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article

# Surveillance of antibiotic susceptibility of *Neisseria gonorrhoeae* in the WHO Western Pacific Region 1992-4

WHO Western Pacific Region Gonococcal Antimicrobial Surveillance Programme\*

**Objective:** To describe the establishment and outcomes of a regional programme of continuing long term surveillance of antibiotic susceptibility of *Neisseria gonorrhoeae* over the period 1992-4.

**Methods:** Laboratories in 17 countries in the WHO Western Pacific Region participated in a continuing programme of surveillance of the susceptibility of gonococci to an agreed group of antibiotics over 3 years. Established techniques were used and these included quality control and proficiency testing systems.

**Results:** About 20 000 gonococci were examined over a 3 year period. Resistance to the penicillins through  $\beta$  lactamase production or chromosomal mechanisms was widespread, with further changes evident over the 3 years. Spectinomycin resistance was infrequently encountered but high level tetracycline resistance was present in most participating centres, with some having high proportions of tetracycline resistant organisms. Quinolone resistance increased and became widespread throughout the region in the 3 years, ultimately involving all but one centre. Both the number and minimum inhibitory concentrations of quinolone resistant isolates increased markedly.

**Conclusions:** Patterns of gonococcal resistance to antibiotics continue to evolve, at times rapidly, and have the potential for wide and rapid dissemination. Regional surveillance programmes can be developed by using and expanding existing resources. Data thus derived were applied to the development of appropriate treatment regimens in the region, and emphasised further the need for a global expansion of the programme of integrated surveillance of gonococcal resistance.

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Keywords: *Neisseria gonorrhoeae*; antibiotic susceptibility; surveillance

## Introduction

Recent WHO estimates put the number of new cases of gonorrhoea worldwide at 62 million annually.<sup>1</sup> The same sources indicate that the significant morbidity that often accompanies gonococcal disease can be greatly reduced by appropriate treatment. For example, for every 100 women with gonorrhoea (25% pregnant) properly treated, 25 cases of pelvic inflammatory disease, one ectopic pregnancy, six cases of infertility, and seven instances of ophthalmia neonatorum are said to be prevented.<sup>1</sup>

Additionally, it is now acknowledged that gonorrhoea (along with other non-ulcerative STDs) is a potent cofactor in the transmission of the human immunodeficiency virus (HIV).<sup>2-4</sup> The "synergy between HIV and STDs is related to both behavioural and biological factors"<sup>3</sup> and it has been shown in longitudinal studies that the rate of transmission of HIV may be amplified by a factor of between three and five in the presence of gonorrhoea.<sup>4</sup> The converse of this situation is that better STD treatment, and through it a reduction in the prevalence of STDs, can contribute to a reduction in HIV transmission.<sup>5</sup> In a population with a high prevalence of HIV infection, effective treatment of 100 cases of gonorrhoea in core groups leads to a cumulative reduction of 425 cases of HIV transmission over a 10 year period.<sup>1</sup> STD prevention and treatment are thus increasingly regarded

as an important component of HIV prevention.<sup>6</sup>

Therefore, there are clearer and more cogent reasons than ever before to ensure that gonococcal disease is properly treated when it cannot be otherwise prevented.<sup>7</sup> The essential point about such treatment is that it must be effective, and for gonorrhoea this means use of an appropriate antibiotic treatment regimen, preferably single dose. Limiting factors in the provision of this appropriate antibiotic treatment are the continuing emergence of antibiotic resistance in the gonococcus and the current distribution of the disease which affects most often patients in resource poor settings where many recommended regimens are unavailable or else too costly.

One strategy adopted by the WHO to obtain information on gonococcal susceptibility patterns and thereby implement appropriate and proper treatment has been to establish a global surveillance network to monitor antibiotic resistance in the gonococcus—the Gonococcal Antimicrobial Surveillance Programme (GASP). This was envisaged as a series of networks in the various WHO regions. The GASP network was to gather data on gonococcal resistance patterns in different countries and make this information available for implementation of effective treatment regimens at global, regional, or national levels.<sup>8</sup> It was also envisaged that there would be dissemination of gonococcal laboratory

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expertise by the network and early identification of new forms of gonococcal resistance with control measures recommended.<sup>8</sup> The relevance of surveillance of antibiotic resistance in gonococci to treatment has been recently reviewed.<sup>9</sup> Factors which have hampered the full implementation of the GASP network include the same limitations in provision of technical resources in less developed nations that restrict access to antibiotics in these settings. None the less, GASP has functioned in the WHO Western Pacific Region (WPRO) since 1992 and is also operating in North and South America and in the WHO South East Asian region more recently. This paper describes the establishment and structure of the WPRO GASP and documents its findings over the years 1992 to 1994. The wider implications of the emergence of antibiotic resistance in the gonococcus in WPRO are discussed.

### Materials and methods

#### ESTABLISHMENT OF THE PROGRAMME

The programme was established under the auspices of the WHO Western Pacific Regional Office (WHO WPRO) to contribute to the aims and objectives of the global GASP network (see above<sup>8</sup>) through continuing long term antibiotic susceptibility surveillance in the region.<sup>10</sup> It was instituted as a distinct subset of a wider programme of antimicrobial resistance surveillance following a meeting of WPRO country representatives (designated as "focal points") in Hong Kong in December 1991.<sup>10</sup> Seventeen centres in the WHO WPRO have participated as focal points in the programme since 1992—Australia, Brunei, China, Fiji, Hong Kong, Japan, Malaysia, New Caledonia, New Zealand, Papua New Guinea, Philippines, Singapore, Solomon Islands, South Korea, Tonga, Vanuatu, and Vietnam. Some of these centres represented relatively small geographic areas—for example, Singapore and Hong Kong, while other centres were already focal points for collection of data from wider sources in their own countries. For example, Australia<sup>11,12</sup> and China had an existing networked system of laboratories, and Malaysia had laboratories serving STD clinics in different geographic areas of the country which referred a standard sample of their isolates for testing in the central laboratory.

#### POPULATION AND ISOLATE SELECTION

A description of the patient population from which isolates were derived was requested from all participants—namely, unselected STD patients—that is, patients presenting for treatment with signs and symptoms; screening/case finding; or unknown. Similarly, participants were asked to record if all or a sample of isolates were tested.

#### ANTIBIOTIC SUSCEPTIBILITY DETERMINATION

A core list of antibiotics for testing, based on WHO recommended treatments, was agreed. Testing for  $\beta$  lactamase (by acidometric or

chromogenic cephalosporin techniques nominated by the WHO<sup>13</sup>) was the minimum requirement for entry into the project. Two methods of testing for chromosomal resistance to the penicillins and for resistance to the other core antimicrobials were nominated. These were the disc, agar inclusion breakpoint, or agar inclusion minimum inhibitory concentration (MIC) techniques of the NCCLS<sup>14,15</sup> and the AGSP,<sup>11</sup> both used extensively in the region.

#### VALIDATION OF RESULTS

WHO reference cultures A–E with assigned sensitivity categories were distributed to all participants together with a comprehensive methodological manual providing details of categorisation of "wild" strains by the zone sizes/MICs obtained with the different methods. These values were verified in the reference laboratory for the two nominated methods. The reference cultures were used in quality control (QC) procedures and were to be incorporated regularly when batches of wild type isolates were examined. Additionally in each year of the project, a series of six quality assurance (QA) strains were distributed as "unknowns" to each centre for examination. Again these strains were first examined in the reference laboratory and categorised on the basis of testing by the two nominated methods. Results of examination of the reference QC and the QA strains were forwarded to the reference laboratory. The QA isolates were specifically chosen to reflect the resistance patterns seen in gonococci isolated in the region and were selected on the basis of MIC/clinical outcome correlates.<sup>16</sup> Assessment of laboratory performance was based on previously established factors.<sup>12</sup> Each laboratory was appraised of its own results but group QA reports did not identify individual participants.

#### COLLATION OF DATA

Results were recorded on standard data processing forms and returned periodically throughout each year to the regional reference laboratory at the Prince of Wales Hospital in Sydney. Because of the limitations in resources in some settings, the standard reporting forms were in a summary format which separately recorded the category of susceptibility of each isolate to each antibiotic, but did not seek to record multiple antibiotic susceptibility/resistance in individual isolates. An additional data recording sheet was available to record this further information but was not used in all centres. Data were summarised and annual reports were prepared, published<sup>17,18</sup> and distributed after examination and agreement by participants. Significance tests were performed by  $\chi^2$  analysis.

### Results

#### DEMOGRAPHIC DATA

A total of 20 365 isolates was examined in the 17 WHO WPRO participating centres in the years 1992–4 inclusive. However, the number of isolates and the number of centres reporting

differed in each of the 3 years. In 1992, 5872 isolates were examined in 14 centres, in 1993, 7176 isolates in 16 centres were available, and 7317 isolates were tested in 16 centres in 1994. Each centre participated for at least 2 of the 3 years. In some centres the number of isolates examined was substantial. However, it was not possible to estimate for each country the proportion of all cases of gonorrhoea that this examination represented. Large or moderate numbers of isolates were examined in Australia, China, Fiji, Hong Kong, Korea, Malaysia, New Zealand, Papua New Guinea, Singapore, and Vietnam. In other centres, such as Japan, only a few isolates were available for routine examination. In the Pacific Island states facilities for culture often exist only in the larger population centres of some countries—for example, the Solomon Islands. In some countries (Australia, China, and Malaysia) the strains were drawn from a wide geographic base by means of existing networks. Other countries such as Hong Kong and Singapore obtained a large number of strains from a small geographic area. Other centres were limited in their access to strains (Philippines) or confined to the same certain parts of the country over the period studied (Korea, Vietnam) or else only had a few isolates but examined them all (New Caledonia). Most strains examined in the participating centres were isolated from unselected symptomatic STD clinic patients although in the Philippines isolates were obtained as a result of case finding. In all focal points the source of isolates remained relatively constant over the period of the study.

Some centres determined the susceptibility

of all or most of the available isolates to all antibiotics (Australia, Fiji) whereas others examined a systematic sample (Malaysia) or else only examined antibiotics pertinent to their situation or resources. In Singapore, while all isolates were examined for  $\beta$  lactamase production in 1992, MIC testing of a systematic sample of these strains was only commenced in the second half of that year. Tables 1-5 provide details of the resistance to the nominated "core" antimicrobials penicillin, quinolones, spectinomycin, and tetracycline (high level only) resistance in the contributing centres in the years 1992-4 inclusive, and the number of isolates examined for susceptibility to each of these antibiotics and to ceftriaxone in each centre. Data from all centres are aggregated into a single figure for each country in the tables. In some of the geographically larger centres—for example, Australia, regional variation in sensitivity within the country was evident. Where this is significant it is specifically mentioned.

#### SUSCEPTIBILITY TO THE PENICILLINS

Resistance to the penicillins was widespread throughout the region (table 1) with only two centres (New Caledonia and Vanuatu) having little or no resistance on a country based analysis. Within Australia there were considerable differences between the larger urban centres with high rates of resistance and rural areas where penicillin based therapy remained effective. Plasmid mediated  $\beta$  lactamase resistance (by penicillinase producing *Neisseria gonorrhoeae*, PPNG) was particularly evident in Korea, the Philippines, Malaysia, Singapore, and Vietnam. Of interest is the

Table 1 Percentage of lactamase mediated, chromosomally mediated, and total penicillin resistance in gonococci in 17 WPRO GASP centres, 1992-4. (Number of strains tested are shown in parentheses)

Country	1992			1993			1994		
	BLR	CMR	All Pen R	BLR	CMR	All Pen R	BLR	CMR	All Pen R
Australia	8.8 (923)	8.1 (923)	16.9 (923)	7.7 (1780)	9.4 (1780)	17.1 (1780)	6.6 (1835)	11.8 (1835)	18.4 (1835)
Brunei	40 (20)	0 (20)	40 (20)	42 (40)	0 (40)	42 (40)			
China	0.3 (323)	61.8 (396)	62.1 (396)	0 (511)	44 (511)	44 (511)	5.5 (344)	48.3 (203)	53.8 (203)
Fiji	9.9 (848)	0.6 (848)	10.5 (848)	9.8 (593)	1.7 (593)	11.5 (593)	9.2 (804)	1.4 (804)	10.6 (804)
Hong Kong	21.8 (1063)	44.4 (1063)	66.2 (1063)	14.5 (2074)	59 (2074)	73.5 (2074)	7.3 (1977)	70.6 (1977)	77.9 (1977)
Japan	4.5 (198)	4 (150)	8.5 (150)	6.9 (72)	11.6 (69)	18.5 (72)	4 (74)	3.6 (55)	7.6 (55)
Korea	71 (52)	38 (38)	90 (38)	71.1 (225)	19.1 (225)	90.2 (225)	69.8 (134)	17.7 (34)	87.5 (168)
Malaysia	41 (356)	19 (111)	60 (111)	47.1 (439)	17 (439)	64.1 (439)	44 (270)	25 (56)	69 (56)
New Caledonia	0 (46)	0 (46)	0 (46)	0 (18)	0 (18)	0 (18)	0 (16)	0 (16)	0 (16)
New Zealand	6.3 (80)	3.8 (80)	10.1 (80)	1.1 (85)	15.3 (85)	16.4 (85)	11.3 (142)	4.2 (142)	15.5 (142)
Papua New Guinea				12.5 (40)	0 (40)	12.5 (40)	8.7 (218)	0 (218)	8.7 (218)
Philippines	80 (79)	3.7 (79)	83.7 (79)				100 (20)	0 (20)	100 (20)
Singapore	35.4 (1755)	3.8 (130)	43 (130)	36.7 (1016)	7.9 (1016)	44.6 (1016)	50.5 (1019)	15.9 (504)	66.4 (504)
Solomon Islands				46.6 (15)	0 (15)	46.6 (15)	20 (20)	0 (20)	20 (20)
Tonga	18.7 (32)			20 (40)			40 (32)	15.6 (32)	55.6 (32)
Vanuatu				1.4 (70)			1 (97)	0 (97)	1 (97)
Vietnam	55 (56)	0 (56)	55 (56)	64.6 (158)	0 (158)	64.6 (158)	88.7 (186)	0 (223)	88.7 (223)

BLR = penicillinase producing gonococci; CMR = chromosomally mediated penicillin resistance; All Pen R = total for lactamase plus chromosomal resistance.

Table 2 Percentage of gonococcal isolates showing altered quinolone sensitivity in 14 WPRO GASP centres, 1992-4

Country	1992			1993			1994		
	Tested	% LS	% Res	Tested	% LS	% Res	Tested	% LS	% Res
Australia	782	2.9	0.13	1570	2.7	0.001	1622	1.4	0.4
Brunei	20	0	0	40	6.6	0			
Fiji	0			24	0	0	804	0.1	0
Hong Kong	0			0			1664	55.9	3.3
Japan	104	21	1.9	53	45.2	3.7	79	35.4	2.5
Korea	43	9	0	225	12	0	192	25	0
Malaysia	185	0	0	280	0.1	0	148	1.4	0
New Caledonia	46	6.5	0	18	0	0	16	6.2	0
New Zealand	12	0	0	85	1.1	0	127	2.4	1.6
Papua New Guinea	0			40	12.5	0	218	0	5
Philippines	0			0			20	95	
Singapore	0			611	2.8	0.33	667	11.2	1.8
Solomon Islands	0			15	0	0	20	0	0
Vietnam	19	0	0	116	2.6	0	218	4.6	6.9

LS = less sensitive; Res = resistant.

increase in PPNG in China and Vietnam over the 3 year period ( $p < 0.05$ ) and the decline in numbers of PPNG in Hong Kong. Also of interest was the presence of PPNG in increasing numbers in some Pacific Island states with high proportions of PPNG in Tonga and the Solomon Islands. Chromosomally mediated penicillin resistant *Neisseria gonorrhoeae* (CMRNG) was also widespread in the region. While the true extent of this phenomenon is difficult to estimate in the presence of PPNG and can only be properly determined by repeat testing of strains after plasmid curing,<sup>19</sup> sufficient data are available to suggest that this was also a considerable problem in the region but with differences apparent in the various centres.

#### SUSCEPTIBILITY TO THE QUINOLONES

A considerable increase in quinolone resistance was observed during the 3 year period surveyed (table 2). In 1992, 1211 strains were tested. In Japan there was a significant proportion of isolates (21%) with low level resistance to quinolone antibiotics. A low prevalence of low level resistance to the quinolones was also observed in two of the other seven centres testing these agents (Australia and New Caledonia). Fully developed high level resistance was seen in only a few isolates in Japan and Australia. In 1993, an additional four centres undertook this examination and a total of 3077 isolates were examined. Low level resistance was present in nine of the 12 centres with again a high proportion of isolates from Japan exhibiting this phenomenon. Additionally Japan, Singapore, and Australia now reported high level resistance, although

again at a low frequency. In 1994, 13 centres tested 5795 strains for quinolone resistance and all but one (Solomon Islands) noted the presence of some form of resistance, some in a very high proportion of isolates examined (Hong Kong, Korea, Japan, Philippines). High level quinolone resistance was present in seven of the 13 centres and in higher proportions than previously recorded. In addition to the high number of resistant isolates observed in Hong Kong and the Philippines in 1994, statistically significant increases ( $p < 0.05$ ) were observed in the numbers of quinolone resistant isolates in separate data from Japan, Korea, Singapore, and Vietnam over the period of the study.

#### SUSCEPTIBILITY TO SPECTINOMYCIN

Examinations for spectinomycin resistance were performed in 13 centres in the 3 years (table 3). The number of strains tested increased from 1440 in eight centres in 1992 to 3687 isolates in 11 centres in 1994. Resistance was consistently seen only in a small proportion of strains in Papua New Guinea and China, the latter observation confirming a prior finding.<sup>20</sup> Sporadic instances of in vitro resistance to spectinomycin were also seen in New Caledonia, Vietnam, and Australia. Specifically, no resistance was seen in 53 isolates in Korea in 1994.

#### HIGH LEVEL TETRACYCLINE RESISTANCE

High level tetracycline resistant *Neisseria gonorrhoeae* (TRNG) were also present in the region (table 4), with Singapore and Malaysia consistently having a high proportion of isolates with this form of resistance. No TRNG

Table 3 Percentage of gonococcal isolates resistant to spectinomycin in 13 WPRO GASP centres, 1992-4

Country	1992		1993		1994	
	Tested	% Resistant	Tested	% Resistant	Tested	% Resistant
Australia	782	0	1570	0	1622	0.06
Brunei	20	0	40	0	0	
China	109	12.8	638	1.4	343	5.3
Fiji	0		0		399	0
Hong Kong	0		1041	0	0	
Japan	149	0	32	0	26	0
Korea	0		0		53	0
Malaysia	185	0	280	0	296	0
New Caledonia	46	0	18	5.5	16	0
Papua New Guinea	0		30	3.3	57	1.8
Singapore	130	0	568	0	667	0
Solomon Islands	0		15	0	20	0
Vietnam	19	0	58	0	188	0.5

Table 4 Percentage of isolates showing high level tetracycline resistance (TRNG) in 15 WPRO GASP centres, 1992-4

Country	1992		1993		1994	
	Tested	% TRNG	Tested	% TRNG	Tested	% TRNG
Australia	782	2.3	1570	2.7	1622	4.1
Brunei	20	0	0		0	
China	117	15.4	0		287	8
Fiji	848	0.4	593	0.3	804	0.1
Japan	148	0	49	2	26	0
Korea	43	2.3	225	8	192	1.5
Malaysia	185	31	280	38.9	148	49.3
New Caledonia	46	8.7	18	0	16	6.2
New Zealand	12	0	85	0	127	3.1
Papua New Guinea	0		40	7.5	218	4.1
Philippines	59	22	0	0	20	100
Singapore	130	43.8	769	38.1	667	47.1
Solomon Islands	0		15	0	20	0
Tonga	32	0	0		0	
Vietnam	41	7.3	157	17.1	220	83.6

TRNG = tetracycline resistant *Neisseria gonorrhoeae*.

were detected in Brunei, the Solomon Islands, or Tonga, but all other centres detected some gonococci of this type. The proportion of TRNG seen in Vietnam increased significantly ( $p < 0.05$ ) over the survey period.

#### SUSCEPTIBILITY TO THIRD GENERATION CEPHALOSPORINS

No clinical resistance to the third generation cephalosporins has yet been reported. However, the programme monitored sensitivity to ceftriaxone in nine centres in 1992, 11 in 1993 and 10 in 1994, examining a total of 9544 isolates in the 3 years (table 5). The lack of definition of precise breakpoints for ceftriaxone resistance and the absence of confirmed clinical resistance precludes comment on "resistance" to this group of agents. Some centres also tested other agents used in their locality and resistance to kanamycin (Malaysia and Vietnam) and chloramphenicol (Vietnam) was recorded.

The results of the proficiency testing programme using reference QC and QA cultures revealed a satisfactory level of participant performance with over 95% of examinations placing the QC and QA cultures in the correct category. Some problems with testing of individual antibiotics were detected in some centres early in the programme. Data from these sources were not included until problems were resolved. Strains from one contributing laboratory were referred to the regional reference centre for testing in the absence of suitable facilities in that country.

Table 5 Number of isolates tested for ceftriaxone susceptibility in 13 WPRO GASP centres, 1992-4

Country	No tested		
	1992	1993	1994
Australia	782	1570	1622
Brunei	20	40	0
China	109	0	151
Fiji	0	24	804
Hong Kong	0	1041	0
Japan	145	57	83
Korea	43	225	192
Malaysia	185	280	148
New Caledonia	40	0	0
Papua New Guinea	0	40	218
Singapore	130	568	667
Solomon Islands	0	15	20
Vietnam	19	115	215

#### Discussion

Considerable progress has been made in the area of organised surveillance of antimicrobial susceptibility of gonococci in the WHO WPRO in the past few years. In this period country based networks have been expanded or established and these have coalesced into a coherent regional programme. The region contains highly developed nations, countries with emerging economies, small Pacific Island states, and underdeveloped areas all of which have contributed validated data to what is now a continuing long term surveillance programme. In order to reconcile the differences in susceptibility testing technique and capabilities of the different participants, a pragmatic approach was adopted which utilised existing resources and accepted data from sources which were limited to  $\beta$  lactamase testing with disc screening methods to full agar incorporation techniques. The variations in methodology in place at the beginning of the programme were reduced by nominating test methods and a quality assurance and quality control programme further overcame effects caused by remaining differences and allowed comparison and validation of data.<sup>12</sup>

The programme expanded in terms of sample size and coverage in the period under review, but the sample base in most instances was from similar sources—namely, unselected symptomatic patients. As the programme settled into a regular pattern, the advantages of longitudinal surveillance, as opposed to point prevalence examinations, became more obvious. The longer term nature of the programme helped to mitigate any effect of possible selection bias resulting from use of a restricted sample base. While it is acknowledged that different groups of patients may be infected with gonococci with different sensitivity patterns—for example, urban and rural, if the source of isolates under surveillance remains relatively constant, alterations in the pattern of sensitivity within that cohort can be validly detected over time and this will provide an indication of shifts in gonococcal susceptibility.

Changes in antibiotic resistance patterns were evident in this study particularly within the quinolone group of antibiotics. In the period of this study, quinolone resistant gono-

cocci appeared in more centres, in a higher proportion of isolates in those centres, and at increasingly high MIC levels. While it was fortuitous that the programme was operating at the time when these strains were appearing, it was reassuring that the programme was able not only to detect these important trends but to also give an assessment of the rapidity and extent of this change. In some centres—for example, Hong Kong, and the Philippines, quinolone resistant gonococci have become endemic while in others (Australia, New Zealand) most isolates of this type are from infected travellers and secondary spread of quinolone resistant gonococci is as yet limited. The observations on quinolone resistance made in the WPRO programme would appear to have been confirmed by other reports of quinolone resistance in isolates from travellers returning to their home country after acquiring infections in the WPR. These reports indicate that the infections were acquired in those parts of the WPR where high levels of quinolone resistance were observed in this study<sup>21-26</sup> and reveal the significance of emerging quinolone resistance on countries outside the WPR. A number of clusters of cases have been identified<sup>22-24</sup> and treatment recommendations for travellers infected in WPR countries have been modified.<sup>24-26</sup>

Fewer changes were noted in the regional patterns of resistance to the other core antimicrobials tested. There were however marked differences in the various parts of the region in terms of resistance to the individual antimicrobials, reflecting the diverse nature of antibiotic usage and availability and different economic conditions in the WPRO GASP participant countries. Although the penicillins are little used because of resistance to them, the spread of PPNG in China and Vietnam and the decline of PPNG in Hong Kong are examples of changes occurring over time in parts of the region. In China and Vietnam the increases could be ascribed to the more frequent international travel in these countries. The decrease in PPNG in Hong Kong has been explained by the prolonged use of quinolone antibiotics.<sup>27</sup> Additionally, the higher rates of TRNG in Singapore and Malaysia reflect a more stable geographic variation. However, the WHO WPRO is a region where gonococcal resistance to a number of antibiotics has emerged previously, the appearance of PPNG and spectinomycin resistant strains being two examples. The availability of certain antibiotics and the consequent potential for their misuse has no doubt contributed to this situation in the past. However, resistant gonococci are seldom restricted to a particular geographic region for long, and the appearance of resistance to one or more antibiotics in this region will see spread of these isolates to more distant localities by infected travellers, as has occurred with the quinolone resistant strains. In this context it is important to continue to monitor antibiotic resistance in gonococci in WPRO so as to be aware of potential difficulties with therapy as they arise and in a wider than local context.

In addition to obtaining information on gonococcal susceptibility to contribute to a global programme, one aim of the project is to help construct or modify appropriate treatment regimens for gonococcal disease in the participating countries themselves. It is known and also evident from this study and others that there are considerable temporal and geographic variations in gonococcal susceptibility patterns. This means that surveillance programmes and the treatment regimens based upon them must be attuned to local needs while maintaining an awareness of changes elsewhere that may impinge on the effectiveness of local measures. This programme initially attempted to have a quarterly reporting period to maximise dissemination of data, but it soon became evident that this was not practical given the number of participants who, in some instances, themselves collated results from other centres. The timeliness of new or changing information was therefore enhanced by the individual centres making their local information available to relevant bodies in their locale as well as reporting it to the central system. The information produced by WPRO GASP has been positively applied in the region. Some options for cheap oral treatment of gonorrhoea—penicillins and tetracyclines—have been greatly reduced in the region because of resistance, and even relatively expensive therapies such as quinolones are becoming less effective. Other antibiotics, even if more expensive in terms of unit cost, have longer term benefits as ineffective cheaper therapies neither treat the individual adequately nor prevent complications or spread of the organism to others. The findings of this surveillance programme have been fundamental to the establishment of a recommended treatment regimen in some countries (for example, Australia, Papua New Guinea, Solomon Islands) and for the modification or reassurance of effectiveness of recommendations in others (New Caledonia). Paradoxically some older agents remain useful in some settings. Spectinomycin resistance is now uncommon, perhaps because its use has declined in recent years, but it is expensive and requires administration by injection.

Cephalosporins, whether oral or injectable, retain their usefulness but their cost makes them difficult to introduce in some circumstances. Additionally, some of the oral third generation cephalosporins are administered in a lower dose equivalent than the injectable agents formerly used, and this, together with the potential for misuse or inappropriate dosing of oral agents means that the cephalosporin sensitivity of gonococci should be closely monitored. The WPRO GASP has contributed significant information thus far, but will need to maintain and perhaps extend surveillance as newer agents are introduced. The programme also aims to improve standards of technical performance and this has occurred by a number of means in the life of the programme. It would thus appear that other considerable benefits, often intangible, have also accrued in this area since the programme's inception.

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