapsall JW. Single dose therapy of uncomplicated ano-genital gonorrhoea. *Med J Aust* 1987;146:254-256.
7. Australian gonococcal surveillance programme. Gonococcal surveillance - Australia (July-September 1981).*Commun Dis Intell* 1981;25:2-3.
8. Australian gonococcal surveillance programme. Gonococcal surveillance. Reporting period 1 January to 31 March 1996. *Commun Dis Intell* 1996;20:499-500.
9. Australian gonococcal surveillance programme. Gonococcal surveillance. Reporting period 1 April to 30 June 1996. *Commun Dis Intell* 1996;20:549-550.
10. Australian gonococcal surveillance programme. Gonococcal surveillance. Reporting period 1 July to 30 September 1996. *Commun Dis Intell* 1997;21:112.
11. 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.
12. 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.