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# WHO/SEAR Gonococcal Antimicrobial Susceptibility Programme (GASP)

*Report of the WHO Regional Reference Laboratory, 2001*

WHO Project: ICP RHR 001



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## 1. INTRODUCTION

Gonorrhoea continues to be a major health problem. Emergence of resistance to antimicrobial agents has made its treatment expensive, prolonged as well as unpredictable. Inadequate treatment, especially in women, may lead to a variety of complications. Formulation of a rational treatment plan for patients with gonorrhoea shall require a continuous feedback from the laboratory. Realizing the importance of laboratory based surveillance, WHO initiated a global Gonococcal Antimicrobial Susceptibility Programme (GASP). This became functional in South-East Asia Region of WHO in 1997. Two regional reference laboratories (one each in India and Thailand) were identified to provide technical and material support to five countries each of the Region. Interregional Reference Laboratory (IRRL) located at Sydney, Australia provides technical support and organizes external quality assessment scheme (EQAS) for laboratories in the SEA Region also. The management of GASP was entrusted to Regional STD Teaching, Training and Research Centre, Vardhman Mahavir Medical College and Safdarjang Hospital, New Delhi, India in December 1999.

Following are the terms of reference of this Regional Reference Laboratory:

- (1) To liaise with national focal point laboratories in Bhutan, India, Maldives, Nepal and Sri Lanka in order to conduct a regional Gonococcal Antimicrobial Susceptibility Programme (GASP) and provide feedback on test results to participating laboratories;
- (2) To obtain and distribute WHO reference cultures to participating laboratories and enable them participate in the quality assurance programme;
- (3) To collate and analyze regional data and transmit it to WHO/SEARO and to participating laboratories;
- (4) To collate technical material for preparation of a GASP newsletter;
- (5) To provide technical advice to participating laboratories, in gonococcal bacteriology and antimicrobial susceptibility testing from time to time, and

- (6) To organize follow up consultation with participants from five SEAR countries.

## **2. ACTIVITIES UNDERTAKEN (June 2001 to December 2001)**

### **2.1 Referral work on isolates received from other laboratories**

Ten isolates were received from Nagpur, five from Calcutta, six from Pune and four from Chennai. Feedback was sent to the concerned laboratories.

### **2.2 Publication of GASP Newsletter**

The Newsletter was released during the intercountry follow-up consultative meeting.

### **2.3 Training of Coordinator**

The Coordinator was trained at WHO Collaborating Laboratory for STD and HIV, Prince of Wales Hospital Randewick, New South Wales, Australia, during March 2001.

### **2.4 Procurement of Reference Strains and Antibiotic Discs**

The WHO Regional Reference Laboratory, Safdarjang Hospital received lyophilized WHO Reference Strains (A to E). WHO/SEARO Provisional Strains (F to J) and QA Strains 1 to 6 and low potency antibiotic discs from IRRL, Sydney, Australia. QA strains 1,4,5,6 could be revived.

### **2.5 WHO - SEAR Intercountry follow up consultative meeting cum Workshop on "Gonococcal Antimicrobial Susceptibility Programme"**

#### ***Introduction***

WHO/SEAR Intercountry follow up consultative meeting on "**Gonococcal Antimicrobial Susceptibility Programme**" was held from 19-21 December 2001. Ten laboratories from four SEAR countries namely Bangladesh, India,

Nepal and Sri Lanka participated. Bhutan and Maldives could not participate. The list of participants and the facilitators is placed at Annex 1 and the programme of work at Annex 2.

### ***Issues for consideration***

The following issues were considered during the meeting:

- Continuous collection of data;
- Interaction of laboratories with physicians;
- Strengthening of laboratories;
- Expansion of present network, and
- Exchange of Information through GASP Newsletter.

### ***Meeting***

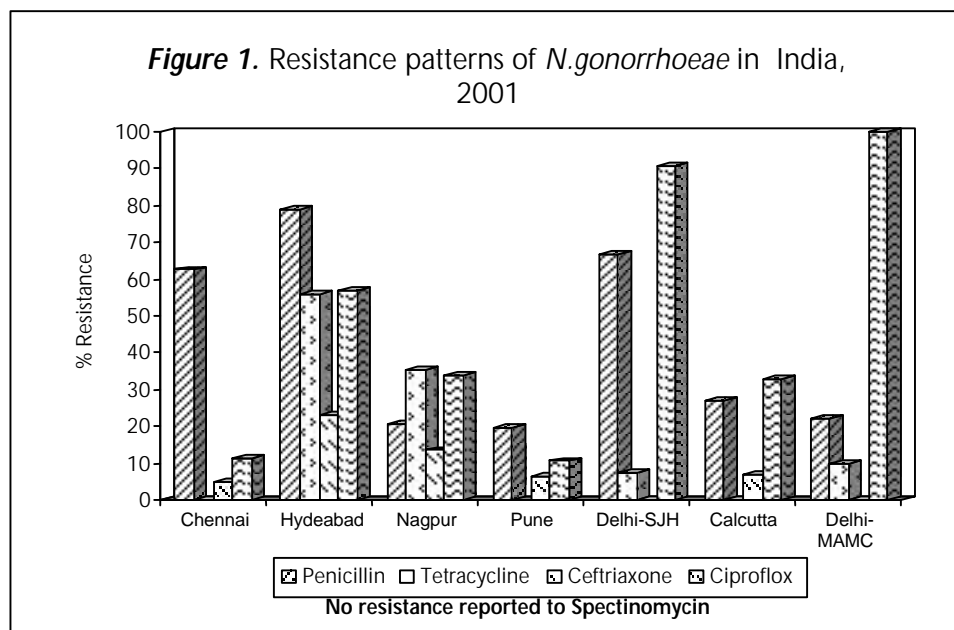
The meeting was inaugurated by Dr Jagdish Prasad, Medical Superintendent and Principal, Vardhman Mahavir Medical College and Safdarjang Hospital, New Delhi. Dr Rajesh Bhatia, STP-BCT/ SEARO highlighted the importance of surveillance as an essential tool in formulating a rational antimicrobial policy and the priority being accorded to this area by WHO. Dr Krishna Ray briefed the participants about the objectives and mechanics of the meeting. On the first day, all the participants made presentations regarding the work done and problems faced by their respective laboratories. On the second day, hands-on training on laboratory techniques of isolation and antibiotic susceptibility of *N. gonorrhoeae* under GASP was imparted to the participants. On the third day discussions were held under the chairmanship of Dr S. Kumari, BCT/SEARO.

### ***Current status of antimicrobial resistance of N.gonorrhoeae***

#### **India**

Figure1 summarizes and compares resistance patterns of *N.gonorrhoeae* reported from seven laboratories in India including the Regional Reference Laboratory.





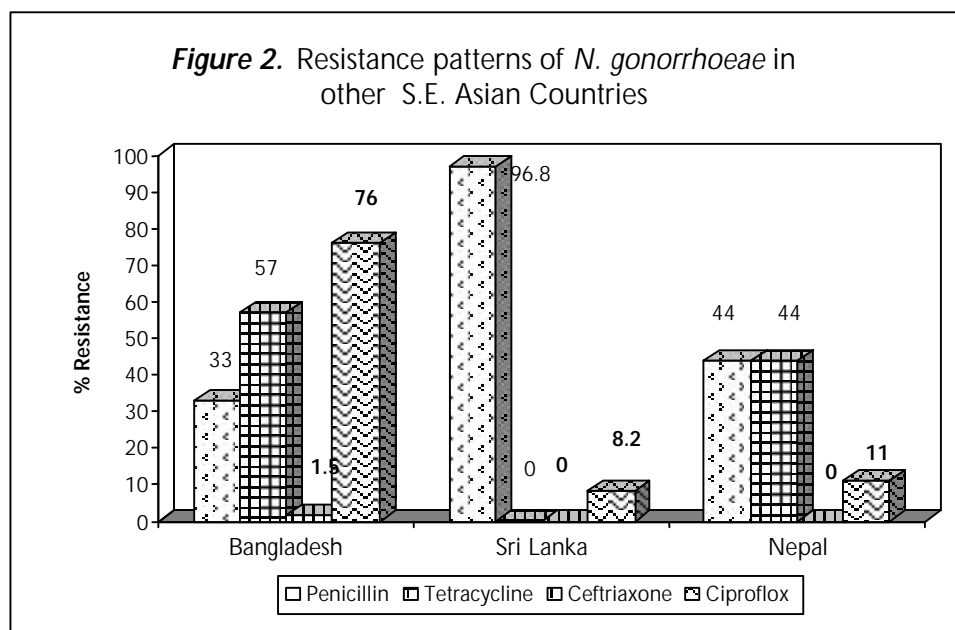
**Ciprofloxacin:** High degree of resistance to ciprofloxacin was reported from Delhi, (Safdarjang Hospital -90.7% and MAMC -100%), Calcutta (67.3%) and Hyderabad (57%), while moderate resistance was reported from Nagpur (35.13%) and low resistance from Pune (10.6%) and Chennai (11.2%).

- (a) **Penicillin:** Resistance to this antibiotic continues to be a problem in India. High degree of resistance was reported from Hyderabad (79%), Delhi (SJH - 66.7%) and Chennai (62.5%).
- (b) **Ceftriaxone:** A low percentage of resistance to ceftriaxone was reported from Chennai (5%), Calcutta (6.9%), Hyderabad (20%), Nagpur (13.3%) and Pune (6.6%). MAMC Delhi reported decreasing zone diameters from 50mm to 40mm(NCCLS) for this antibiotic. Ceftriaxone-resistant strains isolated from Pune were sent to the Reference Laboratory at Safdarjang Hospital, New Delhi for confirmation. The strains showed sensitive results following both NCCLS and CDS technique, but the zone sizes were close to cut off. Ceftriaxone-resistant strains from other laboratories were not received by the Reference Laboratory for confirmation.
- (c) **Tetracycline:** Resistance to tetracycline was reported from all the laboratories except Chennai and Calcutta.

(d) **Spectinomycin:** No spectinomycin resistance has been reported from India.

**Other SEAR countries**

Figure 2 summarizes and compares resistance patterns of *N.gonorrhoeae* reported from other SEAR countries.



**Bangladesh**

High percentage of resistance was reported to ciprofloxacin (87%). The national policy is to use ciprofloxacin for management. The laboratory also reported reduced susceptibility to ceftriaxone and azithromycin in 1.8% and 3.7% of isolates respectively. Resistance to penicillin and tetracycline continues to be a problem.

**Sri Lanka**

Resistance to ciprofloxacin was 10.3% in 1996 and after withdrawal of the antibiotic, reported resistance was 8.2%. Resistance to penicillin continues to be a problem. No resistance was reported for ceftriaxone and spectinomycin. Resistance to cefuroxime was seen in 0.5% strains.

## **Nepal**

The report was based on only nine strains. Only one isolate was resistant to ciprofloxacin. No resistance was reported to ceftriaxone and spectinomycin.

### ***Constraints being faced by GASP***

#### **Preservation facilities**

Most of the laboratories found it difficult to maintain the control strains and the isolates, since facilities of lyophilization was not available even in the Reference Laboratory.

#### **Insufficient sample size**

The centre at Kathmandu, Nepal was testing very few samples and the report was based on only nine culture positive cases. Hence this centre should work in close collaboration with the clinicians to get more specimens. The centres at Hyderabad and Chennai were culturing only smear-negative or treatment failure cases and hence their data may be biased. All the centres felt that there was dearth of clinical material. More samples should be received to produce reliable data and this can only be achieved through adequate support from the clinicians.

#### **Awareness amongst STI physicians**

With the emergence of resistance to ciprofloxacin, it was felt that the clinicians should be made aware of the need of culturing all patients of gonorrhoea even though the management could be based on the basis of syndromic approach or with minimum laboratory support i.e. smear examination. The importance of surveillance of antimicrobial susceptibility should be stressed to the clinicians.

#### **Alarming ciprofloxacin resistance**

As resistance to ciprofloxacin was being reported from all the laboratories, it was also felt that the national and WHO guidelines for management of gonorrhoea by syndromic approach should be modified accordingly.

### **New antimicrobial resistance**

Some of the laboratories reported resistance to ceftriaxone. It was felt that before documenting any new antimicrobial resistance the strains should be sent to the Reference Laboratory for confirmation.

### **Change in testing of resistance pattern of antimicrobials in focal point laboratories**

With the emergence of alarming resistance to ciprofloxacin and reports of reduced susceptibility to ceftriaxone, alternative antibiotics like azithromycin and cefuroxime need to be tested. There are no guidelines for interpreting sensitivity to azithromycin. However, NCCLS guidelines for reporting results for cefuroxime are available.

The centres also felt that as resistance to penicillin and tetracycline continues to be reported, these drugs could be omitted for routine testing and replaced by alternatives that can be used.

### **Difficulties in testing methods**

Some of the laboratories felt that CDS method was not user friendly for the following reasons:

- Difficult to procure low potency disc.
- Not internationally accepted for publications.
- More chances of error while reporting as zone sizes are small compared to NCCLS where zone sizes are larger.

### **Strengthening of Reference Laboratory**

It was felt that the Reference Laboratory at New Delhi should be strengthened for effective coordination with other laboratories.

## **2.6 External Quality Assessment Programme (EQA)**

### **Supply of materials**

For EQA purpose, immediately after the meeting, each participant was supplied with a kit containing the following materials:

- **WHO Reference strains and QA strains:** The strains were supplied in glycerol broth (in dry ice) and on chocolate agar slopes and plates.
- **Culture Media:** 100 gm each of columbia and GC agar base, 2 gms of saponin, one vial of VCNT supplement (in dry ice).
- **Antibiotics discs:** Low conc. antibiotic discs, 10 each of penicillin (0.5 µg), nalidixic acid (30 µg), ceftriaxone (0.5 µg), ciprofloxacin (1 µg), tetracycline (10 µg) and spectinomycin (100µg).

WHO SOP on GASP Techniques was supplied to all.

Proformae for participation under the programme were discussed in detail.

## 2.7 Recommendations

### ***(1) Involvement of STI physicians***

Clinicians should be involved in this programme, as an effective surveillance programme will need more numbers of samples for proper interpretation. The STD physicians should be made aware of the increased resistance of this organism and need for antimicrobial surveillance, by inviting them to future meetings.

### ***(2) Dissemination of information***

The information regarding resistance pattern of *N.gonorrhoeae* from different focal point laboratories should be disseminated through the GASP Newsletter. The Newsletter is important for education of the doctors as well as information of national and international health planners.

### ***(3) Need for review of national treatment guidelines***

Management guidelines for gonorrhoea should be revised urgently, as a high percent resistance to ciprofloxacin has now been reported. For this, Dr Krishna Ray, Co-coordinator, WHO/SEAR GASP should send a concise report of resistance patterns to WHO as well as to NACO.

### ***(4) Provision of contingency funds for focal point laboratories***

Contingency funds should be made available to focal point laboratories to enable them to send the strains to the Reference Laboratories as well as cover small expenditures.

**(5) Availability of low potency antibiotic discs**

If low potency discs are not available, the surveillance programme should not be stopped and laboratories should continue with NCCLS method. However, this problem should be addressed by the coordinator to IRRL .

**(6) Strengthening of Regional Reference Laboratory**

Request for installation of  $-70^{\circ}\text{C}$  deep freezer and supply of CO<sub>2</sub> incubator and lyophilizer to Regional Reference Laboratory should be made to WHO.

**Issues to be addressed to Inter-regional Reference Laboratory**

- Availability of low potency disc
- Interpretation criteria for testing azithromycin
- Reintroduction of ciprofloxacin for clinical management if resistance to ciprofloxacin *in vitro* is seen to decline as seen in Sri Lanka

It was decided to have the next Consultative meeting at Bangladesh.

## Annex 1

### LIST OF PARTICIPANTS

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## Annex 2

### PROGRAMME

#### **19 December 2001**

0900-0930 hrs	Registration	
0930-1000 hrs	Inauguration	
1030-1100 hrs	WHO Perspective on GASP	Dr Rajesh Bhatia
1100-1130 hrs	Antimicrobial resistance of <i>N. gonorrhoeae</i> in SEAR countries	Dr Krishna Ray
1130-1300 hrs	Presentation of reports from <b>Nepal, Bangladesh and Sri Lanka</b>	
1400-1530 hrs	Presentation of reports from India <b>(Calcutta, Chennai, Nagpur, Hyderabad, Pune and Delhi)</b>	
1545-1700 hrs	Presentation of reports (Contd.)	

#### **20 December 2001**

0930-1000 hrs	External Quality Assessment in GASP Techniques	Dr Krishna Ray
1000-1100 hrs	Demonstration on Preparation of Media, Reagents & Identification of Isolates	Dr Manju Bala Mrs L Peter
	– Antimicrobial Susceptibility Testing Disc Diffusion (CDS technique)	
1115-1330 hrs	'Hands on' training on above techniques	Dr Manju Bala Mrs L Peter Mrs Renu, Seema
1430-1700 hrs	– Antimicrobial Susceptibility Testing Agar dilution technique & E-test	Dr Manju Bala Mrs L Peter
	– Preservation of Isolates	Dr Krishna Ray
	– Internal and External Quality Assessment	Dr Manju Bala

**21 December 2001**

0930-1030 hrs	Laboratory- Results of tests	
1030-1100 hrs	Importance of External Quality Assessment in Microbiology	Dr S. Kumari
1115-1215 hrs	Discussion regarding <ul style="list-style-type: none"><li>- Networking in SEAR Transmission of data and QA-consensus</li><li>- Improvement in Laboratory</li><li>- Interface with clinicians</li><li>- Problems faced by different centres</li></ul>	Dr S Kumari
1400-1430 hrs	Valedictory function	Dr S Kumari