SSR Medical College

1st Symposium of International Association of Medical and Biomedical Researchers

IAMBR

Microbial Resistance to Antibiotics

Abstract Book

September 18, 2011

SSR Medical College, Mauritius

Symposium on
Microbial Resistance to Antibiotics

Abstract Book

September 18, 2011

Organized by

SSR MEDICAL COLLEGE, MAURITIUS
Website: http://www.ssrmedicalcollege.com
&
INTERNATIONAL ASSOCIATION OF MEDICAL AND BIOMEDICAL RESEARCHERS | IAMBR
Website: http://www.iambr.info

ABOUT IAMBR

The International Association of Medical and Biomedical Researchers (IAMBR) was founded in a meeting held at SSR Medical College, Mauritius on December 2010 with the objective to motivate and sensitise the people of medical and related profession to participate in medical research through symposiums/workshops/conferences/etc. The IAMBR is an international organization and multidisciplinary in nature including the members of basis science and clinical medical faculty as well as the members from allied sciences.

The International Association of Medical and Biomedical Researchers (IAMBR) was registered on February 16, 2011.

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About S S R Medical college

SSR Medical College, Mauritius prides itself in offering an intimate, collegial environment which fosters human values and genuine learning. The school offers the best education in an environment that supports the practice of new skills as well as an individual student's capacity to learn and serve. A unique emphasis on understanding and discipline in every action is the focal point, and this nurtures the student's intellectual and personal growth. Progressing with a noble idea to transform education from being a cluster of well-understood subject to becoming well-adapted aspects and principles of life, SSR Medical College has become a "Centre of Excellence" in medical education, medicare, training and research.

Mr. R. P. N. Singh, an educationist and social planner from India is the Founder Chairman and Managing Trustee of the Trust.

The College strives to excel in every aspect of education under the direct guidance of honorable chairman whose vision has made every success possible.

Message

It is matter of great pleasure for all of us that the faculty of the IOMIT's SSR Medical College has launched "International Association of Medical & Biomedical Researchers (IAMBR), which has been registered in February 2011 and is conducting a Symposium on" Microbial Resistance to Antibiotics" on 18th Sept.2011, the day which is the birth anniversary of Sir Seewoosagur Ramgoolam, the Father of the Nation and also the annual day of our College.

SSR himself was a doctor and would have been more than happy to give his blessing to such an initiative in Mauritius for which he always had a vision to make a center of science and learning. He was one in line of those greats who always believed that human beings shall make a graceful transition from the role of rebellious teenager to the role of a solid citizen and that without social justice and ethical content, scientific progress may reduce to be a mere tool for exploitation and inequality.

The greatest challenge facing humanity today is the tsunami of new age of technologies: the Information, the Biotechnology and the Neurotechnology. The fundamental challenge for us in coming times is this mismatch between these three new waves of technology and the three basic needs of the needy: affordable housing, affordable health care and affordable education, which concerns even today, almost half of the humanity. The widening gap between technology and human needs can only be filled by addressing ethical issues and restraint in these times of free market economy.

Luckily, the visionary leadership in Mauritius has ensured to do away with this mismatch and has ensured provision of free and affordable health care, education and housing to its people.

We can say with satisfaction that the SSR Medical College has contributed its share in taking forward and living up to this commitment by making provision for quality medical education at a affordable cost.

I extend my best wishes to IAMBR with the hope that it would contribute in propagating these ideals and would provide a vibrant platform for research and propagation of issues relevant to the region.

Best Wishes.

Shri. R P N Singh
Chairman, SSR Medical College, Mauritius
Patron

Message

International Association of Medical and Biomedical Researchers under the aegis of SSR Medical College, is organizing its first symposium, entitled, "Microbial resistance to antibiotics." This is also World health Organization's theme for this year. It gives me immense pleasure to welcome all the participants for the same. The association took birth in February this year with an aim to providing a platform for young researchers to be able to share their experiences and disseminate their knowledge in the various medical and biomedical fields. There could not have been a more suitable seat for this association than SSR Medical College itself, where there is no dearth of highly qualified professors and faculty members, as well as aspiring young students of medicine.

It goes without saying that the association had the full support of the Honourable Chairman, Shri RPN Singh and the Principal Professor Mrs. Shukla, who have always very willingly extended help in every possible way. Without their support, guidance and encouragement the association would not have been able to realize it's goals. I seize this opportunity to thank the Honourable Chairman and the Principal on behalf of the association.

I also wish to thank all the members of the organizing committee who have left no stone unturned in preparing for the symposium as well as arranging for the poster competition in a very scientific manner.

I wish the association and all the young researchers of SSR Medical College the very best in all their endeavours.

Dr. Nilima Jeebun, MD
Professor, Department of Pathology,
SSR Medical College, Mauritius
President

Symposium on:

Microbial Resistance to Antibiotics /September 18, 2011

WELCOME ADDRESS

Dear Delegates,

I extend a warm welcome to all the participants of the symposium on – "Microbial resistance to Antibiotics" organized by SSR Medical College, Mauritius and International Association of Medical and Biomedical Researchers. The symposium intends to focus on the emerging problem of Antimicrobial resistance and its global spread in the community.

I am extremely grateful to our honourable chairman of SSR Medical College Shri RPN Singh for taking the initiative to organize this symposium and providing with all necessary facilities for this event. It is a matter of great joy that this event is being held at our institute. My gratitude also goes to the Principal of SSR Medical College Professor S Shukla for all her guidance and encouragement. I would be failing in my duty if I do not acknowledge the generosity and support of all members of the association.

I am thankful to all the participants for an overwhelming response to the symposium. I am sure that the symposium would provide a platform for healthy scientific deliberations and interactions between students and scientists.

Dr. Arun Kumar Agnihotri, MD
Additional Professor, Department of Forensic Medicine,
SSR Medical College, Mauritius
Organizing Secretary

ORGANIZING COMMITEE

Patron	**Shri. R. P. N. Singh** Chairman, IOMIT's, SSR Medical College, Mauritius
President	**Dr. Nilima Jeebun, MD** Professor, Department of Pathology, SSR Medical College, Mauritius
Vice-president	**Dr. Theeshan Bahorun, PhD** Professor, Department of Biosciences, University of Mauritius, Mauritius
Organizing Secretary	**Dr. Arun Kumar Agnihotri, MD** Additional Professor, Department of Forensic Medicine, SSR Medical College, Mauritius
Co-organizing Secretary	**Dr. Sushil Dawka, MS** Professor, Department of Surgery, SSR Medical College, Mauritius
Treasurer	**Dr. Ashok Pratap Singh, MS** Professor, Department of Anatomy, SSR Medical College, Mauritius
Scientific Committee	**Dr. Smriti Agnihotri, MD** Associate Professor, Department of Pathology, SSR Medical College, Mauritius **Dr. Rimli Barthakur, MS** Additional Professor, Department of Ophthalmology, SSR Medical College, Mauritius
Registration Committee	**Dr. Anju Bala Singh, MS** Associate Professor, Department of Obstetrics & Gynecology, SSR Medical College, Mauritius **Ms. Smita Kachhwaha, MSc** Assistant Professor, Department of Anatomy, SSR Medical College, Mauritius
Souvenir Committee	**Dr. Namrata Chhabra, MD** Additional Professor, Department of Biochemistry, SSR Medical College, Mauritius **Dr. Vandna Jowaheer, PhD** Associate Professor, Department of Mathematics, University of Mauritius, Mauritius
Reception Committee	**Dr. Sudesh Gungadin, MD** Chief Police Medical Officer, Police Medical Division, Mauritius **Dr. Anishta Allock, MBBS** Assistant Professor, Department of Pathology, SSR Medical College, Mauritius **Mr. Amar Nagesh Kumar, MSc** Lecturer, Department of Biochemistry, SSR Medical College, Mauritius

MANAGING COMMITEE OF IAMBR

President	**Dr. Nilima Jeebun, MD** Professor, Department of Pathology, SSR Medical College, Mauritius
Vice-president	**Dr. Theeshan Bahorun, PhD** Professor, Department of Biosciences, University of Mauritius, Mauritius
Secretary	**Dr. Arun Kumar Agnihotri, MD** Additional Professor, Department of Forensic Medicine, SSR Medical College, Mauritius
Assistant Secretary	**Dr. Sushil Dawka, MS** Professor, Department of Surgery, SSR Medical College, Mauritius
Treasurer	**Dr. Ashok Pratap Singh, MS** Professor, Department of Anatomy, SSR Medical College, Mauritius
Assistant Treasurer	**Dr. Smriti Agnihotri, MD** Associate Professor, Department of Pathology, SSR Medical College, Mauritius
Members	**Dr. Sudesh Gungadin**, Chief Police Medical Officer, Police Medical Division, Victoria Hospital, Mauritius **Dr. Rimli Barthakur, MS** Additional Professor, Department of Ophthalmology, SSR Medical College, Mauritius **Dr. Farida Khan, PhD** Assistant Professor, Department of Biochemistry, SSR Medical College, Mauritius **Dr. Namrata Chhabra, MD** Additional Professor, Department of Biochemistry, SSR Medical College, Mauritius
Auditor	**Dr. Vandna Jowaheer, PhD** Associate Professor, Department of Mathematics, University of Mauritius, Mauritius

Scientific Program

September18,2011 **Venue- Anatomy Lecture Hall, SSR Medical College, Mauritius**

8:15 – 9:00 hours	**Registration**
9:00 – 9:10 hours	**Inauguration (By Shri. R P N Singh, Chairman, SSR Medical College, Belle Rive, Mauritius)**
9:10 - 9:15 hours	**Welcome Address by President of IAMBR** Dr. Nilima Jeebun, Professor, Department of Pathology, SSR Medical College, Mauritius
9:15 - 9:30 hours	**Break**
9:30 – 11:00 hours	**Scientific Session** (Chaired by Dr. Bharti Bais MD, Professor, Department of Microbiology, SSR Medical College, Belle Rive, Mauritius)
9:30 – 9:35 hours	**Introduction to topic and speakers** - Session Chairs
9:35 – 10:00 hours	**Microbial Resistance - a clinical perspective** Dr. Sushil Dawka MS, Professor, Department of Surgery, SSR Medical College, Mauritius
10:00 – 10:25 hours	**Mechanisms of antimicrobial resistance in MRSA** Dr. Sanjiv Rughooputh PhD, Department of Molecular Biology and Virology, Central Health Laboratory Candos, Mauritius
10:25 – 10:50 hours	**Microbial Resistance to Antibiotics - WHO Policy Package** Dr. Romesh Munbodh, World Health Organization Country Office, Mauritius
10:50 – 10:55 hours	**Discussion and conclusion remarks by Chairperson**
10:55 – 11:00 hours	**Vote of thanks by Organizing Secretary** Dr. Arun Kumar Agnihotri, Additional Professor, Department of Forensic Medicine, SSR Medical College, Mauritius
10:00 – 10:30 hours	**Poster Session (Venue - A hall near Principal Office)**
11:00 hours onwards	**Prize Giving Ceremony, Lunch and Cultural Program**

Scientific Session

Key notes of speakers

Microbial Resistance - a clinical perspective

Dr. Sushil Dawka MS,
Professor, Department of Surgery,
SSR Medical College, Mauritius

Introduction: Humanity is facing an unprecedented threat, that of a post-antibiotic era. As antimicrobial resistance (AMR) depletes our stock of effective antibiotics, a global public health disaster appears likely. "Superbugs" that make the headlines are merely the proverbial tip of the iceberg.

Hospital-acquired infections (HAI) that resist standard antimicrobials are increasing alarmingly. The Centers for Disease Control and Prevention (CDC) estimates that 2 million hospital patients become infected annually in the US and 90,000 will die as a result. 70 percent of bacteria causing HAI are now resistant to at least one of the common drugs and the patients affected face longer hospital stays and second-choice drugs that may be more expensive, less effective or more toxic.

More than 50% of *Staphylococcus aureus* causing ICU infections are methicillin-resistant. Vancomycin-resistant enterococci are endemic in many hospitals and cause over 25% of enterococcal infections. Gram-negative organisms such as *Klebsiella* and other *Enterobacteriaceae* have acquired extended-spectrum beta-lactamases that resist cephalosporins and consequent wider usage of fluoroquinolones is fostering resistance.

Antibiotics are an environmental selection pressure on microbial populations, ensuring the proliferation of resistant strains. Irresponsible antibiotics use in and outside healthcare such as veterinary usage, food additives in livestock (as growth-promoters) increase exposure. Even in better-regulated human medicine, misuse and overuse, incomplete or inadequate dosage, poor manufacturing practices, patient and medico-legal pressures to unnecessarily prescribe, OTC sale, poor hand hygiene and poor compliance all promote bacteria-drug interfacing and thus AMR.

The Clinical Perspective: One must view the problems of AMR in the context of its setting. Resistance to β-lactam antibiotics in *Streptococcus pneumoniae* results from OPD and domiciliary overuse and is more a community problem. Resistance in *Salmonella*, *Campylobacter* and also in *Escherichia coli* is significantly the result of agricultural and livestock use of antibiotics. In the hospital setting the major players are *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumanni*, *Pseudomonas aeruginosa* and *Enterobacter* species (often referred to as the ESKAPE pathogens) and the blame rests with those who prescribe them in the hospital setting. As the CDC proclaims: ***"Clinicians hold the solution".*** Antibiotic usage should be a deliberate, informed, judicious choice aligned with protocols based on hard global and local evidence.

CDC's Campaign to Prevent Antimicrobial Resistance: *Four strategies* form the framework for the *12 Steps to Prevent Antimicrobial Resistance*. Though antimicrobial use promotes selection of resistant strains of pathogens, the cycle of emerging antimicrobial resistance/multidrug resistance can be broken by:

Preventing infections to reduce the need for antimicrobial exposure and the emergence of resistance.

1. Vaccinate
2. Get the catheters out

Influenza and pneumococcal vaccination of at-risk patients before discharge from hospital as well as influenza vaccination of medical personnel will prevent infections. Catheters and other invasive devices are the leading exogenous cause of hospital-acquired infections.

Effective diagnosis and treatment to decrease the opportunity for development of resistance.

1. Target the pathogen
2. Access the experts

Appropriate antimicrobial therapy (correct regimen, timing, dosage, route, and duration) requires correct diagnosis of the causative pathogen. Cultures are almost always indicated for definitive therapy to identify pathogens and their antimicrobial susceptibility. Empiric antimicrobial therapy should target likely pathogens and match local antimicrobial susceptibility data. Microbiologic and pharmacologic expertise should be sought.

Optimizing antimicrobial use to avoid overuse of broad-spectrum antimicrobials and unnecessary treatment.

1. Practice antimicrobial control
2. Use local data
3. Treat infection, not contamination
4. Treat infection, not colonization
5. Know when to say "no" to vanco
6. Stop treatment when cured

Policies to optimize antimicrobial use are effective. Antibiograms provide a synopsis of common pathogens and their susceptibility patterns. They provide guidelines about empiric antimicrobial treatment decisions, but are not necessarily reliable in the individual case. Contamination of patient specimens often leads to inappropriate antimicrobial use. Hospitalized patients also become colonized with hospital flora which are usually resistant to first-line antimicrobials. Evidence of infection may be attributed to these colonizing organisms inviting unnecessary broad-spectrum antimicrobial usage. Overuse of vancomycin promotes resistance especially among Gram-positive organisms. Unnecessary prolongation of antimicrobial treatment translates to overuse and resistance.

Preventing transmission of resistant organisms.

1. Isolate the pathogen
2. Contain your contagion

Isolation to prevent transmission of pathogens between patients is essential for AMR prevention. Healthcare personnel too can spread resistant pathogens between patients.

WHO warns: "No action today, no cure tomorrow." Pandemics have decimated populations and shaped history in an era when antibiotics were unknown.

Can such a scenario arise today? Yes.

Despite our antibiotics. Because of our antibiotics.

Prevention is Primary!

Fleming warned of antimicrobial resistance as early as 1945

Mechanisms of antimicrobial resistance in MRSA

Dr. Sanjiv Rughooputh PhD,
Department of Molecular Biology and Virology,
Central Health Laboratory Candos, Mauritius

Staphylococcus aureus is one of the major cause of nosocomial infections. Therapy for infections involves β-lactam agents such as penicillin and methicillin. However, since the introduction of methicillin into clinical practice in the 1960s MRSA (Methicillin Resistant *Staplylococcus aureus*) isolates have emerged. MRSA is one of the most significant pathogens responsible for both nosocomial and community acquired infections. Symptoms can range from skin and soft tissue infections to severe, life threatening debilitation.

In recent years, the prevalence of MRSA has dramatically increased. There is always a threat of an emerging MRSA "super bug" strain that is resistant to all antibiotics. According to the National Audit office, between Oct 2003 and Sep 2004, there were 19311 cases of *Staphylococcus aureus* bacteraemia cases reported in England's hospital. During the same time there were 7647 cases of MRSA. In 2002, 800 deaths were associated with MRSA.

On the global scale, MRSA infections account for around 5-10% of hospital acquired infections. The cost of screening, detection and treatment is a significant burden on the health authorities budget. Subsequent intervention on patients with MRSA involves longer bed occupancy and therefore imposes stress on patient management.

MRSA came into existence as a result of acquisition of a large DNA element known as the staphylococcal cassette chromosome *mec* (SCC *mec*), which is similar to a pathogenicity island but does not contain any virulence genes.

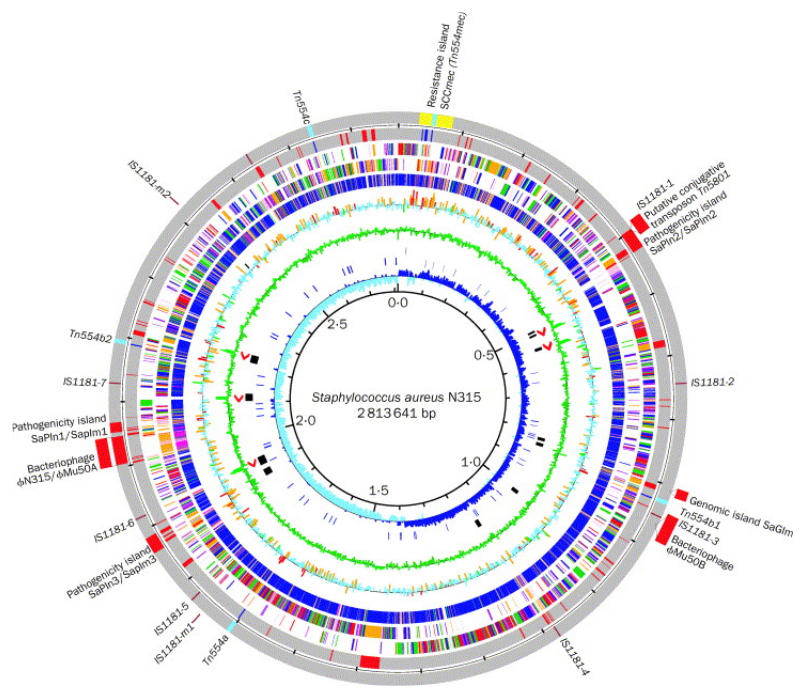

Figure 1: Circular representation of chromosome (N315) and Mu50 of Staphylococcus aureus specific genetic elements. The outer circle shows the positions of various mobile genetic elements (Source : The Lancet 2001; 357:1225-1240)

MRSA is a constantly evolving versatile pathogen whose genome consists of a complex mixture of genes, many of which seem to have been acquired by lateral gene transfer of which 70 are prime candidates for new virulence factors.

The organism has exploited a multitude of ways to become a successful pathogen including:

1. Virulence and quorum sensing mechanisms
2. Genetic diversity and ability to acquire new exogenous genes
3. Ability to establish asymptomatic carriage
4. Remarkable propensity to the acquisition of resistance to multiple antimicrobial agents.

Table 1: Antibiotic resistance genes identified in N315 and Mu50 genomes

Product	Gene name	Location	Function
Bleomycin resistance protein	*bleO*	SCCmec	Resistance to bleomycin
Penicillin-binding protein 2′ (MecA)	*mecA*	SCCmec	Resistance to β-lactams
β-lactamase	*blaZ*	pN315	Hydrolysis of penicillins
rRNA methylase ErmA	*ermA*	*Tn554* in SCCmec	MLS resistance
rRNA methylase ErmA	*ermA*	*Tn554*	MLS resistance
O-nucleotidyltransferase(4′)	*ant(4′)*	SCCmec	Modification of aminoglycosides
O-nucleotidyltransferase(9)	*ant(9)*	*Tn554* in SCCmec	Modification of spectinomycin
O-nucleotidyltransferase(9)	*ant(9)*	*Tn554*	Modification of spectinomycin
Bifunctional AAC/APH protein	*aacA-aphD*	*Tn4001* in pMu50	Modification of aminoglycosides
Tetracycline resistance protein TetM	*tetM*	Putative conjugative transposon *Tn5801*	Resistance to tetracyclines
QacA protein	*qacA*	pMu50	Efflux-mediated antiseptic resistance

MLS=macrolide, lincosamide, and streptograminin B. AAC=6′-aminoglycoside N-acetyltransferase. APH=2″aminoglycoside phosphotransferase

During this presentation, the author will elaborate on the evolution of the organism's resistance mechanisms.

Microbial Resistance to Antibiotics - WHO Policy Package

Dr. Romesh Munbodh,
WHO Country Office, Mauritius

Why Antimicrobial Resistance (AMR) is a global concern?

- Antimicrobial resistance (AMR) kills
- Challenges care and control of infectious diseases
- Greatly increases care costs
- Threatens a return to the pre-antibiotic era
- Jeopardizes healthcare gains for individuals and society
- Compromises health security, damages trade and economy
- Lack of coherent approaches to prevention and containment

AMR - A major challenge

- **Tuberculosis (TB):** 440,000 new multidrug resistance (MDR) TB cases annually; extensively drug resistance (XDR) TB cases reported in 64 countries so far.
- **Malaria:** Emergence of Artemisinin resistance linked to ongoing use of monotherapies.
- **HIV:** With expanded use of antiretrovirals (ARVs), resistance is a concern.
- **Methicillin-resistant *Staphylococcus aureus*:** Lethal infections in hospital settings becoming increasingly frequent.
- **Multi-drug resistant *E.coli, K.pneumoniae and Enterobacter sp.*:** Infections are on the rise and a new beta-lactamase, NDM-1, is causing alarm.
- ***Neisseria gonorrheae* and *Shigella***: Becoming increasingly resistant to drugs.

What drives AMR?

- Plans and resources not comprehensive or coherent; poor accountability.
- Consumers and communities not engaged.
- Surveillance systems weak or absent.
- Systems for ensuring quality and supply of medicines inadequate.
- Use of medicines inappropriate and irrational, including in animal husbandry.
- Infection prevention and control poor.
- Antimicrobials and diagnostics arsenal limited.
- Research and development for diagnostics and medicines insufficient.

WHO Policy Package to combat AMR: WHO recommends 6 priority actions:

1. Commit a comprehensive National Plan
2. Strengthen surveillance and laboratory capacity
3. Ensure uninterrupted access to essential medicines of assured quality
4. Regulate and promote rational use of medicines
5. Enhance infection prevention and control
6. Foster innovations and research and development for new tools

Global policy response to AMR

- **Global Commitment:** WHO Global Strategy for Containment of AMR (2001; Surveillance systems and response strategies being pursued; Task Force and informal network at global and regional levels.
- **Regional Action:** WHO Regional Committee Resolutions (e.g. AFRO, PAHO, SEARO).

- **Political Bill:** World Health Assembly Resolutions; 1998 – Emerging and other communicable diseases AMR; 2005 – Improving the containment of AMR; 2009 – Prevention and control of MDR-TB and XDR-TB.

Despite progress, strategies for AMR containment have not been widely implemented.

AMR - what is blocking process?

- Complex problem requiring a comprehensive response among and between Member States across different sectors.
- Actions needed are clear – but there is a failure of commitment, implementation and accountability.
- Preventing AMR is a "public good" which strengthens health security – but financing is insufficient.

Poster Session

Abstracts

Lethal Meningitis in a Neonate and Salmonella typhimurium

Godfred AM[*], **Anishta Allock**[*], Harish BN[**]
[*]SSR Medical College, Belle Rive, Mauritius.[**]JIPMER, Pondicherry, India

Infections with *Salmonella* spp. are an important public health problem worldwide. On a global scale it has been appraised that *Salmonella* spp. are responsible for an estimated 3 billion human infections each year. Nontyphoidal Salmonellae (NTS) are one of the principal pathogens implicated in food-borne gastroenteritis. Although antibiotics are not usually recommended in cases of *Salmonella* enterocolitis, they are crucial if the infection spreads from the intestine leading to invasive complications, including meningitis, sepsis and bacteremia. Extended-spectrum cephalosporins are preferentially used to treat salmonellosis in children. Treatment failures due to *in-vivo* acquisition of an extended-spectrum β-lactamase (ESBL) gene in NTS are now well established. In this clinical case, a 45 days old male baby presented to the paediatric intensive care unit (PICU) with a history of fever, poor feeding, 2 episodes of seizures of 3 days' duration and recurrent apnoea. At admission, cerebrospinal fluid (CSF), stool and blood cultures were done and *S. typhimurium* was isolated from all the samples. The patient was empirically started on intravenous antibiotics, cefotaxime 125mg sixth hourly and gentamicin 6.5mg eighth hourly. On fifth day of admission baby developed bradycardia and hypotension for which cardiopulmonary resuscitation was started. The baby received adrenaline, calcium gluconate and dopamine infusion. After half an hour the baby developed cardiopulmonary arrest from which baby could not be revived. The baby expired due to acute pyogenic meningitis. The interval between the onset of illness and death was seven days. It is important to note that only the stool isolate was resistant to many antibiotics including the cephalosporins though the isolates from CSF and blood were sensitive. Interestingly *S. typhimurium* isolated from all three samples was clonal, genotyped by Pulsed Field Gel Electrophoresis (PFGE) and Enterobacterial Repetitive Intergenic Consensus PCR (ERIC-PCR). Continued surveillance of the presence of ESBLs in *Enterobacteriaceae*, and rapid elucidation of the mode of spread of these resistance genes in NTS is essential to minimize the risks to future treatment that their widespread dissemination would create.

In search of New Antimicrobial Drugs by the Researchers Across the globe

Manas Kanti Ray, Suranjana Ray
SSR Medical College, Mauritius

Antimicrobial resistance is the ability of microbes, such as bacteria, viruses, parasites or fungi, to grow in the presence of a chemical that would normally kill it or limit its growth. Increasing use of antimicrobials in humans, animals, and agriculture has resulted in many microbes developing resistance to these drugs. Resistance can occur by natural causes, **s**elective pressure, and mutation, and gene transfer, inappropriate use of antibiotics, inadequate diagnostics, and agriculture use of antimicrobials. The discovery of antibiotics in the 1930s fundamentally transformed the way physicians care for patients. Eight decades of medical advances enabled by antibiotics are now seriously threatened by the convergence of relentlessly rising antibiotic resistance. The emerging antimicrobial resistance is of such tremendous global concern that the World Health Organization (WHO) has proclaimed it the central focus. Infectious Diseases Society of America (IDSA) program supports research to study antimicrobial resistance in major pathogens; identify new diagnostic techniques, novel therapeutics and preventive measures to minimize infection with resistant pathogens; prevent the acquisition of resistant traits; control the spread of resistance factors and resistant pathogens; Support basic research of resistance gene acquisition ; Work with academic researchers and biotechnology companies to explore novel therapeutic approaches, such as monoclonal antibodies and natural antimicrobial peptides. In 2010, in recognition of the need for creative, new ideas to address the antibiotic pipeline problem IDSA launched the 10 X '20, the development of 10 novel, safe and effective, systemic antibiotics by 2020. Forty five public health organizations across the spectrum of medicine have endorsed the 10 X '20 initiative. STARS (Scientific Training in Antimicrobial Research Strategies), addressed the urgent need for the development of antimicrobials ,one of the key drivers being the growing number of immunocompromised individuals and transplant recipients. Computer-aided drug design of novel antibiotics project is hosted by InhibOx, which is a drug discovery company in U.K, uses computational methods to discover new drugs. The company's technology is based on the leveraging of computing power from individual PCs around the world. It uses novel software developed to screen libraries of molecules to search for suitable drug candidates. Structure-based design of antimicrobials is emerging as an important area of application in modern drug discovery. Structural models of the target proteins will be prepared using available experimental data and in close collaboration with other STARS partners. Partners in STARS, Spain (Spanish National Research Council), United Kingdom (Medical Research Council), Latvia (Latvian Institute of Organic Synthesis), The Netherlands (Wageningen University), Italy (University of Siena). Minister of Health and Quality of Life of Mauritius announced at a workshop on antimicrobial resistance at Imperial China Trianon, in context of the World Health Day, that a pharmaco-vigilance unit which will be responsible for drug monitoring is expected to come into operation in two months' time in Mauritius. Worldwide health crisis resulting due to enhanced antibiotic resistance and will enhance in the coming decades unless urgent action is taken. The time for debating the problem has passed and immediate action is needed as no action taken today will result in no cure tomorrow.

Stop for Antibiotics Control

Rassool M Yusuf Ali
SSR Medical College, Belle Rive, Mauritius

"…the inappropriate use of penicillin could lead to the selection of resistant 'mutant form' of Staphylococcus aureus…"

Sir Alexander Fleming's interview with The New York Times, 1945

True to this prediction, resistance began to emerge within only 10 years of the wide scale introduction of penicillin. Today patients visit their healthcare provider only with the aim of getting drugs to alleviate their illnesses. Many of them think that only antibiotics would cure them. They are not interested to know the other ways which might help them to get better. When the doctor's prescription does not include any antibiotics, they would often ask for it. While some would request humbly, others would not hesitate to put pressure. Definitely not all doctors would give in. Since most of them are overloaded with work, prescribing broad spectrum antibiotics in the easier way to end the discussion. Some doctors do it just to please their patients; otherwise the latter would not come back and will see another physician. And whenever a doctor prescribes antibiotics, very often the patients do not follow the dose schedule. In this intelligent world of today many people think they know better. The take the tablets the way they feel like. Treatment is stopped as soon as they start to feel better. Some people would discard the rest, and other would save the remaining in their pharmacy box for later use. Many surveys around the world have reported that antibiotics and other drugs in any form are flushed in the toilet. The stored antibiotics would be used later whenever the patients feels unwell or might offer them to their close ones. In this way the mishandling and misprescription of these drugs have transformed the bacterial population such the many antibiotics have partially or entirely lost their efficacy. The problem is sever enough that many experts believe the value of existing antibiotics therapies over the next 100 years is now uncertain. However, some also believe that with a proper response to the current trend in antibiotic resistance, these drugs might once again serve their original function.

"Messieurs, c'est les microbes qui auront le dernier mot"
(Gentlemen, it is the microbes that have the last word)

Louis Pasteur, the father of bacteriology

The alarming presence of Metallo-betalactamases among multi-drug resistant clinical strains in urinary infections from Kolkata, India

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In the complex microbiological *milieu* of the hospital there occurs a duel between man and microbe, which often gets tilted in the latter's favour**.** Our antibiotic choices seldom remain more than a few drugs ahead of the resistant strains. Antibiotic resistance has now been recognized as a phenomenon, which is emerging and reemerging time and again. Carbapenems have been used in clinical settings as a last resort for their broad-spectrum antibacterial activity and stability against various beta-lactamases produced by Gram-negative bacteria. Metallo-beta-lactamases are emerging worldwide as acquired resistance determinant in clinical strains, which can hydrolyze carbapenems. The metallo-beta-lactamase (MBL) a carbapenem-hydrolyzing enzyme, MBLs differ from other beta-lactamases in having a serine moiety at the active site and are inhibited by thiol compounds like 2-mercaptoethanol, 2-mercaptopropionic acids and mercaptoacetic acid. MBL enzymes require divalent cations for activation (especially Zn^{2+}), are resistant to inhibition by clavulanic acid, sulbactam and tazobactam, are inhibited by chelating agents, and do not hydrolyze monobactam like aztreonam. In our study spanning one year 284 non-repeat clinical isolates were collected from patients admitted to various wards in six hospitals of Kolkata. Of these five strains which were multidrug resistant and resistant to beta-lactamase inhibitors and imipenem (IPM) were chosen. The IPM resistant strains were tested by Double Disk Synergy Test of Lee et al using EDTA and 2-mercaptoethanol. These isolates were then tested by Modified Hodge Test to distinguish the MBL producers from the non-producers. Their isoelectric focusing and plasmid profile were determined. Of the 284 non-repeat clinical isolates tested, 123 (43.3 %) were multidrug resistant (MDR) i.e., they were resistant to at least seven antibiotics and also to third-generation cephalosporins (3GC). Of these MDR isolates 5 (1.8%) were found to be resistant to all commercially available beta-lactamase inhibitors i.e., clavulanic acid, sulbactam and tazobactam; and to Imipenem. Of the five imipenem-resistant strains, one was *P. aeruginosa* and four were *P. vulgaris*. These isolates were then tested to distinguish the MBL producers from the non-producers and all five of them gave positive results with 10 µl of 50mM zinc sulfate (140 µg/disk). The imipenem resistant isolates found in our study are the first report of *P. vulgaris* producing MBL in India. pI of 5.4 and 7.8 were obtained in case of beta-lactamases tested by analytical isoelectric focusing. Antibiotic resistant plasmids (R-plasmids) are well known as carriers for spread of antibiotic resistance genes. The plasmid profile of our strains showed plasmid size of 2.1 kb to 6 kb and one common plasmid of greater than 53.4 kb. Similar reports of imipenem resistance in the last few years have shaken the world with the report of NDM-1 from India, Pakistan, UK, USA, and Canada. Hence if the type of beta-lactamase produced by the pathogens is detected along with antibiogram before administering the beta-lactam drug to the patient, the incidence of the therapeutic failure is most likely to be significantly reduced.

Quinolones- a fallacious panacea

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Drug resistance is a global problem - affecting both developing and developed countries. Its spread is helped by the enormous increase in global travel and trade. The 1st generation quinolones began with the introduction of nalidixic acid in 1962 for treatment of UTIs in humans. Nalidixic acid was discovered by George Lesher & coworkers in a distillate during an attempt at chloroquine synthesis. Ciprofloxacin was first patented in 1983 by Bayer A.G. and subsequently approved by the United States Food and Drug Administration (FDA) in 1987. While these drugs originally appeared almost as a panacea, and promised a bright future the scientific community now tends to call for cautious, or even restricted use of these agents for ecological reasons, to avoid the dissemination of resistance. Quinolone Resistance has evolved from urinary tract infections in the early 1970s to infections of almost all body compartments at the present time. As the fluoroquinilones were discovered, it was found out that they had a very wide spectrum of action against microbes, in fact the widest till now. The quinolones are being prescribed, used and abused by the doctors and public widely. From mild sore throat to septicemias, quinolones are the drug of choice. Plasmid-mediated quinolone resistance was first described for a ciprofloxacin-resistant strain of *Klebsiella pneumoniae* in 1998. Fluoroquinolone resistance develops as a result of spontaneous chromosomal mutations in the target of the antibiotic, topoisomerase IV or DNA gyrase, or by the induction of a multidrug efflux pump. Studies demonstrated that ciprofloxacin therapy rapidly increased the proportion of coagulase-negative staphylococcal strains colonizing the nares and skin that were resistant to both ciprofloxacin and methicillin. Pharmaceuticals aggravated this problem by unlicensed production of antibiotics, less stringent quality assurance procedures than those of licensed manufacturers and inadequate prescribing information. The blind promotion of this group of drugs by the medical representatives, worldwide further enhanced the problem. Many prescribers in developing countries have little access to good quality information about diagnosis and drugs. Standard treatment guidelines are often unavailable and health workers are often unsupported and unsupervised. Frequently, drug company representatives are doctors' only source of information. Such information may well be biased. Uncertainties of the diagnosis, fear of poor patient outcome, (and in industrialized countries, fear of litigation), lead to over-prescription of antibiotics. The newly released fluoroquinolones are for treating patients with respiratory tract infections, the single most common group of infections. The convenience of use of fluoroquinolones suggests that use will increase. Shortly after the licensing and use of fluoroquinolone in poultry, fluoroquinolone-resistant Salmonella and Campylobacter were isolated from animals, and soon afterward from humans. WHO, the UN Food and Agriculture Organization and 14 other international governmental and nongovernmental organizations and professional societies have developed a framework of recommendations to reduce the overuse and misuse of antimicrobials in animals and hospitals for the protection of human health. This could prevent further increase in quinolone resistance and emergence of new resistant strains.

Use and Abuse of Antibiotics: A Questionnaire Based Study

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The evidence about patterns of usage of antimicrobial agents is necessary for a constructive approach to the many problems that arise from the diversity of antibiotics now available, their high cost and the ecological sequelae of their use. Patient viewpoints are among the strongest predictors of clinicians' antibiotic prescribing decisions. Beliefs, public knowledge, and experiences of antibiotics may contribute to these viewpoints. Current trends of antibiotic misuse with its associated resistance development necessitated this study to determine perspective and involvement in the use and abuse of antibiotics. The purpose of this study was to look for factors that affect attitudes to antibiotic use. A sampling of 249 individuals (184 students, 35 staffs, and 28 faculties), in SSR Medical College campus was undertaken by administering questionnaires. Of the participants, 57.4% took antibiotic treatment 1-2 times per year. Pertaining to antibiotic usage, 40% of them thought antibiotics give quickest relief. A significant amount of the antibiotics purchased was Amoxicillin (44.6%) whilst Flu (fever/running nose/sore throat/cough), 69.5% were the highest reasons for antibiotic purchases respectively. A 35.8% of individuals discontinued therapy earlier (once symptoms disappear); 17.3% did not follow the correct dosage instructions and 23.7% used leftover antibiotics. Furthermore, a significant number (60%) purchase antibiotics without prescriptions, pharmacist being the main source (47.4%) of antibiotics. Interestingly, in 30.1% of individuals there was change in the antibiotic prescribed because the earlier one did not work. This research work exposes the abuse of antibiotics; medical practitioners should be aware that unnecessary prescribing could facilitate misconceptions regarding use of antibiotics and respiratory tract infections. Expectations of receiving antibiotics were higher for upper respiratory tract infections (URTI) than for other infections. Public beliefs and expectations should be taken into account when developing interventions targeting the public, patients, and physicians to reduce unnecessary prescribing of antibiotics for respiratory tract infections. Inappropriate and irrational use of antibiotics provides favourable conditions for resistant microorganisms to emerge and spread. Particularly, when patients do not take the full course of a prescribed antimicrobial (non-compliance), resistant microorganisms can emerge and spread.

MRSA campaign in a diabetic population: An urgent need in the context of Mauritius

Oodesh Kumar Ramdin

Mauritius health system requires a framework for corrective and preventive actions against antimicrobial resistance (Workshop on Antimicrobial Resistance, 2011). This is highly relevant for the diabetic population because Mauritius has one of the highest rates of prevalence of diabetes mellitus in the world, with around 400 amputations yearly (International Conference on Diabetes, 2009). At least 80% of all limb amputations in Mauritius are due to diabetes complications (Republic of Mauritius Government portal, 2009). Around 30% of hospital's diabetic foot infections are colonised with MRSA, Methicillin-resistant *Staphylococcus aureus* (Podiatry Management, 2009). Abnormalities in cell-mediated immunity and phagocyte function associated with hyperglycemia as well as diminished vascularisation are the causes of infections among the diabetic population. MRSA has been a matter of great concern worldwide because it is associated with severe diabetic foot ulcer, increased mortality and cost of care, and at times longer hospital stay. Several countries have already implemented MRSA campaigns. For example, there has been significant decrease in the rate of MRSA bacteraemia in UK and USA; UK launched the 'wipe it out campaign' in 2005 (Royal college of Nursing, 2005) with result that NHS Scotland shows a drop of 41% of MRSA for the first quarter of 2011 compared to the same period in 2010 (Health Protection Scotland, NHS, 2011). Despite cultural differences between, Scotland, for example, and Mauritius, medical practice and Infection Control Precautions are the same. A comparison of practice between Scotland and Mauritius shows that several measures have been recommended and successfully implemented in Scotland: (1) Guidance on uniforms and work wear (Royal college of Nursing, 2009); (2) Special sinks for visitors at entrance of each ward for hand washing; (3) Upgrading of hospital laundry (Scotland on Sunday, 2005); and, (4) Screening of all patients on admission (Health Protection Scotland, 2011). Based on these gaps and drawing on the success in UK and USA, I am presenting a framework for implementation of a campaign to reduce the risk of MRSA infection in Mauritius. This will lead to a decrease in the number of diabetic foot ulcers infected by MRSA, and help clinicians in their effort to reduce the number of amputations. The proposed framework consists of the following measures:

- Clinics focusing only on diabetes with a multi-disciplinary team.
- Improve infrastructure by creating special side rooms for diabetic patients or diabetic wards.
- MRSA Screening of patients both on admission and discharge.
- Educate public and Health care staffs about MRSA and its impact on diabetes.
- Control antibiotics abuse.
- A Research centre for MRSA surveillance and its impact on diabetes to provide the evidence based to improve practice.
- Special sinks for visitors for hand washing.
- Rapid MRSA screening tool.
- Environmental control.
- Hand hygiene and guidance on uniform and work wear.

It is expected that implementing the measures within this framework can help the Mauritian health care system to attain a standard similar to UK and USA.

Symposium on -
Microbial Resistance to Antibiotics

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