

Surveillance of antibiotic resistance in *Neisseria gonorrhoeae* in the WHO Western Pacific Region, 1998

The WHO Western Pacific Gonococcal Antimicrobial Surveillance Programme¹

Abstract

Effective treatment of gonorrhoea in the World Health Organization's Western Pacific Region is hampered by the emergence and spread of antibiotic resistant strains of *Neisseria gonorrhoeae*. A programme of surveillance of gonococcal susceptibility to antibiotics (GASP) continued in the region in 1998. A high proportion of isolates in many participating countries was resistant to quinolones and penicillins, continuing trends observed by this programme since 1992. Resistance to the later generation cephalosporins and to spectinomycin was absent or infrequent. Options for effective treatment of gonorrhoea in the region have been severely compromised by antibiotic resistance. *Commun Dis Intell*2000;24:1-4

Introduction

Even if considered simply in numeric terms, gonorrhoea remains a major global disease with an estimated 60 million cases of gonococcal disease occurring annually¹. About half of these cases occur in the World Health Organization's (WHO) Western Pacific (WP) and South East Asian (SEA) regions. Control of gonorrhoea (and other sexually transmitted diseases (STDs)), is a difficult and complex issue, but one essential component is the provision of effective antibiotic treatment. As well controlling the disease itself,

appropriate therapy reduces morbidity associated with gonorrhoea such as pelvic inflammatory disease (PID) and neonatal ophthalmia. HIV transmission is also amplified in the presence of gonorrhoea, but this effect can be ameliorated if treatment is provided. In some settings this intervention substantially reduces HIV transmission.² There are thus a number of important reasons why gonococcal disease should be properly treated.

One factor limiting the efficacy of antibiotics in gonococcal disease is the ability of the organism

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to develop resistance to them, and historically much of this resistance has appeared first in the WP and SEA regions. There is however, a strong correlation between likely outcome of antibiotic therapy and the *in vitro* susceptibility of gonococci. This means that if the susceptibility of prevalent gonococci to antibiotics is determined systematically using an epidemiological approach, a reliable guide to the choice of suitable standard treatment regimens can be provided in a country or region. There are a number of examples of country based systems of laboratory based surveillance in existence.^{3,4} The WHO WP Gonococcal Antimicrobial Surveillance Programme (WPR GASP) combines a number of these local networks and functions at a regional level. The WPR GASP has monitored the antibiotic susceptibility of gonococci isolated in the WPR since 1992.⁵ Results have been published annually in *CDI* since 1992.⁶⁻¹⁰

Methods

A full description of the methods used by this programme has been published⁵ and includes details of sample sources, isolate selection, use of standardised testing methods, a programme specific external quality assurance component and the technical support and training provided under GASP auspices. These methods did not alter in 1998.

Results and Discussion

Sixteen countries in the WPR contributed data on about 10,000 isolates in 1998.

As was expected from previous regional surveillance, resistance to the *penicillins* was widespread (Table 1). Both chromosomal (CMRNG) and plasmid mediated (PPNG) forms of resistance were common. The highest rates of penicillin resistance were reported from Korea

(90%), the Philippines (82%), Vietnam (76%), Mongolia (70%), China – Hong Kong (69%), China (62%) and Singapore (59%). These percentages were the total of all forms of penicillin resistance. The proportion of PPNG has been declining in some centres, but CMRNG have become more prominent.

Resistance to the *quinolone* antibiotics (QRNG) continued to increase in a number of centres or else was maintained in a high proportion of isolates in 1998 (Table 2). Quinolone resistance in gonococci results only from different but additive chromosomal changes, and there is no plasmid-mediated transmission. Some of these alterations occur only in the presence of previous mutations. For example, *parC* changes are seen only after alterations in *gyrA* have appeared. This means that levels of resistance in QRNG (as determined by Minimal Inhibitory Concentrations – MICs) show a sequential change. Because of this incremental nature of quinolone resistance, it is relevant to monitor both low (MIC of ciprofloxacin 0.06 to 0.5 mg/L) and high level (MIC of ciprofloxacin \geq 1 mg/L) resistance to quinolone antibiotics. Quinolone resistance was assessed in 13 countries in 1998 and QRNG were found in 11, the exceptions being Fiji and the Solomon Islands. In excess of 90% of isolates in China and China – Hong Kong were QRNG and about half in each setting possessed high level resistance. Both of these focal points had high proportions of QRNG in 1997 but the total QRNG percentages in 1998 were even higher and the proportion of high level QRNG also increased. The Philippines had a high proportion of high level QRNG (63%), also continuing a pattern observed for some time. Korea (62%) and Japan (52%) again reported a high percentage of QRNG, but most were in the category of lower level QRNG. Other centres such as Vietnam, Papua New Guinea and Singapore show a lower proportion of mixed low and high level QRNG. In other

Table 1. Penicillin sensitivity of strains of *Neisseria gonorrhoeae* isolated in countries in the WHO WPR in 1998

Country	Number tested	PPNG		CMRNG		All Penicillin Resistant	
		No	%	No	%	No	%
Australia	3,583	206	5.7	782	21.8	988	27.5
China	939	30	3.2	558	59.4	588	62.6
Fiji	836	33	4.0	40	4.8	73	8.8
Hong Kong (China)	2,255	59	2.6	1,497	66.4	1,556	69.0
Japan	190	1	0.5	15	7.9	16	8.4
Korea	134	99	74.0	21	15.6	120	89.6
Malaysia	na	-	-	-	-	-	-
Mongolia	27	7	26.0	12	44.0	19	70.0
New Caledonia	67	-	-	-	-	6	9.0
New Zealand	490	19	3.9	33	6.7	52	10.6
Papua New Guinea	197	50	25.0	23	12.0	62	37.0
Philippines	245	194	79.0	7	2.8	201	82.0
Singapore	768	439	57.2	12	1.6	451	58.8
Solomon Islands	34	0	-	0	-	0	-
Tonga	37	3	8.0	1	2.7	4	10.8
Vanuatu	89	-	-	-	-	32	35.9
Vietnam	158	99	62.7	22	13.9	121	76.6

Table 2. Quinolone resistance in strains of *Neisseria gonorrhoeae* isolated in countries in the WHO WPR in 1998

Country	Number tested	Less susceptible		Resistant	
		Number	%	Number	%
Australia	3,583	70	2.0	116	3.2
China	912	332	36.4	509	54.2
Fiji	Not stated	0	0.0	0	0.0
Hong Kong (China)	2,255	993	44.0	1,100	48.8
Japan	190	95	50.0	5	2.6
Korea	134	69	51.5	15	11.2
Malaysia	na	na	na	na	na
New Caledonia	67	2	3.0	5	7.5
New Zealand	490	7	1.4	6	1.2
Papua New Guinea	187	1	0.5	6	3.2
Philippines	245	3	1.2	155	63.0
Singapore	768	34	4.4	55	7.2
Solomon Islands	34	0	0.0	0	0.0
Vietnam	160	15	9.4	13	8.1

countries (Australia, New Zealand), QRNG are most often represented by imported strains but with some endemic transmission also occurring. Previous observations summarised the position with regard to QRNG in the WPR as a trend showing more countries recording the presence of QRNG, a higher proportion of QRNG being recorded in these countries each year, and higher MICs in those QRNG present. These observations remain pertinent for 1998.

All isolates remained sensitive to the third generation cephalosporin *ceftriaxone*. These results would also apply to the oral equivalent cefixime, but not necessarily to earlier generation cephalosporins. Some increase in MICs to ceftriaxone was again noted in some centres. Although this decrease in susceptibility has yet to translate into clinical resistance, continued observation of this aspect of evolving gonococcal resistance is advisable.

Spectinomycin resistance is rarely encountered in the WPR and only in sporadic cases (Table 3). Only five strains from over 900 examined in China were

spectinomycin resistant in 1998. This may reflect the low frequency of use of this injectable agent in the region. The aminoglycoside antibiotic gentamicin is sometimes used in the region for the treatment of gonorrhoea because of cost considerations. No data are available on patterns of resistance to this agent.

Tetracyclines are not a recommended treatment for gonorrhoea. However their ready availability and low cost means that they are often used in the informal health sector in a number of countries. A special form of high level resistance to tetracyclines exists and is disseminated by plasmid exchange. Strains with this form of resistance are known as TRNG. Trends in the spread of TRNG have been followed in the WPR as an exercise in the monitoring of emerging antibiotic resistance (Table 4). TRNG have been clustered in certain countries in the WPR, notably Singapore and Malaysia, for some time. Over 80% of isolates in Singapore were TRNG in 1998 and in the Solomon Islands 75% of strains were TRNG. The other centre with a high rate of TRNG was Vietnam (36%). Six

Table 3. Spectinomycin resistance in isolates of *Neisseria gonorrhoeae* in countries in the WHO WPR in 1998

Country	Number Tested	Number	% Resistant
Australia	3,583	0.0	0.0
China	939	5.0	0.5
Japan	190	0.0	0.0
Korea	134	0.0	0.0
New Caledonia	67	0.0	0.0
Papua New Guinea	59	0.0	0.0
Philippines	245	0.0	0.0
Singapore	768	0.0	0.0
Solomon Islands	34	0.0	0.0
Vietnam	156	0.0	0.0

Table 4. High level tetracycline resistance, TRNG, in strains of *Neisseria gonorrhoeae* isolated in countries in the WHO WPR in 1998

Country	Number Tested	Number	% TRNG
Australia	3,583	24	6.7
China	828	24	2.9
Japan	190	0	0.0
Korea	134	0	0.0
Mongolia	27	0	0.0
New Zealand	490	25	5.1
Papua New Guinea	187	9	4.8
Philippines	245	17	6.9
Singapore	768	648	84.0
Solomon Islands	34	25	74.0
Vietnam	156	56	35.9

other centres had TRNG rates of less than 10% and in Japan and Korea no TRNG were detected. The increase in TRNG rates in Singapore and the Solomon Islands was the only real change in TRNG distribution in the WPR in 1998.

Other agents are sometimes used in the WPR mainly because of cost considerations. For example, chloramphenicol/thiamphenicol continues as a recommended treatment in some jurisdictions. Again only scanty data are available on the resistance patterns to these antibiotics. These data do, however, indicate that resistance is present in a significant number of strains tested.

The changes observed in the 1998 susceptibility patterns of gonococci found in the region were incremental. However, this increase was on top of an already high and worrying level of resistance. The observations confirmed the limited options for treatment in the WPR of a disease of high incidence. Those treatment options available are often in a cost bracket that makes their use difficult even when they are a 'recommended' treatment. However, substitution of cheaper but less efficacious agents is in the longer term more expensive and counter-productive.

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Erratum

The captions for Figures 6 and 7 in the last issue of *CDI*, 23(13)345, were transposed.