Surveillance of antibiotic resistance in *Neisseria gonorrhoeae* in the WHO Western Pacific Region, 2000

The WHO Western Pacific Gonococcal antimicrobial Surveillance Programme[1]

Abstract

A long-term program of surveillance of antimicrobial resistance in *Neisseria gonorrhoeae* isolated in the World Health Organization's Western Pacific Region (WHO WPR GASP) continued in 2000. About 11,000 gonococci were examined in 15 focal points. Widespread resistance to the penicillin group of antibiotics was confirmed. Resistance to quinolone antibiotics, already widely dispersed, increased further with a shift to higher levels of resistance in many centres. Gonococci with decreased susceptibility to third generation cephalosporins were observed in 5 centres. Spectinomycin resistance was infrequently encountered. Options for cheap and effective treatment of gonorrhoea in the WPR are increasingly limited. *Commun Dis Intell* 2001;25:274-277.

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

Introduction

Early and successful antibiotic treatment of gonococcal infection is important not only for the individual patient but is also a significant factor in control of disease and the prevention of complications. The ability of *Neisseria gonorrhoeae* to become resistant to cheap and effective antibiotics is well recognised and has significantly compromised both individual and public health management of gonorrhoea. Because treatment of gonorrhoea is best given as single dose treatment on initial diagnosis, standardised treatment schedules have been established. However, antibiotic resistance in the gonococcus can arise quickly. It is therefore important to have available accurate data on antimicrobial resistance in the gonococcus in order to guide selection of an appropriate antibiotic treatment. Antibiotic resistance in gonococci often spreads rapidly between countries, and infected travellers often present for treatment in countries distant from the place of contact. Thus for a number of reasons it is important to have available regional as well as local data on antibiotic resistance.

The WHO Western Pacific Region (WPR) Gonococcal Antimicrobial Surveillance Programme (GASP) is a continuing program of susceptibility surveillance in the Region and has published surveillance data annually since 1992.[1] The Region has an unfortunate history of development of antimicrobial resistance in gonococci with penicillin, spectinomycin and quinolone resistant *N. gonorrhoeae* all appearing in and spreading beyond the WPR. This communication provides an analysis of surveillance of antimicrobial resistance in *N. gonorrhoeae* in the WHO WPR in 2000.

Methods

The methods used by the WHO WPR GASP have been published[2] 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 2000. 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.[3]

Results and discussion

About 10,500 gonococcal isolates were examined in 15 participating countries (listed in the acknowledgments) in 2000.

Resistance to the *penicillins* remained widespread by both chromosomal (CMRNG) and plasmid mediated mechanisms (penicillinase producing *N. gonorrhoeae* — PPNG). Table 1 provides details of CMRNG, PPNG and/or total penicillin resistance in 15 WPR focal points. Very high proportions of combined forms of penicillin resistance (CMRNG + PPNG) were recorded in Korea (91%), the Philippines (89%), China (80%), Brunei (63%), Singapore (58%), Hong Kong SAR (54%), and Vietnam (48%). With the exception of the Hong Kong SAR and Vietnam where penicillin resistance declined somewhat, these proportions approximated those found in preceding years. Apart from New Caledonia (no penicillin resistance), Papua New Guinea (36.5% of strains penicillin resistance), and Tonga (no penicillin resistance), data from some Pacific Island states were unavailable this year. With the exception of Papua New Guinea, low levels of penicillin resistant were observed in these countries in past years. Other participants submitting data in 2000 (Australia, Japan and New Zealand) had proportions of penicillin resistance between 8 and 28 per cent. Malaysia had a high proportion of isolates showing resistance in a small sample.

Resistance to the *quinolone* antibiotics remained a major problem in many parts of the WPR and the situation

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Table 1. Penicillin sensitivity of strains of *Neisseria gonorrhoeae* isolated in 15 countries in the WHO WPR, 2000

Country	No. tested	PPNG		CMRNG		All Pen R	
		No.	%	No.	%	No.	%
Australia	3,468	302	8.7	377	10.8	679	19.5
Brunei	59					37	63.0
China	1,007	344	34.1	464	46.0	808	80.1
Fiji	756	25	3.3	3	0.3	28	3.6
Hong Kong SAR	2,743	292	10.6	1,191	43.4	1,483	54.0
Japan	213	1	0.5	59	27.6	60	28.1
Korea	190	119	62.6	54	28.4	173	91.1
Malaysia	12	9	75.0	1	8.3	10	82.6
New Caledonia	74	0		0		0	0.0
New Zealand	694	20	2.9	35	5.0	55	7.9
Papua New Guinea	224	77	34.3	5	2.2	82	36.5
Philippines	290	259	89.3	0	0.0	259	89.3
Singapore	635	349	55.0	18	2.8	367	57.8
Tonga	50	0	0.0	0	0.0	0	0.0
Vietnam	157	74	47.1	1	0.7	75	47.8

PPNG Penicillinase producing *N. gonorrhoeae*
CMRNG Chromosomally mediated resistance in *N. gonorrhoeae*

deteriorated further in 2000. Data from 12 WPR countries are shown in Table 2 and quinolone resistant strains (QRNG) are divided into 'less susceptible' and 'resistant' categories on the basis of susceptibility determinations. Eleven of 12 WPR countries which examined isolates for quinolone resistance detected QRNG in 2000. High proportions of QRNG were detected in China, Hong Kong, the Philippines, Japan and Vietnam maintaining a situation observed in previous reports. In the above countries and also in Korea and Australia, the proportion of strains fully resistant to quinolone antibiotics increased while the proportion of less sensitive isolates decreased, i.e. there was again an upward shift in overall levels of resistance. In Hong Kong the percentage of 'resistant' QRNG has increased from about 50 per cent in 1998 to about 66 per cent in 1999 to 80 per cent in 2000 and in China quinolone resistance rates again increased markedly in an expanded sample. A shift to higher MICs in Japan saw the proportion of 'resistant' QRNG there increase from about 23 per cent in 1999 to 40 per cent in 2000. In Brunei the proportion of QRNG was essentially unchanged from previous years.

An ominous trend was the presence of a small number of isolates with altered susceptibility to third generation cephalosporins. These strains were seen in Singapore, Brunei, China, Australia and New Zealand. Because of methodological differences in testing, MIC values are not directly comparable between centres, but values ranged up to 0.25 mg/L. Third generation cephalosporins are crucially important agents in the treatment of gonorrhoea as resistance to other agents accelerates.

A small number of spectinomycin resistant strains were found in China, Papua New Guinea, Vietnam, Brunei and Korea. Only very occasional strains resistant to this injectable antibiotic have been found in recent WPR surveys.

Although tetracyclines are not a recommended treatment for gonorrhoea, these agents are widely used and readily available in the WPR. One particular type of plasmid-mediated resistance gives rise to high-level tetracycline resistance (TRNG). About 6,900 gonococci were examined for high-level tetracycline resistance in 12 WPR countries in 2000 (Table 3). High proportions of TRNG isolates were again prominent in Malaysia, Brunei, Singapore, Vietnam, China and Papua New Guinea ranging between 25 and 70 per cent. In other countries the proportions of TRNG ranged between 0.5 and 11 per cent of strains examined. The proportion of TRNG has increased significantly in China in recent years from around 3 per cent in 1998 to nearly 15 per cent in 1999 to 25 per cent in 2000.

The data recorded in 2000 in the WPR indicate that further increases in gonococcal resistance to antibiotics have occurred. Resistance to the penicillins is so widespread that any contemplated use of this group of antibiotics would require prior validation of likely efficacy. A similar requirement would now seem to be appropriate for quinolone antibiotics given the extensive resistance

Table 2. Quinolone resistance in strains of *Neisseria gonorrhoeae* isolated in 12 countries in the WHO WPR, 2000

Country	No. tested	Less susceptible		Resistant	
		No.	%	No.	%
Australia	3,468	334	9.6	285	8.2
Brunei	60	3	5.0	7	12.0
China	1,007	141	14.0	858	85.2
Hong Kong SAR	2,743	459	16.7	2,180	79.5
Japan	213	65	30.5	86	40.0
Korea	190	122	64.2	50	26.3
Malaysia	12	0		0	
New Zealand	694	14	2.0	16	2.3
Papua New Guinea	224	0	0.0	2	0.9
Philippines	290	4	1.4	110	37.9
Singapore	635	39	6.1	121	19.0
Vietnam	157	18	11.5	67	42.7

Table 3. High level tetracycline resistance in strains of *Neisseria gonorrhoeae* isolated in 11 countries in the WHO WPR in 2000

Country	No. tested	No. TRNG	% TRNG
Australia	3,468	318	9.2
Brunei	33	24	72.0
China	1,007	260	25.8
Japan	213	1	0.5
Korea	190	5	2.6
Malaysia	12	3	25.0
New Zealand	694	23	3.3
Papua New Guinea	224	75	33.5
Philippines	290	33	11.4
Singapore	635	453	71.3
Vietnam	155	69	44.5

revealed in this and earlier surveys. Finding suitable alternative treatments is difficult given the cost of suitable antibiotics. The recognition of gonococci with altered susceptibility to third generation cephalosporins is also a matter of concern. Although treatment failure attributable to resistance to this antibiotic is yet to be confirmed, there will be considerable and continuing interest in the number of strains which show this altered susceptibility in future surveys and also in the MICs associated with this phenomenon.

Acknowledgments

The following members of the WHO Western Pacific Gonococcal Antimicrobial Surveillance Programme supplied data in 2000 for the WPR GASP:

Members of the Australian Gonococcal Surveillance Programme throughout Australia; HMH Kassim, Brunei, Darussalam; Y Shunzhang and S Xiaohong, Nanjing, China; S Bavoro, Suva, Fiji; KM Kam, Hong Kong; M Tanaka, Fukuoka and T Kuroki, Yokohama, Japan; K Lee and Y Chong, Seoul, Korea; R Yasin, Malaysia; B Garin, Noumea, New Caledonia; M Brokenshire, Auckland, New Zealand; MV Hombhanje, Port Moresby, Papua New Guinea; CC Carlos, Manila, Philippines; C Ngan and AE Ling, Singapore; AT Ika, Nuku'alofa, Tonga; Le Thi Phuong, Hanoi, Vietnam.

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