ANTIMICROBIAL RESISTANCE IN GONOCOCCI , WHO WESTERN PACIFIC REGION, 1995

The World Health Organization Western Pacific Gonococcal Antimicrobial Surveillance Programme[1]

Abstract

The World Health Organization (WHO) Western Pacific Region Gonococcal Antimicrobial Surveillance Programme tested the susceptibility of about 7,000 isolates to a core group of antibiotics in 16 focal settings in 1995. Resistance to the quinolone antibiotics, which had increased significantly since 1992, was again widespread. Twelve of the 14 centres noted some quinolone-resistant gonococci with particularly high rates being observed in China, Hong Kong, the Philippines and Japan. High rates of resistance to the penicillin group were also common throughout the region. In contrast, resistance to spectinomycin and later generation cephalosporins was infrequent or absent. There was significant geographic variation in the rates of high level tetracycline resistance, but this changed little in 1995 from the distribution seen in earlier years. These results indicate that gonococcal infections in the WHO Western Pacific Region are becoming more difficult and more expensive to treat. ***Comm Dis Intell* 1996;20:425-428.**

Background

The World Health Organization (WHO) Western Pacific Region (WPR) Gonococcal Antimicrobial Surveillance Programme (GASP) commenced in 1992. Recent WHO estimates put the number of new cases of gonorrhoea worldwide at 62 million annually[1]. A significant portion of these cases occur in the Western Pacific Region. The same sources indicate that the serious morbidity that often accompanies gonococcal disease can be greatly reduced by appropriate treatment. It is now also acknowledged that gonorrhoea is a potent cofactor in the transmission of the human immunodeficiency virus (HIV)[2,3,4]. The converse of this situation is that better sexually transmitted disease (STD) treatment and, through it, a reduction in the prevalence of STDs, reduces HIV transmission[5]. There are thus clearer and more cogent reasons than ever before to ensure that gonococcal disease is properly treated when it cannot be otherwise prevented[6].

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 gonococci - the Gonococcal Antimicrobial Surveillance Programme. The WHO WPR GASP network was established to provide reliable data on antibiotic resistance which would benefit not only the Region itself, but also have a wider application.

Methods

Data on gonococcal isolates were provided by participants in focal points in various countries throughout the WHO WPR. A list of members of the programme is contained in the acknowledgements.

Participants were encouraged to examine a recommended core list of antibiotics using one of the standard methods nominated by the programme. However not all isolates were examined for sensitivity to all agents by all participants. A series of reference strains are made available and a quality assurance programme is conducted each year.

Most strains examined were from non-selected STD clinic patients, but some were obtained as a result of case finding. In some countries with a small geographic area (for example Singapore and Hong Kong), isolates were examined in a single centre. Data from other centres represent an analysis of strains referred throughout the country to a central laboratory, as in Malaysia. Other countries (for example Australia and China) have a network of contributors supplying data from a national surveillance scheme.

Results

Approximately 7,000 isolates were examined in 16 focal groupings between 1 January and 31 December 1995.

Trends in susceptibility have become more easily discernible as the period of continuous surveillance has increased. About 27,000 strains have been examined in this programme since 1992.

Penicillins

Interest remains in the extent and type of resistance to the penicillins, although the clinical usefulness of this group of antibiotics has decreased significantly in the WPR over a number of years. The proportion of isolates resistant to the penicillin group by one or more mechanisms ranged between 3% and 98% of isolates in the 16 contributing centres (Table 1). Particularly high levels of penicillin resistance were recorded in Vietnam (98%), Korea (90%), China (84%) and Malaysia (80%).

The programme seeks separate data on the extent of penicillin resistance manifested either through plasmid-

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mediated penicillinase production (PPNG) or through chromosomally controlled intrinsic resistance (CMRNG). Both forms of resistance may exist simultaneously in the one isolate, but the latter type may be masked in PPNG.

PPNG were widespread throughout the WPR in 1995. New Caledonia was the only centre not recording the presence of PPNG, although the proportion of PPNG in Papua New Guinea, Fiji and Japan was also low. A steady increase in the proportion of PPNG has been noted in some countries since the inception of this programme. In Vietnam the proportion of PPNG increased from 55% in 1992 to 93% in 1995. An increasing proportion of CMRNG has also been detected over the life of the programme. In Hong Kong, isolates of this type now represent 73% of all isolates, while the proportion of PPNG has declined to 5%.

Spectinomycin

About 3,500 isolates were examined in 11 countries in 1995. Only three spectinomycin-resistant strains were detected - one in China, one in Papua New Guinea and the other in New Caledonia.

Spectinomycin-resistant strains have been consistently seen only in China (in low numbers) since 1992, and only as sporadic isolates in a few other centres. Notably there was no spectinomycin resistance seen in the sample of isolates from Korea. Spectinomycin resistance was a particular problem in Korea in the 1980s. The current lack of in vitro resistance to spectinomycin in most of the region may reflect the declining use of this injectable agent in recent years.

Ceftriaxone

About 4,400 strains were examined for resistance to ceftriaxone in 12 centres. One isolate from New Caledonia was reported as resistant.

There is no documented case of treatment failure with third generation cephalosporins and consequently no correlation between in vitro findings and clinical outcome is available. However it is recognised that levels of susceptibility to the cephalosporins have decreased in the periods surveyed. If a relationship between these increasing levels of resistance and treatment failure were to be established, it would be a worrying development because of the important place of this antibiotic group in the therapy of gonorrhoea.

Quinolone antibiotics

Particular interest is centred on emerging gonococcal resistance to this group of until-now useful oral antibiotics. In this 12 month period about 6,600 isolates of gonococci were examined in 14 centres for their susceptibility to quinolone agents.

The pattern of increased quinolone resistance was first described in the WPR in 1993 and was maintained in 1994 and 1995. Quinolone resistance was detected in all centres except Fiji and the Solomon Islands (Table 2).

Table 1. Penicillin resistance in gonococci, WHO Western Pacific Region, 1995

Country	Strains tested	Lactamase mediated resistance (PPNG)		Chromosomal resistance (CMRNG)		All penicillin resistance (PP+CMRNG)	
		Number	%	Number	%	Number	%
Australia	2147	161	7.5	179	8.3	340	15.8
China	452	-	-	-	-	380	84
Fiji	977	42	4.3	7	0.7	49	8
Hong Kong	1895	92	4.9	1377	72.7	1469	77.6
Japan	35	1	2.9	8	22.9	9	25.8
Korea	96	74	77	13	13.5	87	90.5
Malaysia	76[1]	36	47.4	141	26.4	-	73.8
New Caledonia	19	0	0	3	15.8	3	15.8
New Zealand	289	27	9.3	17	5.9	44	15.2
Papua New Guinea	87	3	3.4	0	0	3	3.4
Philippines	16	8	50	3	18.8	11	68.8
Singapore	642[2]	315	49	35	5.5	-	54.5
Solomon Islands	4	1	25	0	0	1	25
Tonga	51	24	47	0	0	24	47
Vanuatu	175	-	-	-	-	16	9.1
Vietnam	97	90	92.8	5	5.1	95	97.9

1. 53 of 76 tested for chromosomal resistance.
2. 327 of 642 tested for chromosomal resistance.

Table 2. Quinolone resistance in gonococci, WHO Western Pacific Region, 1995

Country	Strains tested	Resistant		Less sensitive	
		Number	(%)	Number	%
Australia	2108	40	1.9	33	1.6
China	394	61	15.5	318	80.7
Fiji	977	0	0	0	0
Hong Kong	1895	146	7.7	1090	57.5
Japan	34	10	29.4	6	17.6
Korea	96	0	0	15	15.6
Malaysia	53	0	0	1	1.9
New Caledonia	19	0	0	6	31.6
New Zealand	300	1	0.3	7	2.3
Papua New Guinea	86	1	1.2	0	0
Philippines	16	11	68.8	0	0
Singapore	594	17	2.9	48	8.1
Solomon Islands	4	0	0	0	0
Vietnam	73	4	5.5	6	8.2

Quinolone resistance is chromosomally mediated and levels of resistance increase incrementally. The first clinically manifested resistance observed was at a low minimal inhibitory concentration (MIC) level and was accommodated by increasing the recommended dose of antibiotic administered. Subsequently strains with higher MICs were detected and these were not amenable to therapy even with higher dose regimens. These different levels of resistance are shown in Table 2 as less sensitive and resistant groups respectively (these categories have been correlated with clinical outcome data).

The proportion of less sensitive strains increased significantly in many centres since 1992 and the proportion of less sensitive isolates was maintained near or above 1994 figures. The highest rate of less sensitive strains was observed in China (80%) and Hong Kong (58%).

Additionally there was an increase in the proportion of strains classified as resistant in a number of centres. The highest proportion of quinolone-resistant gonococci was seen in the Philippines (69%) and Japan (29%), although sample numbers from both centres were low.

This resistance was noted in only a single centre in 1992 and then in only a few gonococcal isolates. By 1995 the quinolone-resistant strains were present in nine centres and in much higher numbers.

High level tetracycline resistance

Tetracyclines are administered as a multiple dose treatment for gonorrhoea and are not a recommended therapy for gonorrhoea. However, a particular form of plasmid-mediated tetracycline resistance (TRNG) has been recognised for a number of years. The programme has monitored the spread of this form of resistance in the region.

About 4,800 isolates were examined in 1995 in 14 countries. TRNG were present in nine of these centres (Table 3). Particularly high proportions of TRNG were again seen in Singapore, Malaysia and Vietnam, but there was little overall change in the existing distribution of TRNG in 1995.

Other antimicrobials

Six countries tested the sensitivity of their isolates to other antimicrobials (Table 4).

Table 3. High level tetracycline resistance (TRNG) in gonococci, WHO Western Pacific Region, 1995

Country	Strains tested	TRNG	
		Number	%
Australia	2108	113	5.4
China	437	35	8
Fiji	977	0	0
Japan	35	0	0
Korea	96	0	0
Malaysia	53	31	58.5
New Caledonia	19	3	15.8
New Zealand	300	6	2
Papua New Guinea	86	1	1.2
Philippines	16	3	18.8
Singapore	594	379	63.8
Solomon Islands	4	0	0
Tonga	54	0	0
Vietnam	97	41	42.3

Table 4. Resistance to other antimicrobials in gonococci, WHO Western Pacific Region, 1995

Antimicrobial	Country	Strains tested	Resistant	
			Number	%
Kanamycin	Malaysia	53	2	3.8
Cefuroxime	Malaysia	53	0	0
Cephaclor	Vietnam	87	3	3.5
Chloramphenicol	New Caledonia	19	0	0
	Vietnam	97	14	14.4
Augmentin	Fiji	977	7	0.7
Azithromycin	Singapore	253	0	0

Acknowledgements

The following have generously provided support for the programme:

Dr Sima Huilan, formerly Regional Adviser in Health Laboratory Technology, now Director Drug Policy, Environmental Health and Health Technology, WHO Regional Office for the Western Pacific, Manila, Philippines; members of the Australian Gonococcal Surveillance Programme in Australia; Ye Shunzhang and Chen Ping, Nanjing, China; M Shah and K.P. Singh, Suva, Fiji; K.M. Kam, Hong Kong; J. Kumazawa Fukuoka; Toshiro Kuroki, Yokohama Japan; K.H Shin, K. Lee and Y.M. Chong, Seoul, Korea; Rohani M.D. Yasin, Kuala Lumpur, Malaysia; P. Duval and B. Gentile, Noumea, New Caledonia; M. Brett, Wellington, L. Seaward, Christchurch and M. Brokenshire, Auckland, New Zealand; J. Roy, Port Moresby, Papua New Guinea; M. Saniel and C.C. Carlos, Manila, Philippines; A.E. Ling, Singapore; Richard Lucas and Horton Sale, Solomon Islands; Ane Tone Ika, Nuku'alofa, Tonga; H. Wamle and D. Kalorib, Vanuatu; Le Thi Phuong, Hanoi, Vietnam.

The programme was supported by technical services agreement V3 / 181 / 107 with the WHO Global Programme on AIDS (GPA).

References

1. WHO Global programme on AIDS. An overview of selected curable sexually transmitted diseases. World Health Organization, 1995.
2. Wasserheit JN. Interelationships between immunodeficiency virus infection and other sexually transmitted diseases. *Sex Trans Dis* 1992;19:61-77.
3. Quinn TC. Global burden of the IIIV pandemic. *Lancet* 1996;348:99-106.
4. Laga M, Manoka A, Kivuvu M *et al.* Non-ulcerative sexually transmitted disease as risk factor for HIV-1 transmission. Results from a cohort study. *AIDS* 1993;7:95-102.
5. Grosskurth H, Mosha F, Todd J et al. Impact of improved treatment of sexually transmitted diseases on HIV infection in rural Tanzania: randomised controlled trial. *Lancet* 1995;346:530-536.
6. Laga M. STD control for HIV prevention - it works! *Lancet* 1995;346:518-519.

OVERSEAS BRIEFS

Source: World Health Organization (WHO)

Viral meningitis, Romania, update

By 23 September a total of 450 cases of viral meniningitis had been reported in the outbreak which started in Bucharest at the end of July. The number of new cases has decreased. More than half the cases occurred in adults and more than 200 were in people over 60 years of age. Thirty-nine patients died. The WHO Collaborating Centre for Reference and Research on Arboviruses and Haemorrhagic Fevers at the Pasteur Institute, France has confirmed infection with West Nile virus in 89% of the patients investigated. Infection with West Nile virus can be asymptomatic or cause an influenza-like illness. Severe manifestations include meningitis and meningoencephalitis, particularly in the elderly. Migratory birds are the natural reservoir; the virus is transmitted to humans by *Culex* mosquitoes. The virus has been detected in Europe but is more common further south, in the Mediterranean region, Africa and western Asia. Precautions against infection include avoiding mosquito bites either through protective clothing or mosquito repellants

Polio, Albania

An outbreak of paralytic illness has been reported by Albania. The first cases were reported in April 1996, but there was a sharp increase in cases occurring in late July and August. Additional cases continue to be reported. The clinical picture was acute onset, asymmetric flaccid paralysis typical of poliomyelitis. A WHO team is assisting the Albanian Ministry of Health in investigating the outbreak. The team has investigated 66 cases of paralytic illness. There were seven deaths. WHO reference laboratories in Italy and the Netherlands have now isolated wild poliovirus type 1 from seven cases. The Ministry of Health, with the support of WHO, UNICEF and others is planning to immunise both adults and children with oral polio vaccine.