Global efforts in antibiotic stewardship - the BIG picture

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The discovery of antibiotics was one of the most significant event in medical history. Together with vaccination, clean water and other public health measures mortality from infectious diseases was dramatically reduced resulting in great optimism that infectious diseases were no longer a major challenge. This optimism was soon seen to be unfounded due to various reasons including the emergence of antibiotic resistance

Antibiotic resistance is a major challenge world-wide. It occurs in gram positive as well gram negative organisms and in health-care associated as well as community acquired infections. Antibiotic resistance and the inability to treat infections is now considered a global crisis

Resistance is not new. Resistance predates clinical use of antibiotics.Genes encoding for antibiotic resistance to a wide variety of antibiotics including synthetic compounds like quinolones have been found in soil with no prior exposure to antimicrobial agents. Resistant genes including Van A has been found in 30,000 year old permafrost sediments

There is a close association between overuse of antibiotics and emergence of resistance. Surveys worldwide consistently point to a high prevalence of inappropriate antibiotic use. Large quantities are also used in agricultural practices. Antibiotics exert a selection pressure that causes the emergence of resistance. Resistant organisms can then spread between man and man or between animals and man. Global travel results in transboundaryspread which can be rapid and widespread. Antibiotic resistance exacts a tremendous burden in terms of morbidity, mortality and health care costs.

Unfortunately the prospect for new antibiotics is dim and it is unlikely that any major advance in ability to treat antibiotic-resistant infections will be made in the near future.

In 2001 WHO issued the Global Strategy for Containment of Antimicrobial Resistance which describes a comprehensive, multi-faceted strategy which may be adopted by nations to contain antimicrobial resistance. In 2010 the Third Global Patient Safety Challenge was launched with the theme“Tackling antimicrobial resistance”. In 2011 on World Health Day WHO issued a 6 point policy brief to meet the challenge of antibiotic resistance. The brief includes a commitment to a comprehensive, financed national plan with accountability and civil society engagement; strengthening surveillance and laboratory capacity; ensuring uninterrupted access to essential medicines of assured quality; regulating and promoting rational use of medicines, including animal husbandry and ensuring proper patient care; enhancing infection prevention and control and fostering innovations and research and development.

Other WHO efforts has been in Antimicrobial Resistance Monitoring(AMR) and strengthening national capacitiesto establish antimicrobial resistance surveillance. WHO is also establishing international linkages to share information on resistance and its surveillance and to promote the development of containment strategies through the WHO Antimicrobial Resistance Information Bank. In 2014 WHO published its first Global Report on AMR surveillance.

The activities of the European Centre for Disease Prevention and Control are a good example of measures undertaken at a regional level. The mission of ECDC is to identify, assess and communicate about the threats to human health posed by infectious diseases. It has strengthened and developed surveillance and early warning systems for infections in Europe and organises the European Antibiotic Awareness Day Campaign, providing communication materials for use in local and national campaigns.

There has also been some initiatives taken in Asia. The Asia Pacific Society for Clinical Microbiology and Infection (Formerly the Western Pacific Society for Chemotherapy) organizes forums for the exchange of information of resistance information among its member countries. WPRO and SEAROhas also launched some initiatives and there are also industry driven resistance surveillance networks. However all these efforts are largely uncoordinated.

Antimicrobial resistance is now one of the world's greatest crisis and causes significant morbidity, mortality and economic costs. Patients are harmed as a result and antimicrobial resistance is a patient safety issue. Urgent need to put in place measures to combat antimicrobial resistance and requires actions by individuals, institutions, nations and international organisations.

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Victor K E Lim is currently the Vice-President for Education and Professor of Pathology at the Faculty of Medicine and Health, International Medical University in Kuala Lumpur. Prior to this appointment he was the executive Dean of the Faculty of Medicine and Health from 2004 – 2011. He was the Director of the Infectious Diseases Research Centre at the Institute for Medical Research in Kuala Lumpur from 2001 – 2004 and before that he was the Professor of Microbiology and Deputy Dean (Academic Affairs) at the Faculty of Medicine, Universiti Kebangsaan Malaysia.

He obtained his MBBS from the University of Malaya in 1974, MSc in Medical Microbiology from the University of London in 1978, and passed the Royal College of Pathologists examinations (MRCPath) in 1981.

He was the President of the Western Pacific Society of Chemotherapy from 2004 - 2008, the Master of the Academy of Medicine of Malaysia from 2008 – 2011 and the President of the Malaysian Society for Infectious Diseases and Chemotherapy from 1999 – 2003. He is a Fellow of the Royal College of Pathologists, a Fellow of the Academy of Medicine of Malaysia, a Fellow of the Academy of Medicine of Singapore, a Fellow of the Academy of Family Physicians of Malaysia and a Fellow of the Academy of Sciences of Malaysia. He also held the position of Editor-in-Chief of the Malaysia Medical Journal from 1991 – 1998. He is a member of various governmental technical committees including the National Antibiotic and Infection Control Committee and the National Medical Testing Accreditation Committee. His fields of interest include antimicrobial chemotherapy and infectious diseases and has published and presented over 350 scientific papers.

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Ziad Memish obtained his medical degree from the University of Ottawa in 1987. Additional qualifications include those from the American Board of Internal Medicine in 1990 and the American Board of Infectious Diseases in 1992, and the American Certification of Infection Control. He has received Fellowships of the Royal College of Physicians and Surgeons of Canada in Internal Medicine (1991) and Infectious Diseases (1992). He is a fellow of the American College of Physicians (1993), of the Infectious Diseases Society of America (1997), of the Society of Healthcare Epidemiology of America (2000), and Fellow of the Royal College of Edinburgh in 2011 and London 2012 and Fellow of Faculty of Public Health in the UK since 2014..

Positions held include Division Head Infectious Diseases, Chairman Department of Infection Prevention and Control & Executive Director Infection Prevention and Control at King Abdulaziz Medical City and WHO Collaborating Center for Infection control under Saudi National Guard Health Affairs. More recently he has held the position of Assistant Deputy Minister of Health for Preventive Medicine from 2009 till April 2012 and Deputy Minister of health for Public Health from April 2012 till June 2014.

In November 2007, he was awarded by the Custodian of the Two Holly Mosques King Abdullah Bin Abdulaziz Al Saud “The King Abdulaziz Medal from the First Degree” - the highest award on a National level in Saudi Arabia for achievements in the field of infectious diseases and infection control.

Professor Memish has presented more than 250 abstracts internationally and published more than 380 peer reviewed papers and chapters in books. A reviewer for 17 peer reviewed journals, he initiated 2 elsevier journals in the MEA.The Journal of Infection and Public Health (Editor-in-Chief from 2008-2012) and Journal of Epidemiology and Global Health (Editor-in-Chief from 2011 till now). A senior editors of the open access journal Antimicrobial Resistance & Infection Control and ccorresponding editor of the International Journal of Infectious Diseases. Professor Memish is one of the editorial board members of Current Infectious Diseases Reports,and the Journal of Chemotherapy.

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Benefits of Antimicrobial Stewardship in Hospitals: evidence from a recent Cochrane review

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Antibiotic stewardship has been around now for several decades but has received renewed focus as a means of slowing the development of antibiotic resistance (AR). Cochrane reviews include only papers of sufficiently robust methodology and at the date of the last review (2006) there were less than 100 published scientific papers so classified on Antibiotic Stewardship. In recent years a greater proportion of published papers have been included but almost all are from USA and Europe. The majority use interrupted time series analysis, with about a quarter being randomised controlled trials.

Restrictive interventions such as order forms and expert approval have a more immediate effect than persuasive (educational) interventions such as audit and academic detailing but the effects of both are well maintained over at least 2 years. Most are delivered by multidisciplinary teams, followed by ID/micro and pharmacists.

There is robust evidence that effective stewardship, leading to major reduction (34-42%) in the use of key agents such as quinolones and cephalosporins can reduce *Clostridium difficile* infection, MRSA, VRE and multi resistant Gram negatives by 24-68%. Also, improved quality of use can reduce mortality from CAP. No

associated increases in mortality, length of stay or infection specific re-admission have been documented.

In summary, antibiotic stewardship has a valuable role to play, alongside hand hygiene and surveillance/cohorting/isolation/suppression/decolonization in the control of Multi-Drug Resistant Organisms (MDROs).

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Biography& photos for APCCMI

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Vincent Chi-Chung Cheng is currently Consultant Microbiologist and Infection Control Officer at Queen Mary Hospital, Hospital Authority, Hong Kong Special Administrative Region, and Honorary Associate Professor at Department of Microbiology, The University of Hong Kong. He graduated from the Faculty of Medicine at The University of Hong Kong in 1994 with distinction in Medicine, and trained in the field of internal medicine. After acquisition of Membership from The Royal Colleges of Physicians of the United Kingdom in 1997, he pursued further training in Clinical Microbiology and Infectious Diseases at Queen Mary Hospital. He also received training in Clinical Infectious Diseases and HIV medicine under the tutelage of Davidson Hamer, David Snydman, and Sherwood Gorbach at Tufts Medical Center, Boston, USA in 2001. He obtained his Membership and Fellowship from The Royal College of Pathologists in 2004 and 2007 respectively. He was conferredDoctorof Medicine by The University of Hong Kong in 2012, and was awarded the Sir Patrick Manson Gold Medal for the best MD thesis. He has published over 160 international peer reviewed original articles in the areas of clinical infectious disease including SARS and influenza, diagnostic clinical microbiology, proactive infection control for multiple drug resistant bacteria, and respiratory and gastrointestinal viruses, and hospital outbreak investigations for bacteria, virus, and fungus.

Plenary lecture 6: Emerging and re-emerging viruses: Where is the next threat?

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Most of the emerging infections are caused by viruses, which adapt continually to the environment by mutation, recombination or gene reassortment, as exemplified by influenza A. There has been four major influenza A pandemics from 1918 to 2009, intercalated by sporadic occurrence of human infectionsdue to avian influenza A H5N1, H9N2, H7N9, and H10N8. All avian influenza viruses were first reported in mainland China, where wet markets with caged live poultry served to amplify viruses and they serve as a convenient environment with close human and poultry interactions. An unprecedented outbreak of SARS-coronavirus in 2003 was also epidemiologically linked with civet catsfrom wet markets, although the virus was eventually traced to the Chinese horseshoe batswhich are prevalent in Southern China. Research has focused on the discovery of novel viruses from bats, of which coronavirus-HKU4 is phylogenetic closely relatedwith the recentlydescribed MERS-coronavirus in the Middle East. Healthcare facilities become important epicenters for human-to-human transmission for emerging viral infections. Proactive infection control bundleincluding active surveillance of high risk cases, early isolation of index patients with standard and transmission-based precautions, rapid molecular diagnostics, and directly observed hand hygiene are important measures to combat against nosocomial outbreaks due to emerging and re-emerging viral infections in hospitals.International travel facilitates dissemination of emerging and re-emerging viral infections, as illustrated in the diagnosis of sporadic cases of Ebola virus diseases in North America and Europe, which are epidemiologically linked with the largest-ever Ebola outbreak still simmering in West Africa. Global warming also increases the risk of transmission of mosquito-borne arboviruses.

H7N9: A killer in the making or a false alarm?

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The novel influenza A H7N9 first described in March 2013 raised serious public health concerns locally and internationally. Even though influenza A H7N9 appears to be less virulent compared with the penultimate novel avian influenza A H5N1, the former has proven to replicate in both upper and lower respiratory tract. Additionally, evidence has revealed limited airborne transmission in ferret model, with reports of intra-familial spread of H7N9 influenza A, suggesting infection control preparedness may have important implication in minimizing the risk of nosocomial transmission of influenza A H7N9.