Surveillance of antibiotic resistance in *Neisseria gonorrhoeae* in the WHO Western Pacific Region, 2001

The WHO Western Pacific Gonococcal Antimicrobial Surveillance Programme

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 2001. Seventeen focal points contributed data on about 10,000 gonococci. Resistance to quinolone and penicillin antibiotics remained widely dispersed and at high levels. Gonococci with decreased susceptibility to third generation cephalosporins were again observed in four centres. Spectinomycin resistance was infrequently encountered. Control of gonorrhoea in the WHO WPR is compromised by the further reduction in options for cheap and effective treatment of gonorrhoea. *Commun Dis Intell* 2002;26:541–545.

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

Introduction

The World Health Organization (WHO) estimates put the global number of cases of gonorrhoea at about 65 million each year with approximately half of these occurring in the South-East Asian and Western Pacific WHO regions. Control of this disease and its complications requires an integrated approach embracing efforts to reduce transmission through education and early case finding and includes as a key element, the provision of early and effective antibiotic treatment. Regrettably, the WHO Western Pacific Region (WPR) has an unfortunate record in terms of antibiotic resistance in *Neisseria gonorrhoeae*. The emergence and spread of penicillinase producing *Neisseria gonorrhoeae* (PPNG) in the 1970s was followed by the appearance of spectinomycin resistance for a period in the 1980s and by the currently well established quinolone resistance in the 1990s. The year 2000 report of this group documented some decreased susceptibility to third generation antibiotics. The gonococcus has thus become resistant to cheap and effective antibiotics in the WPR and this has significantly compromised both individual and public health management of gonorrhoea. These resistant gonococci have now spread well beyond the WPR. Treatment of gonorrhoea is best given as a single dose treatment on initial diagnosis, and for this reason standardised treatment schedules have been established. It is therefore important to have accurate data on antimicrobial resistance in the gonococcus available in order to guide selection of an appropriate antibiotic treatment. Antibiotic resistance in gonococci can spread 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 regional as well as local data on antibiotic resistance available.

The WHO Western Pacific Region Gonococcal Antimicrobial Surveillance Programme (GASP) is a continuing program of susceptibility surveillance in the Region and has published surveillance data annually since 1992.[1] This report provides an analysis of surveillance of antimicrobial resistance in *N. gonorrhoeae* in the WHO WPR in 2001.

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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 2001. Most isolates were collected from symptomatic sexually transmitted disease 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

Approximately 10,781 gonococcal isolates were examined for susceptibility to one or more antibiotics in 17 participating countries (listed in the acknowledgments) in 2001.

Penicillins

Resistance to the penicillins remained widespread by both chromosomal (CMRNG) and plasmid mediated mechanisms (penicillinase producing *N. gonorrhoeae*). Table 1 provides details of CMRNG, PPNG and total penicillin resistance in 16 WPR countries. Very high rates of forms of penicillin resistance (CMRNG +/- PPNG) were recorded in Laos (96%), Korea (88%), the Philippines (86%) and China (85%). Singapore (58%), Malaysia (56%), Hong Kong (55%), Brunei (45%), Papua New Guinea (40%) and Vietnam (36%) also had high rates of penicillin resistance. Data from some Pacific Island states were again unavailable this year. In past years low rates of penicillin resistance were observed in these countries, and continued to be low in New Caledonia and Fiji. However, continuing surveillance is required if these agents are to be used. Other participants submitting data in 2001 (Australia, Japan and New Zealand) had rates of penicillin resistance between 9 and 29 per cent.

Table 1. Penicillin sensitivity of strains of *Neisseria gonorrhoeae* isolated in countries in the WHO Western Pacific Region in 2001

Country	Tested	PPNG		CMRNG		All penicillin resistant	
	n	n	%	n	%	n	%
Australia	3,641	274	7.5	558	15.3	832	22.8
Brunei	57	21	36.8	5	8.7	36	45.6
China	748	219	21.3	438	58.5	657	85.8
Fiji	522	9	1.7	8	1.5	17	3.2
Hong Kong SAR	2,575	350	13.6	1,064	41.3	1,414	54.9
Japan	300	7	2.3	80	26.6	87	29.0
Korea	177	96	54.2	60	33.9	156	88.1
Laos	160	133	83.0	21	13.0	154	96.0
Malaysia	30	16	53.3	1	3.3	17	56.6
New Caledonia	57	0	–	0	–	0	–
New Zealand	765	29	3.8	39	5.0	68	8.9
Papua New Guinea	369	147	39.8	2	0.5	149	40.3
Philippines	399	268	67.1	76	19.0	344	86.1
Singapore	741	390	52.6	41	5.5	431	58.1
Tonga	32	2	6.3	4	12.5	6	18.8
Vietnam	166	59	35.5	1	0.6	60	36.1

PPNG Penicillinase producing *N. gonorrhoeae*

CMRNG Chromosomally mediated resistance in *N. gonorrhoeae*

Quinolones

Resistance to the quinolone antibiotics has been high and endemic in many parts of the WPR for many years. Additional data from Laos and Cambodia in 2001 confirmed the widespread extent of the problem in the WPR. Data from 14 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. Thirteen of the 14 WPR countries which examined isolates for quinolone resistance detected QRNG in 2001, the exception being Papua New Guinea. Very high proportions of QRNG were detected in Cambodia, China, Hong Kong, Japan, Korea, the Philippines and Vietnam. There was again an upward shift in overall levels of resistance with most of the QRNG in the majority of countries having gonococci with high level resistance.

Cephalosporins

In the 2000 report, the presence of a small number of isolates with altered susceptibility to third generation cephalosporins was noted. Gonococci with this characteristic were again seen in low numbers in 2001 in Singapore, Brunei, China and Australia. Such strains have prevailed for a few years but are only now translating into treatment failure.[4] A report of documented treatment failure with an oral third generation cephalosporin in the WPR has now been published.[5] This is a finding of major significance as this group of antibiotics is crucially important in the treatment of gonorrhoea as resistance to other agents accelerates.

Spectinomycin

A small number of spectinomycin resistant strains were found in Cambodia (1 isolate) and China (3 isolates) with Vietnam reporting two isolates in the less sensitive to spectinomycin category. Only very occasional strains resistant to this injectable antibiotic have been found in recent WPR surveys.

Table 2. Quinolone resistance in strains of *Neisseria gonorrhoeae* isolated in countries in the WHO Western Pacific Region in 2001

Country	Tested	Less susceptible		Resistant		All QRNG*	
	n	n	%	n	%	n	%
Australia	3,641	149	4.1	489	13.4	638	17.5
Brunei	52	1	2.0	10	19.0	11	21.0
Cambodia	42	9	21.0	18	43.0	27	64.0
China	748	83	11.1	650	86.9	733	97.9
Hong Kong SAR	2,575	235	9.1	2,270	88.2	2,505	97.3
Japan	300	42	14.0	192	64.0	234	78.0
Korea	177	94	53.1	70	39.5	164	92.6
Laos	187	11	5.9	42	22.5	53	28.3
Malaysia	30	2	6.7	7	23.3	9	30.0
New Zealand	765	20	2.6	77	10.0	97	12.7
Papua New Guinea	96	0	–	0	–	0	–
Philippines	399	1	0.2	217	54.3	218	54.6
Singapore	741	35	4.7	207	27.9	242	32.6
Vietnam	168	33	19.6	71	42.3	104	61.9

* QRNG Quinolone resistant *Neisseria gonorrhoeae*

High-level tetracycline resistance

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 7,583 gonococci were examined for high-level tetracycline resistance in 13 WPR countries in 2001 (Table 3). High rates of TRNG continue to be reported from Malaysia, Brunei, Singapore, Vietnam, China and now Laos with rates between 34 and 99 per cent. In other countries, rates of TRNG ranged between one and 17 per cent of strains examined.

Discussion

The data recorded in 2001 in the WPR provide no relief from concerns previously expressed in regard to increasing antibiotic resistance in gonococci. Any contemplated use of the penicillins would be restricted to a few settings and would require prior validation of likely efficacy. The same approach would need to be applied to the quinolone group and their use has been discontinued in many WPR countries because of resistance. Selection of suitable alternative treatments is difficult given the cost of available antibiotics. The recognition of gonococci with altered susceptibility to third generation cephalosporins[6] and now, leading to documented treatment failure, is also a matter of considerable concern. It remains to be seen if this treatment failure with oral third generation cephalosporins will extend to injectable agents such as ceftriaxone. The amount of ceftriaxone that can be given by injection exceeds by a considerable margin, that which is absorbed by administration of oral agents of the same class. Considerable attention will need to be given to any further emergence of gonococci with these attributes.

Table 3. High level tetracycline resistance in strains of *Neisseria gonorrhoeae* isolated in countries in the WHO Western Pacific Region in 2001

Country	Tested %	Less susceptible %	All TRNG* %
Australia	3,641	343	9.4
Brunei	47	23	49.0
China	748	256	34.2
Japan	300	4	1.3
Korea	177	2	1.1
Lao PDR	187	185	98.9
Malaysia	30	20	66.6
New Zealand	765	73	9.5
Papua New Guinea	369	56	15.2
Philippines	399	68	17.0
Singapore	741	499	67.3
Tonga	11	1	9.0
Vietnam	168	68	40.5

* TRNG Tetracycline resistant *Neisseria gonorrhoeae*

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