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**Neisseria Reference Laboratory**

**WHO Collaborating Centre for STD and HIV**

16<sup>th</sup> February 2007

Dear Colleague,

Please find enclosed a copy of the annual report on gonococcal surveillance in NSW for 2006.

Antimicrobial resistance in gonococci is starting to sound like the information coming from data on global warming – it is all bad news. However whereas dam levels go down, resistance levels in gonococci go up.

In 2006, resistance levels to such antibiotics as the penicillins and quinolones exceeded the historical highs seen in 2005.

In past years, the NRL also provided estimates of trends in gonococcal disease by analysing the isolates it examined from a relatively constant sample. Increasing use of nucleic acid based amplification assays [NAA] for diagnosis of gonorrhoea from 1999 onwards resulted in a decrease in the number of isolates referred for testing and reduced numbers of gonococci obtained from the previous exclusively isolate-derived sample base. The sample examined however has remained sufficiently large and diverse to monitor gonococcal susceptibility to antibiotics used for treatment.

This sample base is derived by the continuing support of laboratories throughout NSW who provided cultures for examination and is again gratefully acknowledged.

We also thank those who have supplied geographic acquisition data where this is known. This has been helpful in distinguishing between imported and locally acquired infection.

If any further details are required on individual patients or overall patterns, please call us on 9382 9084. (If you wish to receive this report electronically please contact us at the same number or at [j.tapsall@unsw.edu.au](mailto:j.tapsall@unsw.edu.au))

Yours sincerely,

Athena Limnios, Sanghamitra Ray, Tiffany Hogan, Anne Lam and John Tapsall

# *Gonococcal Surveillance NSW Annual Report*

*January - December 2006*

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## **Summary**

### **Numbers of isolates**

The 1198 gonococcal isolates referred to and isolated in the reference laboratory in 2006 approximated the 1216 strains seen in 2005. The highest number tested in any year of this programme was the 1625 examined from the same sources in 2002.

### **Source of isolates**

A high proportion of isolates [92.6%] was again from males and rectal and pharyngeal isolates comprised 36% of strains from men. The number of isolates from females (88) was slightly less than the 95 reported in 2005 and most (79) of these were from the genital tract. Two ophthalmic (one in a neonate) and two disseminated gonococcal infections were recorded.

### **Antibiotic resistance patterns**

Levels of antibiotic resistance in 2006 increased further from the historical highs observed in 2005.

Gonococcal resistance to the [oral] **quinolone** agents was present in 635 (54%) of gonococci tested and nearly all (>99%) was at a high level. In 2005, 555 [46%] of isolates were QRNG. More than 90% of the QRNG were acquired through local contact.

Fifteen isolates (1.3%) displayed decreased susceptibility to **ceftriaxone** and 14 were also quinolone and penicillin resistant. Thus far, this decrease in sensitivity to third generation cephalosporins has not translated into clinical treatment failure with ceftriaxone given as a 250 mg IM dose.

Resistance to the **penicillins** [including ampicillin and amoxycillin] was also at historically high levels. 605 (51.3%) of all isolates were resistant to these agents by one or more mechanisms.

All isolates remained susceptible to the injectable agent **spectinomycin**.

**High-level tetracycline resistance [TRNG]** was observed in 125 [11%] gonococci and two thirds of these were also PPNG. In about half cases, the TRNG were acquired through local contact.

## **Introduction.**

The primary purpose of this programme is the surveillance of antimicrobial resistance in *Neisseria gonorrhoeae* in New South Wales. The Neisseria Reference Laboratory [NRL] receives isolates from private and public laboratories throughout the state. The identity of all isolates is confirmed and the susceptibility to appropriate antibiotics determined for epidemiological purposes *viz.* the formulation of treatment schedules for management of gonorrhoea in NSW. Additionally strain differentiation techniques are applied to all isolates and matched with certain clinical data [e.g. acquisition history - overseas or local] to monitor the introduction and spread of antibiotic resistant isolates.

Successful treatment of gonorrhoea is important for the individual and is also of public health relevance in terms of disease control and prevention of complications. Gonococcal resistance to those antibiotics used in the treatment of gonorrhoea compromises both individual management and efforts aimed at wider disease containment. Significant shifts to increasing resistance in those antibiotics used for the treatment of gonorrhoea in NSW have been recorded in recent years.

Data generated in NSW by the NRL are incorporated into those of the National Neisseria Network Gonococcal Surveillance Programme and into WHO regional programmes of gonococcal susceptibility surveillance.

## **Numbers of Gonococcal Isolates January - December 2006, NSW**

The total number of gonococci isolated and referred in 2006 was 1198. This number does not include duplicate isolates or those diagnoses made by nucleic acid amplification (NAA) techniques such as PCR.

This number approximates the 1216 strains received in 2005. The highest number examined in recent years was in 2002 when 1625 gonococci were available.

Historical data on the numbers of isolates examined are shown in Figures 1 (by year, 1994 - 2006) and 2 (by quarter, 1998 - 2006). Numbers of isolates were higher than usual in the first half of 2006, but decreased in the September and December quarters.

Table 1. Number of gonococcal isolates from men and women in 2006 by quarter and for the whole year.

<u>Period</u>	<u>Men</u>	<u>Women</u>	<u>All isolates</u>
1 January - 31 March	323	24	347
1 April - 30 June	289	25	314
1 July - 30 September	257	21	278
1 October - 31 December	<u>241</u>	<u>18</u>	<u>250</u>
<u>1 January - 31 December</u>	<u>1110</u>	<u>88</u>	<u>1198</u>

Figure 1. Number of NSW gonococcal isolates examined in each year 1994 - 2006 (excludes diagnoses made by NAA based tests).

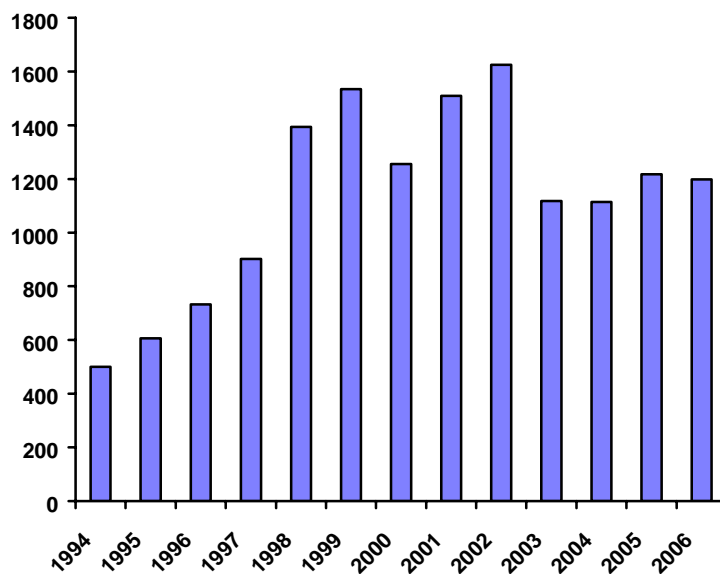
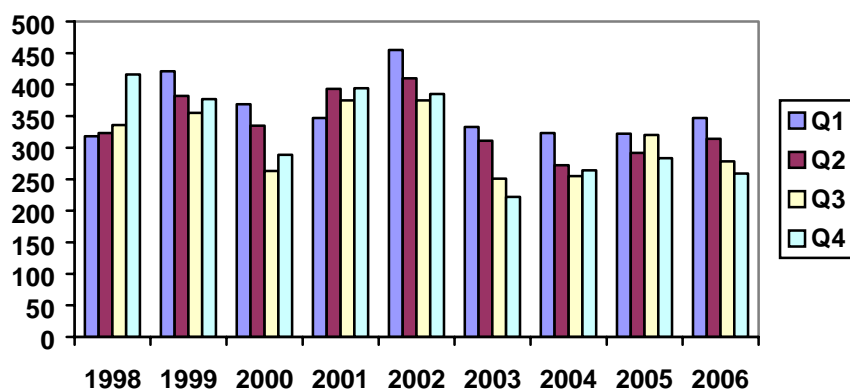


Figure 2. Number of gonococcal isolates by sequential quarters, NSW 1998 – 2006.



### Infected sites - January - December 2006

Table 2. Sites of gonococcal infection in men and women, New South Wales, 2006

<i>Male patients</i>			<i>Female patients</i>		
Urethra	697	[664]	Endocervix/vagina	79	[90]
Pharynx	148	[172]	Pharynx	2	[3]
Ano-rectum	255	[238]	Ano-rectum	3	[1]
Blood/Joint	1	[4]	Blood/Joint	1	[0]
Eye	0	[4]	Eye	2	[0]
<u>Unspecified</u>	<u>9</u>	<u>[38]</u>	<u>Other*</u>	<u>1</u>	<u>[1]</u>
Total	1110	[1120]	Total	88	[95]

[Figures in parenthesis are data from 2005; \*one isolate in women was from the peritoneum]

The male:female ratio of infected patients in 2006 was 12.6:1 [in 2005, 11.8:1]. Sixty three percent of isolates from known sites of infection in men were from the urethra. Rectal isolates in men comprised 23% of isolates and pharyngeal strains 13.5%. There were two disseminated infections. One of the two eye infections was in a neonate, the age of the other case was not specified. Most (90%) of isolates from women were from the genital tract but also included two from the pharynx and three rectal infections.

### **Gonococcal antibiotic sensitivity patterns in NSW gonococci in 2006**

1179 strains remained viable for susceptibility determination. For guidance in considering the following data, WHO recommends that the use of an antibiotic should be discontinued when 5% or more of isolates are resistant.

**Quinolones** [Ciprofloxacin, Norfloxacin, Enoxacin; more recently released fluoroquinolones such as gatifloxacin and moxifloxacin would not be expected to have any advantage over ciprofloxacin in the treatment of gonorrhoea]

In 2005 a major upsurge in the number and proportion of quinolone resistant gonococci occurred when 46% of all isolates were quinolone resistant (QRNG). This was the highest number and proportion of QRNG recorded in NSW in any year to that time (Figure 3). This was part of a significant shift to increasing quinolone resistance over several years, seen when there were 160 (15%) QRNG in 2003 and 331 (30%) in 2004. In 2006 this trend continued when 635 (54%) of gonococci were quinolone resistant. In the fourth quarter of 2006, 60% of gonococci in NSW were quinolone resistant.

Additionally, from the middle of 2000 onwards, there has been a progressive increase in MICs of those gonococci identified as QRNG. The proportion of QRNG with ciprofloxacin MICs  $\geq 1$  mg/l) and of those with even higher MICs has increased while those in the 'less sensitive' ciprofloxacin MIC range [0.06 - 0.5 mg/L] has decreased. [Treatment failure with a 500 mg dose of ciprofloxacin is said to occur in about 6% of cases where 'less sensitive' QRNG are involved and in about 40% at an MIC of 1 mg/l. Rates of treatment failure increase rapidly above this MIC value.]

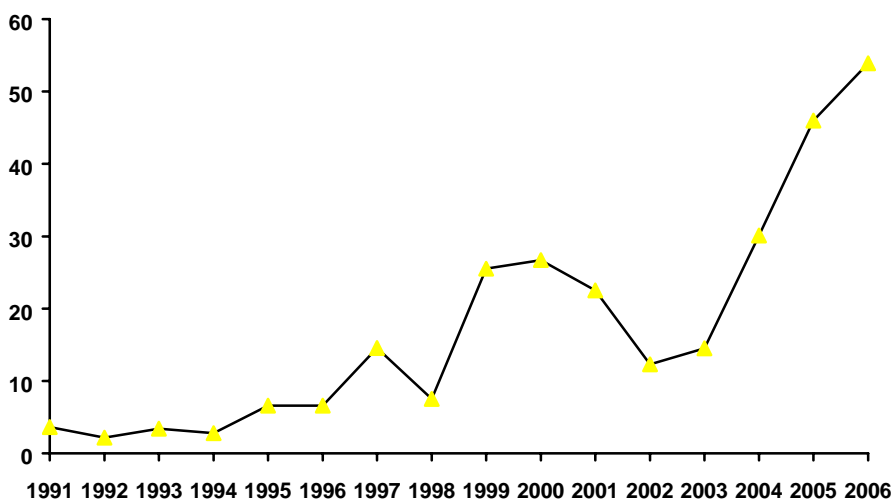


Figure 3. QRNG as a % of all gonococci isolated in NSW, 1991 – 2006.

More than 99% [629, of the 633 QRNG] were resistant to the quinolones over an MIC range 1 – to more than 32 mg/L Of these, 407 (over 80% of all QRNG

or about half of all isolates) had high level resistance with MICs for ciprofloxacin of 8 mg/l or more. A further 6 QRNG [0.5%] only were in the less sensitive range (ciprofloxacin MICs 0.06 – 0.5 mg/l).

Data on geographic acquisition was available in about 37% of the cases of infection with QRNG. The rate of local acquisition of QRNG increased again in 2006, with about 95% of infections with QRNG arising from local contacts. Overseas sources of QRNG acquisition included Brazil, China, Hong Kong, Indonesia (including Bali), Pakistan, the Philippines, Singapore, Thailand, Vietnam and the Netherlands reflecting the wide distribution of QRNG in neighbouring countries.

**Penicillins** [including penicillin, ampicillin and amoxycillin]

Resistance to the penicillins also increased further in 2006 when 605 (51.3%) of strains tested were penicillin resistant. In 2005 the number (574) and proportion (47.5%) of gonococci resistant to the penicillins had increased substantially from the 290 penicillin resistant strains [26.5% of isolates] detected in 2004.

The increase observed in 2005 was due to a rise in the number and proportion of gonococci intrinsically penicillin resistant by chromosomal mechanisms [CMRNG, Minimal Inhibitory Concentration - MIC =, > 1 mg/L] with a slight decrease in the number and proportion of penicillinase producing *N. gonorrhoeae* (PPNG). These trends were accentuated in 2006. There were 504 CMRNG (43%) detected in 2006 compared with 432 CMRNG (37.5%) in 2005 and 130 (11.8%) in 2004. In 2006 the number (101) and proportion (8.6%) of PPNG decreased further from the 142 (11.8%) present in 2005 and the 161 (14.6%) found in 2004 (Figure 4).

In 49 (48% of the PPNG) cases, the geographic source of acquisition of the infection with PPNG was recorded. Of these, 24 were acquired through local contact and 25 from a variety of countries, most prominently Thailand, the Philippines and Indonesia but also China and Singapore.

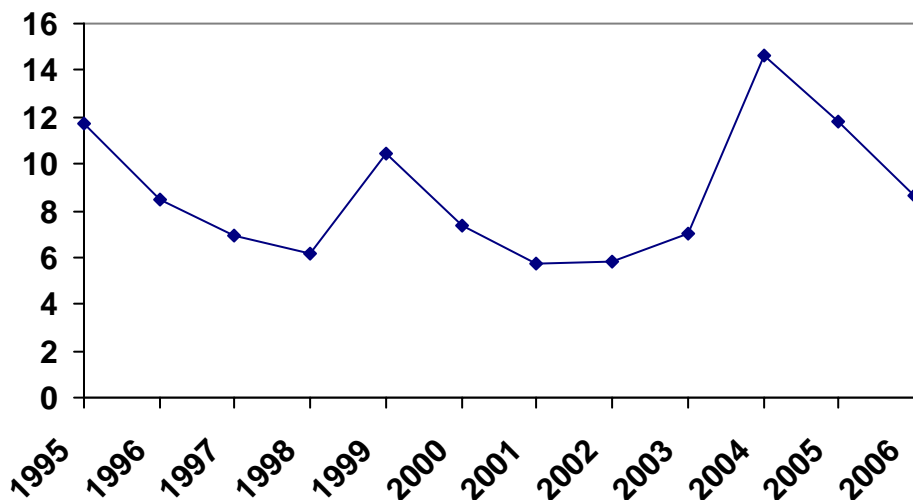


Figure 4. Percentage of NSW isolates which were PPNG, 1995 – 2006

### **Ceftriaxone**

Fifteen (1.3%) isolates of gonococci tested in 2006 had slightly raised MICs to ceftriaxone in the range 0.06 - 0.12 mg/L, compared with 37 (3%) in 2005. All of these gonococci were also penicillin resistant and 14 of the were quinolone resistant. Only one was a PPNG, while the remainder that were penicillin resistant were CMRNG with penicillin MICs in the range 1 – 4 mg/L. Contact details were available in six cases and all of these were acquired locally.

These isolates have altered *penA* genes which phenotypically express a range of ceftriaxone MIC values. Isolates with these features are not regarded as posing any risk of treatment failure with ceftriaxone at MIC levels currently encountered, if the recommended dose of 250 mg IM is used. However, strains with similar characteristics were reported to have failed treatment with *oral* third generation cephalosporin antibiotics in Japan.

### **Spectinomycin**

All strains tested were susceptible *in vitro* to this injectable antibiotic.

### **Tetracyclines**

*Tetracyclines are NOT recommended for treatment of gonorrhoea in NSW*, and the continuing presence of plasmid-mediated high-level tetracycline resistance in gonococci [TRNG] has reinforced this recommendation.

High-level resistance to this agent has also fluctuated over a wide range over time. The number [125] and proportion [10.6% of all isolates] of TRNG seen in 2006 was slightly less than in 2005 [136, 11.4%] and continued a downward trend. In 2004 there were 196 [18%] TRNG detected.

Some countries close to Australia have high numbers of TRNG and in the past TRNG have been seen mostly as imported infections. Geographic acquisition information was again available in about 40% of cases, and half of these were from local contact. The patients where TRNG were acquired overseas nominated China, Fiji, Hong Kong, Indonesia, the Philippines, Singapore and Thailand as sources of contact. Eighty-three (66%) of the TRNG were also PPNG.

### **Acknowledgments :**

The continuing co-operation of private and public hospital laboratories who refer strains for examination is once again gratefully acknowledged.