

# GASP Newsletter

A SEARO Newsletter on Gonococcal Antibiotic Susceptibility Programme



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## Mucosal inflammation due to Sexually Transmitted Infections

### Rapid detection of asymptomatic infection

Sexually Transmitted Diseases (STD), such as gonorrhoea, chlamydial infection and trichomoniasis can cause either symptomatic or asymptomatic infection of the genital tract. Because a substantial number of infections are asymptomatic, rapid diagnosis of chlamydial infection and gonorrhoea with minimally invasive screening tests has become extremely important. These STDs can be detected in "first void" urine specimens, self-administered vaginal swabs, tampons, and sanitary napkins. All these approaches are designed to allow cost-effective screening of a large number of asymptomatic people, especially sexually active adolescents.

Farrell and colleagues from the Queensland Health Pathology Service, Toowoomba, Australia<sup>1</sup>, compared the Abbott LCx vs Roche COBAS Amplicor assays for detection of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* in urine samples. The authors were particularly interested in asymptomatic infections. A total of 282 asymptomatic volunteers were included. The newer COBAS test had a higher false-positive rate for gonorrhoea than did the LCx assay.

Van Dyke and coworkers from Antwerp, Belgium<sup>2</sup>, compared several methods for diagnosis of chlamydial infections and gonorrhoea from endocervical swab specimens. The study demonstrated that the older enzyme immunoassay (EIA) test for chlamydia, which is still widely used, has very poor sensitivity. On the other hand, all the newer amplification tests demonstrated excellent sensitivity and specificity. Indeed, the Probetec ET SDA (Abbott) showed 100% specificity, a very desirable characteristic for screening asymptomatic subjects in whom false-positive results represent a key problem. Now that these new amplification tests are available, the EIA test has limited utility.

Detection of STD pathogens with self-administered devices could also help to find people with asymptomatic infections. While STD pathogens can be detected in urine, management of urine samples adds complexity. Sturm and coworkers<sup>3</sup> from Durban, South Africa, screened 620 pregnant women for *Trichomonas vaginalis* using self-administered vaginal swabs. *T. vaginalis* was diagnosed in 24% of the women. The authors found that the sensitivity of these self-administered tampons by polymerase chain reaction

(PCR) was 100%, compared with 71% for culture. The specificity of PCR was 99% compared with 94% for culture. The authors suggest that tampons also might be used to detect other STD pathogens.

Fortier and colleagues<sup>4</sup> from Quebec, Canada, conducted a similar study using modified sanitary napkins to detect chlamydia. In this study, women attending medical or community clinics were asked to wear sanitary napkins for 4 hours and results from PCR detection were compared with cervical swab samples. The sensitivity of detection of chlamydia with sanitary napkins was 93% and specificity was 98.9%. The authors concluded that sanitary napkins are an effective non-invasive sample collection device.

### Gonococci continue to develop antibiotic resistance

Resistance of gonococci to penicillins can be ascribed to plasmid-mediated beta-lactamase production as well as chromosomal and multidrug resistance. Multidrug resistant strains grow in the presence of penicillins, tetracyclines, and quinolones. Resistance to quinolones is a rapidly growing problem. Ng and coworkers<sup>5</sup> from Winnipeg, Manitoba, Canada, reported that in 1997-1998, 65 strains of *Neisseria gonorrhoeae* resistant to ciprofloxacin were isolated in Canada. These organisms demonstrated resistance mutations in the *gyrA* and *parC* genes as previously reported. In addition, the authors noted increased resistance of gonococci to azithromycin related to alterations in efflux pumping and membrane permeability.

These changes in antibiotic susceptibility can be translated into a failure of therapy. Rahman and colleagues from

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Bangladesh<sup>6</sup>, studied 80 female sex workers who were culture-positive for *N. gonorrhoeae*. These patients were treated with a single dose of 500 mg of ciprofloxacin. A total of 66 women were reevaluated over 7-10 days. In 25 patients (38%), a second specimen was positive for *N. gonorrhoeae*. Twenty-four of 25 recurrent infections were caused by quinolone-resistant gonococci. These investigators found that *in vitro* resistance to quinolones accurately predicts failure of therapy.

Extended-spectrum beta-lactam antibiotics have been effective against gonorrhoea; indeed, ceftriaxone has remained the "gold standard" for treatment of gonorrhoea for more than a decade. Takahashi and coworkers from Kitakyushu, Japan<sup>7</sup>, now report resistance of *N. gonorrhoeae* to a cephalosporin (cefdinir) and the monobactam aztreonam. These investigators found three patients with urethritis who failed clinical therapy with these agents (2 cefdinir, 1 aztreonam). The organisms recovered demonstrated lower susceptibility *in vitro* to these agents and other beta-lactam antibiotics.

### References

1. Farrell DJ, Sheedy TJ, Robertson C, *et al.* Asymptomatic Urinary Screening for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in a high prevalence Australian population: a comparison of Abbott LCx and Roche COBAS AMPLICOR. Abstract 887, page 147.
2. Van Dyck E, Ieven M, Smet H, *et al.* Detection of *N. gonorrhoeae* and *C. trachomatis* in cervical swab specimens by culture (NG), EIA (CT), PCR, SDA, and LCR E. Abstract 888, page 148.
3. Sturm PDJ, Ebrahim S, Nzimande GG, *et al.* Diagnostic PCR on self-collected tampon specimens for detection of *Trichomonas vaginalis* infection in pregnant women. Abstract 884, page 147.
4. Fortier M, Alary M, Poulin C, *et al.* Evaluation of a modified sanitary napkin for self collection of specimens for detection of urogenital *Chlamydia trachomatis* infection in women. Abstract 1197, page 448.
5. Ng LK, Bryden L, Heidebrecht P. Characterization of *Neisseria gonorrhoeae* with ciprofloxacin and azithromycin resistance. Abstract 1570, page 454.
6. Rahman M, Monira S, Sultan Z, *et al.* Treatment failure with ciprofloxacin in gonorrhoea correlates with the prevalence of fluoroquinolone resistant *Neisseria gonorrhoeae* strains in Bangladesh. Abstract 1572, page 454.
7. Takahashi K, Muratani T, Akasaka S. Three cases showed clinical failures in gonococcal urethritis treated with cefdinir or aztreonam: the *N. gonorrhoeae* isolates demonstrated resistance to those agents. Abstract 1571, page 454.

Summary prepared by Ashok Rattan, based on presentations made at the 40th Interscience Conference on Antimicrobial Agents and Chemotherapy; Toronto, Ontario, Canada; September 17-20, 2000 and published by Myron Cohen: *STDs Forgotten but not gone.*

## Condom usage and STDs in sex workers of Sonagachi, Kolkata

The increased evidence that STDs facilitate HIV transmission has led to renewed attempts at STD control. A study was undertaken among commercial sex workers (CSWs) of Sonagachi - the red light area of Kolkata, to determine the prevalence of causative agents of STDs and their relation to condom use and duration in the profession. An intervention project having three components: health services provision; information - education - communication (IEC) and condom promotion was designed.

In 475 CSWs, examined for prevalence of STDs, TPHA positivity was 63.16% whereas VDRL reactivity was 57.4%. Positivity for chlamydial infection was 36.08% followed by *N. gonorrhoeae* 11.81%, *T. vaginalis* 9.47%, HBsAg 6.53%

and *Candida albicans* 4.21%. Total 59.07% samples were positive for infections. Out of these, 38.82% had single infection, 17.30% double infection and 2.95% showed more than two infections.

There was a clear correlation between condom use and infection among CSWs. Among "always" condom users, the infection rate was 43.46%, in "often" users, 73.33% and among "sometimes" users, 80.26%. Maximum infection was seen among sex workers whose duration in the profession was between 1 to 5 years. Duration in the profession over 5 years did not increase the positivity. There was a good relation between condom use and low prevalence of infection. Gopi Thawani and S. Jana, Institute of Serology, Govt. of India, Kolkata & All India Institute of Hygiene & Public Health, Kolkata.

## Consultative meeting cum workshop on Gonococcal Antimicrobial Susceptibility Programme (GASP) SEAR at Safdarjung Hospital, New Delhi

A National Workshop cum Consultative meeting on GASP was held from 12-14 June 2000 in the WHO Regional Reference Laboratory at Safdarjung Hospital, New Delhi. The participants were selected to represent the five Regional STD Reference Laboratories of India as well as from other Indian laboratories.

The workshop objectives were as follows:-

- to impart "hands on training" to the participants in various laboratory techniques involved in GASP, in order to enable them to participate in the External Quality Assurance Programme.
- to sort out the problems encountered by different participating laboratories while carrying out gonococcal bacteriology.
- to distribute the materials including WHO Reference and Quality Assurance strains, media and antibiotic discs to participants.
- to highlight the importance of networking through proper transmission of data to the Regional Reference laboratory and its feed back in the form of publication of GASP Newsletter.

While inaugurating the workshop, Dr. S. Kumari, Regional Adviser, emphasized the importance of the GASP in view of the current HIV/AIDS scenario in the SEAR countries.



Inauguration ceremony of Consultative Meeting cum Workshop



*Demonstration of GASP laboratory techniques*

The discussions revealed that there was an universal reduction in the clinical cases. Most of the laboratories isolated *N.gonorrhoeae* and determined their susceptibility sporadically owing to either non-availability of media/reagents or administrative problems. The laboratories faced difficulties in maintaining the strains and in obtaining low concentration discs that were recommended for use in the GASP/SEARO manual. The problems as well as the strategies to solve them were discussed.

## External Quality Assurance (EQA) Programme under GASP

An EQA Programme on antimicrobial susceptibility of *N.gonorrhoeae* was conducted by the WHO Regional Reference Laboratory, Safdarjung Hospital, New Delhi amongst ten participating laboratories in June / July 2000.

### *Procurement of Reference & EQA strains and low concentration antibiotic discs:-*

The laboratory received lyophilized WHO Reference strains (A to E), WHO/SEARO provisional strains (F to J) and QA strains 1 to 6 and low conc. antimicrobial discs of penicillin (0.5 µg), nalidixic acid (30 µg), ceftriaxone (0.5 µg), ciprofloxacin (1 µg), tetracycline (10 µg) & spectinomycin (100 µg) in May 2000 from Dr. J. Tapsall, Sydney, Australia.

Each participant was supplied with a kit containing the following materials:-

- i) WHO Reference and QA strains in glycerol broth (in dry ice) and on chocolate agar slopes (in candle jar).
- ii) Columbia and GC agar base, saponin, VCNT supplement (in dry ice) and chocolate agar plates.
- iii) Low conc. antibiotic discs.

### *Feedback of EQA results of QA strains: -*

All the participating laboratories could perform the antimicrobial susceptibility of the QA strains provided and did not ask for the strains again. The results after compilation were submitted to Dr. S. Kumari & Dr. J. Tapsall. The feedback results of the EQA received from Sydney, Australia, were sent to each participating laboratory.

### *Analysis of EQA results: -*

The results showed that ceftriaxone, penicillin, tetracycline, quinolone and spectinomycin susceptible strains could be determined correctly by most of the laboratories. However, PPNG and quinolone less sensitive and resistant strains

could not be identified by any of the ten laboratories. In one of the strains, the PPNG plasmid was probably lost. TRNG could not be detected on 73% occasions. The plasmid may have been lost prior to testing.

*Report prepared by Dr. Manju Bala, Microbiologist, WHO Regional Reference Laboratory, GASP, Safdarjung Hospital, New Delhi.*

## Antibiotic resistance in gonococci - USA: 1999

### *Studies show Gonorrhoea control again facing challenge of antibiotic resistance*

As drug-resistant strains of *N. gonorrhoeae* continue to emerge, successful treatment of this STD is becoming more difficult. In the 1980s, *N. gonorrhoeae* became resistant to penicillin and tetracycline, rendering these drugs ineffective for gonorrhoea. As a result, since 1989, Centres for Disease Control and Prevention (CDC) has recommended fluoroquinolone antibiotics such as ciprofloxacin as treatment for gonorrhoea. Increased levels of fluoroquinolone-resistant *N.gonorrhoeae* are being reported in Hawaii now, rising from 1.4% of strains tested in 1997 to 9.5% in 1999<sup>1</sup>.

Consequently, CDC recommends that health care providers ask patients with gonorrhoea if they or their sex partners could have acquired the disease in Hawaii, other Pacific Islands, or Asia, where fluoroquinolone-resistant *N.gonorrhoeae* is common. If so, patients should be treated with cefixime or ceftriaxone, currently recommended for treating gonorrhoea and to which no resistance has been reported so far.

In addition, CDC is seeing the first indication that gonorrhoea may be becoming resistant to yet another drug. The first reported cluster of patients - 12 people - with gonorrhoea, with decreased susceptibility to azithromycin, another commonly used antibiotic, was found in Kansas City, Missouri in 1999<sup>1</sup>.

The resistance in Hawaii and Missouri were discovered through the Gonococcal Isolate Surveillance Project (GISP), a CDC-sponsored surveillance system, which monitors drug resistance of *N.gonorrhoeae*. Throughout the United States, 26 sexually transmitted disease clinics participate in GISP by collecting *N.gonorrhoeae* cultures and submitting them to one of the five regional GISP laboratories for antimicrobial susceptibility testing.

In view of these findings from GISP, if an antibiotic fails to treat a patient infected with gonorrhoea successfully, health care providers are urged to submit patients' specimens to their local laboratories for drug-resistance testing.

Gonorrhoea is the second most common disease in USA reported to CDC, with more than 3,60,000 cases reported in 1999. The estimated direct medical cost of treating gonorrhoea in the United States is \$56 million each year.

<sup>1</sup>*Abstracted from MMWR, 22 Sep 2000 by Susan A. Wang, MD, MPH, Coordinator, Gonococcal Isolate Surveillance Project (GISP), Division of STD Prevention, National Centre for HIV, STD & TB Prevention, Centres for Disease Control & Prevention, Mailstop E-02, 1600 Clifton Road, Atlanta, GA 30333.*

## Rapid increase in *N.gonorrhoeae* strains with reduced susceptibility to fluoroquinolones associated with treatment failure in Delhi.

Gonococcal isolates with decreased susceptibility or resistance to fluoroquinolones have been reported from many parts of the world. In our patient population during 1993-1995, quinolone resistance was detected in only 1.9% of gonococcal isolates, the percentage increasing to 12% in 1995-1996 and to 91.4% in 1999-2000. For the last 2-3 years, because of the observation of treatment failures after ciprofloxacin therapy in our STD clinic, majority of the patients are now being treated with ceftriaxone and some with Cefixime.

A study was undertaken in 35 cases of gonorrhoea treated

**Table 1: Correlation between Ciprofloxacin susceptibility (MIC) and response to treatment with Ciprofloxacin**

MIC (µg/ml)	Category	No. of strains	No. (%) cured
8	HLR	2	0(0)
1-4	R	6	1(16.6)
0.25-0.5	LS	4	2(50)
<0.125	S	2	2(100)
<b>Total</b>		<b>14</b>	<b>5(35.7)</b>

in the STD clinic of Lok Nayak Hospital during 2000. Out of them, 16 were treated with ciprofloxacin and test of cure samples could be obtained from 14 patients for culture. Antimicrobial susceptibility testing of all the isolates was performed by the disc diffusion method (NCCLS, M2-A6, Vol.17, No.1, 1997). A proportion of the strains was also tested for susceptibility to ciprofloxacin by agar dilution method for MIC determination. Quality control of the methods and antimicrobial discs used was ensured by inclusion of

### Susceptibility reports from laboratories in Southeast Asia Region.

Source	Country	Period	No. Tested	Results Obtained
S.Mananwatte	Sri Lanka	April 2000- March 2001	209	PPNG 12, Pen* 48R, 1LS; Cip 19R, 66LS; TRNG 2; Cro** 0R; SH 1R, 1LS; Cefu 2R, 23LS.
A.A.Pathak	Nagpur, India	July 2000- June 2001	13	PPNG 5, Pen 8 LS; Cip 6R; TRNG 3; SH 0R.
P.Bhalla	New Delhi, India	April 2000- Nov. 2000	36	PPNG 4, Pen 8R, 16LS; Cip 33R; TRNG 1; Cro 0R; SH 0R.
K.Ray&Manju	New Delhi, India	April 2000- March 2001	145	PPNG 26, Pen 67R, 44LS; Cip 119R; TRNG 16; Cro 0R; SH 0R.

Pen = Penicillin, Cip = Ciprofloxacin, Cro = Ceftriaxone, Tet = Tetracycline, SH = Spectinomycin, R = Resistant, LS = Low Sensitive, 0R = Zero Resistant, Cefu = Cefixime, \* = 52 strains Tested, \*\* = 121 strains Tested

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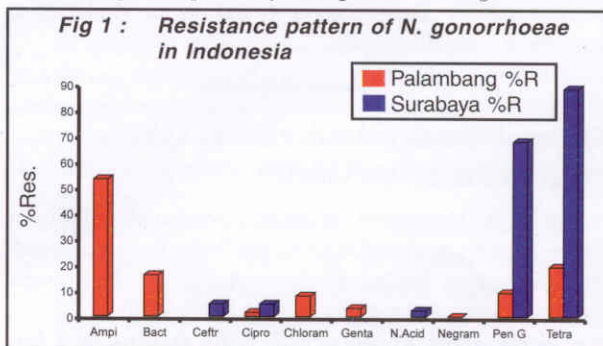
the WHO standard strains A-E.

Treatment failure was detected in nine (64.3%) of these patients, of whom seven were less sensitive and two resistant by disc diffusion method. However, out of the five cured, three were less sensitive and two sensitive. The MIC results of these isolates along with the cure rates are shown in Table 1.

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## *Neisseria gonorrhoeae* and PPNG isolated from Provincial Health Laboratory, Jakarta, Indonesia in 1998

A total of 247 specimens from Palembang PHC and 149 specimens from Surabaya PHC of Jakarta, Indonesia, were processed at Provincial Health Laboratory in 1998. Sixty two and 44 samples respectively were positive for *N.gonorrhoeae*.



In Surabaya, 28 of 44 (63.6%) strains were PPNG positive. PPNG testing was not performed in Palembang. Antibiotic resistance is shown in the figure 1.