APEC Project HWG 05/2010A

Produced by
Asia Pacific Foundation for Infectious Diseases
50 Irwon-dong, Gangnam-gu, Seoul 135-710, Korea

For
Asia Pacific Economic Cooperation Secretariat
35 Heng Mui Keng Terrace
Singapore 119616
Tel: (65) 68919 600
Fax: (65) 68919 690
Email: info@apec.org
Website: www.apec.org

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2nd APEC Expert Forum - International initiatives to control antimicrobial resistance in the Asia-Pacific region

October 15, 2011

Asia-Pacific
Economic Cooperation

2nd APEC Expert Forum

International initiatives to control antimicrobial resistance in the Asia-Pacific region

APEC Health Working Group
October 15, 2011

KOREA CENTERS FOR DISEASE CONTROL & PREVENTION · HEALTHIER KOREA ·

APFID
ASIA PACIFIC FOUNDATION FOR INFECTIOUS DISEASES

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Asia-Pacific
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2nd APEC Expert Forum

International initiatives to control antimicrobial resistance in the Asia-Pacific region

October 15, 2011 Seoul, Korea

APEC Health Working Group
October 15, 2011

Contents

Welcome remarks

Good morning, ladies and gentlemen !

As Director of Korea Centers for Disease Control and Prevention, it is my great pleasure to invite experts on infectious diseases and antimicrobial resistance from Asian countries to the 2nd APEC Expert Forum on future strategies to control antimicrobial resistance in Asia.

The theme that WHO designated for this year's World Health Day is antimicrobial resistance and its global spread. As you are well aware, antimicrobial resistance is emerging as a highly serious public health issue across the world, particularly in Asian countries. Given the current situation of antimicrobial resistance in the region, more comprehensive strategies should be prepared urgently.

Korea, like other Asian countries, has also been facing the challenges of antimicrobial resistance in major pathogens. Recognizing this important public health issue, the Korean government and Korea CDC have been organizing and supporting the efforts to reverse the tide of emerging resistance.

We believe that more effective collaborations between academia and public health system as well as between countries are critically required to control and prevent the emergence and spread of resistance in the region.

It is in this context that we find this APEC project relevant and important as it seeks to prepare the future international strategies for control of resistance in the Asia-Pacific region.

I hope that the 2nd APEC Expert Forum puts the focus not only on defining and understanding the antimicrobial resistance problem in the region, but also on creating multi-level, well-coordinated solutions to this complex and urgent problems of resistant pathogens.

Once again, I extend you a warm welcome to Seoul and wish you all a successful forum and an enjoyable stay in Korea.

Thank you very much.

Byung-yool Jun, MD, PhD

Director
Korea Centers for Disease Control and Prevention
Korea

Opening remarks

I would like to welcome all of you to the 2nd APEC Expert Forum to discuss the “International initiatives to control antimicrobial resistance in the Asia-Pacific region”.

As we are well aware, infectious diseases still remain the major threat to public health in the world. Disease burden of infectious diseases is amplified by the emergence and the spread of antimicrobial resistance among major pathogens. Given the global crisis of antimicrobial resistance, particularly in the Asia-Pacific region, international collaboration and comprehensive strategies are critical to control and prevent the problems. To initiate and encourage the international efforts for this purpose, I have proposed an international project entitled "International initiatives to control antimicrobial resistance in the Asia-Pacific region" to APEC in 2011. Goal of this project is to prepare the future strategies to control and prevent antimicrobial resistance in the region. For this project, we had the first Expert Forum on April 5, 2011 in Seoul to discuss the current status of antimicrobial resistance in the Asia-Pacific region.

At the 2nd Expert Forum, we will discuss the future strategies to control antimicrobial resistance in the Asia-Pacific region. All participants will discuss the future plan and strategies for surveillance, effective measures to control antimicrobial resistance and relevant policies and regulations by Asian countries. I am certain we will have a very productive discussion today to prepare future strategies to control antimicrobial resistance in the Asia-Pacific region.

Once again, I would like to express my gratitude to all of you and I wish you an enjoyable stay in Korea.

Thank you very much.

Jae-Hoon Song, MD, PhD

Project Overseer
Chairman, Asia Pacific Foundation for Infectious Diseases (APFID)
Organizer, Asian Network for Surveillance of Resistant Pathogens (ANSORP)
Professor of Medicine, Samsung Medical Center, Sungkyunkwan University
Korea

Future strategies for the control of antimicrobial resistance in the Asia-Pacific region

Registration ····· 08:30 – 09:00

Opening Remarks ····· 09:00 – 09:05

Jae-Hoon Song (Project Overseer, Asia Pacific Foundation for Infectious Diseases, APFID; Samsung Medical Center, Korea)

PART 1 Current issues on antimicrobial resistance in Asia

Introduction of APEC project ····· 09:05 – 09:15

So Hyun Kim (APFID, Korea)

Current issues on antimicrobial resistance in Asia : Summary of the 1st Expert Forum ····· 09:15 – 09:30

Doo Ryeon Chung (Samsung Medical Center; APFID, Korea)

Strategic plan to control and prevent antimicrobial resistance ····· 09:30 – 09:50

Jae-Hoon Song (APFID; Samsung Medical Center, Korea)

Networking Break ····· 09:50 – 10:00

PART 2 Group discussion : preparation of strategic plans for control of antimicrobial resistance ····· 10:00 – 13:00

(Break 11:30 – 11:50)

I. Surveillance group

Chair : Kyungwon Lee (Yonsei University, Korea)

Po-Ren Hsueh (National Chinese Taipei University Hospital, Chinese Taipei)

- **Discussion**
  - Major issues on antimicrobial resistance and antibiotic uses
  - Future plan of national and international surveillance of resistance

II. Future strategy group

Chair : Jae-Hoon Song (APFID, Samsung Medical Center, Korea)

Christopher Lee (Hospital Sungai Buloh, Malaysia)

- **Discussion**
  - Basic scheme of future strategies to control and prevent antimicrobial resistance
  - Appropriate use of antibiotics, hospital infection control and vaccination as future strategies

III. Policy & regulation group

Chair : Jun-Wook Kwon (Korea Centers for Disease Control and Prevention, Korea)

Shu-Hui Tseng (Centers for Disease Control, Department of Health, Chinese Taipei)

- **Discussion**
  - National health systems, policies, and regulations regarding antibiotic use
  - National and international healthcare system to control and prevent resistance

Lunch ····· 13:00 – 14:00

PART 3 Future strategies to control antimicrobial resistance in Asia

Preparation of summary ····· 14:00 – 14:30

Each group

Summary of group discussion

Chair : Jae-Hoon Song (APFID; Samsung Medical Center, Korea)

Surveillance group ····· 14:30 – 15:10
Future strategy group ····· 15:10 – 15:50
Policy & regulation group ····· 15:50 – 16:30

＊ **Each summay presentation will be 30 min followed by questions and comments for 10 min.**

Closing remark ····· 16:30 – 16:40

Jae-Hoon Song (APFID; Samsung Medical Center, Korea)

2nd APEC Expert Forum

Introduction of APEC project :

International initiatives to control antimicrobial resistance in the Asia-Pacific region

Asia-Pacific Economic Cooperation

International initiatives to control antimicrobial resistance in the Asia-Pacific region

Proposing APEC Economy : Republic of Korea
Project overseer : Jae-Hoon Song, MD, PhD (Korea)
Co-sponsoring APEC Economies : Chinese Taipei, Canada

In collaboration with and APFID

Basic facts of the project

Title of the project	International initiatives to control antimicrobial resistance in the Asia-Pacific region
Proposing APEC economy	Republic of Korea
Co-sponsoring APEC economies	Chinese Taipei, Canada
Project overseer	Professor Jae-Hoon Song, MD, PhD (APFID ; Samsung Medical Center, Seoul, Korea)
Organization	Asia Pacific Foundation for Infectious Diseases (APFID) in collaboration with APEC economies, non-APEC stakeholders and ANSORP (Asian Network for Surveillance of Resistant Pathogens)

Background of the project

Current situation of resistance in the AP region

- Asian countries are the epicenter of antimicrobial resistance
  - Highest prevalence rates of resistance in major bacterial pathogens
  - Two- or three-times higher than those in the western part of the world
- Main reasons for resistance in Asia
  - Widespread abuse and misuse of antibiotics
  - Spread of resistant clones
  - Lack of awareness, weak and unorganized policies and regulations
- Comprehensive strategies for control and prevention of antimicrobial resistance are urgently required in the AP region

Objectives of the project

Long-term goal and objectives

❖ Long-term goal of the project

To control and prevent antimicrobial resistance (AMR) in the AP region

❖ Main objectives of the project

- To organize the Strategic Focus Group (SFG) that will plan the future strategies and coordinate the implementation of the plan
- To organize an Expert Forum to discuss and explore solutions to AMR in the region
- To disseminate the information and future strategies to the APEC economies by websites and documents as well as through available meetings and campaigns

Method of the project

How do we perform the project ?

Strategic Focus Group (SFG)

experts on infectious diseases, health science, veterinary medicine, and healthcare officials from APEC economies and external APEC stakeholders

Expert Forum

Future strategies for AMR

Website | **Documents** | **Meetings/Campaign**

Method of the project

Beneficiaries and relevant stakeholders & engagement

Stakeholders		Target audience
Healthcare professionals	▪ SFG ▪ Expert Forum	Physicians
ID experts	**Strategies and information for control of AMR**	Policymakers
Government officials		General public
Non-APEC stakeholders	▪ Website ▪ Documents ▪ Meetings/Campaign	Advocacy group

Method of the project

Timeline of the project

Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec

- Organization of SFG
- ▪ Summary of the 1st Expert Forum
  ▪ Preparation of the 2nd Expert Forum
- 1st APEC Expert Forum — April 5th, 2011, Seoul, Korea
- 2nd APEC Expert Forum — Oct 15th, 2011, Seoul, Korea
- Future strategies report

Progress of the project

Organization of SFG

Strategic Focus Group (SFG)

- Executive Committee
- • Secretariat ; Scientific Affair
  • Secretariat ; Publication, Finance & Logistics

Surveillance group	Future strategy group	Policy & regulation group
Regional sectors - Southeast Asia - Far East Asia (North & Latin America)	Regional sectors - Southeast Asia - Far East Asia (North & Latin America)	Regional sectors - Southeast Asia - Far East Asia (North & Latin America)

Progress of the project

Organization of Strategic Focus Group (SFG)

1st Working Group of SFG — International, multi-sectoral experts from APEC economies

Economy	Name	Hospital
Korea	Dr. Jae-Hoon Song	Samsung Medical Center
Thailand	Dr. Visanu Thamlikitkul	Mahidol University
China	Dr. Hui Wang	Peking University People's Hospital
Chinese Taipei	Dr. Cheng-Hsun Chiu	Chang Gung Memorial Hospital
Hong Kong, China	Dr. Thomas So	Princess Margaret Hospital
Japan	Dr. Hiroshige Mikamo	Aichi Medical University
Malaysia	Dr. Rohani Md Yasin	Institute for Medical Research
Philippines	Dr. Celia Carlos	Research Institute for Tropical Medicine
Singapore	Dr. Li Yang Hsu	National University Hospital
Viet Nam	Dr. Pham Hung Van	University of Medicine and Pharmacy

Progress of the project

1st Expert Forum

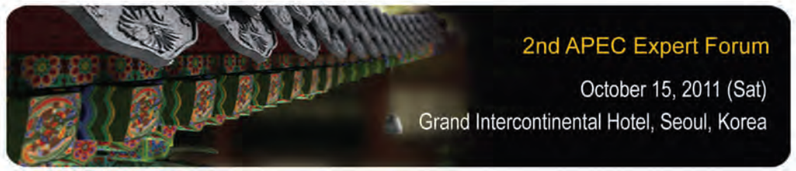
- Date : April 5, 2011 (Tue)
- Venue : COEX Convention Center, Seoul, Korea
- Participants : About 50 experts (11 APEC & 2 non-APEC economies)
  - Experts from 11 APEC economies : China, Hong Kong, China, Indonesia, Japan, Korea, Malaysia, the Philippines, Singapore, Chinese Taipei, Thailand, and Viet Nam
  - Experts from 2 non-APEC economies : India and Sri Lanka


Progress of the project

1st Expert Forum

- Agenda : Current issues on antimicrobial resistance (AMR) in Asia
  - Current situation of AMR in Asian countries
  - Current situation of antimicrobial uses in Asian countries
  - Current regulations and policies related to antibiotics, national health care infrastructure, etc.
  - Panel discussion



- Agenda : Future strategies for the control of antimicrobial resistance in the Asia-Pacific region

- Aims of the 2nd Expert Forum
  - To discuss and envision the future strategies against AMR problems in the AP region
  - To prepare the strategic report on control of AMR in the AP region
  - To discuss plans for implementation of future strategies to control AMR in the AP region

Strategies to control and prevent antimicrobial resistance

Strategies to control and prevent antimicrobial resistance

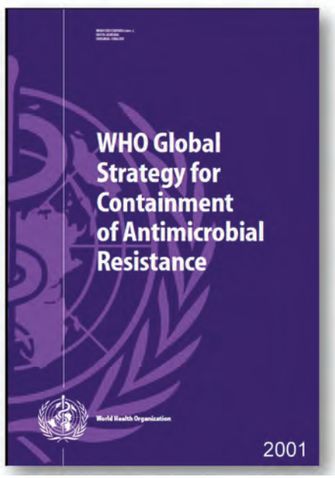
2nd APEC Expert Forum

Jae-Hoon Song, MD, PhD

Division of Infectious Diseases
Samsung Medical Center, Sungkyunkwan University ;
Asia Pacific Foundation for Infectious Diseases
Seoul, Korea

Strategies to control antimicrobial resistance

WHO global strategy



World Health Day, April 7th, 2011

Strategies to control antimicrobial resistance

WHO global strategy

WHO Global Strategy provides a framework of interventions to slow the emergence and reduce the spread of antimicrobial-resistant pathogens

- Reduce the disease burden and spread of infection
- Improve access to appropriate antimicrobials
- Improve use of antimicrobials
- Strengthen health systems and their surveillance capabilities
- Enforce regulations and legislation
- Encourage the development of appropriate new drugs and vaccines

WHO Global strategy for containment of antimicrobial resistance. 2001

Strategies to control antimicrobial resistance

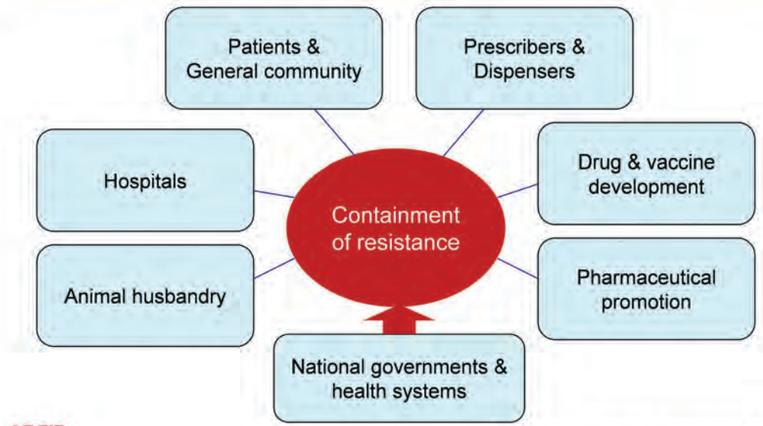
WHO global strategy

- It highlights aspects of the containment of resistance and the need for further research
- It is people-centerd with interventions directed towards the groups of people who are involved in the problem i.e. prescribers, dispensers, veterinarians, consumers, policy-makers, pharmaceutical companies
- It addresses antimicrobial resistance in general (not disease-specific)
- Much of the responsibilities for implementation of the strategy will fall on individual countries
- Prioritization of the implementation of these interventions needs to be customized to national realities
- Containment will require significant strengthening of the health systems

WHO Global strategy for containment of antimicrobial resistance. 2001

Strategies to control antimicrobial resistance

WHO global strategy : general scheme



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WHO Global strategy for containment of antimicrobial resistance. 2001

Strategies to control antimicrobial resistance

WHO global strategy : patients & general community

Education

- Educate patients and general community on the appropriate use of antibiotics
- Educate patients on prevention of infection such as vaccination
- Educate patients on simple measures to reduce transmission of infection such as hand washing
- Encourage appropriate and informed healthcare seeking behavior
- Discourage self-medication of antibiotics

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WHO Global strategy for containment of antimicrobial resistance. 2001

Strategies to control antimicrobial resistance

WHO global strategy : prescribers & dispensers

Education

- Educate all prescribers and dispensers on the appropriate use of antibiotics
- Educate all prescribers on disease prevention and infection control
- Promote student educational programs on diagnosis and management of common infections
- Encourage prescribers and dispensers to educate patients on antibiotic use
- Educate prescribers and dispensers on factors that may influence their prescribing habits such as economic incentives

Strategies to control antimicrobial resistance

WHO global strategy : prescribers & dispensers

Management, guidelines & formularies

- Improve antibiotic use by supervision and support of clinical practice
- Audit prescribing and dispensing practices
- Encourage development and use of treatment guidelines
- Empower formulary managers to limit antibiotic use

Regulation

- Link professional registration requirements for prescribers and dispensers to requirements for training and continuing education

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WHO Global strategy for containment of antimicrobial resistance. 2001

Strategies to control antimicrobial resistance

WHO global strategy : hospitals

Management	▪ Establish infection control programs
	▪ Establish effective hospital therapeutics committee
	▪ Develop and regularly update antimicrobial guidelines
	▪ Monitor antibiotic use
Diagnostic lab	▪ Ensure access to microbiology lab
	▪ Ensure performance and quality assurance of appropriate diagnostic tests
	▪ Ensure the recording of the lab data
Interaction with pharma industry	▪ Control and monitor pharma company promotional activities

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WHO Global strategy for containment of antimicrobial resistance. 2001

Strategies to control antimicrobial resistance

WHO global strategy : national governments & health systems

Advocacy & intersectoral action	▪ **Make the containment of resistance a national priority** - create a national intersectoral task force - allocate resources to promote the implementation of interventions - develop indicators to monitor and evaluate the impact of resistance
Regulations	▪ Establish effective registration scheme for dispensing outlets
	▪ Limit the availability of antibiotics to prescription-only status
	▪ Link presription-only status to regulations regarding the sale, supply, dispensing and promotion of antibiotics
	▪ Ensure that only antibiotics of international standards of quality are granted
	▪ Introduce legal requirements for manufacturers
	▪ Create economic incentives for appropriate use of antibiotics

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WHO Global strategy for containment of antimicrobial resistance. 2001

Strategies to control antimicrobial resistance

WHO global strategy : national governments & health systems

Policies & Guidelines	▪ Establish and maintain national Standard Treatment Guidelines (STGs)
	▪ Establish an Essential Drug List (EDL)
	▪ Enhance immunization coverage and other disease prevention
Education	▪ Maximize the effectiveness of STGs and EDL
	▪ Ensure that prescribers have access to approved prescribing literature
Surveillance of resistance, antibiotic use and disease burden	▪ Designate reference lab to coordinate effective surveillance of resistance
	▪ Adapt and apply WHO model systems of resistance surveillance
	▪ Establish systems for monitoring antibiotic use
	▪ Establish surveillance for key infectious diseases

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WHO Global strategy for containment of antimicrobial resistance. 2001

Strategies to control antimicrobial resistance

WHO global strategy : drug & vaccine development

- Encourage cooperation between industry, government and academic institutions
- Encourage drug development programs
- Provide incentives for industry to invest in R & D of new agents
- Consider fast-track marketing authorization
- Consider using orphan drug scheme
- Make available time-limited exclusivity for new formulations
- Align intellectual property rights to provide suitable patent protection for new drugs and vaccines
- Seek innovative partnerships with pharma industry

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WHO Global strategy for containment of antimicrobial resistance. 2001

Strategies to control antimicrobial resistance

US CDC public health action plan

A PUBLIC HEALTH ACTION PLAN TO COMBAT ANTIMICROBIAL RESISTANCE

Interagency Task Force on Antimicrobial Resistance

Co-Chairs:
Centers for Disease Control and Prevention
Food and Drug Administration
National Institutes of Health

Participating Agencies:
Agency for Healthcare Research and Quality
Centers for Medicare and Medicaid Services
Department of Agriculture
Department of Defense
Department of Veterans Affairs
Environmental Protection Agency
Health Resources and Services Administration
Health and Human Services/ Office of the Assistant Secretary for Preparedness and Response

2011

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Strategies to control antimicrobial resistance

US CDC public health action plan

Focus area	Goals
Surveillance	1. Improve detection, monitoring, and characterization of drug-resistant infections in humans and animals
	2. Better define, characterize, and measure the impact of antimicrobial drug use in humans and animals in the US
Prevention & Control	3. Develop, implement, and evaluate strategies to prevent the emergence, transmission, and persistence of drug-resistant pathogens
	4. Develop, implement, and evaluate strategies to improve antimicrobial use

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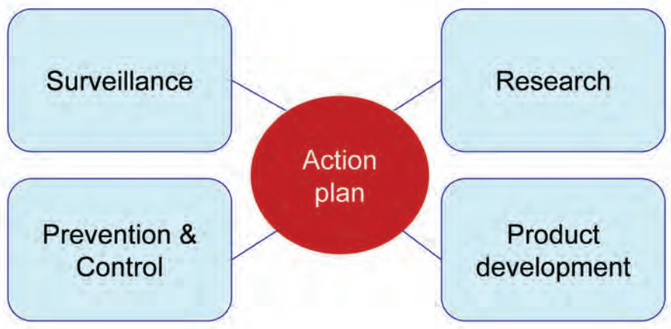
US CDC. A public health action plan to combat antimicrobial resistance. 2011

Strategies to control antimicrobial resistance

US CDC public health action plan : general scheme



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US CDC. A public health action plan to combat antimicrobial resistance. 2011

Strategies to control antimicrobial resistance

US CDC public health action plan

Focus area	Goal
Research	5. Facilitate basic research on antimicrobial resistance
	6. Facilitate the translation of basic research findings into practical application
	7. Facilitate clinical research to improve treatment and prevention
	8. Conduct and support epidemiological studies to identify key drivers of antimicrobial resistance
Product development	9. Provide information on antibacterial drug product development
	10. Consider opportunities foe international harmonization
	11. Encourage development of rapid diagnostic tests and vaccines

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US CDC. A public health action plan to combat antimicrobial resistance. 2011

Strategies to control antimicrobial resistance

Asian strategy : why it should be specific ?

- Asian countries show very unique and serious situation of antimicrobial resistance in most major pathogens
- Antimicrobial agents are very frequently abused or misused and counterfeit drugs are widely used in the Asian region
- Healthcare infrastructure and systems are weak with limited resources in many countries in the region
- Many countries do not have relevant and strong policies or regulations for antibiotic use and prevention of resistance

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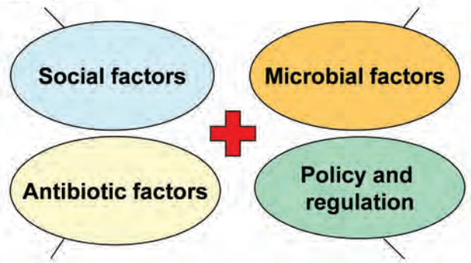
Strategies to control antimicrobial resistance

Asian strategy : what to consider ?

Poverty and inadequate resources
Natural calamities
Human population growth

Epidemic clones
Specific serotypes
Specific resistance genes



Antibiotic abuse/misuse in patients
Agricultural use of antimicrobials
Counterfeit drugs

Poor healthcare infrastructure
Lack of international collaboration

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Antimicrobial uses in Asia

Abuse and misuse in Asian countries

Country	Antibiotic use	Comments
India (2008)	Antibiotic prescription : 82 % (primary and secondary healthcare facilities)	penicillins, sulfonamide, fluoroquinolones
China (2003)	• Antibiotic prescription : 78 % of inpatients • ≥ 2 antibiotics : 55 %	3.8 % : microbiologic investigation
Indonesia (2008)	Antibiotic prescription : 84 % of inpatients (therapeutic : 53 %, prophylactic : 15 % unclear : 32 %)	Appropriate use : 21 %
Turkey (2009)	Self-administration of antibiotics : 19 % for sore throat (59%), fever (46%), cough (40%)	Antibiotics are the most frequently used drug (22 %/ all drugs) in Turkey
Korea (2005)	Prescription rate for URI : 55 %	Primary healthcare clinics
Japan (2009)	Prescription rate for URI : 60 %	3rd cephalosporins (46%), macrolide (27%), fluoroquinolones (16%)

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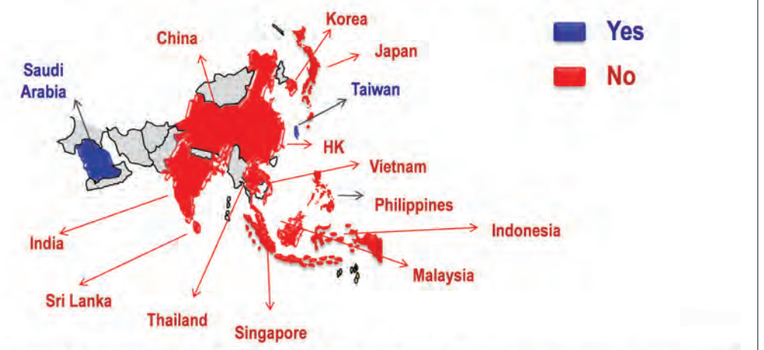
Kumar R et al. J Clin Pharma Thera. 33;625-34, 2008; Hu S et al. J Infect. 46;161-3, 2003;Hadi U et al. Clin Microbiol Infect. 14;698-707, 2008; Ilhan MN et al. Pharmacoepdeimiol Drug Safety. 18;1150-57, 2009; Kim N et al. J Prev Med Public Health. 38;1-8, 2005; Higashi T et al. Intern Med. 48;1369-75, 2009

Antimicrobial uses in Asia

Why are antibiotics abused ? : physician factor

Do general physicians in your country have adequate knowledge on the appropriate use of antimicrobial agents ?



APFID * Based on questionnaire results from ID experts in Asian countries

Song JH et al. Preliminary survey on current status of antimicrobial uses and resistance in Asian countries, APEC project

Antimicrobial uses in Asia

Why are antibiotics abused ? : patient factor

Public's knowledge and attitudes to antibiotic use (Korea, 2010)*

Question	% response		
	Bacterial	Viral	Both
What is an indication for antibiotics ?	20 %	17 %	40 %
What is the cause of common cold ?	8.6 %	53 %	26 %
	Yes	No	
Is an antibiotic effective for common cold ?	51 %	28 %	
Can antibiotics be discontinued if symptoms improve ?	74 %	19 %	
Did you ask doctors to prescribe antibiotics ?	4.6 %	95 %	
Did you self-administer left-over antibiotics ?	28 %	70 %	

* Data from telephone survey with 1,000 persons > 20 years

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Song JH et al. "Evaluation of consumer perception and knowledge on antimicrobial resistance in Korea" supported by Korea FDA (2010)

Antimicrobial uses in Asia

Why are antibiotics abused ? : patient factor

Public's knowledge and attitudes to antibiotic use (Korea, 2010)*

Question	% response			
	Very serious	Serious	Not serious	No problem
How serious is antibiotic resistance in Korea ?	28 %	44 %	12 %	1 %
	Over-prescribing	Overuse by patients	Overuse in food animals	No control in hospitals
What is the main cause of antibiotic resistance in Korea ?	36 %	30 %	12 %	9 %

* Data from telephone survey with 1,000 persons > 20 years

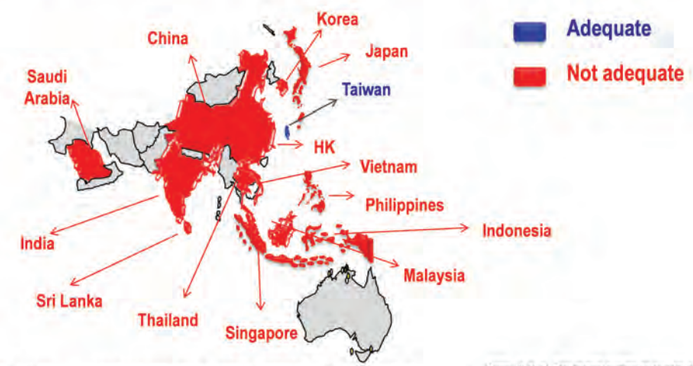
APFID

Song JH et al. "Evaluation of consumer perception and knowledge on antimicrobial resistance in Korea" supported by Korea FDA (2010)

Antimicrobial uses in Asia

Why are antibiotics abused ? : patient factor

Public's knowledge and attitudes to antibiotic use in Asia (2011)*



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* Based on questionnaire results from ID experts in Asian countries

Song JH et al. Preliminary survey on current status of antimicrobial uses and resistance in Asian countries, APEC project

Antimicrobial uses in Asia

Why are antibiotics abused ? : Policy and regulation

Is it possible to purchase antibiotics without prescriptions ?*

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* Based on questionnaire results from ID experts in Asian countries

Song JH et al. Preliminary survey on current status of antimicrobial uses and resistance in Asian countries, APEC project

Antimicrobial uses in Asia

Why are antibiotics abused ? : Policy and regulation

Are you aware that counterfeit antibiotics are used in your country ?*

APFID

* Based on questionnaire results from ID experts in Asian countries

Song JH et al. Preliminary survey on current status of antimicrobial uses and resistance in Asian countries. APEC project

Major factors for resistance in Asia

Counterfeit antibiotics : another form of misuse/abuse

Counterfeit drugs in Asia

Indonesia : 25 % of pharma market

Philippines : 30 % of drug store outlets sell counterfeit drugs as of 2003

Cambodia : 13 % of drugs

China : 8 % of OTC drugs

India : 20 % of total drug market

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IMPACT, International Medical Products Anti-counterfeiting Taskforce, WHO, 2006

Major factors for resistance in Asia

Agricultural use of antibiotics in Asia

Quinolones licensed for use in food animals

Region	Livestock	Poultry	Pet animals	Fish
USA	None	enrofloxacin, sarafloxacin	enrofloxacin difloxacin orbifloxacin	None
Europe	enrofloxacin flumequine marbofloxacin danofloxacin	enrofloxacin, flumequine difloxacin,oxolinic acid	enrofloxacin marbofloxacin difloxacin	sarafloxacin
Asia	enrofloxacin danofloxacin **ciprofloxacin**	enrofloxacin, danofloxacin **ciprofloxacin, ofloxacin** **norfloxacin**, flumequine oxolinic acid	enrofloxacin	oxolinic acid enrofloxacin flumequine

China : total use of quinolones - human 1,350 tons, food animals 470 tons

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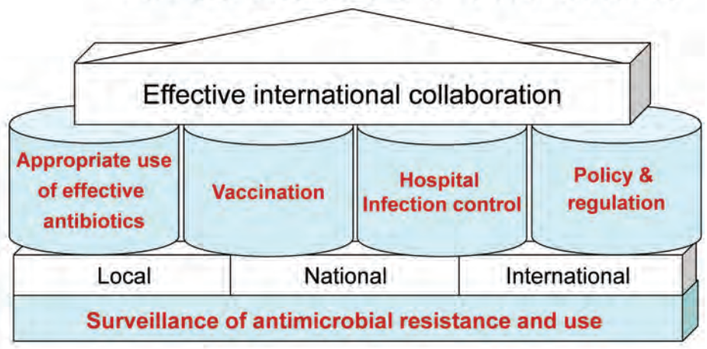
WHO. Use of quinolones in food animals and potential impact on human health. Report of a WHO meeting, 1998

Strategy for control of antimicrobial resistance

Asian strategy : tentative scheme



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Strategy for control of antimicrobial resistance

Asian strategy : focused discussion

Strategy	Major topics	Breakout group
Surveillance	▪ National surveillance of resistance ▪ International surveillance of resistance ▪ National monitoring of antibiotic use	Surveillance
Appropriate use of effective antibiotics	▪ Campaign for appropriate use of antibiotics ▪ Antibiotic stewardship ▪ Appropriate use of antibiotics in food animals ▪ Development of novel antibiotics	Future strategy
Hospital infection control	▪ Infection control measures to control resistance	Future strategy
Vaccination	▪ Vaccination as a tool for control of resistance	Future strategy
Policy & regulations	▪ Control of antibiotic prescribing & dispensing ▪ Regulation of counterfeit drugs ▪ Regulation of antibiotics in food animals	Policy & regulation

ANSORP
ASIAN NETWORK FOR SURVEILLANCE OF RESISTANT PATHOGENS

icare
INITIATIVES TO CONTROL ANTIMICROBIAL RESISTANCE

APFID
ASIA PACIFIC FOUNDATION FOR INFECTIOUS DISEASES

ISAAR
International Symposium on Antimicrobial Agents and Resistance

ABB
Asian Bacterial Bank

Committed to the future of health in Asia

Draft of strategic action plan to control antimicrobial resistance in the Asia-Pacific region

Based on the APEC Project

* This document is a tentative draft of the strategic action plan which will be revised and modified based on the 2nd Expert Forum on October 15th, 2011, in Seoul, Korea

Executive Summary

This “Strategic action plan to control antimicrobial resistance in the Asia-Pacific region” was developed by the Strategic Focus Group, which consists of the experts on infectious diseases, health science, veterinary medicine, healthcare officials from APEC economies, and external APEC stakeholders. This report is based on the First and Second APEC Expert Forum which were held for the APEC project entitled ‘International initiatives to control antimicrobial resistance (AMR) in the Asia-Pacific region” in 2011. APEC Expert Forum was organized by the Asia Pacific Foundation for Infectious Diseases (APFID) and the Korea Centers for Disease Control and Prevention (KCDC). This strategic plan is the first official document for control and prevention of AMR in the Asian region

The Strategic Action Plan consists of five major components that are aligned to achieve effective control and prevention of AMR in the Asian region ; surveillance of AMR and antibiotic use, appropriate use of effective antibiotics, hospital infection control, vaccination, and policy and regulation. The Strategic Action Plan can provide the general concept and the frame of the strategies to address the growing threat of AMR in the region. Since current problems of resistance and antibiotic uses, healthcare system and regulations vary by country, the strategic plan will be implemented depending on the local situation and resources in a stepwise fashion.

Surveillance of antimicrobial resistance and antibiotic use

- The national surveillance system(s) of AMR should be urgently established in every country that can represent the national status of AMR.
- The microbiology laboratory procedures, data collection, and data reporting should be standardized.
- The international surveillance system(s) in the Asia-Pacific region collecting the data from national surveillance networks should be established.
- The Asian Network for Surveillance of Resistant Pathogens (ANSORP) could be an example of multinational network system for surveillance of antimicrobial resistance in the Asian region.
- The national surveillance system(s) for antimicrobial consumption both in patients and in animal husbandry should be established in each country using the standardized methods.

Appropriate use of antibiotics

- Appropriate use of effective antibiotics is a key factor to prevent the further emergence of AMR in major pathogens, which includes the appropriate use of current antibiotics as well as the development of novel agents.
- Appropriate use of current antibiotics can be encouraged by campaigns for both general public and healthcare professionals, which could be implemented as a national program.
- “I Care” (Initiatives to Control Antimicrobial REsistance) campaign prepared by the Asia Pacific Foundation for Infectious Diseases (APFID) can be utilized as an international campaign in the Asia-Pacific region.
- Education of healthcare professionals should be continuously implemented. All countries are encouraged to implement antimicrobial stewardship program in the healthcare setting.
- Antimicrobial use in food animals should be monitored and restricted by the regulations and guidelines.
- Regulations and public policy actions for appropriate antibiotic use are urgently needed in some countries.
- Development of novel antibiotics is very critical to overcome the problems of antimicrobial resistance.

Hospital infection control

- Hospital infection control is a basic procedure to prevent the spread of resistant clones in the hospital as well as in the community.
- Stringent and rigorous infection control procedures should be implemented in all hospitals.
- The microbiology laboratory should provide high quality diagnostic testing to correctly identify nosocomial infections and accurate antimicrobial susceptibility testing.

Vaccination

- Effective vaccination can reduce the prevalence of antimicrobial resistance in major bacterial pathogens.
- National and international efforts should be exerted to increase the awareness of the importance of vaccination both in general public and in healthcare professionals.

Policy and Regulation

- Appropriate and relevant governmental regulations, commitment and support are absolutely necessary for successful control of antimicrobial resistance in each country.
- Relevant policies and regulations to control antibiotic use and to prevent antibiotic abuse or counterfeit drugs are critically required in many Asian countries.
- Any kind of antibiotics should be purchased based on doctor’s prescription by law or regulations in all countries.
- Monitoring and regulation to prevent the production and circulation of counterfeit drugs should be implemented in all countries.
- Antibiotic uses in the animal husbandry should be monitored and regulated by appropriate regulations.

I. Background

1. Global crisis of antimicrobial resistance

Infectious diseases are serious healthcare threats despite the remarkable advances in modern medicine. Recent data from the World Health Organization (WHO) showed that infectious diseases are the second most common cause of death worldwide (a total of 24% of deaths worldwide is caused by infectious diseases) (WHO, 2008; http://www.who.int/healthinfo/ global_burden_diseases/DthInc_ 2008.xls). However, treatment of infectious diseases is becoming more difficult due to widespread emergence of antimicrobial resistance in major pathogens, which makes antimicrobials ineffective, resulting in treatment failure, prolonged illness, disability, greater risk of death and economic loss. In addition, treatment failures caused by antimicrobial resistance lead to longer periods of infectivity, which increase the numbers of infected people moving in the community and thus expose the general population to the risk of contracting a resistant strain of infection. Antimicrobial resistance is a more serious healthcare threat than any single infectious diseases because it encompasses all types of infections. Furthermore, due to slowed development of new antimicrobials internationally, very few antimicrobials are left to treat infections caused by resistant pathogens.

Antimicribial resistance has become one of the most serious concerns in public health worldwide, especially in the Asian region that showed the highest prevalence of antimicrobial resistance in major pathogens. Futhermore, antimicrobial resistance is not a local problem but an international and global issue because antimicrobial resistance can spread between different countries or continents. The massive increases in trade and human mobility brought about by globalization have enabled the rapid spread of infectious agents, including those that are antimicrobial resistant. While

richer countries, to a large extent, are still able to rely on the latest antimicrobials to treat resistant infections, access to these life-saving drugs is often limited or totally absent in many parts of the world.

Recent outbreak and international spread of antimicrobial resistant bacteria, New Delhi Metallo-beta-lactamase-1 (NDM-1) producing *Escherichia coli*, from India to many countries including the UK, Sweden, Austria, Belgium, France, Netherlands, Germany, the USA, Canada, Japan, China, Malaysia, Australia, and Korea could be one of the best examples of transmission of antimicrobial resistance between countries, showing critical impact of antimicrobial resistance on economy and trade in addition to impact on public health. Since the global spread of this new "superbug" was partly due to medical tourism, economic activities related to medical tourism and international travel were seriously affected.

Community pathogens have acquired antimicrobial resistance including penicillin- or macrolide-resistant *Streptococcus pneumoniae*, methicillin-resistant *Staphylococcus aureus* (MRSA), and multidrug-resistant enteric pathogens. Not only these community-acquired infections but also nosocomial pathogens such as MRSA or glycopeptide-resistant *S. aureus* (vancomycin-intermediate or resistant *S. aureus*, VISA or VRSA, respectively), glycopeptide-resistant enterococci (vancomycin-resistant enterococci, VRE), extended-spectrum beta-lactamase (ESBL)-producing enterobacteriaceae, and multidrug-resistant non-fermenters are also being recognized with increasing frequency around the world. The global emergence and rapid spread of antimicrobial resistance in these community and nosocomial pathogens have become serious clinical concerns.

2. Clinical and economic impact of antimicrobial resistance

Antimicrobial resistance is not just a healthcare issue, but a very serious threat to international economy and trade. The economic impact of antimicrobial resistance is devastating with a huge amount of additional healthcare costs for treatment of antimicrobial-resistant infections. The annual health care costs associated with the treatment of antimicrobial resistant infections in the USA were estimated to be approximately US$ 4-5 billion (American Society for Microbiology). Antimicrobial resistance could also significantly affect the international trade. The global trade of food and other agricultural commodities is affected by the regulations to prevent import of the livestock products with antibiotic residues which are due to the use of antibiotics in food animals as growth promoters.

Given the enormous clinical and economic impact of antimicrobial resistance, WHO has identified antimicrobial resistance as one of the greatest threats to human health and the theme of WHO's World Health Day 2011 is antimicrobial resistance with a slogan entitled "Antimicrobial resistance: no action today, no cure tomorrow" (http://www.who.int/world-health-day/2011/en/index.html). Under the theme "Combat drug resistance", WHO has mentioned that "Antimicrobial resistance and its global spread, threatens the continued effectiveness of many medicines used today to treat the sick, while at the same time it risks jeopardizing important advances being made against major infectious killers." and has called for urgent and concerted actions by the governments, health professionals, industry, civil society, and patients to slow down the spread of drug resistance and limit its impact today to preserve medical advances for future generations.

3. Antibiotic use as a driving force

Antibiotics are very important weapons against bacterial infections. However, antimicrobial resistance became a global health problem since the 1990s. Particularly, Asian countries are the epicenter of antimicrobial resistance with the highest prevalence rates of resistance in major bacterial pathogens, which are two- or three-times higher than those in the western part of the world. Although the spread of resistant clones is one of main reasons, widespread abuse and misuse of antibiotics is another important reason for the emergence of resistance in the Asia-Pacific region.

According to many published papers, antibiotics are frequently used for viral infections such as respiratory tract infections although antibiotics are not effective for viral infections (Gonzales R, 1997; Hulsher MEJL, 2010). According to a study in China, antibiotics were prescribed in 78% of inpatients and more than 2 antibiotics were prescribed in 55% of patients (Hu S, 2003). Only 3.8% of cases were treated after microbiologic investigation. In a study performed in Indonesia, antibiotics were prescribed in 84% of inpatients and only antibiotics were used appropriately only in 21% of cases (Hadi U, 2008). According to a study in Korea, prescription rate for upper respiratory tract infection was 55% in primary healthcare clinics in Korea (Kim N, 2005). In Japan, prescription rate for upper respiratory tract infection was 60% and 3rd generation of cephalosporins, macrolides, and fluoroquinolones were prescribed in 46%, 27%, and 16% of patients, respectively (Higashi T, 2009).

Lack of awareness and knowledge on antimicrobial resistance and appropriate use of antibiotics are one of the main reasons for in appropriate use of antibiotics. A survey of general public conducted in Korea revealed that 51% of people thought that despite 72% of people responded that antimicrobial resistance is a serious problem (Song JH, 2010). The first APEC Expert Forum of the project entitled "International initiatives to control antimicrobial resistance in the Asia-Pacific region" to discuss current issues on antimicrobial resistance in Asia was held on April 5, 2011 in Seoul, Korea with participation of 50 infectious disease experts from 13 Asian countries, including China, Hong Kong, China, Indonesia, Japan, Korea, Malaysia, the Philippines, Singapore, Chinese Taipei, Thailand, Viet Nam, India, and Sri Lanka (Proceedings of the 1st APEC Expert Forum, APEC#211-HT-04.1). At the Expert Forum, factors associated with antibiotic abuse or misuse were discussed and according to the survey on current status of antimicrobial uses and resistance in Asian countries of the Expert Forum, both general public and medical personnel do not have adequate knowledge on antimicrobial resistance and appropriate use of antibiotics.

According to the 1st APEC Expert Forum, weak and unorganized policies and regulations in Asian countries are another important factor associated with antibiotic abuse or misuse. Antibiotics can be purchased without prescription in most Asian countries except Japan, Korea, Malaysia, and Singapore according to experts from Asian economies. In China and Chinese Taipei, despite they have policy about separation of prescription and dispensing antibiotics, antibiotics can be purchased without prescriptions. Over-the-counter (OTC) antibiotics can be purchased in pharmacy, supermarket, internet shopping mall, or alternative medicine clinic in those countries. Also, counterfeit antibiotics are used in most Asian countries except Hong Kong, China, Japan, Korea, and Singapore although all countries have regulation to control counterfeit antibiotics. The International Medical Products Anti-counterfeiting Taskforce (IMPACT) of WHO also has reported that counterfeit drugs are used in many Asian countries including Indonesia, the Philippines, China, and India (IMPACT, 2006). Although antimicrobial resistance is a serious public health threat in the Asia-Pacific region, where antimicrobial agents are widely abused and misused, there is still a general lack of awareness on antimicrobial resistance. Weak and unorganized policies and regulations on antibiotic use in many Asian economies are also one of important factors driving the increase of antimicrobial resistance.

Antibiotics are also used in animals for not only therapeutic purposes but also growth-promoting purposes in farm animals. These antibiotics used to promote animal growth are

called “antibiotic growth promoters” and are administered to livestock as feed additives at a low, sub-therapeutic dose. Antibiotic growth promoters are known to improve feed conversion and animal growth and reduce morbidity and mortality caused by clinical and subclinical diseases in animals. However, there have been increasing concerns that the use of antibiotics in animals for therapeutic and growth-promoting purposes could lead to the development of antimicrobial resistance and may transfer antimicrobial resistance between animals and humans through food chain or direct contact. Therefore, in recent years, although there have been considerable efforts to limit the use of antibiotics in animals worldwide, antibiotics are still abused or misused in many Asian countries.

4. Asia-Pacific region as an epicenter of antimicrobial resistance

Although regional situation of antimicrobial resistance may vary by country, it is evident that, Asia is certainly a part of the world in which there are increasing concerns regarding antimicrobial resistance because of a high prevalence of antimicrobial resistance in major bacterial pathogens and existence of many low or low middle income countries. High prevalence of antimicrobial resistance and relatively weak economic infrastructures of developing countries in the Asia-Pacific region make clinical and economic burden of antimicrobial resistance even greater than any other parts of the world. It is expected to be much more detrimental to the economy of Asian countries with regard to the magnitude of the costs and subsequent financial loss. However, in many Asian countries, antimicrobial resistance is still a neglected issue due to lack of awareness. Weak and unorganized policies and regulations in many Asian countries are also contributing to the increase in antimicrobial resistance. Since more than 70% of world population is living in the Asia-Pacific region, problems of antimicrobial resistance in the region are not just a regional issue but a global problem.

In comparison with Western countries, geographic variations in the antimicrobial resistance are notable in Asia because of the uneven policies of antimicrobial usage as well as different standards of public hygiene between countries. According to published papers, very high prevalence rates of beta-lactam and macrolide resistance in *S. pneumoniae*, which is the single most important cause of lower respiratory tract infections in both adults and children, were found in Asian countries (Johnson DM, 2006; Song JH, 1999, 2004, 2008-2009). Particularly, erythromycin resistance has remarkably increased in many Asian countries where >70% of clinical isolates were fully resistant. Based on the published reports, Asia-Pacific region is evidently an epicenter of antimicrobial resistance in the world with the highest prevalence of antimicrobial resistance in major bacterial pathogens. For example, Asian countries like China, Indonesia, Korea, Japan, Thailand and Viet Nam showed very high rates (> 50%) of MRSA, which is the most important cause of hospital-acquired infections such as pneumonia, surgical site infections and bloodstream infection and kills more than 19,000 patients annually in the USA only, suggesting that many Asian countries would have a huge number of deaths due to this infection (Grundmann H, 2006; Song JH, 2011). Carbapenem-resistance rates of *Acinetobacter* spp. and *Pseudomonas aeruginosa* were very high and multidrug-resistant (MDR) non-fermenters were highly prevalent in Asian countries (Chung DR, 2011).

Despite many serious events of antimicrobial resistance internationally, there have been few practical efforts to improve the preparedness for control of antimicrobial resistance based on international collaboration to reduce the economic impact as well as public health impact of antimicrobial resistance. Particularly, although antimicrobial resistance is a serious public health threat in the Asia-Pacific region, where antimicrobial agents are widely abused and misused, it is quite obvious that the lack of awareness of critical situation of antimicrobial resistance prevents Asian countries from preparing comprehensive international strategies for antimicrobial resistance and leads to ineffective responses to antimicrobial resistance in the region. Given its devastating impact on human lives and economy, future strategies should be prepared with multifaceted collaboration among all relevant stakeholders in the Asia-Pacific region and the comprehensive strategies for control and prevention of antimicrobial resistance are urgently required in the region. However, there have been no practical plans or implementations to control this problem based on international and multi-sectoral collaboration in the Asia-Pacific region to date.

Despite the serious problems of antimicrobial resistance in the Asia-Pacific region, many contries do not have adequate national infrastructure and system to control and prevent the problems. Many Asian countries are sharing the same problem of antimicrobial resistance not only due to poor healthcare infrastructure but also due to the spread of resistance between countries. Threfore, effective control and prevention of antimicrobial resistance in the Asia-Pacific region can be achieved only by effective international collaboration based on strong national initiatives. Urgent issues to be addressed in the region would be to establish effective international collaboration system for surveillance of antimicrobial resistance and evaluation of clinical and economic impact of antimicrobial resistance and to prepare the future strategies for control and prevention of antimicrobial resistance in the region based on theses evaluations. The purposes of this report are to discuss and envision the future strategies against antimicrobial resistance problems, to prepare the strategies on control of antimicrobial resistance, and to discuss plans for implementation of future strategies to control antimicrobial resistance in the Asia-Pacific region.

II. Strategic action plan to control antimicrobial resistance in the Asia-Pacific region

The strategic action plan to control and prevent antimicrobial resistance in the Asia-Pacific region consists of five major components as in Figure 1. Surveillance of antimicrobial resistance is the first and basic step to detect and identify the problems of resistance in the region. Appropriate use of effective antibiotics is of utmost importance because antibiotic abuse or misuse is the most critical driving force for the emergence of antimicrobial resistance. This includes the appropriate use of current antibiotics and the development of novel antibiotics. Hospital infection control is also important since it can prevent the spread of resistant clones in the hospitals and in the community. Vaccination can prevent the emergence of infectious disease as well as can reduce the prevalence of resistance in a certain bacterial pathogen, such as *S. pneumoniae*. Finally, adequate and relevant policies and regulation by governmental system for control of antibiotic uses, prevention of counterfeit drugs, and surveillance of antimicrobial resistance are very crucial for successful control of resistance.

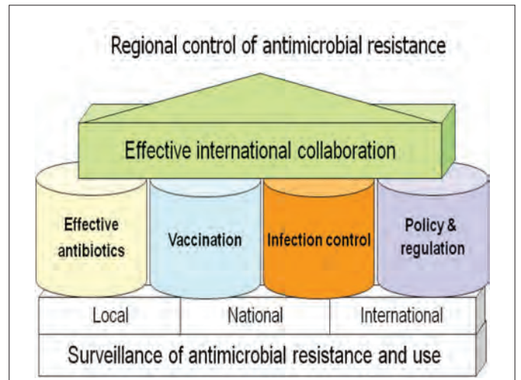


Figure 1. Five major components of strategic plan to control antimicrobial resistance

1. Surveillance of antimicrobial resistance and antibiotic use

1.1. Background

Antimicrobial resistance is now spreading geographically much faster than at any time in the history. Although resistance is spreading worldwide, most serious situation of resistance is now observed in Asian countries. For effective control of antimicrobial resistance in the region, surveillance of antimicrobial resistance based on international collaborations is critically required. Local, regional, or international surveillance of antimicrobial resistance are currently performed with different goals, programs and the quality.

Surveillance of antimicrobial resistance is essential for providing information on the magnitude and trends in resistance. Surveillance of antimicrobial resistance tracks changes in microbial populations, permits the early detection of resistant strains of public health importance, and supports the prompt notification and investigation of outbreaks. Surveillance findings are needed to inform clinical therapy decisions, to guide policy recommendations. Surveillance is needed to monitoring the effect of interventions. The study of antimicrobial surveillance can also collect patient demographic data that may be used to determine which pathogens are more prevalent among various patient populations and how antimicrobial resistance is changing among them.

The actions taken on the basis of surveillance data will depend on the level at which the date are being collected and analyzed. A fundamental principle of any communicable disease surveillance program is defining and standardizing laboratory identification methods. These standards should be compatible with other countries to allow international comparison of local data. International collaboration on surveillance may also be of value, to share information as an early warning of new or unusual resistance events. In addition international quality assurance standards can help to overcome the potential difficulties arising from the use of different methods.

Monitoring of antibiotic uses is also very important because inappropriate use of antibiotics is the most basic driving force for the emergence of antimicrobial resistance. Based on the reports from Asian countries, antibiotics are very frequently abused or misused in most Asian countries not only in patients but also in animal husbandry. Furthermore, counterfeit antibiotics are widely circulated in many Asian countries, which can induce the emergence of resistance due to inadequate dose of antibiotic compound.

1.2. Review of surveillance programs

1) Surveillance programs in the USA

There are numerous surveillance systems that collect data on antimicrobial resistance by the Centers for Disease Control and Prevention (CDC).

- **The Emerging Infections Program (EIP)**

The EIP network is a national resource for surveillance, prevention and control of emerging infectious diseases. The EIP is a network of 10 state health departments and their collaborators in local health departments, academic institutions, other federal agencies and public health and clinical laboratories. The EIP population is roughly representative of the US population on the basis of demographic characteristics. One of EIP activities is Active Bacterial Core Surveillance (ABCs). ABCs is a core component of CDC's EIP and collaboration between CDC, state health departments, and universities. ABCs is an active laboratory and population based surveillance system for invasive bacterial pathogens of public health importance. ABCs data have been used to track disease trends and also contributed to public health policy by providing information and using the basis of revised CDC guidelines.

- **National Antimicrobial Resistance Monitoring System (NARMS)**

NARMS is collaboration among the Food and Drug Administration (FDA, Center for Veterinary Medicine), CDC and U.S. Department of Agriculture. The NARMS program has three components (human, retail, and animal) from which select foodborne bacteria are characterized from human clinical cases, retail meats, and food animals and processing plants. NARMS now includes all 50 states, providing national surveillance for antimicrobial resistance among select foodborne pathogens.

2) Surveillance program in Canada

- **Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS)**

The CIPARS is a nationally integrated antimicrobial resistance surveillance program developed by the Public Health Agency of Canada in collaboration with Health Canada, the Canadian Food Inspection Agency and provincial partners. One of the key objectives of CIPARS is to monitor trends in the development of antimicrobial resistance in the food chain.

3) Surveillance program in Europe

- **The European Antimicrobial Resistance Surveillance Network (EARS-Net)**

The European Antimicrobial Resistance Surveillance System (EARSS) established in 1998 is the predecessor of the current EARS-Net. EARS-Net is a European network of national surveillance systems that maintains a comprehensive surveillance and information system with European reference data on antimicrobial resistance for public health purposes.

The EARS network aimed to serve as a basis for an integrated public strategy for containing antimicrobial resistance. In pursuing this, EARS collaborated closely with other EU-funded projects such as the European Surveillance of Antimicrobial Consumption (ESAC) and Antibiotics Resistance Surveillance and Control in the Mediterranean Region (ARMed). EARS also worked in partnership with the European Society of Clinical Microbiology and Infectious Diseases (ESCMID). At present, EARS-Net includes 900 public health laboratories serving over 1400 hospitals in Europe and providing services to an estimated population of 100 million European citizens.

The main tool for displaying data from the EARS-Net is an interactive database which can be accessed on the website (http://www.ecdc.europa.eu/en/activities/surveillance/EARS-Net/), which allows the user to display selected results in various formats, such as tables, figures and maps.

- **The European Surveillance of Antimicrobial Consumption (ESAC)**

The ESAC collects human and limited animal consumption data from 34 countries. The inputs are largely standardized since countries must adhere to WHO standards regarding measurement (defined daily doses) and classification of antimicrobials.

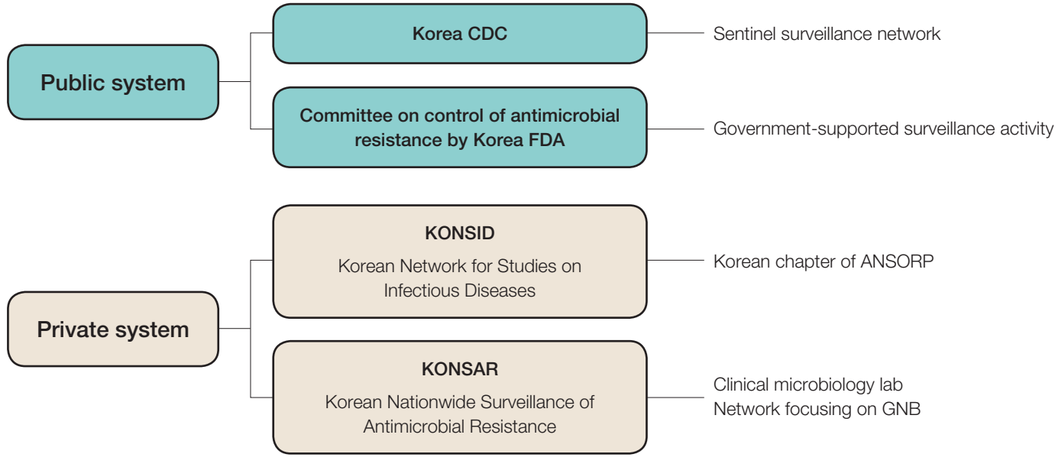
4) Surveillance program in Asia

- **Asian Network for Surveillance of Resistant Pathogens (ANSORP)**

ANSORP was organized as the first multi-country collaborative study group in 1996 to perform the international surveillance studies on antimicrobial resistance in the Asian region. ANSORP is an independent, not-for-profit, non-governmental, international network for collaborative research on antimicrobial agents and infectious diseases in the Asia-Pacific region. ANSORP is the first and the only multinational-coordinated research network to conduct research on antimicrobial resistance and infectious disease in the Asia-Pacific region. As of June 2011, over 100 centers in 14 countries and over 200 researchers are participating in ANSORP.

- **Major surveillance systems in Korea**

In Korea, there are public surveillance systems supported by Korea Centers for Disease Control (KCDC) and Korea Food and Drug Administration (KFDA). In private sectors, Korean



Network for Studies on Infectious Diseases (KONSID), which is a Korean chapter of ANSORP, consisting of 18 hospitals in 9 cities is performing antimicrobial surveillance on major bacterial pathogens. Korean Nationwide Surveillance of Antimicrobial resistance (KONSAR), which is a nationwide network of clinical microbiology labs, is also one of major private surveillance systems in Korea.

• National surveillance system in China

The Chinese Ministry of Health established a national antimicrobial resistance investigation network entitled "Ministry of Health National Antimicrobial Resistance Surveillance Net (Mohnarin)" in 2004 to obtain scientific data for antimicrobial resistance (Xiao YH, 2008). Seventeen tertiary hospitals located in 15 different cities throughout China participated in the Mohnarin as of 2005.

• National surveillance programs in Japan

Japanese Nosocomial Infection Surveillance (JANIS) is supported by the Japanese Ministry of Health, Labour, and Welfare and has been started since 2000. JANIS consists of five components of surveillance including, surveillance on intensive care unit (ICU), clinical microbiology labs, hospital wide, surgical site infections (SSI), and neonatal intensive care unit (NICU). Also, Japanese Society of Chemotherapy (JSC) established a nationwide surveillance network in 2006 to investigate comprehensive antimicrobial resistance of respiratory pathogens (Niki Y, 2011).

• National surveillance in Malaysia

National surveillance program on antibiotic resistance was established in 1990 in Malaysia. It is coordinated by the Infectious Diseases Research Centre at the Institute for Medical Research in Kuala Lumpur and covers all Ministry of Health State hospitals.

• National surveillance in Singapore

Network for Antimicrobial Resistance Surveillance Singapore (NARSS) was established in 2006 by voluntary group of health care workers from all public sector hospitals and affiliated with the society of Infectious Diseases in Singapore.

• National surveillance in Chinese Taipei

To monitor the occurrence of hospital-associated infections (HAIs) effectively, to evaluate the epidemiologic trend of HAIs in Chinese Taipei, and to set up internationally comparable surveillance indicators, Chinese Taipei Centers for Disease Control (CDC) was established the Chinese Taipei Nosocomial Infections Surveillance System (TNIS) in 2007 and publishes annual report.

• National surveillance programs in Thailand

Acute Respiratory Tract Infection in Children (ARIC) was established to monitor resistance situation in *S. pneumoniae* and *H. influenzae* in children (≤5 years old) in 6 provinces. National Antimicrobial Resistance Surveillance of Thailand (NARST) investigates the resistance situation in all organisms from routine isolates in 46-60 hospitals in 48 provinces. Thailand Invasive Bacterial Infection Surveillance (Thai IBIS) was established to monitor both clinical and lab data as well as bacterial characterization in all age group with invasive infection in 48 provinces.

5) International surveillance studies by pharmaceutical companies

• Study for Monitoring Antimicrobial Resistance Trends (SMART)

SMART is an antimicrobial surveillance study looking at intra-abdominal infections conducted by Merck & Co., Inc. The SMART was started in 2002 as a worldwide surveillance study including Asia-Pacific region. It was designed to monitor, globally and longitudinally, the in vitro susceptibility of intra-abdominal bacterial clinical isolates collected from all units of an institution. The centers include both teaching hospitals and community hospitals (http://www.merck.com).

• SENTRY antimicrobial Surveillance Program (SENTRY)

SENTRY was initiated in 1997 by BMS and was designed to monitor the spectrum of microbial pathogens and antimicrobial resistance trends for both nosocomial and community acquired infections on a global scale, by using validated reference quality identification and susceptibility testing methods in designated central laboratories. Consecutive bacterial or fungal isolates, deemed clinically significant by local criteria, are forwarded to the local reference laboratory from various study objectives. The major objectives include blood stream infections, community-acquired respiratory tract infections (*S. pneumoniae, H. influenzae* and *Moraxella catarrhalis*), pneumonias in hospitalized patients, skin and soft tissue infections, and urinary tract isolates from hospitalized patients. The geographic regions in this program included North America, Latin America, Europe and Asia-Pacific region. This program is currently operated by the JMI Lab (USA).

There are other local, regional, or international surveillance programs of antimicrobial resistance currently working for different goals and programs, such as the Alexander Project, Meropenem Yearly Susceptibility Test Information Collection (MYSTIC), Prospective Resistant Organism Tracking and Epidemiology for the Ketolide Telithromycin (PROTEKT), Latin American Surveillance and Epidemiology Research (LASER), etc

1.3. Strategic action plan for surveillance

1) Establishment of national and international surveillance system in the Asia-Pacific region

Surveillance is a key element in the strategy to control and prevent antimicrobial resistance. As described previously, there are many local, regional, or international surveillance programs and project on antimicrobial resistance. The most basic unit for the surveillance of resistance is the hospital. Hospital surveillance should be performed according to the standardized protocols and methods, which are also used for the national surveillance of resistance. National surveillance network should include representative number of hospitals in the country and surveillance of resistance should be performed

based on the standardized protocols and methods.
However, it is more important to evaluate the status of antimicrobial resistance at international level because resistance can spread between countries. International surveillance can be performed either by specific surveillance networks such as ANSORP or SMART or by coalition of national surveillance networks of Asian countries. In order to collate the data from national surveillance networks, it is essential that methods of collecting isolates and in vitro susceptibility tests should be standardized.

2) Standardization of microbiology test, data collection and reporting

Asian countries have different levels of microbiological technologies and may use the different methods and criteria to detect isolates and to perform antimicrobial susceptibility testing. Therefore, designation or development of reference microbiology laboratory for microbiology tests in the region and the standardization of laboratory methods are crucial to get accurate information on antimicrobial resistance, to monitor antimicrobial resistance trends and to compare antimicrobial resistance in different countries in the Asia-Pacific region. Collection of the data and reporting should also be standardized.

3) Surveillance of antibiotic consumption

Antibiotic usage is closely associated with antimicrobial resistance. This information is essential to determine the changing trends of antibiotic usage, further understand the relationship between antibiotic use and resistance, and help to build an interventional strategy for control of antimicrobial resistance. However, the nationwide surveillance system for antibiotic consumption has not been set up in most Asian countries. Therefore, the surveillance system for monitoring and analysis of antibiotic usage in each country should be established. The standardized methods should be promoted in the aspects of the measurement and class of antimicrobials. The defined daily dose (DDD), defined by the WHO, can be used for a statistical measure of drug consumption. It will make standardized comparisons between countries possible.

4) Surveillance of antimicrobial resistance and usage in food animals

Antimicrobials are commonly used as a growth promoter to increase feed efficiency and to prevent infections in food animals. Since antibiotic abuse in animal husbandry is another important factor for the emergence of antimicrobial resistance in major bacterial pathogens, it is critical to monitor the use of antibiotics in food animals as well as to regulate the use of antibiotics as a growth promoter.

Discussion at the Expert Forum : Surveillance group

• National surveillance of antimicrobial resistance

1. What is the current status of national surveillance of resistance ?
2. Which organisms should be included in the national surveillance of resistance ?
3. Which surveillance method would be more useful for national surveillance ; active surveillance vs passive surveillance ?
4. Which methods should be used as standard in vitro susceptibility test in Asian countries ? (CLSI vs EUCAST vs other methods)
5. How can we develop and standardize the microbiology laboratories in the country for surveillance of antimicrobial resistance ?
6. What is the optimal number of hospitals participating in the national surveillance network to generate the representative data of resistance ?
7. What is the role of governmental system and private systems such as academic societies, organizations or companies to build up and maintain the national surveillance system ?

• National monitoring of antimicrobial use

8. How can we develop effective system to monitor the use of antibiotics both in patients and in animal husbandry ?
9. Which antibiotics should be monitored in each country ?
10. How can we monitor the use of counterfeit antibiotics ?
11. How can we associate the use of antibiotics and the prevalence of antimicrobial resistance ?
12. How can we collate the data of antibiotics use from Asian countries ?

• International surveillance of antimicrobial resistance

13. Which organisms should be included in the international surveillance of resistance in the Asian region ?
14. Which surveillance method would be more useful for international surveillance ; active surveillance vs passive surveillance ?
15. What could be the most effective way to transport the bacterial strains across the country ?
16. If transport of the isolates across the country for active international surveillance is impossible, how can we solve this issue ?
17. What could be the most efficient method to report or share the data of resistance in Asian countries from international surveillance studies ?

• Current international networks : ANSORP, SMART, etc

18. ANSORP is already-established international network for surveillance of resistance in Asia. How can we utilize the system of ANSORP for international surveillance of resistance ?
19. What are your personal opinions to improve or strengthen the ANSORP system for international surveillance of resistance in Asia ? What could be the future scope and role of ANSORP activities in the region ?
20. What are your personal opinions about other international systems for surveillance of resistance in Asia ?
21. What are your personal opinions to activate or encourage the national and international surveillance of antimicrobial resistance in the Asian region ?

2. Appropriate use of effective antibiotics

2.1. Background

Because microbes continually adapt and evolve, the selective pressure exerted by antimicrobial agents will promote the emergence and spread of antimicrobial resistance. With the widespread use of antibiotics, the prevalence of resistance to each drug has dramatically increased. Educating the public and prescribers is obviously an important and effective way to achieve the appropriate use of antibiotics and increased awareness of antimicrobial resistance. Appropriate use of antibiotics is defined as use that maximizes therapeutic impact while minimizing toxicity and the development of resistance. Practically, this means using antibiotics only when beneficial to a patient; targeting therapy to the desired pathogens; selecting the right antibiotics; and using the appropriate dose and duration. The most important thing to reduce the selective pressure favoring the spread of antimicrobial resistance is decreasing antibiotic abuse and misuse. In addition, relevant regulations to prohibit purchasing antibiotics without doctor's prescription or production and circulation of counterfeit drugs are very crucial in the Asia-Pacific region.
Appropriate antibiotic use can be facilitated by public awareness campaigns for general public and promoting informed prescribing by healthcare professionals. As for public education, public awareness campaigns have been conducted in European countries and the USA and have shown benefits and effects to increase the awareness of resistance and antibiotic use.

2.2. Strategic action plan for appropriate use of current antibiotics

1) Educational campaigns for general public

Increased awareness of appropriate use of antibiotics by

general public is very essential to control and prevention of antimicrobial resistance in the Asian region. Based on the survey in Asian countries, general public in most Asian countries need to have more adequate knowledge and information about appropriate use of antibiotics and antimicrobial resistance. Among various measures to provide information on antibiotic use and antimicrobial resistance, educational campaign is one of the most effective ways. The main key messages of public campaigns should be customized according to local situations of antibiotic use and antimicrobial resistance.

For more effective public campaign, mass media, on-line campaigns using the website, SNS, and also the printed materials are utilized. Also, a special campaign day or week (such as Antibiotic Awareness Day by European CDC) can be designated.

I Care (Initiative to Control Antimicrobial REsistance) campaign by the Asia Pacific Foundation for Infectious Diseases (APFID) can provide an infra structure for international campaign in the Asian region.

2) Educational campaign for healthcare professionals

Educational campaign for healthcare professionals who are prescribing antibiotics is very important to prevent the abuse or misuse of antibiotics. According to the recent survey in Asian countries, healthcare professionals in most Asian countries need to have more adequate and correct knowledge of antibiotic use and antimicrobial resistance.

The most basic content of educational campaign for healthcare professionals is the current status of antimicrobial resistance, its implications in the clinical practice, and current situation of antibiotic abuse and misuse. This information should be regularly updated and provided to healthcare professionals. Development of clinical practice guidelines for diagnosis and treatment addressing appropriate antimicrobial use is crucial. Treatment guidelines should be based on local and national surveillance of antimicrobial resistance. Educational curricula for medical students and trainees are also important.

3) Policy and regulation on the use of antibiotics

Given a widespread abuse and misuse of antibiotics in the Asian region, any kind of antibiotics should be purchased based on the doctors' prescription. Currently, very few countries have established the separation of prescribing and dispensing antibiotics. It should be defined by law and regulations.

Counterfeit antibiotics should also be strictly prohibited and regulated by law. Since counterfeit drugs are widely used in many Asian countries, international collaboration is also urgently required.

4) Antibiotic stewardship

Antibiotic stewardship in the hospitals is essential for appropriate use of antibiotics. Guidelines for antimicrobial treatment and prophylaxis, and hospital antimicrobial formularies should be developed and regularly updated in the hospitals. These should be based on the institutional, national and international situation of antimicrobial resistance as well as situation of antibiotic uses.

5) Use of antimicrobials in food producing animal

Since antibiotic abuse and misuse in the food animals is an important cause of antimicrobial resistance, unnecessary and inappropriate use of antimicrobials for non-therapeutic use in animals should be reduced. National systems to monitor and regulate antimicrobial usage in food animals should be activated.

2.3. Strategic action plan for development of novel antibiotics

1) Creating a sustained research and development (R & D) infrastructure

Antibiotic pipeline problem can be solved by bringing together global political, scientific, industry, economic, intellectual property, policy, medical and philanthropic leaders to develop creative incentives that will stimulate new antibacterial R&D. Global stakeholders can capitalize on each other's strengths to create a long-term, sustainable R&D infrastructure model that provides incentives for antibacterial drugs. The sustained infrastructure created to achieve this goal would help to recreate the highly skilled scientific workforce that was lost over the past two decades as many companies abandoned antibacterial drug development. Microbial evolution causing antibiotic resistance is constant; the collective efforts at antibiotic discovery should be constant.

2) Cooperation between industry, government, and academic institutions

Drug discovery may be stimulated by cooperative research agreements between companies and academic institutions. These agreements can stimulate basic science research and the sharing of knowledge which may speed up the identification of promising compounds. This approach may potentially reduce overall costs by reducing the duplication of research activities. Public-private partnerships are increasingly being exploited for speeding up drug discovery and development and addressing unmet medical needs where the market opportunities are less attractive. We should encourage cooperation between industry, government bodies, and academic institutions in the search for new antibiotics. Also, incentives for industry to invest in the R & D of new antibiotics should be provided.

3) New regulatory approaches to facilitate antimicrobial development

Several factors have resulted in a market failure of new antibiotic development, including the ability of antibiotics to cure most infections in just a few days, antibiotic resistance which makes the drugs less effective over time, and deliberate and essential measures taken by physicians to limit antibiotics' use to protect their effectiveness over time. Consequently, antibiotics are at a distinct disadvantage compared with most other drug categories, within pharmaceutical companies' internal deliberations about how best to invest R&D resources. Considering together the economic disincentives antibiotic developers currently are facing and the lack of a clear regulatory approval pathway for these drugs over the past decade, one can easily understand why antibiotic approvals have decreased so markedly and companies have withdrawn from antibiotic R&D to pursue more lucrative areas of drug development.

In setting regulatory guidance for antibiotic development, licensing authorities must balance the public health risks of approving a potentially less effective drug with the risk of having no new, critically needed antibiotics available to treat patients infected with resistant pathogens. Specifically, we should balance feasibility of conducting studies (and the resultant public health benefit of facilitating approval of effective new antibiotics) against a desire to narrow the non-inferiority margin. While patients may be harmed if less effective drugs are allowed to reach the market, they also may be harmed if they have an infection for which no effective antibiotics have been developed. Schemes that encourage investment in antimicrobial research must therefore recognize the need for companies to recoup their development costs as well as make a profit from post-licensing sales.

4) New regulatory approaches to licensure and patent protection of new antibiotics

Clinical development of promising antimicrobial agents cannot proceed in the absence of clarity regarding the requirements for licensure of the drugs. To hasten the licensure of some new products, fast-tract evaluation of innovative medicines should be offered by licensing authorities, allowing truly innovative products to reach the public domain as early as possible. The safeguarding of intellectual property rights should be assured for the pharmaceutical industry

Discussion at the Expert Forum : Future strategy group

• Campaign for appropriate use of antibiotics

1. What are the most important requirements for the national campaign for appropriate use of antibiotics for general public ?
2. What could be the most effective ways to implement the national public campaign ?
3. What are the hurdles and barriers to implement the national public campaign ?
4. What are the most important requirements for the international campaign for appropriate use of antibiotics for general public ? What do you think is the possibility of I CARE campaign for Asian countries ? What will be needed to implement it in Asian countries ?
5. What could be the most effective ways to implement the international public campaign ?
6. What are the hurdles and barriers to implement the international public campaign ?
7. What could be the best ways to implement the campaign for healthcare professionals ?

• Antibiotic stewardship

8. How do we strengthen the antibiotic stewardship in the hospitals ? What are the roles of the hospitals and public healthcare systems ?

• Appropriate use of antibiotics in food animals

9. How do we evaluate and investigate the use of antibiotics in food animals ?
10. What could be the most effective way to prevent the antibiotic abuse and misuse in food animals ?

• Development of novel antibiotics

11. What kind of novel antibiotics are needed most in Asian countries ?
12. How do we encourage the discovery and development of novel antibiotics ? What are the best ways to promote it in Asian countries ?
13. Is there any possibility of international collaboration for the development of novel antibiotics in the Asia Pacific region ?

3. Hospital infection control

3.1. Background

Healthcare-associated infections, often caused by antimicrobial-resistant bacteria, are very important cause of increased mortality and morbidity worldwide. Hospital infection control, making efforts to prevent the emergence and spread of antimicrobial-resistant bacteria within the hospital, are an effective way to curb antimicrobial resistance. Since the spread of resistant clones in the hospital and the community is critical factor for the rapid emergence of resistance, it should be controlled to prevent the surge of antimicrobial resistance. Hospital infection control is also important for the control of resistance in the community because resistant pathogens are exchanged between hospital and the community.

3.2. Strategic action plan for hospital infection control

1) Reduced rates of infection transmission through hospital infection control program

Infection control program should be a top priority for healthcare facilities. Infection control in healthcare settings should be enhanced by developing new interventions based on rapid diagnosis, improved understanding of the factors that promote cross-infection, and guidelines for effective infection control. Infection control professionals and practitioners, continuous support by hospital leaders, and multifaceted education and reinforcement of policies are required for successful hospital infection control. Resources must be available for infection prevention and control, including expert consultation, laboratory support, adherence monitoring, and data analysis. Written infection prevention and control policies and procedures must be established, implemented, and updated periodically.

2) Hand hygiene policies

Hand hygiene is the most important way for preventing the spread of antibiotic resistant pathogens in healthcare settings, and appropriate guidelines for hand hygiene should be provided. It is critical that compliance with infection control policies for hand hygiene is monitored regularly. All hand hygiene polices should begin with the use of an alcohol-based hand rub before and after any contact with the patients, dealing with body fluids or any soiled materials, removing gloves and changing bedding or linens. The hands should be thoroughly with soap and water whenever hands are visibly dirty or contaminated with proteinaceous material or are visibly soiled with blood or other body fluids or when dealing with outbreaks caused by spore-forming bacteria such as *Clostridium difficile*.

3) Reduction of transmission of multidrug-resistant organisms (MDRO)

MDROs are usually defined as microorganisms that are resistant to three or more classes of antimicrobial agents. For infection control purposes, MDROs include methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-intermediate *S. aureus* (VISA), vancomycin-resistant *S. aureus* (VRSA), vancomycin-resistant enterococci (VRE), ESBL-producing Enterobacteriaceae, carbapenem-resistant *Acinetobacter baumannii*, and carbapenem-resistant *Pseudomonas aeruginosa*. Successful control of MDROs requires multifaceted interventions including improvement in hand hygiene, contact precautions, active surveillance cultures, education, enhanced environmental cleaning, and administrative support.

Discussion at the Expert Forum : Future strategy group

• Hospital infection control

1. What is the current status of hospital infection control in Asian countries ?
2. Are there any law or regulations for infection control in healthcare settings ?
3. How is the current awareness on hospital infection control to prevent the spread of resistant bacteria?
4. Are there any infection control policies or guidelines for hand hygiene or isolation in healthcare settings?
5. Do we have any specific program to control the spread of MDRO in the hospitals ?
6. What are needed most in your countries to perform successful hospital infection control?

4. Vaccination

4.1. Background

With growing burden of antimicrobial resistance worldwide, we have fewer options for optimal antimicrobial agents against those resistant pathogens. Prevention of infectious diseases by vaccination would eliminate the need for antibiotic usage in diseases and the risk of emerging resistance in bacterial pathogens. Currently, vaccines for various bacterial pathogens include typhoid fever, cholera, tuberculosis, diphtheria, tetanus, pertussis, *Streptococcus pneumoniae*, *Haemophilus influenzae* type b and meningococci. Vaccines targeting bacteria especially with multidrug resistance such as *Staphylococcus aureus* or *Pseudomonas aeruginosa* are also being developed. Among these bacterial vaccines, pneumococcal conjugate vaccine is the most representative example of vaccine that can reduce the prevalence of antimicrobial resistance.

Pneumococcal diseases are the leading cause of death worldwide with 1.6 million deaths. Disease burden of pneumococcal infections has been increasing due to widespread emergence of antimicrobial resistance in *S. pneumoniae*. During the past 3 decades, resistance of pneumococci to beta-lactams, macrolides, and other antibiotic classes has escalated dramatically throughout the world, although it is more severe in the Asian region than in western countries. Pneumococcal infection is also the most common vaccine-preventable disease. In the USA, the 7-valent pneumococcal conjugate vaccine (PCV7) has resulted in 94 % reduction in the incidence of pneumococcal diseases caused by PCV-7 serotype strains and 75 % reduction in invasive pneumococcal diseases regardless of the serotypes. It also reduced the prevalence of antimicrobial resistance in *S. pneumoniae*. These data clearly showed that PCV-7 was a very effective vaccine to prevent pneumococcal infections and pneumococcal resistance.

In Asian countries, according to the ANSORP surveillance study, less than 60% of pneumococcal isolates showed PCV-7 serotypes in most countries which was lower than that in the western part of the world. Also, according to data from WHO-UNICEF, vaccine coverage rates in developing countries including Asia were lower than those of developed countries. Data about pneumococcal conjugate vaccine coverage in children are not available to date in most of Asia.

Although PCV-7 has decreased the incidence of pneumococcal diseases caused by vaccine serotypes, there was a remarkable increase in the incidence of invasive pneumococcal diseases (IPD) caused by non-PCV-7 serotype strains such as serotype 19A worldwide. Since serotype 19A is very frequently related to multidrug resistance, emergence of serotype 19 A is leading to the increased prevalence of multidrug resistance. Therefore, a new conjugate vaccine which can cover these non-vaccine serotypes is urgently required. PCV-13 that includes 6 additional serotypes including serotype 19A was recently approved and introduced to the USA and other countries. PCV-13 is expected to prevent pneumococcal diseases effectively and also to reduce the prevalence of pneumococcal resistance.

4.2. Strategic action plan for vaccination

Given the importance of vaccination to prevent the occurrence of infectious disease and the emergence of resistance, vaccination should be encouraged in Asian countries. Pneumococcal conjugate vaccine is the proven example of bacterial vaccine that can reduce the prevalence of antimicrobial resistance. Currently, PCV-13 would be the best option for this purpose. Therefore, PCV-13 should be introduced and widely used in Asian countries where burden of pneumococcal infections and the prevalence of resistance are the highest in the world. In order to enhance the awareness of pneumococcal vaccination and compliance in the Asia-Pacific region, education and campaign should be implemented for both general public and healthcare professionals. Also, key messages could be disseminated by mass media, leaflets, symposium and medical training.

Discussion at the Expert Forum : Future strategy group

- **Vaccination**

1. What is the PCV-7 vaccination rate in Asian countries ? Is it included in the National Immunization Program ?
2. Are there any data about the changing prevalence of antimicrobial resistance in *S. pneumoniae* after PCV-7 vaccination in Asian countries ?
3. What could be the most effective way to increase the vaccination rate of PCV-13 in Asian countries ?
4. What other bacterial vaccines could reduce the prevalence of antimicrobial resistance in the future ?

5. Policy and regulation

5.1. Background

As documented for the past decades, antimicrobial resistance is not just a medical issue but a very serious socioeconomic issue. Control and prevention of antimicrobial resistance should be based on multidisciplinary approach consisting of medical, legal, social, economical and public measures. In this regard, relevant policies and regulations for control of antibiotic uses, surveillance of antimicrobial resistance, evaluation of clinical and economic impact of resistance, and public implementation of interventional measures are very crucial. However, most Asian countries are not aware of the current status of antimicrobial resistance and its impact on clinical medicine and socioeconomic damage.

The most important policy to prevent antibiotic abuse or misuse is separation of prescribing from dispensing antibiotics. By this law and regulation, antibiotics can be purchased only by doctor's prescription. However, unfortunately, this law has been activated only in some countries such as Korea, Japan, Singapore and Malaysia, while antibiotics can be easily purchased as over-the-counter (OTC) drugs without prescription in many other Asian countries. This is one of the most important reasons for antibiotic abuse in these Asian countries and for increasing emergence of resistance in major pathogens.

Counterfeit antibiotics which contain inadequate concentration of antimicrobial compound are widely circulated in many Asian countries. This is another form of antibiotic abuse and misuse, which can lead to the emergence of resistance. However, in many countries, there is minimal control over public access to OTC antibiotics without prescription. Furthermore, an advertisement for antibiotics or public marketing is allowed in the media in some Asian countries.

5.2. Strategic action plans for policy and regulation

- Legal control of antibiotic supply, distribution and sales

Legal regulation to prohibit purchase of antibiotics without doctor's prescription is of utmost importance to prevent antibiotic abuse in Asian countries. It can be possible only based on multidisciplinary approach by the government, medical society, pharmaceutical companies and public health system. Particularly, the role of government is very crucial. Stringent legislative control of antibiotic prescribing and dispensing should be reinforced.

Financial incentives for prescribing drugs including antibiotics should not be allowed by strict legal regulation. Public advertisement of antibiotics also should be banned because advertising of the drug may lead patients to request the drugs by name. The government should regularly monitor the amount of antibiotic use in patients and assess the appropriateness of antibiotic usage in medical institutions. These data should be provided to the medical community and also to the general public.

- Establishing national clinical practice guidelines for appropriate use of antibiotics

The development of guidance in relation to the appropriate use of antibiotics is an essential part of the strategy and guidance must be developed both in hospitals and in the community. Evidence-based national treatment guidelines encourage appropriate antimicrobial prescribing. Such a strategy requires the promotion of prudent use via education of all prescribers, patients, manufacturers, and other users. Using local laboratory and clinical surveillance data on antimicrobial resistance, these guidelines can be appropriately modified for community and hospital uses in various regions. The use of such guidelines is most effective when combined with supportive interventions such as educational training and supervision programs.

The guidelines should :

- be evidence-based to the greatest degree possible and regularly reviewed.
- exist for both the prescribing and non-prescribing of antimicrobials and recommend treatment options for each clinical situation.
- be group specific, i.e. different bodies of experts should draw up guidelines for different groups of patients.
- include information on the most appropriate antibiotic and information on each antibiotic such as dosage, duration of treatment, effect of alcohol consumption, reactions with other medication, etc.
- highlight areas where antibiotics are often used but not clinically indicated.
- highlight local variation, if any, from national susceptibility data which may influence local recommendations.
- include guidance for the non-antibiotic therapies for infection, e.g. symptomatic therapies for viral respiratory tract infections.

■ Restriction of antibiotic usage in farm animals

Use of antibiotics as growth promoters in animal husbandry should be monitored and regulated.

Discussion at the Expert Forum : Policy & regulation group

• Separation of prescribing and dispensing antibiotics

1. How can we evaluate the current status of antibiotics abuse due to the lack of legal regulation of separation of prescribing and dispensing antibiotics in Asian countries ?
2. What are needed most to establish the legal regulation to prohibit purchase of antibiotics without prescription ? What are the main hurdles for this legal regulation ?
3. How can we monitor the use of antibiotics in the clinical medicine and animal husbandry by governmental system ?

• Regulation of counterfeit drugs

4. How can we prohibit production and circulation of counterfeit drugs in Asian countries ?
5. What are needed most to establish the legal regulation to prohibit counterfeit antibiotics ? What are the main hurdles for this legal regulation ?

• National guidelines for the use of antimicrobial agents

6. How can we develop the national guidelines for the use of antimicrobial agents in our own country ? What are the role of the government and the academic societies ?
7. What are needed most to establish the national guidelines ? What are the main hurdles for this ?
8. How can we monitor and evaluate the compliance and usefulness of the national guidelines of use of antibiotics ?

• Legal regulation of the use of antibiotics in animal husbandry

9. How can we monitor the use of antibiotics ad growth promoters in animal husbandry ?
10. How can we establish the legal regulation of antibiotics in food animals ?
11. What are needed most to establish the legal regulations ? What are the main hurdles for this ?

• Other measures to improve antimicrobial use and to prevent resistance

12. Are financial incentives for appropriate use of antibiotics helpful to improve the use of antibiotics ?
13. What are your personal opinions to improve antibiotic use and to prevent antimicrobial resistance by government ?

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