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# Monitoring of Antimicrobial Resistance

*Report of an Intercountry Workshop  
Vellore, Tamil Nadu, India, 14-17 October 2003*

WHO Project: ICP BCT 001



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# 1. INTRODUCTION

Antimicrobial resistance has emerged as a major problem across the world. Indiscriminate and irrational use of antimicrobial agents is primarily responsible for emergence and spread of resistance in almost all the micro-organisms. This problem has assumed greater magnitude in developing countries because of preponderance of infections and wide misuse, overuse or abuse of antimicrobial agents. Fragmented data available from the countries of SEA Region indicate the gravity of the situation. Organisms such as *Salmonella typhi* and *Neisseria gonorrhoeae* that were considered universally sensitive to chloramphenicol and penicillin respectively do not now respond to these drugs, since more than 80% of isolates of these species are resistant to the respective drug of choice. Multidrug resistant *Klebsiella*, *Proteus*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Acinetobacter* are responsible for an overwhelming number of hospital-associated infections. Data from India and Sri Lanka show the occurrence of 50-90% of resistance to antimicrobial agents commonly used against these microorganisms. Resistant organisms require treatment with toxic and expensive drugs and their irrational use further gives rise to resistant strains.

Resistance in micro-organisms has outpaced the development of newer antimicrobial agents. Concerns have already been expressed in many quarters that the world may soon be heading towards a post-antibiotic era wherein none of the available antimicrobial agents shall be effective against commonly encountered microbes. This will lead to tremendous mortality and morbidity, taking us back to the pre-antibiotic era. Rational use of antimicrobial agents is a globally recognized essential step in containing the spread of resistance. This warrants collection of accurate data on resistance on a continuous basis.

The use of reliable laboratory techniques and real time sharing of analysed data with the user can help in monitoring resistance. At present data is being shared with users and its quality assessed only in Thailand. Other countries in the SEA Region need to set up a mechanism to achieve the same.

WHO developed a training curriculum encompassing these two methods a few years back and used it in various Member Countries. The purpose of the training was to generate quality data for development of rational policies for antimicrobial usage which is the main objective of the

containment strategy. It was felt that the impact of training be reviewed, a network of laboratories forged to share data and a mechanism for assessing the laboratory results discussed to ensure that both clinicians and public health experts had access to reliable data to develop realistic policies for the use of antimicrobial agents. Accordingly, an intercountry training workshop was organized at Christian Medical College and Hospitals, Vellore, Tamil Nadu, India from 14 to 17 October, 2003. The workshop was attended by 17 participants from all the Member Countries of South-East Asia Region except Bhutan, DPR Korea, Myanmar and Timor-Leste. Experts from India, Thailand and the WHO Regional Office facilitated the workshop. See Annexes 1 and 2 for list of participants and the programme of work.

## **2. OBJECTIVES**

The objectives of the workshop were as follows:

- (1) To review and exchange country experiences and status of antimicrobial resistance monitoring (ARM) in selected countries of SEA Region;
- (2) To orient the participants about various key elements of a quality system in antimicrobial susceptibility testing and data (AST) analysis to improve the quality of ARM;
- (3) To develop a national mechanism for external quality assessment scheme for ARM, and
- (4) To develop institution-specific plans of action on integrating quality laboratory- based data in the development of policies for rational use of antimicrobial agents.

## **3. INAUGURAL SESSION**

The workshop was inaugurated by Dr George Chandy, Director, Christian Medical College and Hospitals, Vellore. He emphasized the importance of antimicrobial resistance and also described the role played by his institution in mitigating the misery of thousands of people who came to this hospital from far-flung areas for management of various illnesses including those due to microorganisms. He outlined the community-based health oriented programmes of the institutes. Earlier, the participants were welcomed by Dr Jai Prakash Muliyaali, Principal of the Christian Medical College and Professor MK Lalitha, Department of Microbiology, who were the local organizers. Dr Rajesh Bhatia, STP/BCT, WHO/SEARO presented the

objectives and expected outcome of the workshop. He also elaborated upon the role of WHO in advocating strengthening of laboratories in antimicrobial resistance monitoring and development of policies for the rational use of antimicrobial agents to improve the quality of health care.

## 4. PROCEEDINGS

### 4.1 Status of Antimicrobial Resistance and its Monitoring

Dr Thomas Kurien, CMC gave an overview of the global problem of resistance in microorganisms notably *Staphylococcus aureus*, enterococci, various gram negative enteric bacteria, *Salmonella typhi*, gonococci, pneumococci and *Haemophilus influenzae*. Emergence of multi-drug resistant bacteria has been globally accepted to be associated with increased mortality, morbidity and cost of treatment. Methicillin resistant *S.aureus* (MRSA) were first described in 1961 and currently in many Asian countries 70-80% of isolates of *S.aureus* are MRSA. Vancomycin and teicoplanin are the costly alternatives for infections due to MRSA.

In 2002, 24 cases of infection due to vancomycin-resistant staphylococci have been reported from 11 countries of the world. Till early 1990, most enterococci were sensitive to aminoglycosides and ampicillin, whereas now 20-30% of the isolates are resistant to these agents. In countries like USA, this level has grown to more than 40%, compelling the use of vancomycin and other costlier antimicrobial agents against this common bacterium. As many as 40% of isolates of *Klebsiella pneumoniae* in Latin American countries and 20-30% in Europe are extended spectrum beta lactamase producers and resistant to multiple drugs, mandating the use of imipenem in many of the tertiary care health facilities.

Dr Rajesh Bhatia, STP-BCT described the burgeoning problem of antimicrobial resistance with special reference to developing countries. The problems associated with discovery of new drugs, utilization of disease control tools other than antimicrobial agents and various medical, social, behavioural and economic reasons for emergence and spread of antimicrobial resistance were discussed by him. He also stressed upon the importance of rational use of currently available antimicrobial agents to prolong their utilization, for which policies at the hospital level need to be developed. The microbiologists have to play a critical role in generation of reliable data for resistance by using standardized techniques. WHO has recommended the modified Kirby Baur method which has been

standardized by National Committee on Clinical Laboratory Services (NCCLS) of USA. WHO has also developed a computer software (WHONET) which is very user-friendly, menu-driven and can be used for data storage, retrieval and analysis. The software is freely available and can also be downloaded from the WHO website.

The problem of antimicrobial resistance is common to all the countries of the SEA Region. Though hospital infection control committees have been constituted in many hospitals, policies for rational use of antimicrobials and Committees for Therapeutic Guidance are in existence in very few institutions. Many laboratories use WHO-recommended NCCLS method with varying degrees of functionality of quality system, but the data rarely utilized for understanding of trends in resistance. WHONET is being utilized extensively in Thailand and in selected institutions in other Member Countries.

## **4.2 Orientation on NCCLS Method of AST and WHONET Software**

Prof MK Lalitha, Department of Microbiology, described the NCCLS method of antimicrobial susceptibility testing (AST) and discussed the advantage of this method over various other currently available methods. She, along with her faculty members, demonstrated the disc diffusion, dilution and E-test methodologies to all the participants. The details and common variations that may occur in the conduct of this AST were discussed in detail so that the same could be controlled and quality data can be generated by the microbiology laboratories.

Dr Rajesh Bhatia demonstrated the application of WHONET software in antimicrobial resistance monitoring. Various types of analyses that could be undertaken with this programme, the versatility of the software in importing and exporting data to different computer databases and its potential in real-time analysis of data as well as generation of reports were demonstrated. A computer CD with WHONET software was provided to the participants to enable them to use it in their respective institutions.

## **4.3 Quality System in AST**

An overview of quality, quality assurance and quality system was provided by Dr Rajesh Bhatia, WHO/SEARO, New Delhi. Quality system has five key elements viz organization and management, documentation, standards, training and assessment. The assessment can be continuous and concurrent

(monitoring) or periodic and retrospective (evaluation). It can be undertaken through man (audit) or by sending material (EQAS and internal quality assessment scheme). Accreditation is a tool that recognizes the existence of a quality system in a laboratory. The application of a quality system in improving the quality of AST was emphasized and its various components discussed. The importance of International Standards Organization (ISO) in disseminating international standards to promote quality was highlighted. The objective of a quality system in ARM is to continuously generate reliable data on the basis of accurate and precise testing of the clinical and other materials.

#### **4.4 National External Quality Assessment Scheme for ARM**

Dr Surang Dejsirilert, Head of National Centre for Antimicrobial Resistance Monitoring, Thailand described the objectives, benefits and the process of establishment of a national external quality assessment scheme (EQAS) for AST. She also shared the experiences she has with EQAS in Thailand in which a large number of laboratories are participating. EQAS require characterization and distribution of strains of known but undisclosed antibiograms by the organizer of EQAS to the participating laboratories, which in turn perform AST and submit the results to the organizers within a defined period. An inter-laboratory comparison is established and feed-back given to participants. Those who do not perform as per the expected standards are encouraged to identify the areas which require strengthening and initiate corrective actions for which technical support may be provided by the organizer of EQAS.

#### **4.5 Development of Hospital-based Antimicrobial Policy**

Prof OC Abraham, Department of Medicine, CMC provided a briefing about the genesis of guidelines for rational use of antimicrobial agents developed and used in CMC. The approach adopted was educative and involved top management as well as experts from various specialties. The selection of antibiotics was based upon the local conditions, resources and antimicrobial susceptibility pattern. The members of the team consulted their colleagues in their respective departments to have wider consensus before the finalization of guidelines. The guidelines were launched with a CME for all the users to orient them on the rational use of antimicrobial drugs. Since the basis of guidelines is dynamic, continuous consultation is planned to review and revise them.



#### **4.6 Development of Institution-specific Plan of Action for Formulating Policy for Rational Use of Antimicrobial Agents**

Dr Rajesh Bhatia briefed the participants on the need for planning and the method of development of an action plan by identifying various activities needed to achieve the specific objectives. Various parameters that need to be considered and included in the action plan were: brief description of the activity; time-frame; type of activity; person designated to undertake the same, and the resources required to accomplish the activity and supervision of the whole process. The participants developed institution-specific action plans; two of these were presented and discussed in the plenary session.

Various issues that need to be considered by the participants in implementation of their respective Plans of Action were thoroughly discussed. The technical and managerial problems raised by the participants were discussed and various solutions suggested. Extensive discussions led to the formulation of recommendations that are listed below:

### **5. RECOMMENDATIONS**

#### **5.1 To Member Countries**

- (1) The knowledge and experience gained from the workshop in improving infrastructure and skills in antimicrobial resistance monitoring should be utilized gainfully in developing policies for rational use of antimicrobial agents.
- (2) All laboratories should strive to implement an efficient quality system so that antimicrobial resistance monitoring is reliable and matches the needs of the users.
- (3) Christian Medical College, Vellore and National Centre for Antimicrobial Resistance Monitoring, Ministry of Public Health, Nonthaburi, Thailand may be approached for any technical support and trouble shooting in establishing quality in ARM.

#### **5.2 To WHO**

WHO should continue to provide technical support to all Member Countries in developing and strengthening infrastructure and skills in antimicrobial resistance monitoring.

## Annex 1

### LIST OF PARTICIPANTS

#### Bangladesh

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**Annex 2**  
**PROGRAMME**

**Day 1: Tuesday, 14 October 2003**

- 09.00 – 09.30 hrs      Registration
- 09.30 – 10.00 hrs      Opening ceremony  
Welcome address  
Objectives and mechanics of the meeting  
Special addresses – other dignitaries
- 10.30 – 11.00 hrs      Introduction of participants and their expectations from workshop
- 11.00 – 12.30 hrs      **Introductory lectures**  
Magnitude of resistance: Dr Thomas Kurien  
WHO strategy for containment of resistance:  
Dr Rajesh Bhatia  
Principles and Practice of Quality Assurance:  
Dr Jai Prakash Muliyl
- 13.30 – 14.30 hrs      NCCLS methodology: Recent changes: Dr Lalitha
- 15.00 – 15.30 hrs      Quality assurance for ARM-Thailand experience: Dr Surang
- 15.30 – 16.30 hrs      Country presentations

**Day 2: Wednesday, 15 October 2003**

- 08.30 – 09.30 hrs      AST/Other recent methods vis a vis NCCLS (Lecture):  
Dr Lalitha
- 09.30 – 10.15 hrs      Quality system-an introduction: Dr Rajesh Bhatia
- 10.15 – 12.30 hrs      Demonstration of lab techniques : Dr Lalitha
- 13.30 – 16.30 hrs      Discussion on proper application of NCCLS  
Availability of standard strains: Dr Lalitha

**Day 3: Thursday, 16 October 2003**

- 08.30 – 10.00 hrs      Steps in development of policy for rational use of  
antimicrobial agents: Dr Lalitha
- 10.30 – 11.30 hrs      Internal quality assessment scheme: Local facilitator

- 11.30 – 12.30 hrs      External quality assessment scheme  
Mechanism  
Role of organizer  
Role of participants  
Role of National Programme manager: Dr Surang
- 14.00 – 16.30 hrs      WHONET5: Application  
Utility  
Sharing of data with other labs  
Hands on practice: Dr Rajesh Bhatia

**Day 4: Friday, 17 October 2003**

- 08.30 – 10.00 hrs      Networking of labs  
At national level  
At International level: Dr Lalitha
- 10.30 – 12.30 hrs      How to develop an action plan: Dr Rajesh Bhatia
- 13.30 – 16.30 hrs      Presentation of action plans  
Recommendations  
Valedictory