

Surveillance of antibiotic resistance in *Neisseria gonorrhoeae* in the WHO Western Pacific Region, 1999

The WHO Western Pacific Region Gonococcal Antimicrobial Surveillance Programme¹

Abstract

A long-term programme of surveillance of antimicrobial resistance in *Neisseria gonorrhoeae* isolated in the World Health Organization's Western Pacific Region Gonococcal Antimicrobial Surveillance Programme (WHO WPR GASP) continued in 1999. Over 10,000 gonococci were examined in 18 focal centres. Resistance to the quinolones and penicillins was already high in many parts of the Western Pacific Region and increased further in most centres, the exceptions being a number of Pacific Island States. Although resistance to the later generation cephalosporins was absent, and that to spectinomycin infrequent, options for effective treatment of gonorrhoea in the Western Pacific Region continue to be limited. *Commun Dis Intell* 2000;24:269-271.

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

Introduction

Neisseria gonorrhoeae is, with *Haemophilus ducreyi*, one of the few aetiological bacterial agents of sexually transmitted infection (STI) where antimicrobial resistance (AMR) seriously compromises disease control. Additionally AMR in gonococci, by preventing effective treatment of individuals, increases the rate of complications and morbidity associated with gonococcal disease. One further deleterious consequence of gonorrhoea is the amplification of the rate of transmission of HIV that occurs in its presence. However, effective treatment of gonorrhoea removes this effect. It is therefore important to ensure that gonococcal disease is properly treated, and this in turn depends to a significant degree on having relevant data on AMR patterns to guide selection of treatment regimens.

AMR in gonococci may arise and spread rapidly. The World Health Organization (WHO) Western Pacific Region (WPR) includes countries with high rates of STIs and where different forms of AMR have arisen in the past. Gonococci resistant to the penicillins, spectinomycin and, more recently, the quinolone antibiotics had their origins in countries in the WPR. The potential for spread of AMR gonococci beyond regional confines is also well established so that disease acquired in one setting may present in another. There are thus multiple reasons to ascertain the prevalence and distribution of AMR in gonococci and modify treatment regimens accordingly. The WHO WPR Gonococcal Antimicrobial Surveillance Programme (GASP) has monitored AMR in gonococci in the region since 1992 and results have been published in *Communicable Diseases Intelligence*.^{1,2} This communication provides an analysis of surveillance of AMR in *N. gonorrhoeae* in 18 countries in the WHO WPR in 1999.

Methods

The methods used by the WHO WPR GASP were published in 1997³ and provide full details of the source of isolates, sample populations, laboratory test methods and quality assurance programs used to generate data. These methods were unaltered in 1999. Most isolates were collected from symptomatic STD clinic patients. As a guide to the interpretation of the following data, a WHO expert committee has recommended that treatment regimens be altered once resistance to a particular antibiotic reaches 5 per cent.⁴

Results and discussion

About 10,600 gonococcal isolates were examined in 18 participating countries (listed in the acknowledgments) in 1999.

Penicillins

Resistance to the penicillins remained widespread by both chromosomal and plasmid-mediated mechanisms. Table 1 provides details of chromosomally mediated resistance in *N. gonorrhoeae* (CMRNG), penicillinase-producing *N. gonorrhoeae* (PPNG) and/or total penicillin resistance in 18 WPR countries in 1999. Very high rates of all penicillin resistance (CMRNG + PPNG) were recorded in Korea (95%), the Philippines (94%), China (88%), Hong Kong SAR (73%), Brunei (67%), Vietnam (66%), Singapore (56%) and Mongolia (48%). Resistance to the penicillins in these countries in 1999 approximated that found in 1998. Of interest were the low rates of penicillin resistance found in some Pacific Island States. The Solomon Islands and Vanuatu had no penicillin resistant strains in 1999 and in New Caledonia (4%), Fiji (4.8%) and Tonga (5%), rates were considerably lower than those observed in other parts of the region. The exception to this observation was Papua New Guinea where penicillin resistance was of the order of 59 per cent, equally distributable between PPNG and

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Table 1. Penicillin sensitivity of strains of *Neisseria gonorrhoeae* isolated in 18 countries in the WHO WPR¹ in 1999

| Country | No. tested | PPNG ² | | CMRNG ³ | | All penicillin- resistant | |
|------------------|------------|-------------------|------|--------------------|------|---------------------------|------|
| | | No. | % | No. | % | No. | % |
| Australia | 3,658 | 269 | 7.4 | 525 | 14.3 | 794 | 21.7 |
| Brunei | 64 | | | | | 43 | 67.0 |
| China | 571 | 127 | 21.5 | 338 | 57.1 | 465 | 88.6 |
| Fiji | 860 | 17 | 1.9 | 24 | 2.8 | 41 | 4.7 |
| Hong Kong SAR | 2,482 | 233 | 9.4 | 1,576 | 63.5 | 1,809 | 72.9 |
| Japan | 246 | 3 | 1.2 | 36 | 14.8 | 39 | 16.0 |
| Korea | 86 | 72 | 84.0 | 10 | 12.0 | 82 | 95.0 |
| Malaysia | 54 | 13/44 | 29.0 | 5 | 9.3 | 18 | 38.3 |
| Mongolia | 56 | 10 | 17.8 | 17 | 30.4 | 27 | 48.2 |
| New Caledonia | 53 | | | | | 2 | 3.8 |
| New Zealand | 638 | 18 | 2.8 | 34 | 5.3 | 52 | 8.1 |
| Papua New Guinea | 343 | 73/253 | 28.8 | 103 | 30.0 | | 58.8 |
| Philippines | 313 | 294 | 94.0 | 0 | 0.0 | 294 | 94.0 |
| Singapore | 768 | 399 | 51.9 | 31 | 4.0 | 430 | 55.9 |
| Solomon Islands | 21 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Tonga | 39 | 1 | 2.5 | 1 | 2.5 | 2 | 5.0 |
| Vanuatu | 129 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Vietnam | 194 | 99 | 51.0 | 28 | 14.4 | 127 | 65.5 |

1. World Health Organization: Western Pacific Region.
2. PPNG = penicillinase-producing *N. gonorrhoeae*.
3. CMRNG = chromosomally mediated resistance in *N. gonorrhoeae*.

CMRNG. The other participants submitting data in 1999 (Australia, Japan, Malaysia and New Zealand) had rates of penicillin resistance between 8 and 38 per cent.

Quinolones

Resistance to the quinolone antibiotics has become a major problem in parts of the WPR in recent years and this situation deteriorated further in 1999. Data from 15 WPR countries are shown in Table 2 and allow division of quinolone-resistant strains (QRNG) into 'less susceptible' and 'resistant' categories on the basis of minimal inhibitory concentration (MIC) determinations.³ Twelve of 15 WPR countries detected QRNG in 1999. High proportions of QRNG were detected in Hong Kong, China, Japan and the Philippines, maintaining a situation observed in previous reports. In Hong Kong the percentage of 'resistant' QRNG increased from about 50 per cent in 1998 to about 66 per cent in 1999. A similar shift to higher MICs in Japan saw the proportion of 'resistant' QRNG there increase from 3 per cent in 1998² to about 23 per cent in 1999. The proportion of QRNG also increased significantly in Vietnam in 1999 to about 50 per cent from 17 per cent in 1998. Most of the QRNG in Vietnam were in the higher MIC range. Singapore recorded an increase in resistant strains from 7 per cent in 1998 to 17 per cent in 1999. In both Korea and Australia there were increases in the percentage of QRNG in the less susceptible range. In Korea these increased from about 50 per cent to 71 per cent and in Australia from 2 per cent to 14 per cent as a result of spread of QRNG in homosexually active males. Mongolia reported QRNG data for the first time and about one third of isolates exhibited some form of quinolone resistance; 25 per cent of them had high level resistance. About 17 per cent of strains from Brunei, 3.5 per

cent from New Zealand and 1.8 per cent from Papua New Guinea were QRNG. No QRNG were found in Malaysia, New Caledonia or the Solomon Islands in 1999.

Table 2. Quinolone resistance in strains of *Neisseria gonorrhoeae* isolated in 15 countries in the WHO WPR¹ in 1999

| Country | No. tested | Less susceptible | | Resistant | |
|------------------|------------|------------------|------|-----------|------|
| | | No. | % | No. | % |
| Australia | 3658 | 500 | 13.7 | 128 | 3.5 |
| Brunei | 53 | 4 | 7.5 | 5 | 9.4 |
| China | 591 | 131 | 22.1 | 332 | 52.8 |
| Hong Kong SAR | 2482 | 697 | 28.1 | 1653 | 66.6 |
| Japan | 246 | 80 | 32.5 | 56 | 22.8 |
| Korea | 86 | 61 | 71.0 | 14 | 16.0 |
| Malaysia | 54 | 0 | 0.0 | 0 | 0.0 |
| Mongolia | 56 | 5 | 8.9 | 14 | 25.0 |
| New Caledonia | 53 | 0 | 0.0 | 0 | 0.0 |
| New Zealand | 638 | 8 | 1.3 | 14 | 2.2 |
| Papua New Guinea | 343 | 1 | 0.3 | 5 | 1.5 |
| Philippines | 313 | 8 | 2.5 | 191 | 61.0 |
| Singapore | 768 | 37 | 4.8 | 131 | 17.0 |
| Solomon Islands | 21 | 0 | 0.0 | 0 | 0.0 |
| Vietnam | 194 | 27 | 13.9 | 69 | 35.6 |

1. World Health Organization: Western Pacific Region.

Cephalosporins

There were no isolates resistant to the third generation cephalosporin agents reported in the WPR GASP survey that examined about 7,250 gonococci from 16 of the participating countries.

Spectinomycin

Only two isolates, one each in Malaysia and Papua New Guinea were resistant to spectinomycin amongst about 7,250 gonococci examined in 16 of the participating countries in 1999. Only very occasional strains resistant to this injectable antibiotic have been found in recent WPR surveys.

Tetracyclines

Although tetracyclines are not a recommended treatment for gonorrhoea, these agents are widely used and readily available in the WPR. One particular type of resistance is common in parts of the WPR; this is plasmid-mediated and gives rise to high-level tetracycline resistant *N. gonorrhoeae* (TRNG). About 6,900 gonococci were examined for high-level tetracycline resistance in 12 of the WPR countries in 1999 (Table 3). TRNG were again prominent in Malaysia, Singapore, Vietnam and the Solomon Islands with TRNG rates between 40 and 74 per cent. Rates below 10 per cent were seen in Australia, New Zealand and the Philippines. The TRNG rate increased in China from around 3 per cent in 1998 to nearly 15 per cent in 1999. A similar rate was observed in Papua New Guinea. TRNG were not detected in isolates from Korea, Mongolia and Tonga.

The data recorded in 1999 continue trends noted over several years. Resistance to the penicillins remains widespread, although some island States have low rates of resistance. The effectiveness of the quinolone group of antibiotics continues to decrease and their use in many countries should be discontinued because of the levels of resistance present. However, although alternative therapies are available, their cost limits their use in some settings.

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Table 3. High-level tetracycline resistance in strains of *Neisseria gonorrhoeae* isolated in 12 countries in the WHO WPR¹ in 1999.

| Country | No. Tested | No. TRNG ² | % TRNG |
|------------------|------------|-----------------------|--------|
| Australia | 3,658 | 288 | 7.8 |
| China | 591 | 86 | 14.5 |
| Korea | 86 | 0 | 0.0 |
| Malaysia | 54 | 32 | 59.0 |
| Mongolia | 27 | 0 | 0.0 |
| Papua New Guinea | 343 | 54 | 15.7 |
| New Zealand | 638 | 8 | 1.3 |
| Philippines | 313 | 16 | 5.1 |
| Singapore | 768 | 566 | 73.7 |
| Solomon Islands | 21 | 12 | 57.0 |
| Tonga | 39 | 0 | 0.0 |
| Vietnam | 195 | 79 | 40.5 |

1. World Health Organization: Western Pacific Region.
2. TRNG = tetracycline-resistant *N. gonorrhoeae*.

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