THE BULLETIN OF THE
SRI LANKA COLLEGE OF MICROBIOLOGISTS

30th ANNUAL SCIENTIFIC SESSIONS

VIRTUAL SCIENTIFIC PROGRAMME

in collaboration with
The Ohio State University, USA

24 - 26 AUGUST 2021

Threat of new and re-emerging infections:

ROLE OF NOVEL TOOLS AND TECHNOLOGIES TO FACE CHALLENGES

9 PLENARY LECTURES & 5 SYMPOSIA

with online participation of world's leading experts

FREE PAPER SESSIONS

GUEST LECTURES

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The Bulletin
of the
Sri Lanka College of Microbiologists
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The Sri Lanka College of Microbiologists
Council 2020 / 2021

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Sri Lanka College of Microbiologists

THE OHIO STATE UNIVERSITY

International E-Conference on

Threat of new and re-emerging infections: Role of novel tools and technologies to face challenges

30th Annual Scientific Sessions

of the Sri Lanka College of Microbiologists

held in collaboration with The Ohio State University, USA

Pre-Congress Workshop on

'Advances in Infectious Diseases'

24th August 2021

Inauguration Ceremony

24th August 2021 at 6.15pm

Scientific Programme

25th and 26th August 2021

MESSAGE FROM THE CHIEF GUEST

It is with great pleasure that I send this message of congratulations on the 52nd Anniversary of the Sri Lanka College of Microbiologists, on the eve of your 30th annual scientific sessions. The theme you have chosen, 'Threat of new and re-emerging infections: Role of novel tools and technologies to face challenges' could not be more appropriate at a time when the world is struggling through the second year of global COVID-19 pandemic. The pandemic caught a world not well prepared, and yet we have seen a courageous and swift response by way of developing new tools and technologies through scientific research, and effective strategies from the field of public health. They range from the application of genomics to vaccine development, and the development of effective diagnostics, to less acknowledged but very effective tools through innovation in many other fields such as information technology and communications.

Yet the pandemic, in the control of which in Sri Lanka, the College of Microbiologists has played an admirable role, has shown that the impact of new tools and technologies will only be as good as the strategies through which they are deployed. It has also shown that an inclusive health sector working across disciplines and other sectors is essential for these tools and strategies to have impact. With such instructive lessons from this pandemic I believe that the College of Microbiologists will be ready to deal with future challenges of re-emerging infections even more effectively. I wish the President, Council, Members and Guests, fruitful sessions at your annual meeting, and success in achieving the aspirations of the College.

Professor Kamini Mendis
Former Consultant, WHO
Emeritus Professor, University of Colombo

MESSAGE FROM THE PRESIDENT

It is indeed a privilege to write this message to the Bulletin of the Sri Lanka College of Microbiologists on the occasion of this year's Annual Scientific Sessions, which is the most anticipated event in the calendar of this professional body.

The Annual Scientific Sessions were first held in year 1991 and (named the Academic Sessions at that time), over 2 decades after the establishment of the College of Microbiologists. The Sri Lanka College of Microbiologists (SLCM) has a long history, which goes way back to year 1969 when the Ceylon Association of Microbiologists was formed (which subsequently evolved to be the Sri Lanka College of Microbiologists). This annual tradition of holding scientific sessions has thus continued uninterrupted over the past 3 decades steadily evolving with careful nurturing of respective councils.

Great strides have been made in many areas of infectious diseases and prevention of some dreaded infectious diseases. However, enormous challenges still remain to be addressed with the ongoing pandemic situation due to COVID-19 being a case in point. It spells out the critical need for continuous vigilance and the use of evidence-based approaches to combat infectious disease threats. The theme chosen for this year is "*Threat of new and re-emerging infections: Role of novel tools and technologies to face challenges*" and my address to the membership at the induction ceremony held on 27th February 2021 was titled 'Man vs Parasites: Weapons to combat' to be in line with this theme. Similarly, the Annual Scientific Sessions and the pre congress workshop have been aligned accordingly. Antibiotic resistance is yet another challenge that confront us both at local and global level, which was the topic addressed at this year's Siri Wickremesinghe Oration. The oration was titled "*Fighting the rising tide of antibiotic resistance; exploring non-pharmacological options, challenges and benefits*" and delivered by Professor Nelun Perera, Consultant Microbiologist, University Hospitals of Leicester and Hon. Associate Professor, University of Leicester, UK.

I take this opportunity to thank Professor Kamini N. Mendis, former Consultant, World Health Organization and Emeritus Professor, University of Colombo for accepting our invitation to be the chief guest at the inauguration ceremony. I extend my sincere gratitude to Prof. Abhay Satoskar, Dr. Namal Liyanage and the team at the Ohio State University, USA for partnering with us in organizing and conducting this event. I thank all our guest speakers, both local and overseas, for having accepted our invitations willingly to share their knowledge and expertise with us in spite of their busy schedules. I extend a special word of thanks to all the SLCM members and the Council members who have helped and contributed in numerous ways for SLCM activities during this year.

The busy schedule of the SLCM continues this year too with monthly CME lectures providing us with new insights and knowledge. Successful completion and the launch of the *'Hospital Infection Prevention and Control Manual'*, remains as a significant achievement. This is considered as a 'must have' publication for use of medical and paramedical personnel of all hospitals across the country. I am grateful to the World Health Organization for generously sponsoring printing of copies that will be soon made available for all hospitals across the country. The initial version of this publication was launched in March 2021 and is a result of sustained effort put in by several SLCM members spanning over many years. I would like to thank each and every member of that group. I also would like to thank the members who reviewed and updated the document and for their support to ensure free availability of this valuable resource. Subcommittees of the SLCM have been renewed this year to address many important areas within the field of microbiology and their continued contributions are gratefully acknowledged. We require and request the support and input of all our members in carrying out numerous activities that the SLCM initiates and is called upon to assist with the aim of improving the management of infectious diseases in Sri Lanka and the overall health status of our citizens.

I thank the Honorary Secretaries, Dr. Madhumanee Abeywardane and Dr. Nilakshi Samaranayake, the Editor Prof. Neluka Fernando, all Council members and our office staff, Ms. Priyanga Opatha, Ms. Nilmini Weerasiri who served until February 2021 and Ms. Amanda Jayasooriya who have worked beyond the call of duty to ensure the smooth running of all the activities of the SLCM.

An event of this magnitude would not have been possible without the generous contribution of our sponsors. On behalf of the Council of the Sri Lanka College of Microbiologists, I would like to thank all the sponsors for their valuable contributions.

Let me welcome you all to the Annual Scientific Sessions with a series of plenary lectures, symposia and free papers. I hope there will be something that will interest each and every one of you. A special feature of this year's event is the partnership forged with the Ohio State University, USA that enabled speakers and participants from many countries in the region as well as from the USA. We hope that this Congress will be the launching pad for many fruitful collaborations between clinicians and researchers in Sri Lanka and overseas.

Professor Nadira D. Karunaweera
President
Sri Lanka College of Microbiologists

INAUGURATION PROGRAMME

6.30 pm	Traditional lighting of the Oil Lamp
6.40 pm	Welcome Address **Dr. Madhumanee Abeywardena** *Hon. Joint Secretary*
6.45 pm	Address by the President **Professor Nadira Karunaweera**
7.00 pm	Special Address from The Ohio State University **Dr. Gil Latz** *Vice Provost for Global Strategies and International Affairs* **Professor Abhay Satoskar** *Professor and Vice Chair – Pathology* *Wexner Medical Centre*
7.20 pm	Introduction of the Chief Guest *by the President Professor Nadira Karunaweera*
7.25 pm	Address by the Chief Guest **Professor Kamini Mendis** Professor Emeritus, University of Colombo
7.45 pm	Address by the Guest of Honour **Dr. Alaka Singh** WHO Representative to Sri Lanka
8.00 pm	Award of SLCM Fellowships
8.30 pm	Vote of Thanks **Dr. Nilakshi Samaranayake** Honorary Joint Secretary

PROGRAMME AT A GLANCE

Time	25th August 2021	Time	26th August 2021
7.00 - 7.20am	**Guest Lecture 1** Pathogenesis and biofilm formation of recently circulating strains of Bordetella pertussis	7.00 - 7.30am	**Plenary 6** Defining pandemic preparedness partnerships between universities and government agencies; lessons learned from COVID-19
7.20 - 7.40am	**Guest Lecture 2** Pulmonary infections and the pathogenesis of cardiac dysfunction		
7.40 - 8.00am	**Guest Lecture 3** Altered macrophage phenotype and lipidome abnormalities may contribute to cardiovascular disease risk in aging people with HIV	7.30 - 8.00am	**Guest Lecture 7** Global one health paradigm for interconnected planet - beyond pandemics
8.00 - 8.20am	**Guest Lecture 4** Determinants of SHIV replication in macaque lymphocytes	8.00 - 8.30am	**Guest Lecture 8** Infection prevention and control implications in designing of health care facilities
8.20 - 8.40am	**Guest Lecture 5** Infection prevention and control measures for drug-resistant tuberculosis in healthcare settings		
9.00 - 10.00am	**Free Paper Session 1**	9.00 - 10.00am	**Free paper session 3**
10.00 - 11.00am	**Free Paper Session 2**	10.00 - 11.15am	**Symposium 4** Path to future healthcare
11.00 - 11.30am	**Plenary 1** Pandemic threats from Emerging Coronaviruses	11.15 - 11.45am	**Guest Lecture 9** Climate change and health
11.30 - 12.30pm	**Symposium 1** COVID-19: risks and mitigation of future pandemics	11.45 - 12.45pm	**Poster and Case presentations**
12.30 - 1.00pm	**Plenary 2** The forgotten organ of the body -"THE MICROBIOME"		
1.00 - 1.30pm	**Plenary 3** Ethics and professionalism		
1.30 pm	**End of the first session of the day**	12.45pm	**End of the first session of the day**
4.00 - 5.00pm	**Symposium 2** Advances in pathogenesis, diagnosis and treatment of infectious diseases	4.00 - 4.30pm	**Plenary 7** The COVID-19 response and AMR
5.00 - 5.30pm	**Plenary 4** No respite in the war: resistance to the newest antibiotics	4.30 - 5.30pm	**Symposium 5** Role of insects in the world of microbiology
5.30 - 6.30pm	**Symposium 3** AMR and one health	5.30 - 6.00pm	**Plenary 8** Post-acute COVID-19 syndrome
6.30 - 7.00pm	**Plenary 5** Role of travel and the spread of respiratory infections	6.00 - 6.30pm	**Guest Lecture 10** Clinical approach to manage infections before and after liver transplantation
7.00 - 7.30pm	**Guest Lecture 6** Adjuvants and immunization strategies to enhance mucosal immunity	6.30 - 7.00pm	**Plenary 9** Host targeted therapies for treating infections
7.30pm	**End of the day one proceedings**	7.00 - 7.30pm	**Award ceremony and close of conference**

PRE-CONGRESS WORKSHOP PROGRAMME

Sri Lanka College of Microbiologists

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Threat of new and re-emerging infections: Role of novel tools and technologies to face challenges

30th Annual Scientific Sessions of the Sri Lanka College of Microbiologists held in collaboration with The Ohio State University, USA

Pre-Congress Workshop on 'Advances in Infectious Diseases'

24th August 2021

Chairpersons – Dr. Kanthi Nanayakkara and Professor Namal Liyanage

7.00 - 7.20am	***Advances in immunology*** **Professor Nicholas T. Funderburg** Associate Professor of Division of Medical Laboratory Science College of Medicine, The Ohio State University, USA
7.20 - 7.40am	***Advances in molecular virology*** **Professor Jesse Kwiek** Associate Professor, Vice Chair for Teaching & Undergraduate Affairs Department of Microbiology, The Ohio State University, USA
7.40 - 8.00am	***Advances in vaccinology*** **Professor Purnima Dubey** Associate Professor of Microbial Infection and Immunity, The Ohio State University, College of Medicine, USA
8.00 - 8.20am	***Advances in therapeutics*** **Dr. Bradford McGwire** Infectious Disease – Physician, The Ohio State University – Wexner Medical Center, USA

8.20 - 9.00am	**Discussants** ***On Vaccines*** **Dr. Kanthi Nanayakkara** Consultant Virologist and Vaccinologist, Head / Department of Rabies & Vaccine QC, National Control Laboratory, Medical Research Institute, Colombo, Sri Lanka ***On Immunology*** **Dr. Rajiva De Silva** Consultant Immunologist, Medical Research Institute, Colombo, Sri Lanka ***On Molecular Virology*** **Dr. Rohitha Muthugala** Consultant Medical Virologist, Teaching Hospital Kandy, Sri Lanka ***On Therapeutics*** **Dr. Ananda Wijewickrama** Consultant Physician, National Institute of Infectious Diseases, Angoda, Sri Lanka
9.00am	**End of the first session of the day**
4.00 - 5.00pm	**Scientific writing** **Chairperson – Professor Vasanthi Thevanesam** ***Plagiarism: why and how it should be avoided?*** **Professor Barbara Gastel** Joint Professor of Integrative Biosciences, Humanities in Medicine and Biotechnology, Texas A & M University College of Medicine, USA ***Composing a masterpiece: making your data sing*** **Professor Eugene Oltz** Chair, Department of Microbial Infection and Immunity, Samuel Saslaw, Professor of Infectious Diseases, The Ohio State University, College of Medicine, USA

SCIENTIFIC PROGRAMME

Day 1 – 25.08.2021

Guest Lecture series

Chairpersons – Dr. Geethika Patabendige, Prof. Purnima Dubey and Dr. Madhumanee Abeywardena

7.00 - 7.20 am	**Guest Lecture 1** ***Pathogenesis and biofilm formation of recently circulating strains of Bordetella pertussis*** **Professor Rajendra Deora** Associate Professor, Department of Microbial Infection and Immunity, Department of Microbiology, The Ohio State University, USA
7.20 - 7.40 am	**Guest Lecture 2** ***Pulmonary infections and the pathogenesis of cardiac dysfunction*** **Professor Murugesan Rajaram** Associate Professor, Department of Microbial Infection and Immunity, The Ohio State University, USA
7.40 - 8.00 am	**Guest Lecture 3** ***Altered macrophage phenotype and lipidome abnormalities may contribute to cardiovascular disease risk in aging people with HIV*** **Professor Nicholas T. Funderburg** Associate Professor of Division of Medical Laboratory Science, College of Medicine, The Ohio State University, USA
8.00 - 8.20 am	**Guest Lecture 4** ***Determinants of SHIV replication in macaque lymphocytes*** **Professor Amit Sharma** Assistant Professor, Department of Veterinary Biosciences, Department of Microbial Infection & Immunity, The Ohio State University, USA
8.20 - 8.40 am	**Guest Lecture 5** ***Infection prevention and control measures for drug-resistant tuberculosis in healthcare settings*** **Dr. Rajesh Deshmukh** Public Health Specialist - TB, Division of HIV and Tuberculosis, Centers for Disease Control and Prevention, CDC/DGHT, India

9.00 - 10.00 am	**Free Paper Session 1 – Bacteriology** **Chairperson – Dr. Jananie Kottahachchi**
OP 1	**Gastric microbiota and its association with histopathological findings among a dyspeptic patient population** *Weerasinghe GGYH, Gunasekara TDCP, Weerasekera MM, Fernando SSN* Department of Microbiology, Faculty of Medical Sciences, University of Sri Jayawardenepura, Nugegoda, Sri Lanka.
OP 2	**Effectiveness of two different protocols of daily chlorhexidine bathing in the prevention of nosocomial acquisition of multi-drug resistant pathogens and *Candida* species in the intensive care units at a tertiary care hospital, Sri Lanka** *Sapukotana PM[1], Piyasiri DLB[1], Darshana ILAN[2]* [1]Department of Microbiology, Teaching Hospital Karapitiya, [2]Department of Community Medicine, Faculty of Medicine, University of Ruhuna, Galle Sri Lanka
OP 3	**Optimisation of a loop-mediated isothermal amplification assay for detecting *Chlamydia trachomatis* DNA in urine** *Attanayake H[1], Goonasekara CL[2], Abeygunasekera N[3], Senaratna C[4], Elwitigala J[1], Gunasekera KM[5]* [1]National STD/AIDS Control Program, Sri Lanka, [2]Department of Pre-Clinical Sciences, Faculty of Medicine, General Sir John Kotelawala Defence University, [3]Sexually Transmitted Diseases Clinic, Colombo South Teaching Hospital, Kalubowila, [4]Department of Community Medicine, Faculty of Medical Sciences, University of Sri Jayawardenepura, [5]Department of Microbiology, Faculty of Medical Sciences, University of Sri Jayawardenepura Sri Lanka
OP 4	**Diversity of beta lactamases among Gram-negative blood culture isolates of patients presenting with urosepsis in a tertiary care hospital** *Weerakoon DN[1], Kothalawala M[2]* [1]Faculty of Medicine, Ragama, [2]National Hospital, Kandy, Sri Lanka
10.00 - 11.00am	**Free Paper Session 2 – Virology** **Chairpersons – Dr. Nadisha Badanasinghe and Professor Faseeha Noordeen**
OP 5	**Study on intra-familial transmission of Hepatitis B viral infection in a cohort of Hepatitis B virus infected patients** *Paththamperuma PASR[1], Rajamanthri RGLS[2], Muthugala MARV[2].* [1]Department of Microbiology, National Hospital, Kandy, [2]Department of Virology, National Hospital, Kandy, Sri Lanka
OP 6	**Analysis of accidentally detected COVID-19 patients from a tertiary care hospital in Southern Sri Lanka** *Piyasiri DLB, Withanage V, Wijeweera KDDS, Danthanarayana N, Jayasekara K, Senarathne G, Ubeysekara H, Ubeysekara N* Teaching Hospital, Karapitiya, Sri Lanka

OP 7	**Clinical features and epidemiology of Hantavirus hemorrhagic fever with renal syndrome in Sri Lanka, March 2013 to March 2021** *Muthugala MARV[1,2,3], Dheerasekara WKH[4], Manamperi AAPS[5], Gunasena S[3], Galagoda GCS[3]* [1]Department of Virology, National Hospital, Kandy, [2]Teaching Hospital Anuradhapura, [3]Medical Research Institute, Colombo, [4]Faculty of Allied Health Sciences, University of Peradeniya, [5]Faculty of Medicine, University of Kelaniya, Sri Lanka

OP 8	**Epidemiology of human rabies in Sri Lanka, 2015 to 2020** *Akram MAFA [1], Punchihewa PG [1], Rajapakshe H [1], Wickramasinghe RBM [1], Sampath GGB [1], Jayasinghe KCD[1], Kumarasinghe D[1], Nanayakkara S[1]* [1]Department of Rabies and Vaccine Quality Control, Medical Research Institute, Colombo, Sri Lanka
11.00 - 11.30am	**Plenary 1** **Chairperson – Professor Vasanthi Thevanesam** ***Virus Variants: What to do about Delta*** **Professor Malik Peiris** Chair Professor in Virology, School of Public Health, University of Hong Kong, Hong Kong
11.30 - 12.30pm	**Symposium 1 – COVID-19: risks and mitigation of future pandemics** **Chairpersons – Professor Jennifer Perera and Dr. Vaithehi Francis** ***Virological aspects of COVID-19*** **Dr. Rohitha Muthugala** Consultant Medical Virologist, Teaching Hospital Kandy, Sri Lanka ***COVID-19 vaccines and immune response*** **Professor Neelika Malavige** Professor and Head, Department of Immunology and Molecular Medicine, Faculty of Medical Sciences, University of Sri Jayawardenepura, Sri Lanka ***Management of COVID-19*** **Dr. Ananda Wijewickrama** Consultant Physician, National Institute of Infectious Diseases, Angoda, Sri Lanka
12.30 - 1.00pm	**Plenary 2** **Chairperson – Dr. Madhumanee Abeywardena** ***The forgotten organ of the body – "The Microbiome"*** **Dr. Rohini Wadanamby** Consultant Clinical Microbiologist, Lanka Hospital PLC, Colombo, Sri Lanka

1.00 - 1.30pm	**Plenary 3** **Chairperson – Dr. Veranja Liyanapathirana** ***Ethics and professionalism*** **Professor Panduka Karunanayake** Specialist Physician, Professor, Department of Clinical Medicine, Faculty of Medicine, University of Colombo, Sri Lanka

1.30pm	**End of the first session of the day**
4.00 - 5.00pm	***Symposium 2 – Advances in pathogenesis, diagnosis and treatment of infectious diseases*** **Chairpersons – Dr. Kushlani Jayatilleke and Professor Rajendra Deora** ***Diagnosing Fungal Infections: selecting the right tools*** **Professor Nelun Perera** Consultant Microbiologist & Virologist, University Hospitals of Leicester & Hon. Associate Professor, University of Leicester, UK ***Wiring schemes for innate and adaptive lymphoid cells*** **Professor Eugene Oltz** Chair, Department of Microbial Infection and Immunity, Samuel Saslaw Professor of Infectious Diseases, USA ***De novo fatty acid biosynthesis and HIV replication*** **Professor Jesse Kwiek** Associate Professor, Vice Chair for Teaching & Undergraduate Affairs, Department of Microbiology, The Ohio State University, USA
5.00 - 5.30pm	**Plenary 4** **Chairperson – Professor Neluka Fernando** ***No respite in the war: resistance to the newest antibiotics*** **Professor David Livermore** Professor of Medical Microbiology, Norwich Medical School, University of East Anglia, Norwich, UK

5.30 - 6.30pm	***Symposium 3 – AMR and one health*** **Chairperson – Professor Ajith Nagahawatte and Dr. Roshan Jayasuriya** ***Animal Health: at the center of one health approach for combating antimicrobial resistance*** **Professor Ruwani Kalupahana** Professor in Veterinary Public Health, Department of Veterinary Public Health and Pharmacology, Faculty of Veterinary Medicine and Animal Science, University of Peradeniya, Sri Lanka ***Environmental health*** **Dr. Priyanie Amerasinghe** Emeritus Scientist (Human and Environmental Health), International Water Management Institute, Colombo, Sri Lanka ***Antimicrobial resistance from a food safety perspective*** **Dr. Sujatha Pathirage** Consultant Microbiologist, Additional Approved Analyst (Food microbiology), Head, Department of Food Microbiology, Medical Research Institute, Colombo, Sri Lanka

6.30 - 7.00pm	**Plenary 5** **Chairperson – Professor Nadira Karunaweera** ***Travel and the Spread of Respiratory Infections*** **Professor David R. Hill** Professor of Medical Sciences, Director of Global Public Health, Senior Medical Advisor, Frank H. Netter MD, School of Medicine, Quinnipiac University, USA
7.00 - 7.30pm	**Guest Lecture 6** **Chairperson – Professor Nicholas T. Funderburg** ***Adjuvants and immunization strategies to enhance mucosal immunity*** **Professor Purnima Dubey** Associate Professor of Microbial Infection and Immunity, The Ohio State University, College of Medicine, USA
7.30pm	**End of the day one proceedings**

Day 2 – 26.08.2021

7.00 - 7.30am	**Plenary 6** **Chairperson – Professor Nelun De Silva** ***Defining pandemic preparedness – partnerships between universities and government agencies; lessons learned from COVID-19*** **Professor Michael Oglesbee** Professor of Virology and Comparative Pathology, Director of the Ohio State University Infectious Disease Institute, USA
7.30 - 8.00am	**Guest Lecture 7** **Chairperson – Professor Nelun De Silva** ***Global one health paradigm for interconnected planet – beyond pandemics*** **Dr. Getnet Yimer** Physician Scientist and Consultant Medical Specialist, Director for Global One Health Initiative of Eastern Africa Office and a Senior Researcher at the Ohio State University, USA
8.00 - 8.30am	**Guest Lecture 8** **Chairperson – Dr. Dhananja Namalie** ***Infection prevention and control implications in designing of health care facilities*** **Mr. Janaka Wickramarachchi** Consultant, Biomedical Engineering, Technomedics International (Pvt.) Ltd. Battaramulla, Sri Lanka
9.00 - 10.00am **OP 9**	**Free paper session 3 – Parasitology and Virology** **Chairpersons – Professor N.P. Sunil-Chandra and Professor Hasini Banneheke** **The increasing infection rate of *Leishmania donovani* in *Phlebotomus argentipes* highlights the need for Leishmaniasis control in Sri Lanka** *Kumarasiri RWCK[1], Senanayaka SASC[2], Shantha DS[2], De Silva BGDNK[3], Karunaweera ND[2]* [1]Post Graduate Institute of Medicine, University of Colombo, Sri Lanka, [2]Department of Parasitology, Faculty of Medicine, University of Colombo, Sri Lanka, [3]Department of Zoology, Faculty of Applied Sciences, University of Sri Jayawardenepura, Sri Lanka
OP 10	**Antibody levels against hepatitis B virus surface antigen among haemodialysis patients at two major nephrology units in Sri Lanka** Asmir WM[1], Mathu S[2], Noordeen F[3] [1]Post Graduate Institute of Medicine, University of Colombo, [2]National Institute for Nephrology Dialysis and Transplantation, Maligawaththa, [3]Department of Microbiology, University of Peradeniya, Sri Lanka

OP 11	**Demography, clinical features, outcome, and source of infection in healthcare workers infected with COVID-19 in a leading children's hospital in Sri Lanka** *Kariapper MAKB, De Silva SHCK, Karunasekara HCI, Wijesuriya G, Nallainathan A* Lady Ridgeway Hospital for Children, Colombo, Sri Lanka
OP 12	**The re-emerged *Brugia malayi* infection in Sri Lanka is transmitted by mosquitoes of *Mansonia* spp. mosquitoes** *Mallawarachchi CH[1], Wijerathna ACT[2], Gunathilaka PADHN[2], Chandrasena TGAN[2]* [1]Department of Parasitology, Medical Research Institute, Colombo, [2]Department of Parasitology, Faculty of Medicine, University of Kelaniya, Sri Lanka
10.00 - 11.15am	***Symposium 4 – Path to future healthcare*** **Chairpersons – Dr. Rohini Wadanamby and Dr. Wasana Kudagammana** ***ISO 15189: medical laboratory accreditation*** **Ms. Chanditha Ediriweera** Deputy Director (Accreditation), Sri Lanka Accreditation Board for Conformity Assessment, Ministry of Trade, Sri Lanka ***Issues related to implementation of technical requirements for microbiology in medical laboratory accreditation in Sri Lanka*** **Dr. Kushlani Jayatilleke** Consultant Microbiologist, Sri Jayawardenepura General Hospital, Nugegoda, Sri Lanka ***From PCR to next generation sequencing: how to establish a diagnostic lab*** **Professor Andreas Nitsche** Professor in Virology and Head of the Division Highly Pathogenic Viruses, Head of German Consultant Laboratory for Poxviruses, Robert Koch Institute, Berlin, Germany
11.15 - 11.45am	**Guest Lecture 9** **Chairperson – Dr. Geethani Galagoda** ***Climate change and health*** **Ms. Elena Villalobos Prats** Technical Officer, Lead for Capacity Building and Country Support on Climate Change and Health, Climate Change and Health Unit, Department of Environment, Climate Change and Health, World Health Organization Headquarters, Geneva

11.45 - 12.45am	**Poster and Case presentations** **Chairpersons – Dr. Deepika Priyanthi and Dr. Sumudu Suranadee**
PP 1	**Distribution of vancomycin minimum inhibitory concentration and antibiotic sensitivity pattern in *Staphylococcus aureus* clinical isolates at a university hospital in Sri Lanka** *Musadik FF[1], Karunaratne HMS[2], Nakkawita WMID[2]* [1]School of Applied Sciences, University of Wolverhampton, [2]Department of Paraclinical Sciences, Faculty of Medicine, General Sir John Kotelawala Defence University, Ratmalana, Sri Lanka
PP 2	**Eczematous skin colonization pattern with potential bacterial pathogens among paediatric population at a tertiary care setting in Sri Lanka** *Karunathilake KRP[1], Vidanapathirana G[3], Weerasooriya BWMS[1], Ekanayake EWMA[3], Dissanayake UPRU[3], Seneviwickrama KLPD[2], Herath A[2], Liyanapathirana V[3], Kudagammana HDWS[3]* [1]Department of Medical Laboratory Science, Faculty of Allied Health Sciences, University of Peradeniya, [2]Sirimavo Bandaranaike Specialized Children's Hospital, Peradeniya, [3]Department of Microbiology, Faculty of Medicine, University of Peradeniya, Sri Lanka
PP 3	**The demography, clinical features and outcome of paediatric patients and their bystanders infected with COVID-19 in the largest children`s hospital in Sri Lanka** *Phazyl DLLM, Marapana KPK, Premathilaka WP, Jayatilake JMSD, De Silva SHCK, Karunasekara HCI, Wijesuriya G* Lady Ridgeway Hospital for Children, Colombo, Sri Lanka
PP 4	**Sero-prevalence and factors associated with past exposure to hepatitis E virus infection in pregnant women attending a major maternity hospital in Sri Lanka** *Akram MAFA[1], Niyas ARJP[2], Noordeen F[3]* [1]Post Graduate Institute of Medicine, Colombo, [2]De Soysa Maternity Hospital for Women, Colombo, [3]Department of Microbiology, Faculty of Medicine, University of Peradeniya, Sri Lanka
PP 5	**A case of subcutaneous infection caused by *Basidiobolus ranarum* in a child** *Abeywardena HMW[1], Ekanayake SD[1], Jayasekera PI[2], Hettiarachchi M[3], Sigera LSM[2], Rajamanthri A[1]* [1]Department of Microbiology, Sirimavo Bandaranaike Specialized Children's Hospital, Peradeniya, [2]Department of Mycology, Medical Research Institute, Colombo, [3]Department Surgery, Sirimavo Bandaranaike Specialized Children's Hospital, Peradeniya, Sri Lanka
PP 6	**Mycotic aneurysm in melioidosis: a case report** *Jayasundera MCT[1], Piyasiri DLB[1], Ubayasiri R[1], Corea EM[2], Wagaarachchige YA[1], Liyanage N[1]* [1]Teaching Hospital Karapitiya, [2]Department of Microbiology, Faculty of Medicine, University of Colombo, Sri Lanka

PP 7	**Acute pneumonia due to melioidosis following near-drowning: two case reports** *Liyanage N[1], Piyasiri DLB[1], Jayasundera MCT[1], Wijeweera KDDS[1], Corea EM[2], Dadallage Cv[1]* [1]Department of Microbiology, Teaching Hospital, Karapitiya, [2]Department of Microbiology, Faculty of Medicine, University of Colombo, Sri Lanka
PP 8	**Actinomycosis in the oropharynx** *Thuduvage VS[1], Nakkawita WMID[1], Kumarasinghe IHS[1], Pathirage MVS[2], Dissanayake HTRW[1], Weerasinghe WMDKB[1]* [1]General Sir John Kotelawala Defence University, Ratmalana, [2]Medical Research Institute, Colombo, Sri Lanka
12.45 - 1.00pm	**Empowering microbiology applications and infectious disease testing with next-generation sequencing** **Dr. Cara Lim** Senior Applied Genomics Specialist (South Asia), Illumina
1.00pm	**End of the first session of the day**
4.00 - 4.30pm	**Plenary 7** **Chairperson – Professor Enoka Corea** ***How COVID-19* is accelerating the threat of antimicrobial resistance** **Dr. Adam Roberts** Reader, Antimicrobial Chemotherapy and Resistance, School Lead for AMR and DR Policy advisor for RSTMH, Liverpool School of Tropical Medicine, UK
4.30 - 5.30pm	***Symposium 5 – Role of insects in the world of microbiology*** **Chairpersons – Dr. Shalindra Ranasinghe and Dr. Nilakshi Samaranayake** ***Transgenic technology to combat dengue mosquito vector Aedes aegypti*** **Professor Ranil Dassanayake** Senior Professor in Biochemistry and Molecular Biology, Department of Chemistry, Faculty of Science, University of Colombo, Sri Lanka ***Changing trends in bionomics of phlebotomine sandflies: vectors of leishmaniasis*** **Dr. Sanath Senanayake** Senior Lecturer, Department of Parasitology, Faculty of Medicine, University of Colombo, Sri Lanka ***Vectors and the filarial worms: Present and future*** **Professor Channa Yahathugoda** Professor in Parasitology, Faculty of Medicine, University of Ruhuna, Galle, Sri Lanka

5.30 - 6.00pm	**Plenary 8** **Chairperson – Dr. Dhanushka Dasanayake** ***Post-acute COVID-19 syndrome*** **Professor Namal Liyanage** Assistant Professor, Department of Microbial Infection and Immunity, College of Medicine, The Ohio State University, USA
6.00 - 6.30pm	**Guest Lecture 10** **Chairperson – Dr. Geethika Patabendige** ***Clinical approach to manage infections before and after liver transplantation*** **Dr. Anita Verma** Consultant Medical Microbiologist, King's College Hospital, London, UK
6.30 - 7.00pm	**Plenary 9** **Chairperson – Professor Nadira Karunaweera** ***Host targeted therapies for treating infections*** **Professor Abhay Satoskar** Professor and Vice Chair, Departments of Pathology and Microbiology, The Ohio State University, USA
7.00 - 7.30pm	**Award ceremony and close of conference**

LIST OF SPEAKERS

Professor Nicholas T. Funderburg

Associate Professor of Division of Medical Laboratory Science,
The Ohio State University,
USA

Professor Jesse Kwiek

Associate Professor, Vice Chair for Teaching & Undergraduate Affairs
Department of Microbiology, The Ohio State University,
USA

Professor Purnima Dubey

Associate Professor of Microbial Infection and Immunity,
The Ohio State University, College of Medicine,
USA

Dr. Bradford McGwire

Infectious Disease Physician, The Ohio State University,
Wexner Medical Center,
USA

Professor Barbara Gastel

Joint Professor of Integrative Biosciences, Humanities in Medicine and
Biotechnology, Texas A & M University College of Medicine,
USA

Professor Eugene Oltz

Chair, Department of Microbial Infection and Immunity, Samuel Saslaw
Professor of Infectious Diseases, Microbial Infection and Immunity,
USA

Professor Rajendar Deora

Associate Professor, Department of Microbial Infection and Immunity, Department of Microbiology, The Ohio State University, USA

Professor Murugesan Rajaram

Associate Professor, Department of Microbial Infection and Immunity, The Ohio State University, USA

Professor Amit Sharma

Assistant Professor, Department of Veterinary Biosciences, Department of Microbial Infection & Immunity, The Ohio State University, USA

Dr. Rajesh Deshmukh

Public Health Specialist-TB, Division of HIV and Tuberculosis, Centers for Disease Control and Prevention CDC/DGHT, India

Professor Malik Peiris

Chair Professor in Virology, The School of Public Health, University of Hong Kong, Hong Kong

Professor Nelun Perera

Consultant Microbiologist & Virologist, University Hospitals of Leicester & Hon. Associate Professor, University of Leicester, UK

Professor David Livermore

Professor of Medical Microbiology, Norwich Medical School,
University of East Anglia, Norwich,
UK

Professor David R. Hill

Professor of Medical Sciences, Director of Global Public Health, Senior Medical Advisor, Frank H. Netter MD, School of Medicine,
Quinnipiac University, USA

Professor Michael Oglesbee

Professor of Virology and Comparative Pathology, Director of the Ohio State University Infectious Disease Institute,
USA

Dr. Getnet Yimer

Physician Scientist and Consultant Medical Specialist, Director for Global One Health initiative of Eastern Africa office

Professor Andreas Nitsche

Professor in virology, Robert Koch Institute, Berlin, Germany

Ms. Elena Villalobos Prats

Technical Officer, Lead for Capacity Building and Country Support on Climate Change and Health, Climate Change and Health Unit, Department of Environment, Climate Change and Health, World Health Organization Headquarters, Geneva

Dr. Adam Roberts

Reader, Antimicrobial Chemotherapy and Resistance, School Lead for AMR and DR Policy advisor for RSTMH Liverpool School of Tropical Medicine, UK

Professor Namal Liyanage

Assistant Professor, Department of Microbial Infection and Immunity, College of Medicine, The Ohio State University, USA

Dr. Anita Verma

Consultant Medical Microbiologist, King's College Hospital, London, UK

Professor Abhay Satoskar

Professor and Vice Chair, Departments of Pathology and Microbiology

The Ohio State University, USA

Dr. Kanthi Nanayakkara

Consultant Virologist and Vaccinologist, Head / Department of Rabies & Vaccine QC, National Control Laboratory, Medical Research Institute, Colombo, Sri Lanka

Dr. Rajiva De Silva

Consultant Immunologist, Medical Research Institute, Colombo, Sri Lanka

Dr. Rohitha Muthugala

Consultant Medical Virologist, National Hospital Kandy, Sri Lanka

Dr. Ananda Wijewickrama

Consultant Physician, National Institute of Infectious Diseases, Angoda, Sri Lanka

Professor Neelika Malavige

Professor in Microbiology and Director, Centre for Dengue Research, Professor in Department of Immunology and Molecular Medicine, Faculty of Medical Sciences, Nugegoda, Sri Lanka

Dr. Rohini Wadanamby

Consultant Clinical Microbiologist, Lanka Hospital PLC, Colombo, Sri Lanka

Professor Panduka Karunanayake

Specialist Physician, Professor, Department of Clinical Medicine, Faculty of Medicine, University of Colombo, Sri Lanka

Professor Ruwani Kalupahana

Professor in Veterinary Public Health, Department of Veterinary Public Health and Pharmacology, Faculty of Veterinary Medicine and Animal Science, University of Peradeniya, Sri Lanka

Dr. Priyanie Amerasinghe

Emeritus Scientist (Human and Environmental Health), International Water Management Institute, Colombo, Sri Lanka

Dr. Sujatha Pathirage

Consultant Microbiologist, Additional approved analyst (food microbiology), Head, Department of Food Microbiology, Medical Research Institute, Colombo, Sri Lanka

Mr. Janaka Wickramarachchi

Consultant, Biomedical Engineering
M/s. Technomedics International (Pvt.) Ltd. Battaramulla, Sri Lanka

Ms. Chanditha Ediriweera

Deputy Director (Accreditation), Sri Lanka Accreditation Board for Conformity Assessment, Ministry of Trade, Sri Lanka

Dr. Kushlani Jayatilleke

Consultant Microbiologist, Sri Jayewardenepura General Hospital,
Nugegoda, Sri Lanka

Professor Ranil Dassanayake

Senior Professor in Biochemistry and Molecular Biology,
Department of Chemistry, Faculty of Science, University of Colombo,
Sri Lanka

Dr. Sanath Senanayake

Senior Lecturer, Department of Parasitology,
Faculty of Medicine, University of Colombo, Sri Lanka

Professor Channa Yahathugoda

Professor in Parasitology, Faculty of Medicine, University of Ruhuna,
Galle, Sri Lanka

ABSTRACTS OF THE GUEST LECTURES, PLENARY LECTURES AND SYMPOSIA

Guest Lectures

Guest Lecture 1

Pathogenesis and biofilm formation of recently circulating strains of *Bordetella pertussis*

Professor Rajendra Deora

Despite high vaccination coverage, pertussis or whooping cough caused by the Gram-negative obligate human pathogen *Bordetella pertussis (Bp)* is resurging in many countries. In contrast to whole cell pertussis vaccines, current acellular vaccines elicit feeble and short-lived immunity and fail to prevent nasopharyngeal colonization and transmission. Airborne or aerosolized respiratory droplets generated by sneezing or coughing leads to *Bp* circulation, spread to, and infection of new hosts. Upon repeated laboratory passage, bacterial pathogens undergo rapid and substantial genotypic and phenotypic changes. *Bp* research and vaccine formulations are largely based on bacterial strains isolated seven decades ago. This raises serious questions about the relevance and usefulness of studies focusing solely on laboratory reference strains in understanding pathogenic mechanisms or the development of effective vaccines and therapeutics. Work from our laboratory and others show that CBp strains exhibit enhanced pathogenesis/virulence, survive better in the mammalian respiratory tract and escape vaccine-induced immunity. We have additionally found that CBp strains exhibit enhanced biofilm forming capacity, autoaggregate better and differentially produce key virulence factors. The overarching hypothesis of our research is that CBp strains survive and transmit because phenotypic changes in these strains allow them to subvert and resist host immunity more effectively than reference strains. We are using geographically distinct CBp strains isolated from three countries to (1) identify altered interactions with and susceptibility to host immune components; (2) determine variations in colonization, biofilm formation and pathogenesis utilizing adult and infant mouse models and primary well-differentiated nasal and bronchial human epithelial cells and (3) discover gene expression differences and regulatory networks during both liquid and biofilm growth. Our research will simultaneously enhance fundamental scientific knowledge of *Bp* pathogenesis and inform the development of more effective next generation pertussis vaccines.

Guest Lecture 2

Pulmonary infections and the pathogenesis of cardiac dysfunction

Professor Murugesan Rajaram

Pneumonia in ICU patients carries a bleak prognosis with high risk for the development of cardio vascular complications, largely due to cardiac inflammation with subsequent tissue remodeling and fibrosis. The bacterial and viral infections are major cause for pneumonia in the general public and ICU patients. In general, infectious agents can disseminate into the heart and cause cardiac infections which lead to severe cardiac arrest. Also, infection mediated systemic inflammation, release of pathogen associated molecular patterns (PAMPs) and damage associated molecular patterns (DAMPs) into the circulation is responsible for cardiac dysfunction. Growing evidence indicates that the resident macrophages are important regulators of cardiac electrical activity and damage following myocardial infarction/ infection. After tissue injury, inflammatory monocytes are recruited to the heart and differentiate into macrophages, which contribute to cardiac dysfunction. MicroRNAs have a key role in the regulation and maintenance of macrophage function and cardiac inflammation. However, it is unclear if microRNAs regulate immune cell recruitment or the function of cardiac resident macrophages. To investigate how bacterial pneumonia promotes cardiac dysfunction, we used *P. aeruginosa* infection in a murine pulmonary model of infection. Our results show an aberrant cardiac electrical activity, and compromised pump function in *P. aeruginosa* infected animals. Notably, we found increased cardiac fibrosis mainly due to the accumulation of inflammatory macrophages in the heart. Additionally, we found that miR-155 deficiency reversed the *P. aeruginosa* mediated cardiac dysfunction by limiting the immune cell migration in to the heart. These findings demonstrate that *P. aeruginosa* infection induces miR-155 dependent immune cell recruitment to the heart, which changes the phenotype and function of resident macrophages, resulting in elevated cardiac fibrosis and heart function.

Guest Lecture 3

Altered macrophage phenotype and lipidome abnormalities may contribute to cardiovascular disease risk in aging people with HIV

Professor Nicholas T. Funderburg

The number of people with HIV (PWH) over the age of 50 is increasing worldwide. Even with suppressive antiretroviral therapy (ART), chronic inflammation persists in PWH, likely complicating the aging process and accelerating development of comorbidities. Both HIV infection and ART are associated with dyslipidemia and increased cardiovascular disease (CVD) risk. Macrophages accumulate in vessel walls and produce factors that contribute to vascular inflammation and development of atherosclerosis. The relationships among lipids and macrophage phenotype in PWH are not well understood. Coronary artery calcification (CAC) in people with (n=43) and without (n=25) HIV was quantified by computed tomography scanning. PBMCs from people with (n=20) and without (n=20) HIV were cultured for 5 days in autologous serum to generate monocyte-derived macrophages (MDMs). Concentrations and composition of serum lipids were measured by mass spectrometry. MDM transcriptomes and differential gene expression (DGE) were analyzed using our R Bioconductor pipeline. Foam cell formation was assessed by Bodipy staining and DiI-OxLDL uptake. Metabolic analyses were performed using an Agilent Seahorse FXp instrument. PWH (ages 27-67) had increased CAC compared to people without HIV (ages 25-70) (CAC=367 v 25, p=0.01). Traditional risk assessments categorize individuals with CAC <100 at low risk, and >400 at high risk for CVD. Older (over 55) PWH (n=17) had an average CAC of 423, compared to 51 in older people without HIV (n=8). Proportions of inflammatory monocytes were increased in PWH, and were directly associated with CAC. Among PWH, CAC correlated with serum inflammatory biomarkers, CRP, sCD14, VCAM-1, IL-6, TNF-R1, TNF-R2, D-Dimer, and Endothelin-1, whereas age was the only factor associated with CAC in people without HIV. Among older PWH, we measured increased levels of CRP, D-Dimer, and OxLDL compared to younger PWH. CAC was also directly associated with CRP, Endothelin-1, IL-6, and PCSK9 in older PWH. Metabolic analyses of MDMs from PWH demonstrated increased dependence on glucose oxidation to meet basal energy demands, and a reduced capacity to use glutamine and fatty acids as fuel sources. PWH had significant alterations in serum lipidome composition, including enrichment of saturated fatty acids (SaFAs) and reduced polyunsaturated fatty acids (PUFAs). DGE analysis identified alterations in innate immune signaling, cell cycle regulation, DNA damage repair, replication complexes, mitochondrial dysfunction, and lipid processing pathways in MDMs from PWH. SaFAs and PUFAs correlated with unique DGE signatures and altered metabolic pathway activation in MDMs. MDMs from PWH displayed greater lipid accumulation (Bodipy) and DiI-OxLDL uptake. MDMs from PWH also produced more TNF, IL-6, and ROS, and had increased HLA-DR surface expression. SaFA levels were directly related, whereas PUFAs were inversely related to HLA-DR expression on MDMs from PWH. Lipid abnormalities in PWH may contribute to a pro-atherogenic MDM phenotype. MDMs from PWH readily form foam cells, have altered transcriptional and metabolic profiles, and produce mediators of vascular inflammation, which may enhance CVD risk. Identifiying mechanisms of immune dysregulation in PWH will likely be of particular importance for management of comorbidities in the aging HIV population.

Guest Lecture 4

Determinants of SHIV replication in macaque lymphocytes

Professor Amit Sharma

The host type-1 interferon (IFN) response upregulates expression of a number of IFN-stimulated genes (ISGs) and the proteins encoded by certain ISGs, referred to as restriction factors, potently block HIV-1 and Simian Immunodeficiency Virus (SIV) replication. HIV-1 does not persistently infect macaques due to restriction by several macaque-specific restriction factors. To overcome these restrictions chimeric SIV/HIV-1 viruses (SHIVs), which encode the SIV antagonists of the known restriction factors and HIV-1 Envelope glycoprotein (Env) to permit viral entry, are used to infect macaques to model HIV-1 infection. Existing SHIV/macaque models typically employ SHIVs that encode HIV-1 *env* variants isolated from chronic stages of infection that were further adapted by viral passage in cell culture (lab-adapted viruses). Moreover, these SHIVs require further adaptation *in vitro* in macaque cells and/or *in vivo* by serial macaque-passage. The adaptation of *env* sequences in macaques increases replication and pathogenicity of SHIVs but also leads to changes in its antigenic properties. Thus, SHIVs encoding circulating HIV-1 *env* variants isolated from the newly infected patients near the time of transmission including the transmitted/founder variants (termed circulating, unadapted SHIVs) are desired as challenge viruses for vaccine and therapeutic studies. However, most

attempts at generating these SHIVs have failed as circulating, unadapted SHIVs replicate poorly, if at all, in macaque cells and do not establish persistent infection. Our current research is characterizing the viral and host determinants that restrict replication of circulating, unadapted SHIVs in macaque lymphocytes.

Guest Lecture 5

Infection prevention and control measures for drug-resistant tuberculosis in healthcare settings

Dr. Rajesh Deshmukh

COVID-19 pandemic has reemphasized the need for strengthening infection prevention and control practices (IPC) in healthcare facilities especially in HIV and tuberculosis (TB) care facilities. Effective IPC practices stop the spread of antibiotic resistant organisms and protects patients and healthcare workers from avoidable infections. International and national guidelines on IPC emphasize TB infection control in healthcare settings, still there is a practice gap in implementing IPC measures. The session emphasizes urgent need to address this practice gap in context of COVID-19.

Guest Lecture 6

Adjuvants and immunization strategies to enhance mucosal immunity

Professor Purnima Dubey

Increasing evidence suggests that generation of mucosal memory T and B cell responses by vaccination is critical for long-lived immunity against respiratory pathogens. Activation of such responses depends in large part on the properties of the adjuvant and the route of immunization. We identified Bordetella Colonization Factor A (BcfA) as an adjuvant that elicits Th1/17 polarized immune cellular and humoral responses to a variety of protein antigens derived from bacterial and viral pathogens. Notably, BcfA has the unique ability to downregulate Th2 responses, particularly when combined with the widely used adjuvant, alum. Systemic priming with BcfA-adjuvanted vaccines followed by intranasal booster vaccination elicits strong systemic responses, tissue-resident memory T cells and mucosal IgA and Th1 polarized IgG antibodies in the respiratory tract. Experimental vaccines adjuvanted with BcfA and alum and delivered by this prime-pull regimen provide protection against the bacterial pathogens *Bordetella pertussis* and *M. tuberculosis* and the viral pathogen SARS CoV-2. Thus, leveraging the unique properties of BcfA to generate strong systemic and mucosal immunity has the potential to provide long-lasting protection against respiratory illnesses.

Guest Lecture 7

Global One Health paradigm for interconnected planet-beyond pandemics

Dr. Getnet Yimer

Our planet is highly interconnected with the current population of 7.6 billion and expected to add more than 140 million babies in 2021 alone. The increase in population has several expected consequences that create additional pressure including urbanization (with current 55% of the world living in urban areas expected to rise to 70% by 2050), changes in land use pattern, industrialization and increased animal production to meet the growing protein demand. As such, the interaction among humans, animals and the collective environment is greater than ever before. The Global One Health paradigm envisions building capable institutional systems globally addressing issues at the interface and tackling the world's toughest health challenges including Antimicrobial Resistance, Zoonotic Epidemics and Pandemics, Chemical hazards, non-communicable diseases such as Cancer among others. The presentation will highlight key priorities and discusses how Ohio State and Global partners solve priority issues using integrated One Health system.

Guest Lecture 8

Infection prevention and control implications in designing of health care facilities

Mr. Janaka Wickramarachchi

The field of infection prevention describes a hierarchy of removal of microorganisms from surfaces including medical equipment and instruments in the Operation Theatres.

Infection control addresses factors related to the spread of infections within the healthcare setting, whether among patients, from patients to staff, from staff to patients, or among staff. This includes preventive measures such as hand washing, cleaning, disinfecting, sterilizing, and vaccinating.

Design concept of Surgical Facilities;

1. Environment (Air conditioning and Humidity Control, Air Changes, Positive Pressure, Laminar Flow);

   HTM: Health Technical Memoranda (HTMs) give comprehensive advice and guidance on the design, installation and operation of specialized building and engineering technology used in the delivery of healthcare.

   i. HTM 00: Policies and principles of healthcare engineering
   ii. HTM 02-01: Medical gas pipeline systems
   iii. HTM 03-01: Provide guidance on the design and management of heating and specialized ventilation in health sector buildings
   iv. HTM 06-02: Electrical services - electrical safety guidance for low voltage systems.
   v. HTM 05-02: Fire code Guidance in support of functional provisions (Fire safety in the design of healthcare premises)

2. Surfaces (Flooring, Wall, Surgeon Control Panel, Service Supplies – Surgical Pendent/Supply Pendent)
3. Modular OT: Broadly involves use of modular pre-fabricated wall panels, modular ceiling with embedded laminar flow system, hermetically sealed doors and anti-static flooring to form the shell.
   i. ISO Theatre Classification
4. Sterilization
   i. Laundry Designing
   ii. Central Sterilization Supply Department (CSSD) Designing.

Guest Lecture 9

Climate change and health

Ms. Elena Villalobos Prats

The presentation on “Climate change and health” will provide an overview of key interlinkages between climate change and health as well and of the main responses and actions being promoted by World Health Organization to address those. Furthermore, additional opportunities to promote health in the context of climate change, including in the face of COVID-19, will be discussed.

Guest Lecture 10

Clinical approach to manage infections before and after liver transplantation

Dr. Anita Verma

The infectious complications before and after liver transplant (LT) are affected by the severity of liver disease and immunosuppression intensity after transplantation. Both cirrhosis and immunosuppression contribute to dysfunction of defensive mechanisms of the host. When a patient is evaluated for transplantation, the opportunity arises to assess the individual’s risk for infection and how one may modify those risks through prophylactic and therapeutic strategies. Pretransplant infectious disease evaluation focuses on exposure history, prior infections, serologic testing for latent infections, distant exposures, identify colonization patterns of multi drug resistant organisms (MDRO), and administration of vaccines. The risk of acquiring rare infections is increasing because of greater global mobility. Additional evaluation should be considered for some endemic infectious diseases, beyond recommended standard testing for transplant candidates and donors.

It is important to have knowledge of risk factors, local epidemiology and resistance pattern of organisms for management of infections in post-transplant period. Infections are often recipient or donor derived or can be associated with surgical and nosocomial complications during 1st month after LT. Opportunistic infections are common during first year after transplantation due to higher intensty of immunosuppression, while the risk goes down with time but is never zero as intermittent augmentation of immunosuppression can bring the risk back. The risk factors for infection after LT is both donor and recipient derived, as well as aspects related to the transplant operation. In recent studies genetic polymorphisms in the innate immune system, from both donor and recipient, have been identified as important risk factor for infection after LT. Early diagnosis of infections using advanced diagnostic approaches, closer surveillance and targeted treatment protocols are required to manage infectious complications in LTR. Rigorous screening of both donor and recipient for latent and active infections is essential for best outcome after liver transplantation. Most of the liver transplant centers have dedicated physicians with expertise in transplant infectious disease and it is advisable if these experts are consulted when the patients admitted to non transplant centers.

Plenary presentation 1

Pandemic threats from emerging coronaviruses

Professor Malik Peiris

Emerging viral infections continue to pose major threats to global health, wealth and well-being. COVID-19 has illustrated the societal impact of such events but it was not the first and will not be the last such event. Research is important in identifying and risk assessing potential pandemic threats, using this information to reduce risk of their emergence and in developing countermeasures. Understanding the origins of SARS led to understanding that other endemic coronaviruses (229E, OC43) also arose from animal reservoirs within the past few hundred years, highlighting the pandemic potential of coronaviruses. The knowledge that SARS-CoV-like viruses were common in insectivorous bats with potential to infect humans, the emergence of MERS in 2012, the spill over of bat coronaviruses to cause a lethal swine acute diarrhoea syndrome (SADS) in pigs in China in 2016, highlighted the threat posed by zoonotic coronaviruses of diverse groups. Although SADS coronavirus had not been shown to cause human disease so far, it is able to infect human respiratory and intestinal epithelium and poses potential risk to humans. Although MERS-CoV has caused human zoonotic disease only in the Middle East, the majority of MERS-CoV infected dromedary camels are found in Africa. Why zoonotic MERS has not been reported in Africa has been unclear. We have used immunological and virological methods to investigate the pathogenic potential of MERS-CoV in Africa for humans. The rapid development of vaccines for COVID-19 was enabled by prior research on coronaviruses that identified the spike protein as the key protective target for protection and that the spike protein existed in different conformations, all factors that had to be taken into account in vaccine design.

Plenary presentation 2

The forgotten organ of the body – "The Microbiome"

Dr. Rohini Wadanamby

It is very exciting to explore the microbiomes of the human body which is a highly evolving field. Evidence showed, the highly complex collection of microbes extensively helps in maintaining human health while preventing the majority of both communicable and non-communicable diseases. Many studies were evidenced that dysbiosis of the microbiomes (especially the gut) can lead to a plethora of metabolic, inflammatory, infective, immunological, neurological, psychological, autoimmune diseases, and more. Therefore, understanding more on "Microbiomes" may be a hope to find answers to many unresolved medical problems.

Plenary presentation 4

No respite in the war: resistance to the newest antibiotics

Professor David Livermore

After a long fallow period, new anti-Gram-negative antibiotics are finally becoming available. They include ceftolozane/tazobactam, ceftazidime/avibactam, meropenem/vaborbactam, imipenem/relebactam, cefiderocol, eravacycline and plazomicin. All these have shown some utility in infections due to multi-resistant bacteria, including carbapenemase producers in several cases. These are welcome developments.

Disturbingly, though, resistance has already been seen emerging to these newest agents.

In the case of ceftolozane/tazobactam – a combination mostly of interest due to its activity against *Pseudomonas aeruginosa* – structural mutations in pseudomonal AmpC chromosomal b-lactamase can confer resistance and have been selected during therapy. Interestingly, these changes typically also confer resistance to ceftazidime/avibactam, but lower resistance to imipenem, which co-depends on AmpC activity as well as loss of porin OprD.

For ceftazidime/avibactam –– a combination active against Enterobacterales with KPC and OXA-48 carbapenemases -mutations to the bla_{KPC} gene can confer resistance. The most frequent and important leads to an Asp179Tyr substitution in the enzyme, making it a more powerful ceftazidimase, and therefore harder to inhibit. Meropenem/vaborbactam – a combination principally of interest against Enterobacterales with KPC carbapenemases – can be compromised through porin mutations, reducing uptake by these organisms. Again, such mutations have been seen emerging during therapy, leading to clinical failure.

There is less experience so far with the catechol cephalosporin cefiderocol, which has the widest spectrum of all the new agents. However, its MICs are quite widely scattered within resistance types, suggesting a major influence of factors beyond those normally considered potentially including lesions in the iron uptake system. Notably, resistance evolved in several *Acinetobacter* strains during a Phase III resistant pathogens, although the precise mechanism(s) remain to be established.

Before leaving the novel β-lactams, it should be added that several, as well as the developmental agent aztreonam/avibactam, can be compromised by 4-amino-acid insertions, typically Tyr-Gly-Ile-Asn/Lys, in PBP3 of *E. coli*, making this target less vulnerable to inhibition. *E. coli* with this modification are scattered across Asia, Europe and the Middle East, and seem particularly prevalent in India.

For eravacycline, like tigecycline, increased expression of chromosomal RND efflux pumps can confer resistance. This has been described as emerging in vivo during therapy for tigecycline, and (so far) only in vitro for eravacycline.

Another risk is that new agents suppress pathogens with mechanisms that are covered, whilst facilitating expansion of strains with uncovered mechanisms. Thus, deployment of ceftazidime/avibactam in Patras (Greece) was followed by a surge of *Klebsiella* with metallo carbapenemases, which evade inhibition by avibactam. Plazomicin overcomes most resistance due to aminoglycoside-modifying enzymes but carried the hazard of instead selecting strains with ArmA and Rmt ribosomal methyltransferases. These confer aminoglycoside pan-resistance and are often genetically linked with NDM carbapenemases; they are prevalent in Asia, less so in Europe and are very uncommon in North America.

In all this, one thing is clear: that the new agents are no more immune to resistance than their predecessors. It is vital therefore that we use them prudently. This should increasingly be facilitated using rapid diagnostics, better matching the choice of antibiotic to the pathogen's specific resistances.

Plenary presentation 5

Travel and the spread of respiratory infections

Professor David R. Hill

The devastating global pandemic of SARS-CoV-2 (COVID-19) has brought into clear focus the role that travel across and within international borders contributes to the spread of respiratory pathogens. In addition to infections with pandemic potential, such as the SARS-coronaviruses and influenza viruses, other respiratory infections, tuberculosis and measles, continue to challenge public health control measures, and contribute to ongoing morbidity in at risk populations. This presentation will examine the driving forces for the international spread of respiratory illness and recommend control measures based on the dynamics of each of the pathogens. Improved country and global surveillance, detection and response, implementation of effective vaccination strategies, and personal protection measures can lead to effective control.

Plenary presentation 6

Defining pandemic preparedness – partnerships between universities and government agencies; lessons learned from COVID-19

Professor Michael Oglesbee

COVID-19 highlighted the importance of partnerships between universities and government agencies in mitigating the impact of the pandemic. At the Ohio State University, contributions in 2020 and 2021 included predictive modeling to ensure adequate hospital resources and to establish the effectiveness of state government policies designed to limit the spread of infections. State-wide serological surveys and monitoring wastewater for SARS-CoV-2 in nine cities was performed as a means of gaging the extent of infections. The university itself was a model for pandemic responses, representing one of the largest student bodies in the United States and located in a major metropolitan area. The university Infectious Disease Institute performed over 550,000 screening tests of saliva samples over the course of the 2020/2021 academic year, guiding effective contact tracing, isolation and quarantine measures in concert with local public health agencies. Sequence analysis of positive samples showed the dramatic rise of variants of concern and their association with vaccine breaks, data that is essential in modeling the future course of the pandemic. Methods for SARS-CoV-2 sequence analysis of wastewater were developed and provided as a service to the state as a cost-effective surveillance strategy. Such environment surveillance efforts should be maintained as a means of pandemic preparedness for zoonoses caused by coronaviruses and influenza viruses, adding to surveillance in domestic and wild animal species. While wastewater provides a regional signal, needed is a cost-effective means of localizing presence of virus in specific locations and for this we propose the detection and characterization of virus in dust samples from built environments.

Plenary presentation 7

The COVID-19 response and AMR

Dr. Adam Roberts

The COVID-19 pandemic has affected the lives of most people on the planet, forcing us to think about our response to an infectious disease for which we have no treatment. Our response to COVID-19 has been both extraordinary and at the same time reactive and chaotic. Our ability to develop effective vaccines and treatments within a year of first detection is remarkable however our use of antimicrobials normally reserved for bacterial infections has far exceeded the need based on emerging data of co- and secondary infections in COVID patients. In this presentation we will review the data on antibiotic usage during the pandemic and discuss the ways in which our behavioural changes, as a response to the pandemic, may affect the selection, emergence, and persistence of antimicrobial resistance (AMR) in bacteria pathogens.

We will consider how and where to monitor the effects of the pandemic on AMR to detect any differences before they become a problem in healthcare environments and finally, we will ask if there are lessons that can be learned in terms of pandemic preparedness in order for us to be proactive in terms of AMR rather than reactive as we have had to be with COVID-19.

Plenary presentation 8

Post-acute COVID-19 syndrome

Professor Namal Liyanage

COVID-19 is now recognized as a multi-organ disease with a broad spectrum of manifestations. An increasing number of publications report persistent and prolonged effects after acute COVID-19 resolution. Post-COVID syndrome is multi-factorial and more implicated in several clinical manifestations. The long-term consequences of the disease remain largely unknown and are being investigated in several patient populations. Our current studies suggest that the dysregulated innate and adaptive immune responses during COVID-19 infection play a crucial role in its pathogenesis and may account for neurological, renal, and cardiovascular complications despite clearance of the infection.

Plenary presentation 9

Host targeted therapies for treating infections

Professor Abhay Satoskar

More than 350 million people worldwide are at risk of contracting leishmaniasis. Current treatments for all forms of leishmaniasis are lengthy, and highly toxic. Most commonly pentavalent antimonials are used, but also the teratogens paromomycin and miltefosine. Liposomal Amphotericin B (AmBiosome) is also used, but requires intravenous application. Besides safety concerns with current medication, drug resistant parasites are becoming more and more commonplace. Clearly new treatments for leishmaniasis are needed. Host directed therapy (HDT) is a viable alternative which targets the host pathways responsible for parasite survival and pathogenicity. HDT has gained significant momentum with the recent innovative combinations of different genomics, proteomics and computational biology approaches. Given the success of HDT in the field of cancer and autoimmunity, there is potential for its employment in treating infectious diseases. This talk will be overview of current discoveries by our team demonstrating efficacies of host-directed interventions in prevention and treatment of cutaneous and visceral leishmaniasis.

Symposium 1

Virological aspects of COVID-19

Dr. Rohitha Muthugala

In late December 2019, an outbreak of viral pneumonia was reported from Wuhan, China. The infectious agent responsible for this outbreak was a novel coronavirus. Subsequently, the disease spread globally and became a pandemic. WHO has officially named the disease as COVID-19 and responsible virus as SARS-CoV-2. SARS CoV-2 is a beta coronavirus, closely related to the SARS virus.

Direct or indirect contact with respiratory droplets, released via coughing, sneezing and speaking is the primary mode of transmission of the SARS-CoV-2 virus. Incubation period ranges between 2 and 14 days. It causes wide spectrum of disease manifestations, ranging from asymptomatic to mild, moderate and critical, life-threatening infections. The fatality rate of SARS-CoV-2 infection is around 1-3% and is commonly linked to the development of acute respiratory distress syndrome results from uncontrolled immune activation, which is known as a cytokine storm.

The gold standard diagnostic test for SARS-CoV-2 is real time RT-PCR. Detection of viral antigen using rapid ICT is currently widely used for identifying infectious patients. These tests play discrete roles concerning large-scale population testing, hospital, and point of care testing. To date, there are no strong clinical evince to support the efficacious drug for SARS CoV-2 infection and there are few therapeutics with modest effect.

Social distancing efforts, case isolation and contact tracing are vital to reduce the incidence. Furthermore, the usage of masks and the practice of hand washing and disinfection are paramount to reduce or eliminate the viral spread. Currently, over 100 vaccine candidates are being developed and tested in clinical trials and this accelerated effort has created several efficacious vaccines, which are now being used to mitigate the COVID-19 pandemic.

Symposium 2

Diagnosing fungal Infections: selecting the right tools

Professor Nelun Perera

There are many different tools to diagnose invasive fungal infections, yet, diagnosing invasive fungal infections poses many challenges. Knowing the tools, it's performance and selecting the right tool/s for the right patient is critical to make an informed diagnosis and treatment plan. A good understanding of the local epidemiology of invasive fungal infections, patients at risk, risks of exposure, the context of performing the tools (e.g surveillance, pre-emptive diagnosis etc.) have direct bearings on results interpretation. Tools should be easy to access and results should have a good turn-around time. Finally, tools have an associated cost and should be cost effective. Selecting the right tools is an art; mastering this art can overcome the challenges of diagnosing invasive fungal infections.

Wiring schemes for innate and adaptive lymphoid cells

Professor Eugene Oltz

A delicate regulatory balance must be achieved in cells of the innate and adaptive immune systems to effectively eliminate pathogens, while minimizing damage to neighboring tissues. Defects in regulatory mechanisms that govern expression of cellular or soluble mediators can interfere with pathogen clearance or lead to unchecked inflammatory responses associated with autoimmunity. Integral components of the innate immune response are natural killer (NK) and innate lymphoid cells (ILCs), which lack antigen-specific receptors, but respond rapidly to microenvironmental cues upon pathogen exposure or tissue damage. These cells also have direct functional counterparts in the adaptive immune system, namely CD4+ helper and CD8+ cytotoxic T cells, whose responses are more specific, but develop more slowly. Over the past few years, we have elucidated gene regulatory circuits within these cell lineages to understand the key players involved in setting the transcriptional programs for their identities and functions. These studies uncovered an evolutionarily conserved hierarchy of activating and repressing transcription factors, including TCF-1 and BLIMP-1, which set programs for self-renewal, cytokine expression, and differentiation to effector subsets in both innate and adaptive lymphoid cells. Functional dissection of key enhancer elements and factors that control the expression of signature cytokine genes in these cells will also be discussed. These studies highlight how integrative-omics approaches can provide new insights into the cis- and trans-factors that govern

fundamental immunologic processes. In turn, such information is valuable in generating testable hypotheses and, ultimately, may be leveraged to engineer cells into better therapeutics for our battles against cancer, infections, and chronic inflammatory diseases.

De novo fatty acid biosynthesis and HIV replication

Professor Jesse Kwiek

HIV-1 engages host cellular machinery to produce progeny, and thereby imposes a substantial burden to cellular metabolism. The development of CCR5-targeted therapy and several siRNA and CRISPR-based screens have identified hundreds of host dependency factors that highlight the potential to drug host proteins. Drugging host proteins could provide several advantages over viral targets, including a higher barrier to drug resistance (human proteins cannot evolve in a relevant time frame), and the potential development of a pan-antiviral (if several viruses require the same host pathway). The challenge is to identify a non-essential host pathway that is also critical for viral replication. Our research suggests that human fatty acid synthase (FASN) meets these criteria. We recently discovered that cellular FASN is upregulated by HIV-1. FASN is a multifunctional enzyme that generates palmitate, a 16-carbon FA. Owing to FA acquisition from the diet, FASN expression is limited in most cell types (including CD4+ T-cells), and yet FASN is both upregulated and required by many viruses (*e.g.* HCV, West Nile Virus) and several cancers (*e.g.* colorectal, breast). Using siRNA targeting of FASN and small-molecule mediated ablation of FASN activity, we revealed that HIV-1 replication also requires FASN activity. When FASN activity is blocked, intracellular Pr55 Gag levels remain constant, but nascent virion production is reduced by 90%, indicating that FASN activity contributes to a late step in the HIV-1 replication cycle. How could FASN activity and resulting *de novo* FA production affect a late stage of HIV-1 replication? The final product of FASN activity, palmitate, can be metabolized into myristate or other long chain FAs. Long chain FAs have many cellular functions, including roles in membrane structure, energy storage, and regulation of subcellular protein localization. This presentation will examine how FASN activity contributes to the production of lipids for post-translational fatty acylation of proteins. We posit that a greater understanding of HIV-stimulated *de novo* FA biosynthesis will reveal the potential utility of FASN inhibition among PLWH.

Symposium 3

Animal Health: at the center of one health approach for combating antimicrobial resistance

Professor Ruwani Kalupahana

Animal health is at the centre of One Health. Healthy animals and healthy production systems in terrestrial, aquatic, domestic and wild animal sectors are of paramount importance to ensure the health and welfare of animals as well as to improve public health, food security and source of livelihood.

When it comes to ensuring the health and welfare of animals, antimicrobials are essential therapeutic agents in veterinary practices, but acquired resistance of microorganisms against many antimicrobials has threatened effective treatment of infectious diseases. Antimicrobial Resistance (AMR) is a topic of concern not only in veterinary practice but across human, animal, plant, food and environmental sectors. Due to the fact, animal health includes prevention, treatment and control of vast array of infectious diseases in diverse group of animal species and in consideration of biomass, the challenges faced by veterinary sector is huge.

Use of sub therapeutic doses of antimicrobials without prescriptions, for prophylaxis, growth promotion and masking poor bio-security are the key concerns related to livestock production despite a legal framework in place. Recent research studies conducted in different livestock production systems and companion animal practices have indicated the gravity of the problem. Additionally, wildlife as sentinels shows environmental contamination with resistant bacteria. Development of guidelines on the responsible and prudent use of antimicrobials based on scientific evidences via surveillance has become an urgent requirement. However, considering the interconnectivity of all biological systems, combating AMR will only be achieved through multi-sectoral one health approach.

Antimicrobial resistance and its implications for environmental health

Dr Priyanie Amerasinghe

The natural environment is becoming a reservoir of antimicrobial compounds, which is driving the antimicrobial resistance (AMR) processes. Drug resistant microbes

in humans, animals and food also enter the environment through all types of waste disposal systems, making antimicrobial resistance build-up a complex phenomenon which is still poorly understood. Thus, it is important to unpack the different linkages to better understand the role of the environment in the spread of AMR and its impact on the environment. The "One Health" approach is holistic in its conceptualization and affords a framework within which to understand the health of people, animals, and plants living in this shared natural environment and also plan the necessary mitigation efforts.

In general, environmental health is considered as a branch of public health that focuses on the interrelationships between people and their environment, promotes human health and well-being, and fosters healthy and safe communities. One health approach also embraces the same principles, but identifies more specifically the key components (animals and food systems) that can enhance the environmental resistome.

Antimicrobial resistance in the environment can be triggered by three major groups of chemicals: (i) antimicrobials (antivirals, antibiotics, antifungals, anti-parasitics); (ii) biocides (surfactants and disinfectants); and (iii) heavy metals. Basin level studies are showing that large waterways are being contaminated with antimicrobial compounds from drug manufacturing processes, human and animal waste disposal systems, and hospital waste. Modelling studies can now predict the source reduction that is required to limit the resistance selection. While the generation of resistant genes is a natural phenomenon and exists in our environment, its substantial increase in terms of prevalence and diversity has become an environmental concern that is driving global attention.

Despite the large body of knowledge that is emerging, there are fundamental gaps linked to the ecology and drivers of AMR in the environment across geographies. This presentation discusses the "One Health" approach to addressing AMR in the environment and how countries are taking steps to address this global problem.

Antimicrobial resistance from a food safety perspective

Dr. Sujatha Pathirage

Antimicrobial resistant microorganisms in food are a major public health challenge and an economic problem. Use of antimicrobials in the food producing animals/crops/aquaculture leading to emergence of antimicrobial resistance microbes in food is increasing threat to human, plant and animal health. Use of sanitizers and biocides further contribute for AMR in food chains. It needs a one health approach to address this issue.

In food producing animals' antibiotics are used as therapeutic and also for nontherapeutic uses like metaphylactics, prophylactics and growth-promoters. Antimicrobial use at production level led to food safety issues associated with the presence of antimicrobial residue, antimicrobial resistance bacteria and the antimicrobial resistance genes in food animal as well as food products

Food can act as a potential route of AMR bacteria. Food of animal origin can become contaminated during slaughter and during carcass dressing while food of plant origin can get contaminated from environment, water and from manure. In addition, food can get contaminated during post-harvest stage from food handler if proper hygienic measures are not practiced or improper food processing and from unhygienic food processing environment.

When AMR food pathogen access human, AMR gene may transfer from food borne microorganism to human microbe by horizontal gene transfer through mechanisms such as transformation, transduction or via conjugation. Regardless of the original source of selective pressure for development of drug resistance – human, livestock, or aquaculture – there exists an interplay between multiple ecosystems to disseminate and exchange antimicrobial resistance determinants (ARDs) For this reason, a unified, multifaceted approach (e.g., One Health) is needed in order to address both the causes and sequelae of antimicrobial resistance (AMR).

Direct and indirect transmission of antibiotic resistance bacteria and antibiotic resistance gene in the food chain increases the likelihood of their entrance and spread in to communities and hospital jeopardizing the health care system.

A total of 73 nontyphoidal Salmonella enterica isolates, 33 from raw chicken meat and 40 from routine clinical specimens, were collected between 2015 and 2017 from eight cities in Sri Lanka for a pilot study of whole genome sequencing for Salmonella surveillance. Among the chicken meat isolates, 87.9% (29/33) of them had at least one resistance gene and multidrug resistance (MDR; defined as resistance to three or more classes of antibiotics) was observed in 15.2% of them (5/33), including two Salmonella enterica serovar Kentucky ST314 strains, which harbored six different classes of antimicrobial resistance (AMR) determinants. In contrast, among the human isolates, 17.5% (7/40) of them had at least one resistance gene and only two isolates (5%, 2/40) were found to be MDR, which were both Salmonella

enterica serovar Chester ST2063 strain that contained five AMR determinants, belonging to five different antibiotic classes. However out of 73 isolates, only one human isolate contained extended-spectrum beta-lactamase (ESBL) gene, blaCTX-M-15. Among all the identified AMR genes, the most frequent resistance genotype was fosA7 and was found in all 16 Salmonella Agona (ST13) strains from different chicken meat samples.

Study done in 2017 at for 12 isolates of campylobacter, overall Campylobacter resistance to erythromycin, tetracycline and ciprofloxacin were 22.22%, 66.66% and 83.33% respectively.

Management of AMR in food chain is complex and need comprehensive approach involving multiple sectors with international cooperation as it is a global problem.

It should start from primary production and continuing through to consumption. Improved regulatory frameworks and better enforcement of existing regulations by governments together with good food safety management practices, Sustainable farming practices, good hygiene and biosecurity measures is necessary.

The international food safety and standard setting agency, Codex Alimentarius Commission is in the process of reviewing the 10-year-old AMR policy as directed by government as a part of global response to AMR.

Codex standard on Maximum Residue Limits (MRLs) and Risk Management Recommendations (RMRs) for Residues of Veterinary Drugs in Foods CX/MRL 2-2018 is already available to guide industry on veterinary drugs. Integrated monitoring and surveillance to track the use of antimicrobials and spread of AMR through food chain together with veterinary drug residue monitoring should be implemented by each country.

Symposium 4

ISO 15189: Medical laboratory accreditation

Ms. Chanditha Ediriweera

Medical laboratories are the key partners in patient safety. Laboratory results influence 70% of medical diagnoses. Quality of laboratory service is the major factor which directly affects the quality of health care. The clinical laboratory as a whole has to provide the best patient care promoting excellence.

To demonstrate the quality and reliability of their services, medical laboratories can be accredited to ISO 15189: Medical laboratories. Requirements for quality and competence, an internationally recognised standard that contains the requirements necessary for diagnostic laboratories to demonstrate their competence to deliver reliable services. ISO 15189 covers the essential elements for medical laboratories to demonstrate the quality and competence of their services, as well as to consistently deliver technically valid test or “examination” results as they are referred to in the standard. The standard, which was developed with strong involvement from the medical, scientific and clinical community, is for the use of medical laboratories to foster a culture of continuous improvement through developing their management systems and maintaining their own technical competence; and for accreditation bodies to confirm or recognise the competence of these laboratories through accreditation.

Accreditation is a tool to demonstrate the competence of medical laboratories and ensure the delivery of timely, accurate and reliable results.

ISO 15189 accreditation involves an independent assessment of the medical laboratory that includes an examination of personnel qualifications and competence, equipment, reagents and supplies, quality assurance, and analytical, pre-analytical, and post-analytical factors. Qualified assessors conduct a thorough evaluation of all factors affecting the production of test data.

To ensure continued compliance, accredited laboratories are regularly reassessed to check that they are maintaining their standards of technical expertise. These laboratories will also be required to participate in regular proficiency testing programs (known as external quality assurance programs or EQAS) as an on-going demonstration of their competence.

Accreditation is an enabler of quality and a core component of good clinical management.

Issues related to implementation of technical requirements for microbiology in medical laboratory accreditation in Sri Lanka

Dr. Kushlani Jayatilleke

There are many issues faced when implementing technical requirements in clinical microbiology laboratories. Firstly, specific trained staff responsible for maintaining quality, such as quality managers are not available in most of the laboratories. This hinders the organization and implementation of quality system in laboratories. Unsuitable storage facilities also lead to poor

quality in reagents, and proper maintenance and calibration of equipment are also not feasible in most laboratories. Not having certified material with traceability and non-availability of proficiency testing programmes for all the tests is a major problem that most laboratories face. Lack of properly validated information systems also contribute to the problem.

In this setting the consultant microbiologists need to think of different ways to assure that the quality system is properly functioning, making the reports issued by the laboratories accurate and timely.

Symposium 5

Transgenic technology to combat dengue mosquito vector *Aedes aegypti*

Professor Ranil Dassanayake

Dengue is currently the most important mosquito-borne viral disease globally having a huge impact on the wellbeing of the human society. The incidence of dengue has increased substantially over recent decades, with about half of the world's population now at risk of infection in more than 140 countries and territories, resulting in about 100 million symptomatic cases and 10,000-20,000 deaths annually. Sri Lanka has also been affected by the dengue epidemics every two to three years causing heavy socio-economic burden on households, health care systems, and the government.

Vector control is currently the main strategy to reduce dengue virus transmission; however, vector control has not halted the spread of *Aedes aegypti*, the main dengue vector, and dengue outbreaks. The transgenic (TG) insect methods are a potentially promising approach to control dengue. TG mosquitoes prove to be safer than conventional vector control methods and effective in controlling dengue vectors. The technology behind TG is species-specific, self-limiting and may potentially reduce pesticide use. Further, dengue mosquito, *Ae. aegypti* is an invasive species and the reduction of this mosquito population is expected to have little or no impact on ecosystems. TG technology can address the problem of hidden or difficult to reach breeding sites of *Ae. aegypti*, which are inaccessible through conventional technologies. Furthermore, in this technology only the male mosquitoes will be released to the environment, which does not generally bite the human and through mating they transfer mosquito or pathogen killing genetic trait to their progeny and thus it is a safer method for controlling vector population and in this way it neither have significant impact on the society and nor to the ecosystem. There have been recent trials of TG mosquitoes in the Cayman Islands, Malaysia, Brazil and Florida Keys with promising results.

In this presentation, our recent development based on advanced cutting-edge technologies, blocking the replication dengue virus serotypes inside the mosquitoes using an effecter molecule engineered to exert RNA interference on dengue RNA and also our ongoing research based on self-limiting gene constructs designed [technology is known as Release of Insects carrying Dominant Lethal genes (RIDL)] to suppress mosquito population and editing mosquito sex determinant gene using CRISPR/Cas9 to achieve male only phenotype will be discussed.

Vectors and the filarial worms: Present and future

Professor Channa Yahathugoda

Sri Lanka has eliminated lymphatic filariasis as a public health issue in 2016. However, the ongoing post-elimination surveillance programmes have documented cases due to human *(Wuchereria bancrofti)* and zoonotic *(Brugia malayi, Dirofilaria repens)* filarial worms. Moreover, vector *(Culex quinquefasciatus)* surveillance – molecular xenomonitoring – has documented hot spots in the country even after 2016. Data on vector (*Armigeres* and *Mansonia* spp,) infectivity rates related to zoonotic filarial diseases are scanty. Thus, successful and sustainable elimination of mosquito-vectored diseases is often challenged by the reintroduction of new infections and resurgence from human infections. At present, strengthening the research on vector-pathogen systems and vector biology to refine vector-harnessed control strategies has become a global priority. Therefore, this presentation will cover some new understandings of the mosquito-filaria relationship and novel approaches to achieve the elimination of lymphatic filariasis.

A community survey carried out after certification of elimination has documented evidence of a threatening level of residual infections (3% of circulating filarial antigenemia, 1% microfilaremia and 5.2% filarial DNA in vectors) in an endemic area of Sri Lanka. Molecular xenomonitoring studies conducted in 2016 have documented that 27% of the collected pools of *Culex* mosquitoes were positive for *W. bancrofti* DNA. Moreover, ongoing transmission was also evident in areas outside of endemic zones. In Trincomalee, a 1.8% urine antibody positive rate was found, and nine of the 630 (1.4%) examined became positive for circulating filarial

antigenemia. Another study carried out in an endemic district of Sri Lanka in the recent past has documented residual cases of bancroftian filariasis and re-emergence of zoonotic brugian filariasis. Therefore, interventions other than preventive chemotherapy and basic vector control is required.

The new trend is to harness more advanced techniques to study genetic factors influencing mosquito resistance or susceptibility to filarial parasites and incorporating them in the control programmes. Recent work on transcriptome analysis and proteomic profiling of *B. malayi* has provided an opportunity to identify and explore genes or proteins expressed in the filarial parasites' life stages, thus providing an important tool to understand the molecular foundation of these parasites. These new understandings of parasites' adaptation, survival, development and physiological activities in the vector have unveiled biological information paving the pathway for novel transmission-blocking therapeutics, vaccines, and identifying target genes for transgenetic mosquito technologies for vector control.

OP 1

Gastric microbiota and its association with histopathological findings among a dyspeptic patient population

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Introduction

Despite the declining prevalence of *Helicobacter pylori (H. pylori)* infection in Sri Lanka, many patients seek treatment for dyspepsia. This highlights the question if other microorganisms residing in gastric mucosa may have a role in gastric pathology. Data on other gastric microorganisms and their role in gastric pathology is still an unexplored area. Present study investigated the presence of gastric bacterial and yeast species and its association with gastric histopathology.

Design, setting and methods

Three gastric biopsies were taken from each patient during the endoscopic procedure. Presence of *H. pylori* was determined by an in-house biopsy urease test (IBUT) and/or histology. Pathology of the gastric mucosa were graded according to the updated sydney classification system. Presence of bacteria (including *H. pylori*) and yeast species in the gastric mucosa were determined by PCR using the universal bacterial (HDA1/HDA2) and yeast (NL1/LS2) primers respectively.

Results

A total of 70 dyspeptic patients were enrolled for the study. Thirty-eight were male and thirty-two were female. Fourteen patients (20%) were positive for *H. pylori*. Most prevalent dyspeptic symptoms were abdominal pain (n=66, 94%), nausea (n=58, 82%), belching (n=24, 34%), emesis (n=14, 20%) and abdominal rumbling (n=8, 11%). According to histopathology, 42 (60%) patients had mild chronic gastritis while 20 (28%) had active chronic gastritis and 8 (11%) had normal gastric pathology. Out of 70 specimens NL1/LS2 PCR for yeast species were positive in 10 specimens and HDA1/HDA2 PCR for bacterial species positive in 65 patients. All *H. pylori* positive specimens were positive for eubacterial PCR. Among the yeast positive group 6 had active chronic gastritis, interestingly all 6 were positive for eubacterial PCR. However, there was no statistically significant difference observed between histopathological findings and the presence or absence of bacterial or yeast species among this study group.

Conclusion

This study demonstrates the presence of yeast species and bacteria in gastric mucosa of dyspeptic patients. Future studies are needed to identify the organisms and understand their role in gastric pathology.

Acknowledgement

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OP 2

Effectiveness of two different protocols of daily chlorhexidine bathing in the prevention of nosocomial acquisition of multi-drug resistant pathogens and *Candida* species in the intensive care units at a tertiary care hospital, Sri Lanka

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Introduction

Healthcare associated infections (HAI) due to multi-drug resistant organisms (MDRO) and *Candida* spp in the intensive care set-up (ICU) increase mortality and morbidity. A large proportion of HAIs are considered preventable; however, many preventive interventions are complex and challenging.

Objectives

The aim of this study was to assess whether daily chlorhexidine gluconate (CHG) bathing is effective in reducing the nosocomial acquisition of MDROs in adults in ICUs.

Design, setting and methods

An intervention study was carried out in patients who were admitted and staying for 48 hours or more in the two main ICUs with total 14 beds in a tertiary care hospital, over a period of 4 months from November 2019 to March 2020. In the pre-intervention period of 2 months, normal soap and water bath was continued in both ICUs. In the

next 2 months, two different protocols of 2% chlorhexidine baths were introduced to both ICUs. One ICU was instructed to follow the CHG leave-on protocol and other ICU, the washout protocol. Screening cultures were done on admission to ICU and on every 3rd day. End point was determined as nosocomial acquisition of multidrug-resistant pathogens and *Candida* species. The rates were calculated according to the total patient days.

Results

Intervention vs pre-intervention (RR, 0.721; 95% CI, p=0.0317), and CHG leave-on protocol vs pre-intervention (RR, 0.652; 95% CI, p=0.0383) had statistically significant difference in the nosocomial acquisition of multidrug-resistant pathogens and *Candida* species. However, no statistically significant difference was identified between CHG washout protocol vs pr-intervention (p=0.1659). CHG leave-on protocol vs CHG washout protocol had no significant difference (p=0.4492). Both CHG washout protocol and leave-on protocol were less likely to have nosocomial acquisition compared to normal soap and water bath.

Conclusions

Daily bathing with 2% chlorhexidine can reduce nosocomial acquisition of multidrug resistant organisms and *Candida* spp significantly. Both CHG washout protocol and leave-on protocols are protective from nosocomial acquisition of MDRO compared to patients who had soap and water bath only.

OP 3

Optimisation of a loop-mediated isothermal amplification assay for detecting *Chlamydia trachomatis* DNA in urine

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Introduction

Chlamydia trachomatis (CT) is one of the most common sexually transmitted infections worldwide. Nucleic acid amplification tests are the gold standard for diagnosis of CT infections. Commercial real-time polymerase chain reaction (PCR) kits with high sensitivity and specificity are prohibitively expensive for countries like Sri Lanka.

Loop-mediated isothermal amplification (LAMP) is cheaper, faster and does not require expensive equipment. We have used published primers of CT LAMP and optimized the assay for use with urine. These primers used by others with endocervical samples reportedly had an analytical sensitivity of 0.17fg. Urine specimens are preferred to endocervical swabs as they are non-invasive.

Objectives

We aimed to optimize a LAMP test, using published primers, for the detection of CT DNA in urine.

Design, setting and methods

Six published primers, F3, B3, FIP, BIP, LF, LB (Patent no.1503002132) targeting the *omp1* gene of CT, were used. Urine samples positive and negative by both CT in-house and real-time PCRs were used as controls for optimization. Crude DNA extraction was done by boiling 40µl of urine with 20µl of 10mM Tris and 1mM EDTA buffer (pH 8) at 95°C for 5 minutes and cooling on ice. Supernatant was used as template.

Optimization was done for Betaine (0.5M, 0.8M), $MgSO_4$ (6-10mM), *Bsm* DNA polymerase (4, 6, 8 units), template volume (5-9µl), incubation temperature (55°C-60°C) and reaction time (40 and 60 minutes), using both gel electrophoresis and 150µM hydroxyl naphthol blue (HNB) for detection.

Analytical sensitivity of LAMP was determined using tenfold dilutions of quantitated CT DNA spiked urine. Specificity of primers were confirmed with urine spiked with DNA of HSV, *Neisseria gonorrhoea*.

Results

Optimal conditions for the one-step CT LAMP-HNB assay were, 0.8M Betaine, 8mM $MgSO_4$, 8U *Bsm* DNA polymerase,1.4mM deoxynucleoside triphosphate, 1.6 µM FIP/BIP, 0.2 µM F3/B3, 1.4 µM FLP/BLP with 7µl crude DNA incubated at 56°C for 60 minutes. The analytical sensitivity by gel detection was 74.9fg ($5.26x10^4$) for crude DNA and 7.49fg ($5.26x10^3$) for DNA purified by commercial extraction kit.

Conclusions

This LAMP assay needs further modifications to increase the analytical sensitivity in urine.

OP 4

Diversity of beta lactamases among Gram-negative blood culture isolates of patients presenting with urosepsis in a tertiary care hospital

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Introduction

Urosepsis contributes for nearly 25% of patients with sepsis. The key characteristics, which contribute to negative out-come are the virulence factors and antibiotic resistance expressed in uro-pathogens. Expression of beta-lactamases in uro-pathogens is one of the most important mechanisms of antibiotic resistance. Elucidation of these resistance characteristics is important but not routinely undertaken in most diagnostic laboratories.

Objectives

To describe the diversity of Gram-negative bacterial species causing urosepsis and to utilize the Advanced Expert System (AES) in a commercial platform (VITEK® 2) and commercial combined discs (Mast® discs) in predicting different types of beta lactamases among target isolates.

Design, setting and methods

This laboratory based prospective (Descriptive) study was conducted over 4 months. Forty-seven blood culture isolates obtained from patients confirmed to have bacteremic uro-sepsis, based on clinical features and investigation results, were analyzed. All isolates were identified to species level with antibiotic sensitivity and minimum inhibitory concentration (MIC) using VITEK 2 platform. Resistance mechanisms were extrapolated using MIC values and AES data according to CLSI-M100-S28. Then isolates were tested for ESBL, Amp C and carbapenemase using quality-controlled combination discs according to manufacturer's instructions.

Results

Main uropathogens identified were: *Escherichia coli* (n=29, 62%), *Klebsiella pneumoniae* (n=11, 24%), *Enterobacter cloacae* (n=3, 6%), *Serratia marcescens* (n=2, 4%), *Proteus mirabilis* (2%) and *Pseudomonas aeruginosa* (2%). According to AES and MIC interpretations, 20 (42.5%) of the isolates were ESBL producers. Eleven (23.4%) were probable carbapenemase producers. There were 6 (12.7%) probable Amp C producers. Only 2 isolates demonstrated wild type phenotype. With combined discs, there were 20 ESBL producers and 2 Amp C producers together with 3 ESBL and Amp C co-producers. Three isolates were shown to produce metallo beta lactamases. Nineteen showed no demonstrable resistance mechanisms with commercial disc kits used.

Conclusion

Gram-negative bacteria causing urosepsis, produced a wide variety of beta lactamases. Nearly 50% of the isolates causing urosepsis were ESBL producers. MIC distributions predicted high rates of Amp C and carbapenemase producers among target isolates but combination discs demonstrated low rates.

OP 5

Study on intra-familial transmission of Hepatitis B viral infection in a cohort of Hepatitis B virus infected patients

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Introduction

Hepatitis B is an infection of liver caused by Hepatitis B Virus (HBV). Sri Lanka is considered as a country of low endemicity and prevalence of HBV infection is estimated to be less than 2%. Among family members and close contacts of infected patients, there is a high risk of transmission of HBV. Preventing intra-familial transmission is important in management of Hepatitis B.

Objectives

To evaluate HBV infection status among family contacts of HBV infected patients followed-up at National Hospital, Kandy.

Design, setting and methods

Laboratory data on serological markers of 148 family contacts of 42 index cases were analyzed. All the index cases were followed up at Department of Virology at National Hospital, Kandy referred from Gastro-enterology clinic, STD clinic and medical clinics for contact screening from March 2017 to February 2021. Serum samples of family members were tested for Hepatitis B serological markers.

Results

Out of 148 family members 25 (16.89%) showed evidence of exposure to hepatitis B (Core total antibody positive)

at the time of screening. Six (4.1%) were positive for HBs antigen. Of them two had evidence of active infection (HBe antigen positive/ HBe antibody negative) and four had sero-conversion to Anti-HBe. Among exposed contacts nineteen (12.8%) were negative for HBs Ag indicating past infection of whom thirteen (8.7%) were positive for HBs antibodies indicating immunity following infection.

Among 32 spouses, six (18.75%) showed evidence of exposure to HBV infection. In two index cases all the family members had evidence of HBV infection. Thirty-six (24.3%) family members had taken HBV vaccine prior to screening. Among them 26 (17.6%) family members showed adequate immunity against Hepatitis B (Anti HBs antibody titer > 10 IU/ml) and all were negative for HB core total antibodies indicating immunity following vaccination.

Conclusion

There is a high HBV infection rate among family members (16.9%) when comparing to the general population (<2%). Proper understanding of transmission kinetics of intra-familial transmission of HBV infection is important for the prevention of HBV infection among family contacts.

OP 6

Analysis of accidentally detected COVID-19 patients from a tertiary care hospital in Southern Sri Lanka

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Introduction

We are a major tertiary-care hospital and a COVID sentinel center, thus transfers all COVID positive patients to specific treatment centers following diagnosis. The hospital has an on-admission triage system to prevent suspected COVID-19 patients getting admitted to wards other than isolation/quarantine units. Nevertheless, COVID-19 patients are accidentally detected from other wards being admitted with atypical/asymptomatic presentation and/or absence of known epidemiological risk factors or adequate information.

Objectives

To analyze the presentation of accidently detected COVID-19 patients and the efficacy of the triage.

Design, setting and methods

This descriptive study was conducted retrospectively for four months (November 2020 to February 2021) utilizing patient records and laboratory data. The diagnosis of COVID-19 was made by RT-PCR and rapid antigen test (RAT).

Results

During this period, 47 COVID-19 patients were accidentally discovered. Respiratory symptoms were absent in 39 (83%) patients on admission/diagnosis. Patients with respiratory symptoms (8/47, 17%) had alternative confirmed diagnoses like chronic kidney disease, heart failure, tuberculosis or bacteraemia.

Routine pre-procedural testing was positive in 23.4% (11/47) in which 3 revealed a positive contact history retrospectively. A cluster of 17 (17/47) patients in an oncology ward found during screening following an accidental identification of a positive patient-carer and was successfully contained, while none of the others caused any hospital clusters. Mortality rate was 4.3% (2/47) and one of them was diagnosed postmortem.

Only 30 (17/47 were from the oncology cluster) had escaped the triage which handled 45,305 admissions. There were 85 positives from 877 admissions to isolation wards. The total COVID positive admissions during the period were 115 (30 plus 85), thus, the efficacy of the triage was calculated as 74% (85/115).

Conclusions

Since COVID-19 patients can present asymptomatically or with a myriad of symptoms, a high degree of suspicion and protected exposure are the keys to contain the infection, while pre-procedural testing can also contribute to minimize the spread. RT-PCR and RAT both contribute to the efficient detection of patients. The mortality rate in the studied group was higher than the national figures.

OP 7

Clinical features and epidemiology of hanta-virus hemorrhagic fever with renal syndrome in Sri Lanka, March 2013 to March 2021

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Introduction

Hemorrhagic fever with renal syndrome (HFRS) is caused by Euro-Asian hantaviruses. Clinical features and basic hematological investigations often mimic leptospirosis.

Objectives

To describe the clinical features and epidemiology of hantavirus infection with HFRS in Sri Lanka from March 2013 to March 2021.

Design, setting and methods

Clinically suspected patients with HFRS who were referred for laboratory diagnosis of hantavirus infection from March 2013 to March 2021 were included in the study. Acute serum samples from these patients were tested for anti-hanta virus IgM antibody. Convalescent samples, when available, were tested for rising IgG antibody titre. Patients' clinical and demographic data were analyzed.

Results

Of the 1032 patients' samples tested, 168 (16.3%) were positive for IgM antibodies; 64.8% (n=109) of the patients were males. Fever, thrombocytopenia and at least one feature of renal involvement were observed with all positive patients. Out of the positive patients, 129 (76.7%) had myalgia, 65 (38.6%) had liver involvement or hepatitis, 41 (24.4%) had difficulty in breathing and 49 (29.1%) had bleeding manifestations. The following complications were observed in the positive patients: 51 (30.3%) acute renal failure (ARF), 27 (10.1%) non cardiogenic pulmonary oedema, 08 (4.7%) myocarditis, 09 (5.3%) massive hemorrhage, 02 (1.1%) encephalitis and 27 (10.1%) developed multi-organ failure. There were 29 (17.2%) fatalities and the majority were (19/29) due to multi-organ failure following ARF. Blood investigations indicated, 85.8% (139/162) of patients had leukocytosis and 80.19% (81/101) had elevated CRP.

Majority of the cases (n=121, 72.0%) were detected during paddy harvesting seasons and 151 (89.9%) of positive patients had significant history of exposure to rodents. Majority (53/168) of positive cases had been reported from Western Province and second highest (51/168) was from North Central Province.

Fourfold rise of anti-hantavirus IgG antibody was detected in 31/35 of patients. Antibodies detected strongly cross reacted with Seoul, Hantaan and Puumala viruses.

Conclusions

Typical characteristic of HFRS have been seen with majority of the cases. Significant number of patients had developed severe complications with a high fatality rate. Hantavirus infections were frequently reported in Western and North Central part of the country during paddy harvesting seasons.

Acknowledgement

Financial assistance by WHO is acknowledged.

OP 8

Epidemiology of human rabies in Sri Lanka, 2015 to 2020

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Introduction

Rabies is a vaccine-preventable viral zoonosis. It causes an invariably fatal acute encephalomyelitis which is nearly 100% preventable by timely administration of post-exposure prophylaxis.

Objective

To describe the socio-demographic data and to analyze the trend of confirmed human rabies from 2015 to 2020 in Sri Lanka.

Design, setting and methods

This study was performed in the Department of Rabies, Medical Research Institute (MRI). Brain samples received for confirmation during the study period were mainly tested using a direct fluorescent antibody test. Socio-demographic and clinical details were obtained from request forms and clinicians.

Results

A total of 147 human rabies deaths were confirmed from 2015 to 2020. Of them, 143 were laboratory confirmed. Cases reported were, 25 in 2015, 21 in 2016, 26 in 2017, 18 in 2018, 26 in 2019, 31 in 2020. This shows a static incidence during the last 5 years with a relative increase in 2020. The highest incidence was reported from Kurunegala District (n=23,15.6%). Kalutara, Gampaha, Jaffna, Galle, and Anuradhapura reported 15,10,8,9 cases respectively. Male: female ratio of the victims was 3.2:1. Of them 21 (14.2%) were reported under the age of 15 years and 84 (57.1%) were in the age group of 15 to 60.

Out of 109, 93 (85%) were following dog bites, 6 (5.5%) cat bites or scratches, and 10 (9.1%) wild animal bites including 2 deaths within one month, following jackal bites in 2020. Out of 93 dog bites, 59 (63%) were following stray dog bites. Out of 147, 133 (90.4%) had not taken any form of rabies post-exposure prophylaxis (PEP), 8 (5.4%) have taken partial treatment, and 6 (4%) patients developed rabies despite recommended PEP. Clinically, 119/128 (93%) were furious rabies, 6 (4.6%) were paralytic, and 3 (2.3%) with atypical symptoms. Out of 75 available histories, 39/41 (95%) adult males were in the lower socio-economic group.

Conclusions

The majority of patients were adult males of earning age and belong to a low socio-economic group. Furious type of rabies is the commonest presentation and the main source was stray dogs.

Although PEP is freely available, the majority had not sought proper medical advice after exposure. Reported treatment failures might be due to inadequacy of wound infiltration with anti-rabies serum or direct inoculation of the virus to nerves.

OP 9

The increasing infection rate of *Leishmania donovani* in *Phlebotomus argentipes* highlights the need for Leishmaniasis control in Sri Lanka

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Introduction

Leishmaniasis is a neglected tropical disease with a heavy global health burden. There is a steady rise in cutaneous leishmaniasis (CL) cases in Sri Lanka over the last two decades. Sri Lankan vector *Phlebotomus argentipes glaucus* transmits *Leishmania donovani* MON-37 parasite.

The prevalence rate of Leishmania parasites within *P. argentipes* is used as a parameter to assess the leishmaniasis transmission intensity. Previous molecular-based studies have shown an infection rate of 0.3% locally and 5-17% regionally.

Objective

A molecular-based evaluation of the infection rate was done as part of the first vector-based island-wide study to understand the changing trends in bionomics among Sri Lankan sandflies.

Design, setting and methods

DNA was extracted from 1520 (1085 blood-engorged and 435 non-engorged) previously collected and preserved *P. argentipes* sandflies covering all provinces of Sri Lanka. *Leishmania*-specific primers were used to amplify the partial sequence of kDNA using conventional PCR. A second nested PCR using *donovani*-specific primers targeting ITS-rDNA was done to confirm the presence of parasites within *P. argentipes.* All positive PCR amplicons were sequenced. The sequences were aligned with those in the NCBI-GenBank repository and phylogenetic analysis was performed. The infected sandflies were molecularly confirmed as *Phlebotomus argentipes*.

Results

There were 15 positive PCR amplicons in both PCRs. The sequence analysis confirmed the identity as *Leishmania donovani*. Two *L. donovani* sequences were identified in DNA extracts from non-engorged sandflies. The infection rate of the Sri Lankan sandflies was 1% (15/1520). The demonstration of *L. donovani*-infected sandflies supports the view of *P. argentipes* incriminated as the Sri Lankan leishmaniasis vector. The Neighbour-joining tree topology showed the close relationship of Sri Lankan *L. donovani* with *L. donovani* in regional countries.

Conclusion

The notable increase in the infection rate of *L. donovani* in *Phlebotomus argentipes* in Sri Lanka may explain and is in accordance with the leishmaniasis burden's escalating trend. The changing trend of the vector's bionomics and its relationship with the host and parasite may be exploited to implement successful vector control strategies in the future.

OP 10

Antibody levels against hepatitis B virus surface antigen among haemodialysis patients at two major nephrology units in Sri Lanka

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Table 1. Anti-HBs levels in 235 haemodialysis patients

HBV vaccination schedules	Anti-HBs levels in mIU/mL			Total
	<10	10-100	>100	
Schedule A (0,1,2 months)	49 (33.1%)	45 (30.4%)	54 (36.5%)	148 (100%)
Schedule B (0,1,3 months)	13 (41.9%)	10 (32.3%)	8 (25.8%)	31 (100%)
Schedule C (0,1,6 months)	11 (19.6%)	13 (23.2%)	32 (57.2%)	56 (100%)
	70 (29.8%)	71 (30.2%)	94 (40.0%)	235 (100%)

Introduction

Haemodialysis patients are susceptible to hepatitis B virus (HBV) infection and it is recommended to test for antibody levels against HBV surface antigen (anti-HBs) annually in dialysis patients and if levels are less than 10mIU/mL, a booster dose is required. Currently, anti-HBs is not measured in dialysis patients in Sri Lankan nephrology units and thus the need for repeat vaccination cannot be identified.

Objectives

This study aimed to quantify anti-HBs levels, identify the factors associated with anti-HBs levels in haemodialysis patients and test for HBsAg on samples with anti-HBs levels below 10mIU/mL.

Design, setting and methods

This was a descriptive cross-sectional study done at the National Hospital of Sri Lanka and the National Institute for Nephrology, Dialysis and Transplantation from November 2019 to April 2020. End stage renal disease patients on haemodialysis who have received HBV vaccine in a schedule within the last ten years with the last vaccine dose given at least one-month before the commencement of the study were included. Anti-HBs levels were quantified and analysed with demographic factors such as gender, age, duration of chronic kidney disease, duration of dialysis, cycles of dialysis done per month, body mass index, serum creatinine and haemoglobin. Furtheranti-HBs levels in each group were analysed with the duration from the last dose of vaccine.

Results

(Table 1)

The overall seroconversion rate was 70.2% with schedule C showing 80.4%. Females had a better sero-conversion level compared to males in schedule A. Other factors did not show any association with HBV sero-conversion levels. Two patients with no protective immunity were positive for HBsAg giving a prevalence of 0.8% for HBV infection.

Conclusion

Schedule C showed a better sero-conversion compared to others.

OP 11

Demography, clinical features, outcome, and source of infection in healthcare workers infected with COVID-19 in a leading children's hospital in Sri Lanka.

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Introduction

Coronavirus disease 2019 (COVID-19) is an ongoing, rapidly evolving global pandemic causing dramatic impact on healthcare. This study was conducted in a major tertiary care hospital for children in Sri Lanka with 1,016 beds. There are 2,462 healthcare workers (HCWs) currently working in this hospital. A significant number of HCWs became positive for COVID-19 at this hospital. This research is conducted to fill the gap in data regarding this infection and HCWs.

Objectives

To assess the demography, clinical features, outcome, and source of infection in confirmed COVID-19 infected HCWs at this hospital.

Design, setting and methods

This is a retrospective cross-sectional study done at this hospital including all HCWs infected with SARS-CoV-2 virus from 09th October 2020 to 09th February 2021.

Data extracted from the infection control unit database using an investigator administered questionnaire, and the characteristics were analysed.

Results

Out of 2,462 HCWs, 74 (3%) tested positive for COVID-19 during the study period. The majority of positive cases were from 20-30 age group (27%) and 51- 60 age group (27%). There was a female predominance (51.4%, n=38). Healthcare assistants (HCAs) were infected mostly (68.9%, n=51) followed by nursing officers (10.8%, n=8) and medical officers (9.5%, n=7). Most of them were asymptomatic (44.59%). In the symptomatic population majority had respiratory symptoms (29.73%) followed by body aches (28.38%). Fever was present in 24.32% of the HCWs. However, the least prominent symptom was diarrhoea (5.41%). Most of the HCWs contracted the infection from their colleagues (58.1%), whereas none contracted the disease from patients. All HCWs were admitted to hospital according to the national policy, but no one needed ICU care. All HCWs (100%) recovered completely with 0% death rate.

Conclusions

COVID-19 presented mostly as asymptomatic disease in this population and the majority of infected HCWs were HCAs. The reason for high acquisition of infection among HCA may be lack of infection control precautions while contacting their colleagues. However further research required to conclude this fact.

OP 12

The re-emerged *Brugia malayi* infection in Sri Lanka is transmitted by mosquitoes of *Mansonia* spp. mosquitoes

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Introduction

Brugian filariasis has re-emerged in Sri Lanka after four decades of quiescence. The re-emerged *Bruguia malayi* microfilaria exhibited nocturnal sub-periodicity and was shown to be a variant strain of zoonotic origin. Mosquitoes of genera *Mansonia* and *Anopheles* are the known vectors of *B. malayi* infection. The *B.malayi* subspecies found in Sri Lanka in the past exhibited nocturnal periodicity and was transmitted by mosquitoes of *Mansonia* spp. Entomological investigations were performed to identify the vector species of the re-emerged B.malayi.

Design, setting and methods

A mosquito surveillance was carried out in April 2019, in Kelaniya and Wattala Medical Officer of Health areas, in Gampaha. Both selected areas reported human and animal *B.malayi* (nocturnal- subperiodic) infections in the recent past. Cattle-baited net-traps were used in capturing mosquitoes. The field-caught mosquitoes were identified using taxonomic keys. Heads and thoraces of all *Mansonia* spp mosquitoes were dissected to identify filarial larvae. The lysate of the dissected mosquitoes with filarial larvae were taken for genomic DNA extraction followed by Polymerase Chain Reaction. Pan-filarial primers that spanned the internal transcribed spacer region two (ITS-2) of the ribosomal DNA were used. Amplified DNA was run in 1.5% agarose gel and visualized in a gel documentation apparatus. The species identity was confirmed by size discrimination in the agarose- gel.

Results

A total of 672 mosquitoes belonging to six species were collected. Among field caught mosquitos species, 82 (12.2%) belonged to the genus *Mansonia* namely; *Mansonia annulifera* 65 (9.67%), *Mansonia uniformis* 14(2%), *Mansonia indiana* 3 (0.44%). Rest were *Culex gelidus* 280 (41.6%), *Culex tritaeniorhynchus* 255 (37.9%), *Armigeres subalbatus* 55 (8.18%). Seventeen (20.73%) *Mansonia* spp. specimens were positive for filarial larvae. The majority of the infected mosquitoes were *M. annulifera* (94.11%; 16/17). The DNA extracts of all infected *Mansonia* mosquitoes elicited the expected band at 615bp by pan-filarial primer specific PCR, confirming the filarial larvae as that of *B. malayi*.

Conclusion

Mansonia spp. mosquitoes predominantly *(M. annulifera* and *M. uniformis)* were implicated as vectors of the re-emerged nocturnally-subperiodic *B.malayi* parasite in Sri Lanka.

PP 1

Distribution of vancomycin minimum inhibitory concentration and antibiotic sensitivity pattern in *Staphylococcus aureus* clinical isolates at a university hospital in Sri Lanka

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Introduction

Methicillin sensitive and methicillin resistant *Staphylococcus aureus* (MSSA and MRSA) frequently cause superficial to deep-seated infections in human. Due to the multidrug resistance, treatment options are limited for MRSA, making vancomycin the drug of choice for severe and complicated infections. Recently, there have been reports of reduced susceptibility of MRSA to vancomycin.

Objectives

Study was conducted to determine the minimum inhibitory concentration (MIC) of vancomycin in MRSA and MSSA isolates and to analyse the antibiotic sensitivity patterns of them.

Design, setting and methods

Staphylococcus aureus isolates (n=40) from clinical samples received to microbiology laboratory during the study period (3 months) from January 2020, were tested for vancomycin MIC using broth microdilution method (BMD) with a concentration gradient 0.25-512µg/ml, and Epsilometer strips (E strips: Liofilchem, Italy) with a concentration gradient 0.016-256µg/ml. Isolates were identified by Gram stain, catalase, tube coagulase, DNase tests and cefoxitin 5µg disc. Antibiotic sensitivity was performed by disc diffusion method. (CLSI 2019).

Results

Among the 40 *Staphylococcus aureus* isolates, 15/40 (37.5%) were MRSA. Isolates were from wound swabs (42%), pus samples (30%) ear swabs (17%), nasal swabs (5%), blood cultures (3%) and urine cultures (3%). MIC of vancomycin to MRSA strains ranged from 1 µg/ml to 2 µg/ml by BMD with a mean MIC of 1.87 µg/ml and from 0.5 µg/ml to 1µg/ml by E strips with a mean MIC of 0.93 µg/ml whereas MSSA ranged from 0.5µg/ml to 2 µg/ml with a mean MIC of 1.7 µg/ml by BMD and 0.5 µg/ml to 2 µg/ml with a mean MIC of 0.93 µg/ml by E strips. Antibiotic sensitivity of MRSA and MSSA to other antibiotics were erythromycin (0%, 20%), clindamycin (20%, 76%), gentamycin (67%, 56%), ciprofloxacin (60%, 64%), Cotrimoxazole (80%, 100%) and tetracycline (43%, 31%) respectively.

Conclusion

Our findings concluded that prevalence of MRSA isolated from clinical samples was relatively high. None of the MSSA or MRSA isolates were found to be vancomycin resistant. High MIC values were observed in BMD method than by vancomycin E strip in both MSSA and MRSA.

PP 2

Eczematous skin colonization pattern with potential bacterial pathogens among paediatric population at a tertiary care setting, in Sri Lanka

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Introduction

Atopic dermatitis (AD) is a chronic relapsing inflammatory skin disease primarily in childhood which leads to a substantial psycho-social morbidity for the child and parents. AD skin is at greater risk of colonization by pathogenic bacteria due to its altered epidermal barrier, increased bacterial adhesion and reduced innate immune responses.

Objectives

To identify and evaluate antibiotic sensitivity of colonizing bacterial flora associated with eczematous skin of paediatric patients.

Design, setting and methods

It was a prospective cross-sectional study carried out at a paediatric dermatology clinic of a specialized children's

hospital. Surface swabs of eczematous lesions were collected from 50 consecutive patients who attended the outpatient dermatology clinic during the study period and the swabs were transported immediately to the laboratory. Isolates were identified with Gram stain and standard biochemical tests. Further identity of *Staphylococcus* isolates was confirmed by molecular typing using spa gene. Antibiotic susceptibility patterns were determined using quality-controlled disc diffusion method (CLSI 2019).

Results

A total of 98% (n=49) of subjects showed bacterial colonization and of those, 34% (n=17) were confirmed as due to *Staphylococcus aureus*. Of 101 different bacterial isolates from 49 subjects, 65.3% (n=66) accounted for coagulase negative staphylococci (CoNS), *S. aureus* 18.9% (n=19), micrococci 11.8% (n=12), *Acinetobacter* sp. 3% (n=2) and further *Bordetella bronchiseptica* (n=1) and *Streptococcus agalactiae* 1% (n=1). Among *S. aureus* isolated, 68.4% were methicillin sensitive, 31.6% were MRSA and showed resistance to erythromycin (36.8%) and clindamycin (21%). Some of the isolated CoNS were resistant to cefoxitin (68.2%), erythromycin (65.2%), clindamycin (33.3%) and tetracycline (1.5%). The two isolated *Acinetobacter* sp. were sensitive to gentamycin, ceftazidime and meropenem.

Conclusions

The incidence of *S. aureus* colonization (34%) is much lower compared to the previous data available locally of which 31.6% were MRSA. However, MRSA colonization rate among populations with eczema needs to be evaluated periodically to avoid related complications and spread.

PP 3

The demography, clinical features and outcome of paediatric patients and their bystanders infected with COVID-19 in the largest children's hospital in Sri Lanka

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Introduction

Coronavirus Disease 2019 (COVID-19) is a deleterious pandemic. This study was done in the largest paediatric tertiary care hospital in Sri Lanka with 1,016 bed strength.

Objective

To describe demographic characteristics, symptoms, outcome and possible source of contact in children and their bystanders with laboratory confirmed COVID-19 at the largest children's hospital in Sri Lanka.

Design, setting and methods

A retrospective cross-sectional study was conducted recruiting all paediatric patients and their bystanders diagnosed with COVID-19 by positive Polymerase Chain Reaction (PCR) and Rapid Antigen Test (RAT) following admission from 24/03/2020 to 24/02/2021. Data extracted from the hospital database were analysed using an investigator administered questionnaire.

Results

During the study period 6395 patients and 2183 bystanders underwent either PCR or RAT. Out of them, 174 patients (3%) and 139 bystanders (6%) were confirmed of COVID-19 infection. Among the positive patients, 59 (34%) were under 2 years, whereas 12 (7%) were in the 12-14-year group and 93 (53.44%) were male. Among the positive bystanders 61 (44%) were between 30-40 years and 114 (82.01%) were female. A total of 294 (93%) of the positive cases were from Western Province (the main draining area of this hospital) with 256 (82%) from Colombo District. Among 120 positive patients, 69 (57.5%) were symptomatic. 63 (52.5%) experienced at-least either fever or respiratory symptoms, whereas only 6 (5%) developed diarrhea. Only 10 (10.52%) out of the 95 infected bystanders were symptomatic. Only 50 (29%) of the positive patients and 25 (18%) of positive bystanders gave a positive contact history. Among them 60 (19%) had household exposure and 5 (1.6%) from the community. Out of all positive patients, severe illness requiring ICU care were 10 (5.7%), severe disease leading to death were 3 (1.7%) and rest of the patients and all the bystanders had mild to moderate illness with recovery. Bystander mortality was 0.

Conclusion

Proportion of symptomatic children were more than among bystanders (adults) in this population probably because the study was done in a children's hospital. Younger children are mostly affected and their commonest features were fever and respiratory symptoms.

PP 4

Sero-prevalence and factors associated with past exposure to hepatitis E virus infection in pregnant women attending a major maternity hospital in Sri Lanka

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Introduction

Hepatitis E is an enterically transmitted disease, which may cause fulminant hepatitis in pregnant women and the immunocompromised. There were very few published data on the sero-prevalence of hepatitis E virus (HEV) infection in Sri Lanka. This project has been undertaken to determine the sero-prevalence of HEV infection in a selected sample of pregnant women.

Objectives

To determine the sero-prevalence of HEV exposure and to identify the factors associated with past exposure in the study sample.

Design, setting and methods

This was a descriptive cross-sectional study, carried out in a maternity hospital from December 2019 to April 2020. The study sample was consecutive pregnant women (age 16-42 years) who attended the OGTT clinic. A total of 260 blood samples were collected with data related to socio-demography and associated factors using a questionnaire. Sera were tested for anti-HEV IgG using an ELISA at the Virology Laboratory of the University of Peradeniya to determine the sero-prevalence rate with associated factors.

Results

Only one tested pregnant woman was positive for anti-HEV IgG among the 260 participants with an overall sero-prevalence of 0.38%. The mean age of the study sample was 28 (SD ± 7.7) years and the mean gestational age was 21 weeks (SD ± 7.9). The majority (n=149; 57%) were with multi parities, 68% (n=176) in 2nd trimester and 62% (n=161) were Sinhalese. They had a literacy rate of 99.6% (n=259), 80% (n=209), had secondary level education 90.3% (n=235) reported using hygienic practices, 82% (n=214) reported using purified chlorinated water for drinking and 97% (n=252). reported to have water sealed toilets with proper sewage disposal

Conclusion

Overall, anti-HEV IgG sero-prevalence of 0.38% suggests a low exposure to HEV. Exposure to enteric infections is generally through improper sewage disposal, contaminated drinking water and poor sanitary facilities, which were not identified by the study sample. Large scale studies in different communities would help to determine the actual exposure to HEV in Sri Lanka.

PP 5

A case of subcutaneous infection caused by *Basidiobolus ranarum* in a child

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Introduction

Chronic abscesses in children are usually rare. Recurrent subcutaneous infections occur due to virulent organisms like *Staphylococcus aureus* or in patients with dermatological disorders or in immune-deficiencies. *Basidiobolus* species is an occasional human pathogen which can cause subcutaneous infections involving the thigh, trunk, buttock and perineal areas.

Case report

A 3-year-old girl presented to a local hospital in August 2020 with a history of a gradually enlarging painless, non-tender lesion of one week in the posterior aspect of the right mid-thigh. No associated fever or history of any trauma. Local examination revealed a lump measuring 2x3 cm. Systemic and general examination revealed no abnormalities. Sample taken for bacterial culture during incision and drainage, had no growth.

The child was discharged on syrup co-amoxiclav. Poor wound healing with discharges were noted during subsequent follow-ups and managed with cleaning and dressing and antibiotics. Six weeks later wound toilet was repeated and necrotic tissues were excised. Treatment with co-amoxiclav was continued. At follow-up after four months, healing was noted but hyperpigmentation of a vast area of the posterior mid-thigh and a subcutaneous mass solid in consistency was noticed beneath the surgical scar which raised suspicion of a deep fungal infection. The child was referred to a tertiary care hospital for further management.

Ultra-sound scans revealed an irregular hypoechoic lesion beneath the surgical scar measuring 23mm ×16mm × 5mm,

which raised suspicion of a superficial abscess with surrounding cellulitis. Incisional biopsy done on the 5th month since initial presentation and sent for histology and culture. Pure growth of fungal isolate on blood agar plate was identified as *Basidiobolus ranarum* at Medical Research Institute. Histology report suspected of fungal infection. Treatment with oral itraconazole started after liver function tests and was discharged on the same. Follow up in two weeks showed significant reduction of the swelling, pain, pigmentation and induration. Treatment continued till complete clinical recovery and for a further period of four weeks.

Discussion

Subcutaneous infections with *Basidiobolus ranarum* have been reported in Asian and African countries, occasionally in Sri Lanka. Timely suspicion of fungal etiology could save children from treatable deformities.

PP 6

Mycotic aneurysm in melioidosis: a case report

Jayasundera MCT[1]*, Piyasiri DLB*[1]*, Ubayasiri R*[1]*, Corea EM*[2]*, Wagaarachchige YA*[1]*, Liyanage N*[1]

[1]Teaching Hospital Karapitiya, [2]Department of Microbiology, Faculty of Medicine, University of Colombo

Introduction

Although melioidosis can result in a range of clinical manifestations, cardiovascular infections are extremely rare. Mycotic aneurysms comprise about 1-2% of melioidosis cases.

Case report

A 66-year-old, retired security officer who is a diabetic, an ex-smoker and an occasional farmer was admitted with pain and weakness of the right lower limb for three days. He had no history of trauma or fever. Absent pulse was noted in the right lower limb. CT aortogram detected a large saccular aneurysm in the right common iliac artery measuring 6 ×10cm^2. The patient had pancytopaenia with a white blood cell count of 0.17×10^3/mL with 22% neutrophils. CRP was 207mg/L while ESR was 85mm/ 1st hr.

Aneurysm exclusion and femoro-femoral crossover grafting was done. The patient developed fever on second post-operative day. The aneurysm wall culture and blood culture grew a non-lactose fermenting, oxidase positive, Gram-negative bacillus. Upon suspicion of the typical colony morphology and antibiotic sensitivity profile, the bacterium was preliminarily identified as *Burkholderia pseudomallei*, which was confirmed at the reference laboratory by latex agglutination. Melioidosis antibody titer was 1:160. Echocardiogram revealed no vegetations.

Antibiotics were optimized as intravenous meropenem, oral co-trimoxazole and doxycycline. This regime was continued for 5 weeks. Patient improved clinically with a reduction of inflammatory markers. Patient was discharged on a plan to continue oral co-trimoxazole and doxycycline for a minimum of 20 weeks.

Discussion

Mycotic aneurysms in melioidosis are associated with a high rate of morbidity and mortality. Only a few cases have been published worldwide and this could be the first case reported in Sri Lanka. Diagnosis is challenging due to the non-specific presentation and rare incidence. Risk factors like diabetes, smoking and soil exposure may have contributed to the development of the disease in our patient. Positive cultures from aneurysm wall and blood confirmed the diagnosis even with a low antibody titre.

Treatment includes ceftazidime or a carbapenem, with co-trimoxazole, for 4-6 weeks followed by eradication therapy for a minimum of 3 months. Wide surgical excision and repair of the aneurysm is the surgical gold standard therapy.

PP 7

Acute pneumonia due to melioidosis following near-drowning: two case reports

Liyanage N[1]*, Piyasiri DLB*[1]*, Jayasundera MCT*[1]*, Wijeweera KDDS*[1]*, Corea EM*[2]*, Dadallage CV*[1]

[1]Department of Microbiology, Teaching Hospital Karapitiya, [2]Department of Microbiology, Faculty of Medicine, University of Colombo

Introduction

Melioidosis, caused by the saprophytic bacillus *Burkholderia pseudomallei*, is acquired by inhalation, ingestion or traumatic inoculation and presents as acute, sub-acute and chronic presentations. Here we report two cases of acute pneumonia due to melioidosis following aspiration and near-drowning.

Case 01

A 65-year-old, otherwise healthy gentleman from Weligama was admitted with fever and cough for one

week and diagnosed as having pneumonia. He had aspirated muddy water from a drain after crashing his motorbike under the influence of alcohol, two days before the onset of fever. His white cell count was 9×10^9/L and CRP was 271 mg/L. Blood culture grew *B. pseudomallei* and the melioidosis antibody titre was 1/640. He was treated with IV meropenem, oral cotrimoxazole and oral doxycycline for 2 weeks and given a further 10 weeks of oral eradication therapy. He recovered fully and his antibody titre reduced to 1/80 at 12 weeks.

Case 02

A 19-year-old, previously healthy young male from Aluthgama was admitted with fever and difficulty in breathing for 5 days after an episode of near-drowning in a river one week previously. His white cell count was 15.2×10^9/L and CRP was 172 mg/L. Blood culture grew *B. pseudomallei* while the melioidosis antibody titre was 1/80. He was treated with IV meropenem and oral co-trimoxazole for 10 days and discharged on oral eradication therapy after which he fully recovered.

Discussion

In both these cases, the patients had no significant risk factors and the likely source was contaminated water. However, we failed to culture the bacillus from either drain or river water despite repeated attempts at enrichment and prolonged incubation. Initial treatment regimen for acute community acquired pneumonia targeting pneumococci and other pathogens was not effective in both cases and response was only achieved following targeted antibiotics for melioidosis. Therefore, melioidosis should be considered in cases of acute pneumonia with poor response to standard antibiotics following aspiration of water.

PP 8

Actinomycosis in the oropharynx

Thuduvage VS[1]*, Nakkawita WMID*[1]*, Kumarasinghe IHS*[1]*, Pathirage MVS*[2]*, Dissanayake HTRW*[1]*, Weerasinghe WMDKB*[1]

[1]General Sir John Kotelawala Defence University, Ratmalana, Sri Lanka, [2]Medical Research Institute, Colombo, Sri Lanka

Introduction

Actinomycosis is a rare infectious bacterial disease caused by Actinomyces species. Actinomyces are gram positive facultatively anaerobic bacteria who are ubiquitous in nature. They occur in soil and in microbiota of animal including human.

Case Report

A 56 years old patient presented to ENT outpatient department of University Hospital KDU (UHKDU) with irritation and foreign body sensation in the throat without having throat pain for a period of two months. He was a carpenter and a diagnosed patient with diabetes mellitus. Throat examination showed white patches over the posterior pharyngeal wall and rest of the oral cavity was normal. Fiberoptic laryngoscopy examination was performed under local anesthesia through the nasal route and found whitish patches over the tongue base, posterior pharyngeal wall, and vallecular area. Lesions appeared as penetrated the mucosa and multiple samples were taken for culture and histology. Biopsy specimens taken from the lesions showed multiple basophilic spherical clusters of densely packed filaments suspicious of *Actinomyces* colonies in the tissue specimen. Bacterial culture of specimens from the lesions were performed. Inoculated blood and chocolate agar plates were incubated in the CO2 incubator under microaerophilic conditions at microbiology laboratory at UHKDU. Pure growth of whitish dry colonies grew after 72 hours of incubation and appeared as branching Gram-positive bacilli on Gram stain. These colonies were later identified as *Actinomyces meyeri* (remel: RapdID ANA11 positive rods) at the reference laboratory. Antibiotic sensitivity report showed susceptibility to penicillin and co-amoxiclav. Patient was initially treated with intravenous penicillin for 5 days and later converted to IV co-amoxiclav and continued with oral co-amoxiclav for total 8 weeks. Repeated fibro optic laryngoscopy examinations were initially done weekly to evaluate the response and showed complete recovery of lesions after 8 weeks of antibiotic treatment. Patient was asymptomatic at the end of the treatment and was followed up for 6 months in the clinic and no recurrence was observed.

Discussion

Actinomyces infections of the head and neck, although uncommon, represent an important entity because of its varied presentation, difficult diagnosis, and long course of treatment.

FELLOWSHIPS OF THE SRI LANKA COLLEGE OF MICROBIOLOGISTS 2020

Fellowships of the Sri Lanka College of Microbiologists were awarded to Dr. Pranitha Somaratne, Dr. Philomena Chandrasiri and Dr. Geethani Wickramasinghe on 14th August 2020 at the 'Lionel Memorial Auditorium', Wijerama House, Colombo 07.

Dr. Pranitha Somaratne

MBBS, Diploma in Medical Microbiology, Diploma Micro. (KL, Malaysia), MD Medical Microbiology

Dr. Pranitha Somaratne (nee Jayasekera) had her primary and secondary education at Southlands College, Galle and Visakha Vidyalaya, Colombo. She graduated in MBBS in 1979 from the Faculty of Medicine, University of Colombo and did her Internship at Professorial Surgical Unit, General Hospital, Colombo and Paediatric Medicine at Lady Ridgeway Children's Hospital.

Dr. Somaratne joined Bacteriology department of the Medical Research Institute in 1989 and obtained post-graduate qualifications, Diploma in Medical Microbiology in 1993, Diploma in Medical Microbiology from the Institute of Medical Research, Kuala Lumpur in 1995 with distinction and winning 'Best Student' award, and MD Microbiology in 1998. She was Board Certified as a Specialist in Medical Microbiology in 1999 and served as a Consultant Microbiologist of Medical Research Institute (MRI) until 2011.

As a consultant, she headed several laboratories in Bacteriology and received training in many components of the subject, mainly at WHO and JICA endorsed centers and contributed to improve laboratory standards. She contributed to multi-center Antimicrobial Resistance Surveillance Project, Phase 1, in 2009. She organized training on laboratory diagnosis of *Clostridium difficile*, with experts from Australia, UK and Belgium and received input to improve Anaerobic bacteriology diagnostic standards.

She worked closely with WHO to up-grade Leptospirosis Reference Laboratory. She established serovar classification of local isolates with training and partnership received through WHO Leptospirosis Reference Center, Andaman and Nicobar Islands, India and WHO National Collaborating Centre for Reference and Research on Leptospirosis in Netherlands. Received assistance from Pasteur Institute for preliminary work on molecular diagnosis of leptospirosis.

Dr. Somaratne presented a paper at Sixth International Leptospirosis Conference 2009, in India. She contributed to research projects with clinicians and university scientists and jointly won E M Wijerama Prize at Sri Lanka Medical Association Sessions 2009. She supervised two MD trainees to conduct dissertations on leptospirosis, organized trainings and was a member of National Advisory Committee on Prevention of Leptospirosis.

Dr Somaratne contributed to improve Bacteriology External Quality Assurance (EQAS) programme since inception in 1995. These include procuring and making available reference cultures, training, audits, initiating joining of new participants and co-production of hand-book on 'Bacteriology QC'. In 2010 she arranged registering MRI for participation in International EQAS in Microbiology by Indian Association of Medical Microbiologists.

After the terrorist attacks of September 11, 2001 in the USA, anonymous letters carrying deadly anthrax spores began arriving in America. Five people died from inhaling anthrax and 17 were infected. The threat became global, not sparing us. Since 2001 more than 150 'samples' suspected as anthrax were received within Sri Lanka. Each of these were tested in only one Bio-safety Level 3 laboratory in the country at MRI. Dr Somaratne headed, supervised and worked in processing suspected samples. She was trained by WHO in international hands-on workshops and forums in Thailand, India and Sri Lanka. In 2002 she co-authored 'WHO Manual on Laboratory Diagnosis of Anthrax'. She has trained several technologists in processing samples and infection prevention on handling Category 'A' pathogens.

While working at MRI, Ministry of Health appointed her as a Visiting Microbiologist to several District General and Base Hospitals, before they had their own Microbiologists. Several infection outbreaks in these hospitals were investigated and managed successfully. Public health outbreaks were also investigated and controlled including a major outbreak in an Army camp.

Dr. Somaratne was involved in investigation of the outbreak of meningitis-associated- with-spinal-anesthesia in 2005, in major maternity and other hospitals. She was a member of the Task Force in this investigation and contributed to 'Final Report on Containment'.

She has co-authored several research papers in national and international journals and contributed for 'Infection Control Manual 2005', 'WHO manual on Guidelines for labour-room management', 'Laboratory Manual in Microbiology' First and Second Editions. She co-authored 'Biosafety Manual for Medical Laboratories' 2004 and, as President of Sri Lanka College of Microbiologists initiated the revision of Second Edition 2014. Her pledge in biosafety was a result of exposure to international training and consultative meetings on laboratory bio-safety and bio-risk assessment.

Dr Somaratne was a Visiting Lecturer, Examiner or Chief Examiner for Medical Laboratory Technology training schools since 1990 until her retirement in 2011.

She was a Member of Board of Study (BOS) Microbiology from 2005 to 2012 and BOS in Venereology from 2006 - 2009. She was the Course Coordinator and trainer for Diploma in Medical Microbiology from 2006 - 2012 and Chief Examiner or Examiner for PGIM examinations from 2001 to 2012 in Microbiology, Virology, Venereology and Pathology. She was a Visiting lecturer for Diplomas in Medical Administration, Reproductive Health, Pathology and Family Medicine, a supervisor and reviewer for MD Microbiology projects and contributed for 'Training of Trainer' workshops of PGIM.

She was a member of the Task force in Microbiology and is a Technical Assessor for Sri Lanka Accreditation Board since 2015. Dr. Somaratne is a member of the SLCM and held many portfolios since 1993 and was the President of the College in 2010/2011.

Since her retirement from state service, she continues to provide microbiology services at private hospitals, empowering them to achieve international standards of accreditation.

On a personal note, Dr. Somaratne was the supervisor for my MD dissertation and my mentor. I am fortunate to be bestowed with her kind and loving guidance throughout my career.

Madam President, it is my privilege and honour to present Dr. Pranitha Somaratne to offer her with the highest honour of the Sri Lanka College of Microbiologists as an Honorary Fellow.

Citation read by **Dr. Jananie Kottahachchi**
Senior Lecturer, Faculty of Medical Sciences,
University of Sri Jayawardenepura

Dr. Philomena Chandrasiri

MBBS, Diploma in Medical Microbiology, MD Medical Microbiology

Dr. Philomena Chandrasiri entered the faculty of Medicine, University of Colombo from Anula Vidyalaya, Nugegoda and graduated in1979. She completed her internship at the General Hospital, Ratnapura and obtained her post graduate qualifications, Diploma in Medical Microbiology in 1990 and MD in Medical Microbiology in 1996 from the Post Graduate Institute of Medicine, University of Colombo. After obtaining her MD she completed her overseas training at the St. Vincent's Hospital in Sydney, Australia from 1998 to 1999. Following her return, she was posted to the Medical Research Institute (MRI) as a consultant microbiologist. After the retirement of Dr. Sri Wickremesinghe, she served as the head of the department of bacteriology until she took up the post as consultant microbiologist, Colombo South Teaching Hospital in 2004.

During her tenure at MRI, she served as the offsite microbiologist for Lady Ridgeway Hospital and the Central Laboratory at Chest Hospital, Welisara. While serving at the MRI, with the assistance of World Health Organization she conducted many workshops in different parts of the country to upgrade the microbiology services provided by hospital laboratories. Through these training programs, she initiated the urine culture services in laboratories of five base hospitals.

In addition, she established Leptospira culture in artificial media, in order to prevent animal inoculation of clinical specimens done as a confirmatory test for leptospirosis. Along with other researchers she developed a PCR test to diagnose leptospirosis from clinical specimens and also demonstrated a relationship between Leptospirosis in humans and in Buffalos.

Furthermore, she established stool culture for campylobacter detection at Enteric Reference Laboratory, MRI. In 2005, she assumed duties at National Hospital of Sri Lanka where she served until her retirement in 2013. During this period, she offered her services as the Consultant Microbiologist to National Eye Hospital, De Soyza Hospital for Women and Castle Street Hospital for Women. Dr. Chandrasiri was a senior member of the Task force in Microbiology, National Healthcare Waste Management Committee and Drug Evaluation sub-Committee of Ministry of Health. She was a member of research and ethics committees at MRI and NHSL during the period she served in these institutions.

She made an immense contribution for medical education in the field of microbiology. Dr. Philomena Chandrasiri served as a member of the Board of Study in Microbiology from 2001 to 2013 and the Board of Study in Critical Care from 2010 to 2013.She contributed as a trainer and an examiner for both undergraduate and post graduate medical students as well as for medical laboratory technologists and as a research supervisor for postgraduate students. Moreover, she offered her services as chief

examiner for diploma and MD in medical microbiology and for diploma in medical laboratory technologists' examinations.

Contributions made in her capacity as an editorial board member for biosafety manual for health laboratories first published by MRI in year 2004, the first edition of the Hospital Infection Control Manual of Sri Lanka College of Microbiologists in year 2005, national guidelines on waste management for sexually transmitted diseases (STD) and chest clinics and national antibiotic guidelines are some of her involvements for publications for the improvement of medical microbiology in the country.

She also made her valuable contribution for the first and second editions of Microbiology Manual for Healthcare Laboratories and the National Guidelines of Healthcare Waste Management. She was the author of "antibiotic guideline" – a booklet for the clinicians" done during her tenure at National Hospital of Sri Lanka.

There are many research publications including the first isolation of *Helicobacter pylori* in Sri Lanka to her credit and she presented several research papers both at local and international conferences.

She is a trained as an assessor on ISO 15189 and served as a technical assessor and a member of expert committee in microbiology of Sri Lanka Accreditation Board for few years.

Her interests were not limited to microbiology and is a founder member of Allergy and Immunology Society of Sri Lanka and served as a member of critical care faculty of the College of Anesthesiologists.

Dr. Philomena Chandrasiri held the position of the president of Sri Lanka College of Microbiologists during the years 2011/2012. During her tenure as the president, she was able to conduct several workshops on infection control for nurses, medical officers and paramedical staff and she initiated and prepared the groundwork for the development of National Antibiotic guidelines published in 2016.

Her passion for infection prevention and control has led her to present position as the head of infection prevention and control of several leading private hospitals in the country. Infection control and preventive practices of these hospitals were brought to the standard required by Joint Commission International (JCI), and the Australian Council on Healthcare Standards (ACHS) by her untiring effort. She authored an infection control manual to be used by staff of these hospitals.

Dr. Philomena Chandrasiri is a loving mother of three children.

Madam President, I have the privilege and honour to present to you Dr. Philomena Chandrasiri, to confer her with the highest honour of the Sri Lanka College of Microbiologists and admit her as an honorary fellow.

Citation read by **Dr. Sujatha Pathirage**
Consultant Microbiologist,
Medical Research Institute, Colombo

Dr. Geethani Wickramasinghe

MBBS, Diploma in Medical Microbiology, Diploma in Family Medicine, MD Medical Microbiology

President and members of the Sri Lanka College of Microbiologists, Distinguished invitees,

The story of Dr Geethani Asokamali Wickramasinghe, starts with in the cool month of December in the year, 1952. She had her primary education at St. Thomas Girls High School, Matara and later at Sangamiththa Balika Maha Vidyalaya, Galle. She entered the Faculty of Medicine, Colombo in 1973 from Dharmapala Vidyalaya, Pannipitiya and obtained her MBBS in 1978.

She completed her internship at General Hospital, Ragama in 1979. Thereafter, she worked as medical officer at the Mental Hospital, Angoda and the ENT unit of the then General Hospital, SL. She obtained Diploma in Family Medicine in 1988.

She joined the Rabies Department at the Medical Research Institute (MRI) in 1991 and gained experience in laboratory diagnosis of rabies and the management of patients. She greatly acknowledges the training given to her by Dr. A. Sathasivam during this period. She completed the Diploma of Medical Microbiology in 1993, MD in Medical Microbiology (Virology) in 1997.

Her post graduate training was at the Victorian Infectious Disease Reference Laboratory in Australia and she also worked as a Grade 1 scientist in Royal Children's Hospital till July 2000. She returned to Sri Lanka as a Consultant Virologist and later, was appointed as the Head of the Department of Virology at the MRI until her retirement in December 2012.

After retirement, she joined the Post Graduate Institute of Medicine as a Senior Lecturer in 2014 and continued to work until 2018. During her time at MRI, she studied Respiratory Syncytial Virus infection in children below 2 years, with lower respiratory tract infection. Isolation of the virus by tissue culture technique and direct detection by fluorescent technique were compared and submitted as a dissertation for the MD Microbiology examination under the supervision of Dr. Nalini Withana.

The experience she has gained during her pre- and post-MD training influenced her to establish the first respiratory virus laboratory at the MRI. She carried out a vast number of surveillance studies for Influenza and other respiratory viruses during outbreaks of respiratory infections in Sri Lanka. She supported the Ministry of Health and the Epidemiology unit to establish respiratory viral surveillance in the country. She has trained medical staff from 20 sentinel sites in collection and transport of samples. She initiated egg isolation technique under the guidance of then Senior Medical Laboratory Technician, Mr. Upali Hettiarachchi, but later abandoned it, and continued with the tissue culture technique.

She was the first person to start molecular diagnosis with real time PCR technique, which was a turning point in influenza surveillance. She contributed to the influenza vaccine selection for the Southern hemisphere by identifying the circulating virus types through World Health Organization Reference Laboratories. Professor Sriyal Malik Peiris and the staff of the Hong Kong University gave her optimum support with advice, training and even consumables, at times of emergencies. The present-day crisis with the corona virus outbreak has shown us the value of the respiratory virus laboratory.

Similarly, she established antigen detection, culture and molecular techniques for the Measles and Rubella surveillance programs in Sri Lanka. She was the first person to identify the circulating genotypes and sequence analysis of measles and rubella viruses in Sri Lanka. She managed to obtain accreditation for the Measles and Rubella Laboratory at the MRI by an external Quality Assurance Team. The support given by Dr. Nalini Withana as a WHO Consultant was invaluable in this regard.

She was also able to establish the Cytomegalo virus (CMV) antigenaemia assay to detect CMV disease in immuno-compromised populations. As a supervisor, she encouraged a post graduate trainee in virology to conduct a study using quantification of CMV viral load by PCR and establish the test at MRI.

Dr. Wickremasinghe has presented most of her work at the Annual Academic Sessions of Sri Lanka College of Microbiologists. She was the orator of the Siri Wickremesinghe Memorial Oration in 2013 and she has been rewarded with the Presidential Award for Research in 2014.

She has attended many local and international workshops and meetings in the fields of Influenza, Measles and Rubella and BSL 3 laboratory. She has also acted as the chairperson of various local and international conferences. She has been involved in teaching undergraduates, post graduate medical officers as well as other categories of staff of the Ministry of Health. She has also been an examiner for the Diploma and MD Microbiology and Virology examinations.

Dr. Wickremesinghe has been actively involved in activities of the Sri Lanka College of Microbiologists. She has acted as the secretary in the year 2002, a council member on several occasions, convener, and a member of the advisory group in MD Microbiology (Virology).

After joining the PGIM, she acted as a member of the Board of Study in Microbiology, Dental Surgery, Otorhinolaryngology, Ophthalmology.

Today, in retirement, she is enjoying a peaceful, fully satisfied life, practicing Buddhist teachings, reading medical journals and engaging in social and philanthropic activities.

On a personal note, I have observed her courage and perseverance in establishing the respiratory virus laboratory and surveillance system in Sri Lanka. She never let her personal issues affect her work. To borrow the words of another colleague of ours, she is a person who works at 110% of her capacity.

Ladies and gentlemen,
It is my honour and privilege to present Dr. Geethani Asokamali Wickramasinghe for the Fellowship of the Sri Lanka College of Microbiologists.

Citation read by Dr. Geethani Galagoda
Consultant Virologist,
Lanka Hospital PLC, Colombo

FELLOWSHIPS OF THE SRI LANKA COLLEGE OF MICROBIOLOGISTS 2021

Dr. Sunethra Gunasena
Medical Virologist, Senior Lecturer,
Department of Microbiology,
Faculty of Medicine, University of Ruhuna

Dr. Kumudu Karunaratne
Consultant Microbiologist

Prof. Sirimali Fernando
Senior Professor and Chair of Microbiology,
Faculty of Medical Sciences,
University of Sri Jayawardenepura

PRIZE WINNERS AT THE 29TH ANNUAL SCIENTIFIC SESSIONS OF THE SRI LANKA COLLEGE OF MICROBIOLOGISTS

Following oral presentations were awarded first, second and third places at the 29th Annual Scientific Sessions of the Sri Lanka College of Microbiologists held on 13th and 14th August 2020

Oral presentations

1st prize

OP 7

The diagnostic accuracy of a modified nested PCR-RFLP method in the diagnosis of cutaneous leishmaniasis caused by *Leishmania donovani*

De Silva NL[1], *De Silva VNH*[2], *Deerasinghe ATH*[3], *Kato H*[4], *Itoh M*[5], *Takagi H*[5], *Weerasooriya MV*[1], *YahathugodaTC*[1]

[1]Department of Parasitology, Faculty of Medicine, University of Ruhuna, [2]Base Hospital, Tangalle, [3]District General Hospital, Hambantota, [4]Division of Medical Zoology, Department of Infection and Immunity, Jichi Medical University, Japan, [5]Department of Microbiology and Immunology, Aichi Medial University School of Medicine, Japan.

2nd prize

OP 8

Establishment of an in-house SARS CoV-2 real-time PCR and investigation of first few suspected cases of COVID-19 in Sri Lanka

Jayamaha CJS[1], *Witahnage VH*[1], *Jayathunga RCS*[1], *Ekanayake DHP*[1], *Wepathairage LH*[1], *Neelambari S*[1], *Chu DKW*[2], *Peiris M*[2]

[1]National Influenza Centre, Department of Virology, Medical Research Institute, Colombo, [2]School of Public Health, LKS Faculty of Medicine, The University of Hong Kong

3rd prize

OP 6

Preliminary study to detect mutations in UL97 gene in suspected ganciclovir resistant CMV patients' samples, presented to a diagnostic laboratory in Sri Lanka

Thambyrajah JC[1], *Jayamaha CJS*[2], *Ratnayake AKDVY*[1], *Handunetti S*[1], *Fernando N*[1].

[1]Institute of Biochemistry, Molecular Biology and Biotechnology, University of Colombo, [2]Department of Virology, Medical Research Institute, Colombo

Following poster presentations were awarded first, second and third places at the 29th Annual Scientific Sessions of the Sri Lanka College of Microbiologists held on 11th August 2020

Poster presentations

1st prize

PP 5

Effect of bundle care on central line associated blood stream infection at medical intensive care unit at the National Hospital of Sri Lanka

Sugathadasa MRDN [1] *, Kottahachchi J* [2] *, Patabendige CGUA*[1]

[1]National Hospital of Sri Lanka, Colombo, [2]Department of Microbiology, Faculty of Medical Sciences, University of Sri Jayawardenepura

2nd prize

PP 12

In vitro antibacterial and antibiofilm activity of *Tribulus terrestris* L. against planktonic and biofilm models of common uropathogens

Gunasekara SP[1]*, Bandara DS*[1]*, Nishadhya S*[1]*, Aluthwaththa MG*[1]*, Pathirana R*[2]*, Widanagamge R*[2]

[1]Department of Microbiology, Apeksha Hospital, Maharagama, [2]Department of Medical Laboratory Sciences, General Sir John Kotelawala Defence University

3rd prize

PP 8

Filarial parasites among two dog communities in selected filariasis endemic and non-endemic areas in Sri Lanka

Rathnayake SP[1]*, Mallawarachchi CH*[2]*, De Silva LAPNF*[3]*, Gunathilaka PADHN*[4]*, Chandrasena TGAN*[4]

[1]Department of Animal Production and Health, Northern Province, [2]Medical Research Institute, Colombo, [3]Department of Community Medicine, Faculty of Medicine and Allied Sciences, University of Rajarata, [4]Department of Parasitology, Faculty of Medicine, University of Kelaniya

Dr. C. Palasuntheram Prize

OP 7

The diagnostic accuracy of a modified nested PCR-RFLP method in the diagnosis of cutaneous leishmaniasis caused by *Leishmania donovani*

De Silva NL[1]*, De Silva VNH*[2]*, Deerasinghe ATH*[1]*, Kato H*[4]*, Itoh M*[5]*, Takagi H*[5]*, Weerasooriya MV*[1]*, YahathugodaTC*[1]

[1]Department of Parasitology, Faculty of Medicine, University of Ruhuna, [2]Base Hospital, Tangalle, [3]District General Hospital Hambantota, [4]Division of Medical Zoology, Department of Infection and Immunity, Jichi Medical University, Japan, [5]Department of Microbiology and Immunology, Aichi Medial University School of Medicine, Japan.

Presidential address delivered at the Induction of President and Dr. Siri Wickremesinghe Memorial Oration 2021 of the Sri Lanka College of Microbiologists on 27th February 2021

Professor Nadira D. Karunaweera

Medical Parasitologist, Chair Professor, Department of Parasitology, Faculty of Medicine, University of Colombo

Distinguished invitees, past presidents, board of directors, fellow council members, members of the Sri Lanka College of Microbiologists including those who have joined us online, colleagues, friends, ladies, and gentlemen.

First let me declare the theme for the scientific activities of the College this year: 'Threat of new and re-emerging infections: Role of novel tools and technologies to face challenges. To be in line with this theme, I wish to talk on the topic: 'Man, vs Parasite: Weapons to Combat'.

There are zillions of organisms that continue to affect human health since time immemorial. Majority are harmless, however, there are disease-causing or pathogenic organisms, which could be broadly categorized as viruses, bacteria, and parasites. Infectious diseases cause a very heavy toll on human health with over 14 million deaths caused each year as per figures available, which are likely to be the numbers before COVID came in. I am sure it must have drastically increased by now. Human-pathogen relationship is often recognized as a co-evolutionary arm-race. Each trying to outsmart the other.

In this backdrop, I would like to take two parasitic diseases as examples and explain to you a few studies that we have done in the field of malaria (as part 1 of my presentation) and secondly, in the field of leishmaniasis (part 2) to elaborate on related work. The studies selected here were aimed at developing and testing novel tools for efficient disease management and control. In other words, our attempts at expanding the arsenal that we could fight with.

To start off with malaria: it is a mosquito borne disease and Sri Lanka has been quite successful in shrinking the malaria map. In fact, by end of 2012 Sri Lanka was able to get rid of all locally acquired cases of malaria; and in view of this success the World Health Organization awarded the certificate of malaria elimination to the country in 2016 and it was a huge achievement especially when one considers, where we were in mid 1930s, way before most of us were born. There had been millions of cases of malaria with nearly 80,000 deaths at that time (we can't even imagine that scale from where we are now). One might wonder why we need malaria studies, if

we have achieved elimination. If you look at this figure (Figure 1) which gives the number of malaria cases, the dark blue bars indicate the locally acquired ones and there were no cases after 2012 after achieving elimination. However, the orange-coloured ones, which indicate imported malaria or travelers' disease continue. These patients who are carrying malaria come from various countries, but the majority are from the region that include India and Pakistan If we look at the numbers that are brought in, around 50 cases are encountered each year. What are the risks involved in malaria being brought in by travelers? The risks are due to the persistence of the vector mosquitoes in the country. Although we got rid of the locally acquired cases, the mosquitos persist in addition to the susceptible hosts; that include you and I, and a suitable environment for malaria transmission particularly in the dry zone of the country. Therefore, introduction of malaria cases through travelers causes significant risk of re-emergence and resurgence of this disease. The services of the anti-malaria campaign of the Ministry of Health have continued in the post elimination period quite commendably, and their focus has been on active surveillance to detect and treat cases, to look at vector surveillance, vector control etc. We also have continued our studies, both during the pre and post elimination era with a focus on developing and testing new tools to facilitate disease management and control.

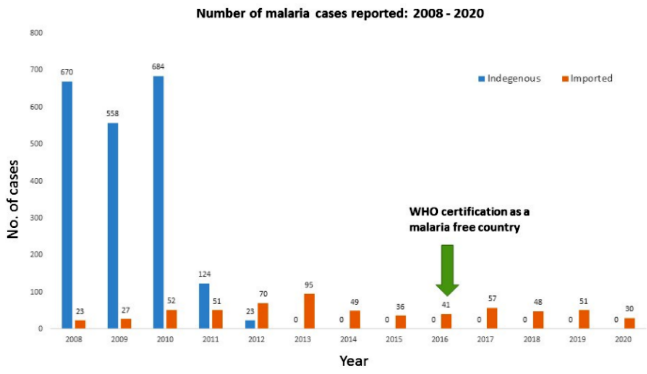

Figure 1.

Source: Anti Malaria Campaign, Ministry of Health

I have selected a couple of studies that we did on genotyping of parasites to track them to their geographic origin. Genotyping is considered as a tool that one could use to strengthen surveillance in the post elimination era in Sri Lanka. Out of the two common species i.e. *Plasmodium* vivax and *Plasmodium falciparum* that cause malaria in the world, we focused on *P. vivax* because it is the most prevalent species in the Asian region. We examined the genome of *P. vivax* parasite and selected genotyping markers in the form of microsatellites, which are nucleotide repeat regions in the genome that could be used for genotyping. Molecular experimental conditions were optimized (PCR conditions) to amplify these loci. These markers have been described in detail giving the location on the genome, the nucleotide repeat regions of each one of them and primers used [1]. What we did was we labeled these products/primers with four fluorescent dyes. Length variation of labeled PCR products could be visualized using capillary gel-electrophoresis using the machine called the ABI sequencer. The output of this machine enabled read-off the size or length variation of the PCR products using a scale. So, it was possible to look at length variations of alleles or the haploids in different isolates we tested. We tested isolates from Sri Lanka (n=140), from Ethiopia (n=118) and from Myanmar (n=167), counties where *P. vivax* is endemic. We got a whole heap of results, which was very informative given the number of alleles, diversity figures and so on which I am not going to dwell into. But I will try to explain the population structure studies that came out of it. We did the analysis using the STRUCTURE software to look at the clustering of these haplotypes/ alleles according to geographic origin. Figure 2 summarizes the results which indicated basically how these parasites that come from different geographic regions vary from each other. There was a clustering of these parasites according to geography, which was very interesting to see [2, 3]. This work was done by Prof. Shamini Gunawardhena as a part of her post MD training.

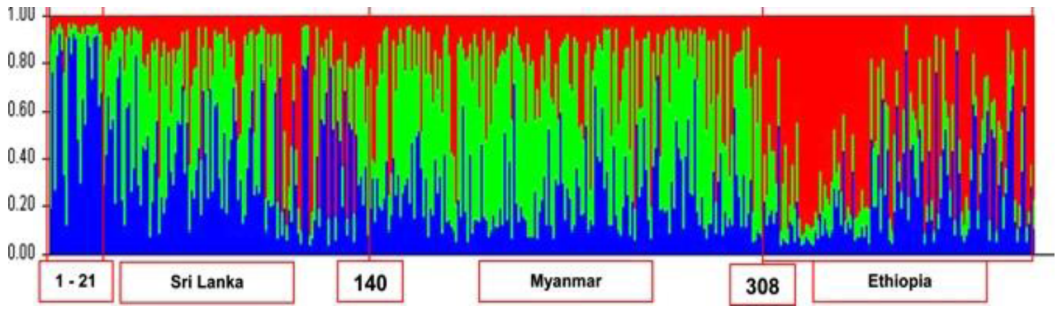

Figure 2. Population structure of *P. vivax.*

Gunawardena GSA, Karunaweera ND, Ferreira MU et al., (2010). Am J Trop Med Hyg. 82(2): 235–242.

As I mentioned there were lots of information on polymorphism, diversity, clonality and so on. I would like to focus on the last point which simply indicated that microsatellite typing is indeed a useful tool in predicting the geographic origin of an isolate and also map outbreaks of malaria, which remains as a challenge even in countries that have wiped out the disease.

We did not want to stop there because the microsatellite typing is a laborious technique and not really easy to repeat as a routine measure. We were on the lookout for more efficient tools. We found one in the form of single nucleotide polymorphisms (SNPs) that could be used to identify the genetic variation within species using a very short genetic sequence from a standard part of the genome that contains the SNP. We used this method called SNP barcoding which contains a combination of selected SNPs that together express a unique pattern of variation.

The concept is basically similar to that is used to identify products in the supermarket. Basically, you may have seen how the cashier at the supermarket counter scans the barcode printed on the product packaging to get the details of the product out from the computer, including the price. The concept used in this SNP barcoding is similar, but it's to identify different alleles. It was possible to compare the genetic diversity between the populations using a software called Principal component analysis (PCA) that enables us to identify the alleles which varies together across samples. When we got the barcoding done on all the isolates that we tested and arranged according to the similarity of genetic composition, we got a complicated picture. In order to simplify we used principal component analysis again that generated figures as in Figure 3 [4] .

These experiments enabled us to demonstrate that these alleles can be separated out based on geography. Simply it was possible to conclude that SNP barcoding can be used to distinguish locally-acquired or indigenous from the imported parasites and therefore, this will be useful to track imported malaria. This part of work was done primarily by Dr. Rajika Dewasurendra as part of her PhD.

I gave you only a snapshot of these studies because of the time concerns, but if anyone interested in details, one could find in these publications [1-4].

To move on to the next part of my presentation, which will be on leishmaniasis; it remains as a relatively new health challenge in Sri Lanka. We were interested in looking at new tools to test, and validate them to facilitate better patient management and infection control. We were interested to look at this causative agent, which is the *Leishmania* parasite in order to understand the disease, epidemiology, disease burden and pattern of spread: to help plan future control measures and also to find ways to enable better patient care or management.

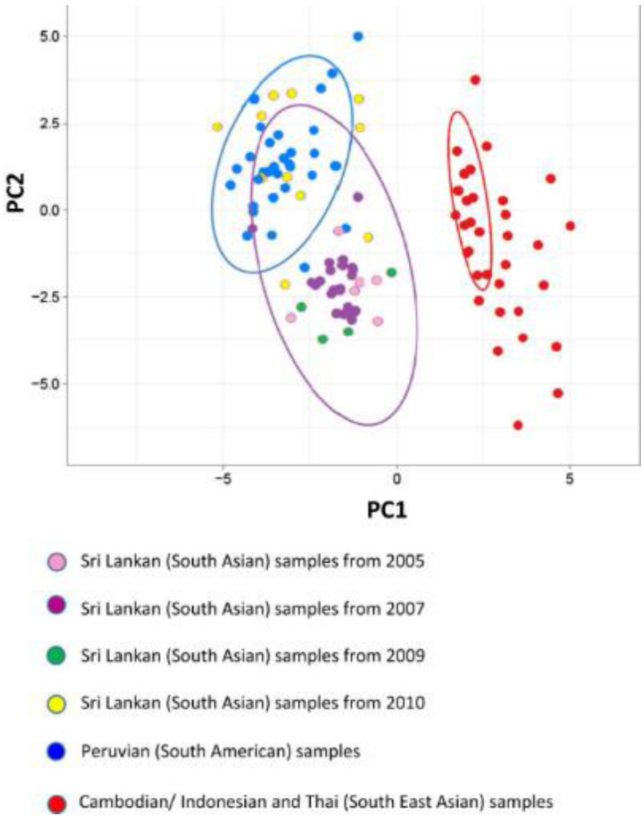

Figure 3. Principle component analysis of *P. vivax* isolates.

Leishmaniasis is not a single disease entity. It is a range of diseases with varying clinical forms. It ranges from mild forms, which is confined to the skin to most severe fatal form that affects organs, which is called visceral leishmaniasis. This is caused by the *Leishmania* parasite and transmitted through a tiny insect called the sand-fly. It is a disease that is found in many tropics and the sub tropics. In Sri Lanka the first case of skin form of leishmaniasis or cutaneous leishmaniasis was recorded in early 1990s, however things were fairly quiet until an outbreak was reported in 2001 from Welioya that is in the North Central province. The subsequent studies revealed that the causative agent is *Leishmania donovani* which is the same species that is found in the regional counties, which causes a very different and dangerous form of disease [5]. The vector is the sandfly *Ph. argentipes* it's a tiny insect about 1/3 of the size of a mosquito. If you look carefully, I'm sure you will identify this insect in your backyard, because they are fairly frequent in areas with vegetation and they are found almost all over the country now.

Parasite is a protozoan parasite (a single celled organism) that is found inside hosts mononuclear cells. Quite thankfully the predominant clinical form that we see in Sri Lanka remains as the skin form or cutaneous leishmaniasis. And these skin lesions are characteristically non-itchy and non-painful sores found on exposed areas of the skin accessible to sand-fly bites. You get the lesions at the site of the sandflies bite. There are different types of lesions we see: tiny papules, nodules, ulcers or plaques [6].

How are they treated? The most frequent drug used is sodium-stibogluconate, which is given as intra-lesional injections, in other words it's injected into skin tissue surrounding the lesions and it is a fairly painful procedure. You need weekly injections to be given for several weeks up to about three months in most cases to achieve cure. To make matters worse there are more and more cases reported that fail to respond to the regular treatment with recent reports giving drug failure rates of over 70%, which is alarming. It is not a very encouraging picture there. Cryotherapy was used before Sodium Stibogluconate (SSG) but again it wasn't a very popular form of treatment. Cryotherapy is simply the use of liquid nitrogen that is sprayed onto the lesion. You have to repeat it at weekly intervals for several weeks. There are other drugs like amphotericin B that maybe used, but again those are toxic and not that popular.

In addition to the skin forms, we also have seen other forms of disease in Sri Lanka that effect mucosal tissue involvement in the mouth or nose. It can cause massive tissue destruction in immunocompromised patients such as those with tuberculosis and other complications related to immune deficiency. Leishmaniasis may cause total destruction of nasal septum and also the upper palate in such patients, which may be fatal.

There have been few cases of visceral leishmaniasis reported in Sri Lanka. As mentioned earlier it is a serious disease which affect the organs like the spleen, liver and bone marrow. Unless you detect these patients very early during the infection and treat them effectively, they succumb to this disease.

The causative organism is *L. donovani* and it is better known to cause visceral disease in other countries including India. In fact, ours was the first isolation of this particular strain of skin form of disease [1]. We were interested in dissecting it out using molecular methods. We did molecular typing using micro-satellite markers. The phylogenetic tree based on genotyping data showed genetic relationship between parasites from different regions (Figure 4) [7]. The Sri Lankan parasites are quite close in genetic structure to those in the neighboring countries like India, Nepal and Bangladesh. However, they separated out in the phylogenetic analysis since they have a distinct genetic structure. This might at least partly explain why we are seeing different clinical forms or phenotypes. This work was done by Dr. Yamuna Siriwardhane as a part of her PhD back then. This work was continued thereafter, to look at the sequence diversity or sequence differences in different clinical forms that we see in Sri Lanka.

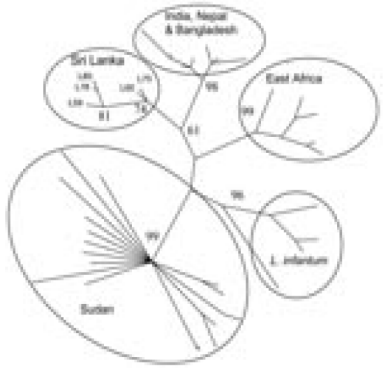

Figure 4. Phylogenetic tree of isolates.

Parasite isolates that were derived from the cutaneous leishmaniasis patients, those from visceral leishmaniasis and those from cutaneous leishmaniasis that did not respond to the regular drug SSG were then used in the whole genome analysis. The phylogenetic tree demonstrated that the different phenotypes could be separated out (Figure 5) [8]. Therefore, the genetic structure appeared to be different in each of these phenotypes. This work was done by Dr. Udeshika Kariyawasam who completed her PhD in our laboratory recently and now is a post-doc at Johns Hopkins University, USA.

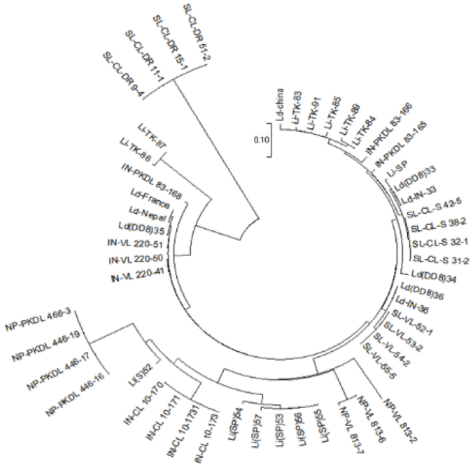

Figure 5. Association of phenotypes (disease types observed) with the genotypes (genetic structure) in leishmaniasis.

We proceeded to carry out whole genome sequencing of selected isolates from Sri Lanka. This is a heat map that shows the grouping of these isolates that were sequenced and the analysis is based on their SNP profiles (Figure 6) [9]. The sequencing was done in the genetics lab in our faculty, which is headed by the current dean, Prof. Vajira Dissanayake. This figure shows the SNP profile analysis and the associated dendrogram, shows three different clades or three different groupings. These were due to different clinical forms: the cutaneous, visceral and the suspected drug resistant isolates from poor responding patients. This work was done by Ms. Sumudu Samarasinghe, a young scientist and Dr. Nilakshi Samaranayake who is a senior lecturer in our department.

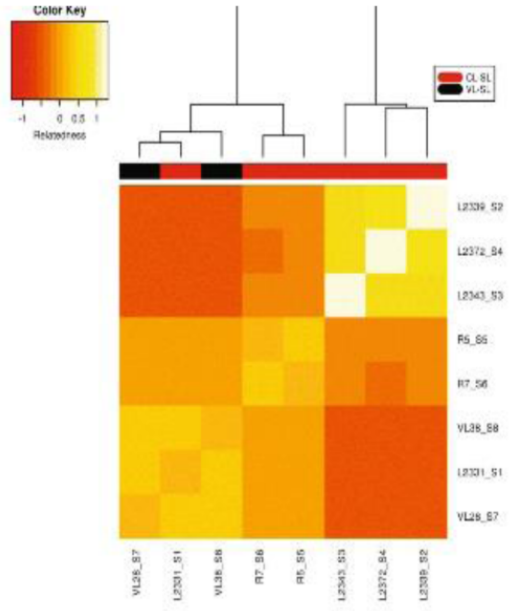

Figure 6. Heat map based on profile of single nucleotide polymorphisms (SNPs) of fully-sequenced *L.donovani* isolates with varying clinical phenotypes.

In this back drop, you will be interested to hear that there is an ongoing programme of leishmaniasis elimination. It's called the 'Elimination of leishmaniasis from the Indian subcontinent' and it's a program facilitated by the World Health Organization, which was started in 2005 with governments of India, Nepal and Bangladesh signing up for this program as partners. There were couple of other countries that joined in for this program later on, however Sri Lanka is not a part of it yet. This figure (Figure 7) gives the number of cases in each of these countries that's in the elimination program [10]. There is a downward trend indicating a reduction in the number of cases since 2005 when they joined the elimination program, although they still haven't reached the elimination targets. The countries remained hopeful that they will do so within the next few years.

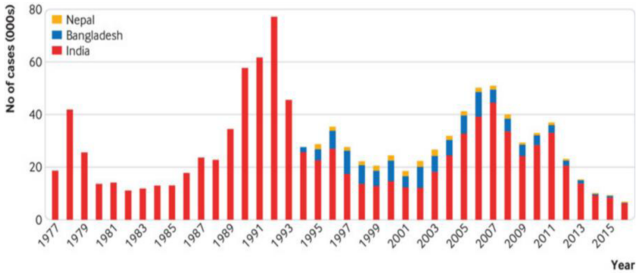

Figure 7. Number of leishmaniasis cases in India, Nepal and Bangladesh.

In contrast to this picture, what we are seeing in Sri Lanka is rather disappointing, particularly during last three years (Figure 8). We used spatial mapping tools to look at the disease burden trends from 2001 (beginning of this outbreak) onwards (Figure 9) [11]. Even at a glance you can see how it has across the country starting from the north central province. If you look at the color coding you can see, how the colors have become darker pink appearing then the red and then maroon and so on indicating increasing disease burden over the years. There is a spatial spread eventually affecting all the districts in the country and increasing burden in affected areas.

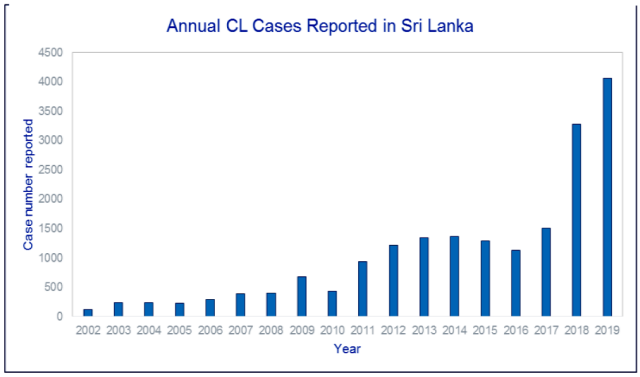

Figure 8. Leishmania case numbers.
Source: Epidemiology Unit, Ministry of Health

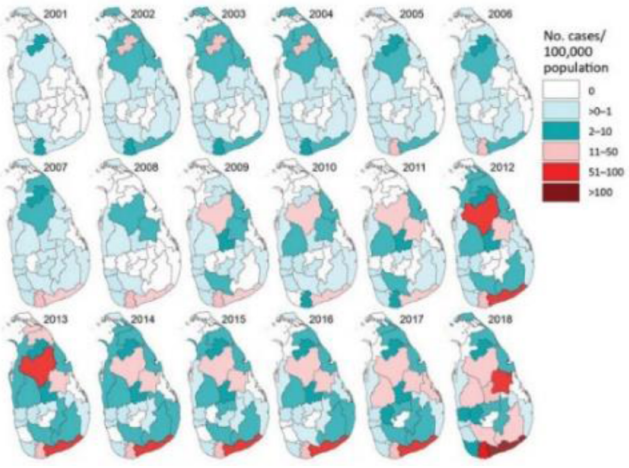

Figure 9. Disease burden and spatial spread of CL 2001-2018.

When we put all this data together, you can see that all the districts have had cases, however, the most number of cases were from three districts Anuradhapura, in the North Central area and Matara and Hambantota from the South. In fact, five district accounts for over 85% of cases that are reported from the country with the trend seen in 3 districts closely mimicking the trend that is seen in the entire country [11]. We used the hotspot analysis to look at this hotspot areas or high burden areas in the North Central and Southern parts (Figure 10) from 2015 onwards. As you can see, in the North Central area the hotspot has shifted and it also has shrunk. But in the South, it has expanded and the disease burden has become even more as years passed by [11].

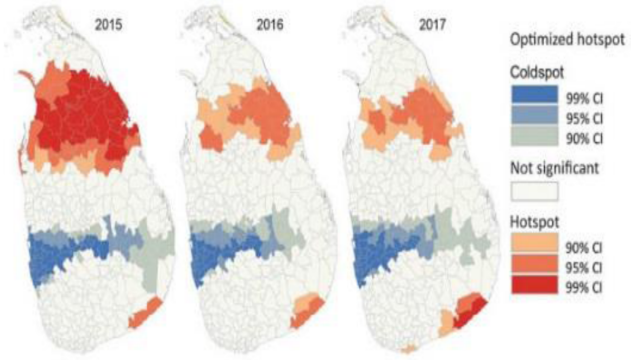

Figure 10. Shift in spatial distribution and hotspots of disease.

In addition to looking at the parasites and the epidemiology, we also looked at new tools for patient management in the form of thermo therapy. We did a controlled clinical trial using a machine called the thermo-therapy machine (it is also called radio frequency heat therapy). This emits radio frequency waves which comes through a wire and through an electrode it is introduced on to the skin surrounding the lesion. These radio frequency waves cause rapid molecular movements in the skin tissue which generates heat. It's believed to induce a good immune response that promotes lesion healing. That is the principle behind using it. In the clinical trials we used two arms. In the control arm we used the regular drug intra-lesional SSG weekly injections up to a period of three months, and in the test arm we used radio frequency heat therapy which was applied only once at the beginning of the trial and these patients in both the study arms were followed up weekly up to a period of three months and thereafter less frequently up to one year. Just to summarize the finding, the comparison is between the single applications of thermotherapy vs weekly injections of intra lesional SSG. The lesions in patients included in the thermo-therapy arm healed rather fast. However, as the time passed by, the healing rates became similar. By the end of 3 months, it was comparable.

The key conclusion of the trial was thermotherapy is an effective treatment method for cutaneous leishmaniasis in Sri Lanka. The single application was found to be safe and effective and the per patient cost of treatment is 7 to 8 times cheaper than the routine therapy. It's patient friendly as well because they need to come to the hospital only once, to get the treatment as opposed to the multiple visits the patients need to make for the weekly doses of intra-lesional injections. We replicated this trial later on poor responding patients to SSG because it is a huge problem in the field. The second trial also demonstrated similar efficacy and safety in patients who haven't responded to SSG earlier. The first trial was done by Dr. Wardha Refai who is a Parasitologist at the MRI and she conducted this as part of her MD training and the second trial was done by Dr. Hermali Silva who is a lecturer in our department.

In leishmaniasis there is a notable increase in the case burden and spread since 2001 with a prominent increase in 2018. There is a steady expansion in risk areas with persistent 02 hotspots in the North Central and Southern parts of the country. Thermo-therapy is a cost-effective and patient friendly alternative that we could use to overcome challenges in patient management, including those who fail to respond to SSG. There is evidence of sub-species diversity of this parasite and we are pursuing this work to look further as to how that diversity translates into pathogenesis and its implications on patient management and treatment outcome.

Finally, to get back to the title that I started off with: 'Man vs parasites: weapons to combat':

In the case of malaria: parasite genotyping markers, particularly SNP barcoding were identified as useful tools for genomic surveillance and to track parasites to their geographic origin, which may supplement the current and patient surveillance based on patients' travel history.

In the case of leishmaniasis: genetic tools are available for parasite typing at sub species level with significance in understanding of disease pathogenesis. Spatial and epidemiological tools are ready to track and monitor hotspots of disease, which can assist in planning and directing future control programs that can be put in place. Novel treatment options are available as safe and cost-effective treatment methods for these patients.

Finally, the recommendations that could be made:

In the case of malaria: In the post-elimination period as we are in now: one could introduce more effective methods for parasite surveillance to aid management of travelers' malaria which remains as a challenge to the country.

To contain the spread of leishmaniasis: It is required to enhance the surveillance, public awareness and intervention that are urgently needed in targeted areas to halt these outbreaks. The existing treatment protocols in CL are required to be reviewed and replaced with new treatment options that are effective and more cost effective.

Before I end, I would like to thank all those people who were responsible for my existence. To start off with my parents: my late father, my mother who is in the audience. My husband Cecil, two daughters Ayesha and Sajani, my brother Nalin and sisters Purnima and Sadhana: I am so thankful for their love, understanding and I am particularly grateful to Cecil and the 2 girls for their enormous patience and putting up with my crazy schedules.

Whatever the distance that I have travelled in my career, I owe to this lady: Prof. Kamini Mendis, who took me under her wings from day one that I joined the department. She has guided me throughout my career path and even now I reach out to her when I meet with challenges. I'm truly grateful to her for her role in my life. There are other people who have helped me in my career: my co-supervisor Prof. Richard Carter, Dyann Wirth, Dominic Kwiatkowski, Geoges Grau and so many others from different parts of the world. I am really thankful for the trust and confidence that they placed in me and giving me opportunities that made me the person that I am today. I never could have done all these work on my own. The team, colleagues from our department as well as outside and the project staff both from past and present. I remain very grateful to each and every one of them for being part of my life and for their contributions to our studies including the foreign collaborators from various parts of the world, who are too many to name.

I am truly grateful to the College Council members for the support they continue to offer in each and every activity that we have undertaken, which I hope will continue for the rest of the year as well. I should especially mention the role of the co-secretaries of the council Dr. Nilakshi and Dr. Madumani who work tirelessly, they've been particularly busy during the past several weeks leading up to this event. I would like to extend my sincere thanks to them. Then my office secretary Priyanga who is the rock that we all lean on. She has very bravely shouldered all the responsibilities because the junior person left a few weeks back. Thank you Priyanga for everything. Last but not least I would like to thank everyone here, for scarifying your long weekend to be with us today.

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Fighting the rising tide of antibiotic resistance; exploring non-pharmacological options, challenges, and benefits

Professor Nelun Perera
Consultant Microbiologist and Hon. Associate Professor
University Hospitals of Leicester and University of Leicester, UK

The President of the Sri Lanka College of Microbiologists, Mrs. Ranganie Wickremesinghe, family members and friends of the late Dr. Wickremesinghe, members of the Council, members of the Sri Lanka College of Microbiologists and distinguished invitees.

I am honoured to be invited to deliver the 2021 Siri Wickremesinghe Oration in memory of one of my dear teachers' Dr Rakkitha Sirimal Bandara Wickremesinghe.

Rakkitha Sirimal Bandara Wickremesinghe was born on 28th November 1937 to Dr Artie and Helen Wickremesinghe. He had his education at Royal College Colombo and obtained his MBBS in 1963 from the Faculty of Medicine, Colombo. He started his medical career in the field of dermatology which we understand was his first love and worked in the Dermatology Unit at Kandy. Thereafter he joined the Medical Research Institute (MRI) where he fell in love with microbiology. To further his postgraduate education, he obtained the Diploma and Master of Science in Microbiology from the University of Manchester, and MD with Board Certification in Microbiology from the Postgraduate Institute of Medicine, University of Colombo. He also worked in laboratories overseas that included Addenbrooks at Cambridge, a CDC-linked laboratory in Michigan and Fairfield Hospital in Melbourne.

Throughout his career he dedicated major part of his life, to the life and soul of the MRI where he always belonged and where he served as Director of MRI from 1996 to 1998.

Dr. Wickremesinghe was actively involved in the Sri Lanka College of Microbiologists and was a member of the Council even at the time of his death. As an eminent

Microbiologist, he was very much interested and concerned in the ever-increasing problem of antimicrobial resistance and together with the WHO was in the forefront of many workshops and seminars conducted to explore measures to alleviate this global problem.

Dr. Wickremesinghe a renowned and scholarly microbiologist has taught a good number of practicing Microbiologists in Sri Lanka. He taught me between 1994 and 1999 when I enrolled for the Diploma and thereafter the MD Microbiology.

He was a great teacher and a great mentor. His teaching though very didactic, which may not be endorsed by modern day educationists, gave his students a good foundation of basic microbiology, and all of us who have listened to his lectures know how much of an effort he took to impart knowledge, some of which were hard to find in textbooks.

I still remember him encouraging his students to have two pocketbooks, one he called the book of "gems" and the other the "don't know" book. The best CPD I could think of. I still maintain both books and I constantly remind all my students to maintain these books. In addition to the theoretical knowledge, he was very thorough with his practical skills, a skill that is fading away from modern day microbiologists due to all the wonderful machines that have taken over traditional diagnostic microbiology. The pace at which manual diagnostic microbiology is disappearing one wonders what will happen to diagnostic microbiology if the world is struck by a computer bug, it will be only those who can start thinking from basics and do things from basics as taught by Dr Wickremesinghe can come to the rescue.

Dr Wickremesinghe was a sportsman and was a long-standing member of the Health Department Sports Club. He was also an avid nature lover his most outstanding passion was turtle conservation to which he gave his utmost by establishing the Kosgoda turtle hatchery.

I will now move to the topic of my Oration: Fighting the rising tide of antibiotic resistance; exploring non-pharmacological options, challenges, and benefits.

I will first introduce the evolution and spread of anti-microbial resistance and the measures available to combat antimicrobial resistance. The main body of the oration will explore the role of antimicrobial stewardship in turning the tide of antimicrobial resistance, with discussion of the challenges and benefits. This will include a description of a study undertaken by myself and colleagues which examined the moral and contextual dimensions of "inappropriate" prescribing in Secondary Care in three countries including Sri Lanka, and my personal experience in developing an antifungal stewardship programme in a Teaching Hospital.

Finally, where, and how Microbiologists fit in the bigger picture will be briefly discussed.

Introduction

1. Background

The serendipitous discovery of penicillin in 1928 by Alexander Fleming marked a new era of modern medicine [1]. Before the discovery of antibiotics, there were soaring deaths due to postpartum sepsis, pneumonia, skin, and soft tissue infection. Discovery of the first antibiotic penicillin by Alexander Fleming in 1928, synthesis of the first sulfonamide, prontosil by Gerhard Domagk in 1935 and synthesis of many other antibiotics thereafter brought down infection rates significantly across the globe. A US study in 1999 calculated that the introduction of antibiotics in 1936 caused a fall in deaths by 220 per 100,000 within 15 years. All other medical technologies combined over the next 45 years reduced deaths by only 20 per 100,000 people [2].

Today, we have a myriad of antibiotic classes that are effective against a wide range of bacteria. Despite their benefits, we must acknowledge that antibiotics are not infallible and can do more harm than good if misused. The over-reliance on antibiotics comes with a cost, a cost we were warned about by Alexander Fleming in his 1945 Nobel Prize acceptance speech [3]. He expressed his concern about improper use of penicillin and how easily resistance is acquired with insufficient treatment dosages. It is clear we did not heed this warning and now we are battling with the consequences.

In the past few decades, the world has seen an unprecedented emergence and spread of antimicrobial resistance (AMR) resulting in a global threat to public health. There is ample reason to fear for the future of treatment of many infections due to the dwindling reserves of antimicrobial agents. Such infections include community-acquired urinary tract infections, gonorrhoea, typhoid and tuberculosis and infections in hospital patients caused by Gram-negative and Gram-positive pathogens such as *Escherichia coli*, *Klebsiella* spp, *Acinetobacter* spp, *Pseudomonas* spp and vancomycin resistant enterococci. As recently as 2014, the World Health Organization (WHO) highlighted that AMR is a "serious threat happening right now in every region of the world and has the potential to affect anyone, of any age, in any country" [4]. Attributable mortality due to AMR is

also significant. It is estimated that by 2050, 10 million lives a year could be lost due to AMR, exceeding the 8-2 million lives a year currently lost to cancer and the cumulative economic loss to world economies could be as high as US$100 trillion [5]. Studies comparing attributable mortality due to carbapenem-resistant *K. pneumoniae* with sensitive *Klebsiella* have shown a significantly higher mortality, and the same has been shown with methicillin-resistant *S. aureus* bacteremia, relative to methicillin-sensitive *S. aureus* bacteremia [6].

2. Emergence of antimicrobial drug resistance

AMR is an expression of the ability of microorganisms to counteract antimicrobial agents commonly used to treat infections. It is due to microorganisms developing mechanisms that render them resistant to these agents. However, it is important to note, antimicrobial use does not cause the initial emergence of resistance. If an antibiotic causes resistance it would be a mutagen and would be denied a license. Resistance originates by random processes – mutations and the acquisition of resistance genes mobilized from the chromosomes of other bacteria.

Microorganisms display two major resistance mechanisms. Microorganisms that are intrinsically resistant to antimicrobial agents are referred to as having innate or intrinsic resistance. This is related to the general physiology or anatomy of the microorganism that confers resistance. Intrinsic resistance is an inherent trait and is not affected by use (or misuse) of antimicrobial agents. Acquired antimicrobial resistance commonly originates due to random mutations. Although mutations are relatively rare and occur at about 1 per 107 to 1010 cells, due to the high replication rate of microorganisms there is a high probability of having a large increase in numbers of resistant microorganisms [7]. If these mutations are genetically 'unfit' and do not confer survival benefit to the microorganism they will disappear from the microbial population. On the other hand, if the mutation confers survival benefit to the microorganism it can find its way to other clinically significant microorganisms through acquisition of mobile genes – a phenomenon called 'gene escape'. For example: mecA gene originated in *Staphylococcus fleurettii* and later spread to *Staphylococcus aureus* to confer resistance to methicillin, blaCTX-M originated in *Kluyvera* spp. and later reached *Enterobacteriaceae* to confer resistance to B-lactam antibiotics including oxyimino cephalosporins [8]. Microorganism can also acquire multiple mutations that confer resistance to many classes of antimicrobial agents. This is called 'multi-drug resistance' (MDR). For instance, the MDR *Salmonella Typhimurium* phage type DT104, which is disseminated worldwide, carries the genomic Island 1 (SGI1) that encodes resistance to multiple antibiotic classes. Because of its virulence and resistance gene repertoires, isolates with a SGI1 variant have been implicated in rapid dissemination [7].

The selective pressure exerted by inappropriate use of antimicrobial agents is the main driver of emergence of resistance and not surprisingly the higher the volume of antimicrobials used, the stronger the correlation with emergence of resistance. The varying strengths of such selective pressures encountered in human medicine, animal husbandry, aquaculture and agriculture have all been implicated in rising AMR. Microorganisms acquire mutations and or mobile genetic elements through horizontal gene transfer (HGT) which confers resistance to antimicrobial agents. In response to this selective pressure, following the Darwinian process of natural selection such mutants can survive, multiply and produce a resistant progeny that will ultimately replace the original susceptible microbial population.

In a population of microorganisms, the maintenance of antimicrobial resistance is determined by several factors. These include the mutation supply rate, the level of resistance conferred by the resistance mechanism, the growth of the resistant mutant at different drug concentrations and the strength of various selective pressures [9].

Some examples of how the selective pressure has driven AMR:

Patients with cystic fibrosis carry abundant populations of *Pseudomonas aeruginosa* that are subject to strong drug-induced selective pressure over a long time. Because of the relatively low population turnover in these patients, resistant bacteria emerge and rapidly increase in numbers.

Emergence of methicillin resistance in *Staph aureus* due to the selective pressure of flucloxacillin that led to outbreaks of MRSA in hospitals, and as community-acquired MRSA outside the healthcare environment.

Emergence of resistance by itself is not enough for transmission. A good example is emergence of vancomycin-resistant *Staphylococcus aureus*, due to acquisition of the vanA gene cluster through HGT from co-infecting *enterococci*. This did not create a resistance problem in clinical settings or lead to major health problems worldwide. The success in transmission is thus as important (or even more important) as emergence of resistance, which is generally facilitated by strong antibiotic selection.

Selective pressure in non-clinical settings is also implicated in emergence of resistance in microorganisms infecting humans.

An example of antibiotic selective pressure in animals that has led to resistance in humans is the detection of plasmid-borne colistin resistance due to the mcr-1 (mobilized colistin resistance) gene in clinical isolates of *Escherichia coli*, *Salmonella enterica*, *Klebsiella pneumoniae* and Enterobacter aerogenes/cloacae. Several lines of evidence indicate that it was the extensive use of colistin as a growth promoter in livestock that facilitated its subsequent transmission to humans.

In addition to the selective pressures encountered in human medicine, animal husbandry, aquaculture and agriculture, there are number of factors that exert strong or weak selective pressures on microorganisms in the environment. These include natural production of antimicrobial agents by microbes, influx of waste (urine, stool etc) enriched with excreted antimicrobial agents from individuals treated with antimicrobial agents and pollution from pharmaceutical manufacturing [9]. These, chemically stable antimicrobial agents ultimately end up in rivers, lakes, soils and/or in food products, where they continue to exert a selective pressure on microorganisms, promoting the selection of antimicrobial resistant genes. Such genes from the environment can reach microorganisms found in animals and humans leading to spread of AMR.

For example: a case-control study conducted in Pennsylvania from 2005 to 2010 on more than 400,000 primary care patients revealed that the community exposure to crop fields where swine manure was used as fertilizer was a significant risk factor for both community and healthcare-associated MRSA strains [7].

3. Dissemination of antimicrobial resistance

Microorganisms are exposed to a number of different antimicrobial agents in diverse ecosystems creating a complex web of selection pressures that facilitates emergence of AMR. Dissemination of AMR commonly occurs through direct and indirect contact with a person carrying bacteria or by touching contaminated surfaces. Transmission is also seen between humans and pets (and vice versa), farm animals and contaminated animal meats. AMR can also spread through fruits and vegetables contaminated from water and manure.

Population density, travel, international trade etc facilitates dissemination and provides a landscape that shapes the dimensions of AMR.

Specific genetic lineages have become highly transmissible which has contributed disproportionately towards the global burden of AMR. Just to name a few of such successful and highly transmissible genetic lineages that is causing major challenges to the control the rising AMR are CTXM in E coli, Cabepenemases such as KPC, NDMs, OXA48 etc

4. Mitigating antimicrobial resistance

AMR needs to be tackled on multiple fronts. In this talk, strategies mainly applicable to AMR affecting human medicine will be discussed. Nevertheless, measures targeting use, misuse, and overuse of antimicrobial agents in animal husbandry, livestock, agriculture and aquaculture have a high impact (or a higher) and are crucial for controlling the spread of resistance worldwide.

4.1 Develop antimicrobial agents against new targets

There is a growing clinical need to develop new antimicrobial agents with a low propensity for resistance. Despite the clinical need, the pace of development of new antimicrobial agents has been remarkably slower with a dwindling pipeline. The major reason for this mismatch is the high investment cost. As a result, the pharmaceutical industry does not see research into new antimicrobial agents as economically viable. The average cost to bring one antimicrobial agent successfully to the market is between $800 and $900 million and takes about 10-15 years per approved agent [7] [10]. In addition, there is also the possibility that the new drug may become ineffective in the short-term. Added to all this is the increased regulatory conditions and strict price controls imposed by many governments.

There is an urgent need for an international effort to repair the pharmaceutical market by reducing developmental costs and barriers to entry, thereby pulling in new players and diverse innovation, regardless of whether these involve conventional small molecules or non-conventional approaches [8]. Without such efforts tackling AMR with new antimicrobial agents is a far-fetched reality.

4.2 Reduce selective pressure

A more direct and efficient way to reduce the emergence of AMR is to reduce the selective pressure that provides the microorganisms with a fitness advantage. Infection prevention and control (including hand hygiene), which reduces the need to use antimicrobial agents, with their contingent selection pressure, is vital to containing AMR. Also important are measures to optimize use of antimicrobial agents. These measures however are mainly

applicable in reducing the selective pressure in the hospital setting. About 90% of antimicrobial use in humans is in community settings and in many cases, antimicrobials are prescribed to treat mild, self-limiting community-based infections [9]. It would therefore seem reasonable to focus more on community antimicrobial use, especially for the most common infections, e.g., respiratory and urinary tract infections. For optimum benefit this would require improving diagnosis such as the use of biomarkers (e.g., procalcitonin) to distinguish viral from bacterial infections. Also, rapid identification and susceptibility tests would enable the choice of antimicrobial drugs to be evidence-based rather than empirical, which in turn would allow de-escalation of treatment more rapidly.

4. 3 Improve diagnosis

Access to laboratory tests with good turn-around time is critical to reducing diagnostic uncertainty and optimizing the use of antimicrobial agents. The reality is that the methods used by most microbiology laboratories haven't changed much, typically taking at least 2 days to complete: 1 day to grow the bacteria and another day to test susceptibilities, with the patient being treated empirically in the interim. There is a need for rapid tests to detect infecting microorganisms directly in specimens or from culture isolates and detecting drug resistant markers to narrow the window of empirical and targeted treatment. The most welcome progress to date is the introduction of mass spectroscopy (i.e., MALDI-TOFF) which has accelerated identification of microorganisms, but not susceptibility testing.

4.4 Improve population wide vaccination against common infections

Immunity plays a direct role in preventing or delaying the emergence of antimicrobial resistant organisms. Vaccination against viruses, such as influenza, reduces host susceptibility to bacterial infections. This will minimize the number of cases where diagnostic uncertainty favours antibiotic usage, reduce the number of antibiotic treatable co-infections that are secondary to viral illnesses and prevent the increased transmission rate of resistant bacterial pathogens between hosts that is associated with viral infections.

Role of antimicrobial stewardship in AMR

Antimicrobial stewardship (AMS) is defined as "the optimal selection, dosage, and duration of antimicrobial treatment that results in the best clinical outcome for the treatment or prevention of infection, with minimal toxicity to the patient and minimal impact on subsequent resistance" [6].

AMS interventions are aimed to:

1. Ensure each patient receives the most appropriate antimicrobial agent with the correct dose and duration. This means treating patients with the correct, properly dosed antimicrobial agent and one that has the least likelihood of causing resistance.
2. Prevent antimicrobial overuse, misuse, and abuse.
3. Minimize the development of resistance.

AMS teams commonly consist of a microbiologist or an infectious disease physician and a pharmacist and tend to adopt either a front-end (pre-prescription) or back-end (post-prescription) approach to stewardship. The front-end approach primarily uses a restrictive approach with antimicrobial prescribing, whilst the back-end approach uses prospective review of prescriptions with feedback. Both approaches have their merits and demerits. The restrictive approach targets specific antimicrobials for specific indications based on local resistance patterns and the hospital formulary. Antimicrobials are approved for a specific duration and a review is prompted after culture data have been obtained. The approach aims to reduce overuse, abuse and misuse of antimicrobials and has shown to bring significant reductions in expenditures of the targeted antimicrobial but there is a risk of increasing the use of antimicrobials that are not restricted. Prospective review of prescriptions has shown improved clinician satisfaction and has the potential to decrease antimicrobial use. There is also the advantage of being able to focus on de-escalation, a critical aspect of appropriate antimicrobial use [6].

AMS also attempts to use other strategies to optimize antimicrobial use. These include:

1. Formulary restriction
2. Order sets and treatment algorithms
3. Clinical guidelines
4. Education
5. Pharmacodynamic dose optimisation
6. Computer-assisted decision support programmes
7. Intravenous to oral switch programmes
8. Advice on dosing programmes and antimicrobial cycling

Some of the common barriers to AMS programmes include overuse of antimicrobial agents in patients with viral infections, non-infectious processes (i.e., acute pancreatitis), bacterial infections that do not require antibiotics (i.e. skin abscesses that will resolve with incision and drainage), and bacterial colonization (i.e. positive urine culture result in a patient with a bladder

catheter). Similarly, abuse of antimicrobial agents has been seen among clinicians due to aggressive promotion by pharmaceutical representatives or sometimes because of financial interest.

One of the greatest challenges of AMS is demonstrating a clear causal association between implementation of AMS programmes and decreased rates of antimicrobial resistance. Nevertheless, indirect benefits such as improvement in infection rates of *C. difficile* have been shown with decreased use of cephalosporins and fluoroquinolones (Figure 1). However, such interventions can come at the cost of increased use of extended-spectrum β-lactam/β-lactamase inhibitors and carbapenems, and other consequences may be experienced [6].

Making AMS part of our daily practice, has the potential to improve patient safety and care, reduce the unnecessary use of valuable resources, and reduce resistance.

Having provided the background information, I will now move to my own work on optimising antimicrobial prescribing, antimicrobial stewardship and the associated challenges and benefits.

The impact of risk perceptions and antimicrobial prescribing decision-making processes on AMR

I will first present an exploratory qualitative study undertaken by a team of microbiologists, social scientists, psychologists and sociologists from England, South Africa, and Sri Lanka. This study looked into the social and contextual factors impacting on prescribing decisions on the use of broad-spectrum antibiotics for acute medical patients in hospitals.

The background to this work came from the observations of wide variations in patterns of antibiotic prescribing and antibiotic consumption across countries. This variation was difficult to fully explain by differences in case mix and infection prevalence only; rather it reflected variations in prescribing practices and stewardship activities.

Drawing on previous research by Eva Krockow [11] and Carolyn Tarrant [12] (two of the members in our team) on the determinants of prescribing in hospitals, as well as theoretical literature on social dilemmas, a study was designed between 2016 and 2017 using qualitative interviews. This involved semi-structured interviews with prescribers in secondary care in Sri Lanka, South Africa, and the United Kingdom. The participants included prescribers with different roles and levels of seniority, from a total of seven different hospitals across the three countries. These hospitals included public and private hospitals from high and lower resource settings, with diverse challenges in terms of resourcing and patient population. The topic guide contained 17 questions about antibiotic use, exploring a range of aspects of antibiotic use, with several questions focusing specifically on identifying the participant's understanding of inappropriate

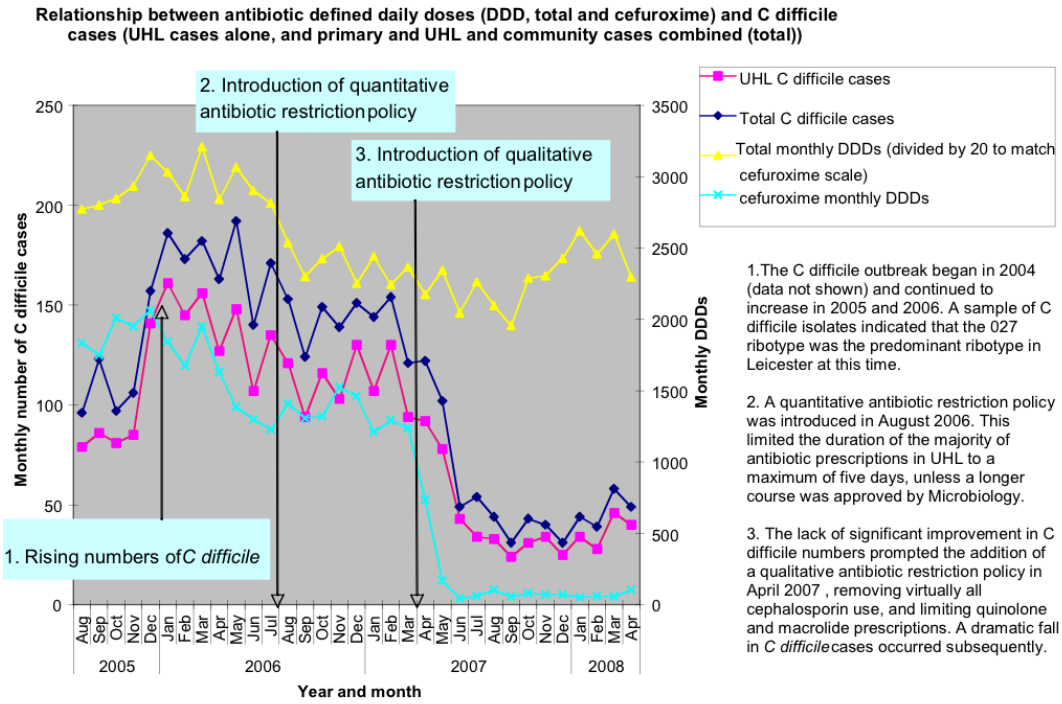

Figure 1.

prescribing and asking for examples. The interviews were conducted by local researchers and were audio recorded and ranged in length between 20 and 80 min.

In all three countries the participants demonstrated that they were in a state of constant tension in balancing the interests and risks to individuals and society. There was a general acceptance that being responsible prescribers and avoiding overuse and inappropriate use of antibiotics minimizes the risks of AMR. At the same time the participants recognised they have a moral responsibility, on a daily basis, to prioritise the wellbeing of the individual patient.

The data captured showed three distinct behaviours of prescribing: (extracted from reference 13)

1. Unambiguous "inappropriate" use of antibiotics:

   Overall, participants from all hospitals and countries shared similar opinions about what constituted an unambiguously clinically "inappropriate" decision about antibiotic prescribing. These included situations where antibiotics were prescribed but where infection was unlikely or the presentation indicated a different root cause such as a viral infection, when the diagnosis was unambiguous and where clear guidelines about antibiotic choice, dose, and duration existed, but the prescriber failed to prescribe in accordance with these guidelines. The common reasons for such "inappropriate" prescribing were unjustified individual preferences and habits, lack of appropriate knowledge, or, for more junior doctors, a lack of experience or senior supervision. Organizational systems and processes were also seen as contributing to this, for example, a lack of access to guidelines, workload and demand on practitioners, or inefficient systems for monitoring and regulating antibiotic use.

2. Balancing the interests between different stakeholders in antibiotic prescribing decisions:

   The tensions in balancing the interests of individuals and society, together with uncertainty of the diagnosis and moral framing of antibiotic prescribing decisions led to the ambiguity of "inappropriate" prescribing. Where there was uncertainty about the likelihood of infection, the likely source of infection and infective agent, the decision to prescribe a targeted narrow-spectrum antibiotic as opposed to a broad-spectrum antibiotic was less easy to classify as appropriate or inappropriate in objective terms. Factors that determine the threshold for prescribing varied from patient to patient, depending on their vulnerability and level of risk (e.g., young children, frail older people). The threshold also varied according to the individual prescriber's experience and confidence in assessing risk and tolerating uncertainty. Participants recognized that setting a low threshold – i.e., erring on the side of caution and prescribing antibiotics to acutely ill patients "when in doubt," was an easy and low risk approach to avoid the risks of deterioration and death for their patients.

3. "Inappropriate" prescribing as contextually dependent
   There were a number of contextual factors that shaped the views of prescribers in low resource settings that constrained the choices of antibiotics that were potentially seen as over-use of antibiotics, or excessive reliance on broad-spectrum antibiotics. These included high patient throughput, patients presenting at a late stage when they were acutely ill, and patients who had already taken (often unspecified) antibiotics in the community prior to coming into hospital. Such antibiotic use was exacerbated in some contexts by the lack of rapid and high-quality testing services. Unsanitary and overcrowded environments which increase the risk of hospital-associated infections were also seen as another factor in reliance on antibiotics. Finally in private health-care settings prescribers favoured the use of broad-spectrum antibiotics for social and financial gains to the patient even at a cost of increased antibiotic resistance.

Our study highlights how prescribers made judgements about the appropriateness of antibiotic use, and how they justified their own and others' use of antibiotics. Not all decisions about antibiotic use could, however, be judged as objectively appropriate/inappropriate in clinical terms. Participants varied in their views of their responsibilities in relation to public health and consideration of wider society in their decision making, most focussed on the individual patient. This tension between attending to the needs of individual patients vs. tending to the needs of the population as a whole has been recognized as a central ethical problem in diverse areas of medicine, particularly preventative medicine [14] [15]. Our study highlights how this tension underpinned the judgements about antibiotic use: what one prescriber judged to be excessive antibiotic use, based on their perceptions of duty to consider public health, could be seen by another as an appropriate response based on their sense of responsibility to minimize risk to the individual patient in front of them.

Changing behaviours of prescribing to turn the tide of rising AMR is challenging. This study outlines a number of clinical, moral, and contextual factors that frame antibiotic decision-making processes among prescribers.

Stewardship interventions that directly target behaviour change using techniques such as education, restrictions and controls on prescribing, and audit and feedback may have value where there is consensus that prescribing is wrong or suboptimal. These types of interventions may, however, be less effective at addressing the underpinnings of moral reasoning about antibiotic use, or the structural and contextual factors, that from the point of view of prescribers can make antibiotic overuse a rational and justifiable action.

Design and implementation of stewardship programmes should have a more holistic approach that considers the broader drivers of antibiotic use in secondary care settings globally, issues such as sanitation, hospital environment, diagnostics, community healthcare, and the financial implications for patients of hospitalization etc to turn the tide of rising AMR

Is stewardship a game changer?

I would now like to move onto my own personal experience in establishing an antifungal stewardship (AFS) programme in an adult haemato-oncology unit in a teaching hospital.

In 2005 following my appointment as a Consultant Microbiologist in the Department of Clinical Microbiology, University Hospitals of Leicester (UHL), I undertook to establish an AFS programme in the adult haemato-oncology unit in my hospital. At this point in time there was no agreed guideline for antifungal prescribing in the unit. My 1st task was to gather baseline information on antifungal prescribing to establish existing practice. There were 9 patients over a 4 month period who were prescribed empiric antifungal drugs for presumed invasive fungal infections due to a fever unresponsive to broad spectrum antibiotics. Antifungal prescription charts of the 9 patients were reviewed. The findings did not support a consensus approach to antifungal prescribing (Figure 2).

The next task was to form an AFS team and write an antifungal treatment guideline.

Working with three other members (Haematologist, Pharmacist and Radiologist) in 2006, the 1st antifungal treatment guideline for adult haemato-oncology was finalised. Based on risk stratification for invasive fungal infection (IFI) patients were offered antifungal prophylaxis and patients unwell for more than 72-96 hours on antibiotics were offered empiric antifungal treatment.

In 2007 and 2012 the AFS team performed audits to review compliance with the guideline and costs associated with antifungal treatment. Despite improvements in compliance with implementing the guideline, it became apparent that an empiric treatment approach exposed a significant number of patients without radiological and mycological evidence of IFI to "unnecessary" antifungal drugs thus exposing the patients to the toxic side effects of the drugs. The selective pressure of antifungal drugs had an associated risk of emergence of antifungal drug resistance, in addition to a significant additional financial cost pressure to the haemato-oncology department (Figure 3).

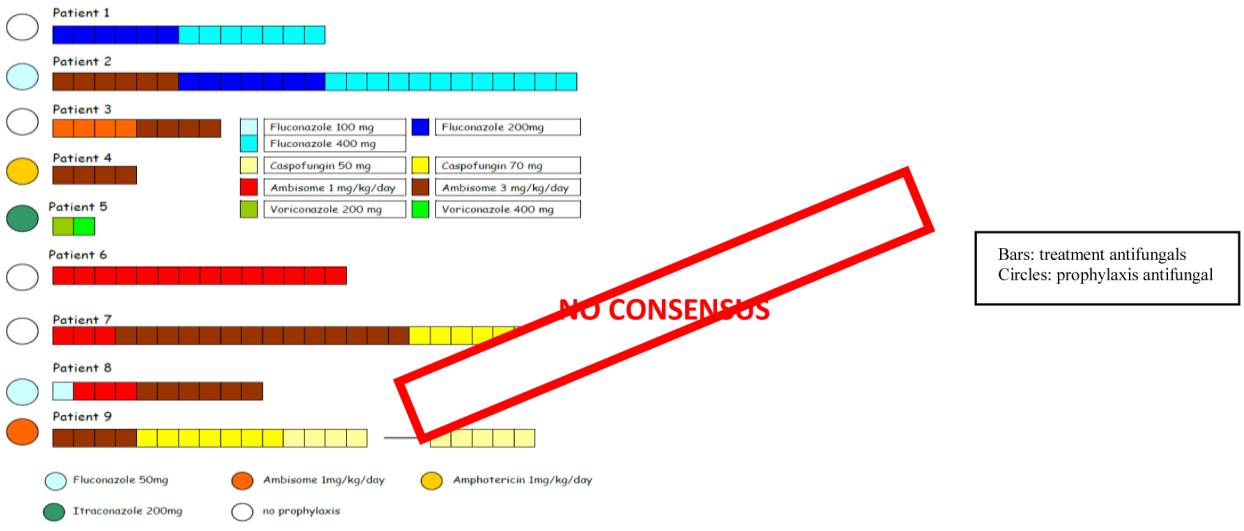

Figure 2. Antifungal treatment and prophylaxis, adult haematology and oncology, UHL Nelun Perera, personal data (unpublished).

Number of patients with IFI	Cost (£)
Probable (4)	14,750
Possible (19)	47,760
Total (probable & possible)	62,510
No evidence (14)	51,070
Total	113,580

Figure 3. Cost of antifungal treatment for IFI 37 patients in 2012. Cost of antifungal agents is based on institution specific pricing.
Nelun Perera, personal data (unpublished).

Recognising the significant number of patients exposed to "unnecessary" antifungal drugs, the AFS team proposed moving away from the empiric treatment guideline. At the same time to reduce "uncertainty" of diagnosis and improve timely diagnosis of IFI, 3 fungal biomarker tests with a turn-around time of 48-72 hours were commenced in the laboratory. By 2014 a directed antifungal treatment guideline was adopted in adult haemato-oncology. The AFS team also introduced regular AFS ward rounds and worked with the clinical team, reviewing every antifungal prescription for appropriateness (agent, dose and route) and duration of treatment and supported the clinical team to develop confidence in assessing risks, tolerating uncertainty and setting thresholds for treatment.

Two further audits performed in 2014 and 2015 showed the immediate benefits of the AFS efforts with a reduction in the number of patients treated with antifungal drugs and the costs associated with antifungal treatment. Since diagnosis of IFI had been improved this reflects a reduction in "unnecessary" antifungal prescribing and lower selective pressure and promotion of drug resistance (Figure 4).

	2013[1]	2014[2]	2015[2]
Number of patients	69	31	24
Annual antifungal cost (£)	241,752	123,453	98.070

Figure 4. Comparison of costs of antifungal treatment [1]empiric treatment guideline, [2]directed treatment guideline.
Cost of antifungal agents is based on institution specific pricing.
Nelun Perera, personal data (unpublished).

AFS has continued in adult haeamto-oncology and the benefits have continued even to-date. The annual antifungal expenditure for 2020 was £136,240.

My personal experience shows it is possible to make stewardship work. It can reduce inappropriate and overuse of antimicrobial agents and has the potential to reduce the emergence of antimicrobial resistance. To make it work there has to be a dynamic AMS team, there should be robust treatment guidelines and access to appropriate diagnostic tests with a good turn-around time. The clinical teams have to be supported with the necessary education and training on antimicrobial prescribing to achieve confidence and balance the risks to individual and society. In my experience regular audits are powerful tools to identify barriers to appropriate antimicrobial prescribing of individuals or issues with processes and consolidate appropriate antimicrobial prescribing behaviour.
I will now move to the final part of my oration.

Where and how do microbiologists fit in the bigger picture?

Clinical microbiologists are best placed to steer AMS programmes and should be taking a lead role in optimising antimicrobial prescribing behaviours.

At a local level, microbiologists should ensure prescribers have access to antimicrobial prescribing guidelines, microbiological tests with good turn-around times, and microbiology advice. They should organise education and training to prescribers to impart knowledge and best practice on principles of antimicrobial prescribing and the risks associated with inappropriate prescribing to individuals and society. Efforts should be made where possible to make prescribers inclusive in the AMS programmes and also keep them informed of local data such as laboratory data, antimicrobial consumption data, resistance data, etc to be able to reflect on their own and other's prescribing behaviours and encourage learning from each other. Communication between microbiologists should be improved and there should be a platform to share experience and learn from each other to identify gaps and improve practice.

At a national level, microbiologists should be part of all decision-making strategies to tackle AMR and should offer leadership in all policy making decisions pertaining to guideline development, workforce development, procuring equipment, AMR surveillance, education and training, etc.

Closing remarks

There is an urgent need to use antimicrobial agents responsibly in clinical practice. It is impossible to predict

what the future resistance landscape will look like. Even with improvements in infection control, stewardship and diagnostics, resistance will present new challenges.

AMS remains one of the single most important low cost, non-pharmacological interventions to tackle the rising tide of AMR.

Although this has been clearly stated and embraced in principle, and even adopted by policymakers, there appears to be very little measurable change to reflect the urgency and magnitude of this public health crisis.

AMR is not limited to clinical medicine. The drivers of AMR are also not limited to clinical medicine. There is an urgent need to generate a roadmap to improve clinical, agricultural, animal husbandry, aquatic and environmental control of AMR, and prevent further escalation of this public health crisis.

"The often-repeated mantra 'prudent use of antibiotics' and the successful French slogan 'les antibiotiques c'est pas automatiques'reflect the belief that any unjustified increase in antibiotic use will increase the prevalence of AMR".

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Review article

ANTIFUNGAL STEWARDSHIP – THE WAY FORWARD

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Introduction

Antimicrobial stewardship has been defined as the optimization of antimicrobial usage, with the end-points being favourable patient outcomes, cost-effectiveness of therapy and diminished adverse effects [1]. Although similar importance has not been given for antifungal agents, antifungal stewardship is as important, especially considering the very limited armamentarium of antifungal agents and the ever-expanding list of fungal pathogens and at-risk population due to novel therapies. Inappropriate antifungal usage leads to collateral damage such as emergence of resistance, which in turn leads to hospital acquired infections, increased patient morbidity, mortality and healthcare expenditure. Therefore, antifungal stewardship aims to increase favorable patient outcomes, reduce drug toxicities, expedite fungal diagnosis, reduce emergence of resistance with streamlined healthcare costs [2].

Establishing an antifungal stewardship program

The Centre for Disease Control has updated the core elements of antimicrobial stewardship in 2019 [3]. These principles are also applicable for antifungal stewardship.

Forming a multidisciplinary team with the necessary expertise is a key component for the successful implementation of any stewardship program. The essential members of the antifungal stewardship team should include a physician / infectious disease specialist, a clinical pharmacist and a clinical microbiologist / mycologist [4].

The stewardship team needs to allocate adequate time and resources (human, financial and information technology) to ensure success of the program [3]. Team leaders should include a pharmacist and microbiologist. The core components of the stewardship program are prospective audit and feedback, pre-authorization and institution-specific treatment recommendations, which have been shown to improve antimicrobial use. Timely de-escalation of antimicrobials and regular updates to prescribing physicians on the antibiotic usage, resistance data and adverse effects are useful adjuncts. These same strategies may be used for antifungal stewardship, along with the integration of rapid diagnostic tests and therapeutic drug monitoring of azoles [1,3].

Guidelines formulated on prescription of antifungals should be accessible at the point-of-care and should be easily available for reference of physicians and junior doctors, which will increase its acceptability [1]. Prophylactic and empirical antifungal therapy constitutes for a large portion of antifungal prescriptions. Empirical therapy constitutes 63% of antifungal prescriptions, and prophylactic therapy accounts for 13% of same in haemato-oncology patients. Therefore, these areas should take prominence when formulating institutional guidelines [5]. Furthermore, the extent of adherence to therapeutic guidelines was found to be more, when there was direct interaction between the prescribing clinician and the stewardship team [2].

Pre-authorization requires the clinician to get prior approval for an antimicrobial before it is prescribed. This enables the stewardship team direct control over its use, optimizing empiric antimicrobial choices and negates indiscriminate use. However, this strategy can be used for a limited number of antimicrobials, and may even delay the initiation of therapy [6].

Prospective audit and feedback allow the stewardship team and the clinician to review the antimicrobials prescribed. This helps to build mutual respect for each other and promote de-escalation and optimize the duration of therapy. However, this method is labor-intensive and requires good collaboration between both teams [6].

A Cochrane review on antimicrobial prescription practices found that restrictive techniques which limits antibiotic prescriptions such as requiring pre-prescription approval, and enablement techniques which aim at education and evaluation of prescription practices were the most effective interventions [7]. These restricted antimicrobials should

not be withheld for critical patients but should be reviewed by the microbiology team within 24 - 48 hours of starting the antimicrobials [1].

The management of fungal infections should be diagnostics-driven. Traditional fungal diagnostics lack the sensitivity and rapid turn-around-time to be of value in reducing empirical antifungal use. However, they can be used as an adjunct for early cessation of antifungals when the results are negative. Also, newer non culture-based methods such as β-D-glucan, galactomannan and aspergillus PCR have good negative predictive value. Thus, they should be used as a guide to discontinue antifungal therapy. These methods should be implemented with the support of the antifungal stewardship team, as this approach has been shown to reduce healthcare costs and hospital stay, without compromising on mortality due to fungal infections [8].

Therapeutic drug monitoring (TDM), although not widely available, can be useful to optimize antifungal therapy, and minimize its adverse effects. Patients on triazole antifungals, with their unpredictable pharmacokinetics benefit most from TDM. Critically ill patients are at increased risk for sub-optimal drug exposure, which in turn leads to selection and overgrowth of resistant strains. Those on long-term therapy with antifungals also benefit from TDM, to optimize their management. Overall, TDM plays an important role in antifungal stewardship, by directing towards the best possible doses, routes of administration and formulations for ideal antifungal concentrations [8].

Difficulties unique to antifungal therapy

Antifungal stewardship shows some unique hurdles that must be kept in mind. De-escalating therapy when the susceptibility results are available and using pathogen targeted therapy is an integral component of the antibiotic stewardship program. However, clinicians are still reluctant to step down on antifungals when a critically ill patient is recovering on broad spectrum antifungal agents. This trend is partly due to the non-availability of optimal diagnostics for invasive fungal diseases. This situation can be circumvented by the development of sensitive and specific fungal diagnostic tests and antifungal sensitivity testing with minimum turn-around time. However, for most fungal pathogens, the optimum tests have yet to be introduced [1].

Another problem is to limit the use of empiric antifungal agents. This may be achieved by utilizing non culture-based tests with a high negative predictive value (NPV), such as serum galactomannan assay [NPV 98% (95% CI 97-99%)] and PCR. These tests allow for the exclusion of invasive fungal infections with confidence, thereby saving on empirical antifungal therapy. On the flipside, certain subgroups such as acute leukaemics undergoing remission induction, do benefit from empiric antifungal therapy, due to high incidence of IFIs [1].

Special populations

Patients with malignancies, especially those with haematological malignancies are at various times given antifungal drugs with prophylactic or therapeutic intent. However, these exposures may increase the likelihood of emergence of resistance. Implementing a stewardship program in cancer patients is challenging, due to the complex nature of the patients and difficulties in arriving at a timely and accurate diagnosis. Therefore, it is imperative for the stewardship team to collaborate with haematology/oncology, transplant teams to develop institution-specific, evidence-based guidelines. The clinicians' input is especially necessary as the guidelines should encompass diverse populations such as those on novel chemotherapy regimens and cancer-related immune-dysfunctions. Attention should be given to discontinuing anti-fungal prophylaxis when deemed no longer necessary, to prevent drug toxicities and emergence of resistance, and developing therapeutic end-points for proven/probable invasive fungal infections. Due to the inability to obtain invasive samples and the need for rapid presumptive diagnosis, non-culture-based tests such as serological biomarkers and imaging will help to provide targeted therapy [9].

Solid organ transplant recipients are often prescribed antifungals due to their complicated medical and surgical co-morbid conditions, the atypical clinical presentations and need for high dose immunosuppression. Using broad-spectrum antifungals for prolonged durations lead to drug interactions and opportunistic infections with resistant fungal pathogens, which lead to poor clinical outcome. Also, dysbiosis of the gut microbiome may contribute to allograft rejection. Involving the transplant physicians and employing pharmacists with some experience in transplant pharmacology will increase compliance and success of the stewardship program, as well as reduce adverse patient outcomes. As previously mentioned, employing rapid diagnostics would be beneficial, even though their cost and other logistics impede their use in a clinical microbiology laboratory [10].

The commonest invasive fungal infection plaguing critically ill patients is invasive candidiasis. Diagnostic challenges owing to poor sensitivity of traditional cultures and high mortality of the condition, inevitably leads to the overuse of antifungals in this population. This leads to drug interactions and emergence of resistant strains, which further compound the problem [11]. Antifungals are mostly prescribed empirically or as pre-emptive therapy in critically-ill patients, and should be used with infectious disease advice as many have hepatic and renal

impairment or receive renal replacement therapy. Every effort should be taken to arrive at a mycological diagnosis, and de-escalation based on the results, avoiding unnecessary and prolonged therapy [12].

Measurement of outcomes

The effectiveness of a stewardship program can be quantified by "process" and "outcome" measures. Process measures are used to compute the antimicrobial usage, while outcome measures calculate the changes in the antimicrobial resistance and patient outcomes. Factors considered for process measures are antifungal drug consumption and compliance with institutional guidelines, with regards to appropriate drug, dose, therapeutic drug monitoring, de-escalation, conversion from intravenous-to-oral formulations, as well as the utilization of appropriate diagnostic tests and source control. Outcomes can be quantified by the percentage of episodes of invasive fungal infection in vulnerable populations, percentage of patients where clearance of fungaemia was achieved and percentage with recurrence, percentage with fluconazole resistant invasive fungal infections and the total cost for antifungals in the institute [13].

Stewardship initiatives

The first of-its-kind dedicated antifungal stewardship program implemented in England, used measures such as annually updated antifungal guidelines and formulary restrictions for off-guideline antifungals use and regular prescription reviews. It was found that the stewardship program was implementable and sustainable, and enabled unnecessary prescribing, with no increased patient mortality and good acceptance from clinicians. However, the challenge remained to enroll rapid and accurate diagnostics [14].

Antimicrobial stewardship programs are not routinely implemented in Sri Lanka. However, several programs have been initiated in selected hospitals with the services of a clinical microbiologist. One such program implemented formulation of national/local guidelines and its availability at point-of-care, education of prescribers, formation of a multidisciplinary team and pre-authorization of selected antibiotics. Outcomes showed reduction of defined daily doses of carbapenems, cost savings and reduction of carbapenem resistance rates [15].

Antifungal stewardship programmes are yet to be formally introduced in Sri Lanka. We hope that will change in the future. Some positive aspects to look forward to include,

- Expansion of the mycology services in the country, with more specialist mycologists, who will be able to offer their services for the initiation and maintenance of antifungal stewardship programmes,
- Increasing the armamentarium of mycology diagnostics, with precedence for non-culture based rapid diagnostic tests
- Initiation of Candida surveillance to cover the entire country under WHO GLASS programme
- Updating institutional / national guidelines on the usage of antifungals, based on available laboratory data
- Initiation of audits on prophylactic and therapeutic use of antifungals
- Liaising with clinicians with regards to management of invasive fungal infections
- Updating the diagnosis and management of fungal infections among all clinicians including microbiologists by conducting presentations, lectures, literature publications etc.

Conclusions

Initiating stewardship programs with the involvement of all stakeholders is essential. This includes the private sector healthcare providers, traditional medical practitioners and veterinary and agricultural services [16]. Antifungal stewardship is a long way from being implemented in Sri Lanka, with no hospital based medical mycologists at present, and no specialized fungal diagnostics offered in the clinical microbiology laboratories. Although invasive fungal infections have lesser incidence than multi-drug resistant bacterial infections, the health and economic implications are higher, and stands to increase further with the expansion of vulnerable population [1].

The time to act is now...

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IMPLICATIONS OF CUTANEOUS LARVA MIGRANS AND ITS MANAGEMENT IN A PATIENT WITH COEXISTING FILARIAL LYMPHOEDEMA IN SOUTHERN SRI LANKA

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Introduction

Lymphatic filariasis (LF) is a leading cause of disability. Skin breaches due to trauma or dermatoses act as entry points for pathogenic bacteria, causing progression of lymphoedema [1]. We report a case of cutaneous larva migrans (CLM) and its implications in a patient with filarial lymphoedema.

Case report

A 28-year-old married female from Habaraduwa, presented to the Filariasis Research Training and Services Unit (FRSTU), University of Ruhuna for further evaluation of left sided ankle oedema of one-month duration, after being found positive for anti-filarial IgG antibodies (FAT). The oedema did not reverse completely on limb elevation. She didn't experience episodes of lymphangitis or adenitis. However, she complained of a gradually expanding, intensely pruritic rash, over bilateral soles, of five days' duration (Figure 1: clinical timeline). She has been a seamstress at a garment factory in Koggala for eight years and works eight-hour shifts in the standing position. Her source of bathing water is a well, situated about 100m from her house, towards which she usually walks barefoot. She does not own pets but her garden is unprotected garden is frequented by stray dogs and cats.

On examination, she was afebrile and bilateral lower limb grade 2 pitting oedema was observed, more pronounced on the left. There were no skin changes, varicose veins, ulcers or cellulitis. Inflamed serpiginous tracts with entry points and erythematous papules were visible on the

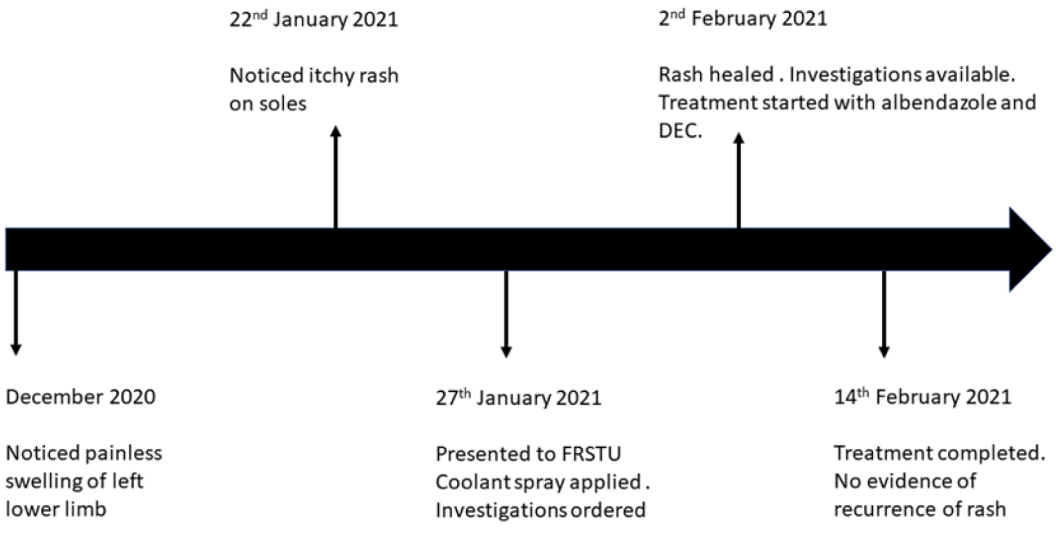

Figure 1. Timeline of important clinical events.

medial plantar aspect of both feet (left more affected); Figure-2A. Onychomycosis involving the left big toe, bilateral web space fungal infections and cracked skin were observed (Figures-2B-C). Inguinal lymph nodes were not enlarged. She was weakly positive for *Wuchereria bancrofti (Wb)* AD-12 antigen by the Filariasis Test Strip (FTS). Full blood count, erythrocyte sedimentation rate, C-reactive protein, liver functions, renal functions and fasting blood sugar were normal. Urine hCG by strip test was negative. Skin thickness ultrasound measurements were; L/lateral-0.280cm, L/medial-0.548cm; R/lateral-0.239cm, R/Medial – 0.297cm. Limb circumference measured by infra-red 3D scanning at 12, 20 and 30 cm limb height respectively (in cm) were; L-21.6, 26.4, 34.5 and R- 21.1, 26.7, 34.6.

A coolant spray, was applied to bilateral soles, following which the patient's symptoms improved (Figure-1D). She was started on diethylcarbamazine citrate (DEC) 6mg/kg daily for 12 days and albendazole 400mg single dose. Entry lesions were managed with miconazole, soframycin, and 15% urea application for cracked skin. Patient was trained on morbidity management and disability prevention (MMDP) protocol, which includes limb hygiene, managing entry lesions, elevation, exercise and limb protection [2]. She is being followed up at FRSTU.

Discussion

LF was eliminated from Sri Lanka as a public health problem in 2016. Ongoing low-level-transmission of bancroftian filariasis is reported in several minor foci such as Habaraduwa and Koggala while brugian filariasis is reported sporadically [3]. 891 new cases of lymphoedema (no hydroceles) were reported locally in 2019 (Personal Communication, Director, Anti Filariasis Campaign). Although the annual mass drug administration from 2002-2006 contributed to disease elimination, cases are still seen due to the chronic, nonfatal, heterogeneously distributed nature of the disease. Diagnostic tests tend to be negative in people with chronic sequalae, as it occurs due to the immune response upon parasite clearance [1]. This patient was non-pregnant and lacked features of cardiac, hepatic or renal disease. Living in an endemic focus, and working night shifts probably increased her exposure to the vector, *Culex quinquefasciatus*. Oedema may have persisted longer as it was staged grade 2 at first contact. Positive filarial antibodies only indicate past exposure, but positive FTS, indicated the presence of adult worms, warranting treatment [1]. Regrettably, night blood filming for microfilaraemia was not performed due to patient's busy work schedule.

Progression of lymphedema and development of elephantiasis are complications of LF which occur secondary to repeated acute dermato-lymphangio adenitis (ADLA) episodes [1,2]. Interdigital fungal infections, paronychia, injuries and eczema act as entry lesions for bacteria [1,2]. The lesions on the soles were clinically diagnosed as Cutaneous Larva Migrans (CLM),

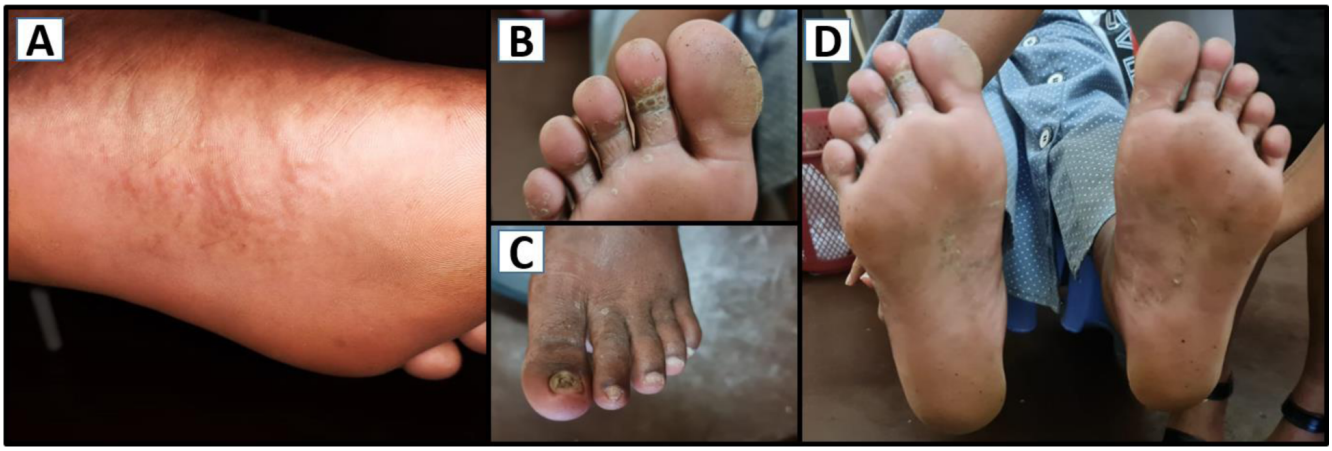

Figure 2.

A = Left foot before treatment; shows serpiginous tracts of cutaneous larva migrans

B = Entry lesions of left foot

C = Onychomycosis of left big toe

D = Healed lesions of cutaneous larva migrans, one week after treatment with coolant spray

a zoonosis caused by dog and cat hookworms; *Ancylostoma braziliense, A. caninum* and *Unicaria stenocephala* [1]. Third stage larvae penetrate skin on contact with contaminated soil, and creep, causing serpiginous tracts in the epidermis. Walking barefoot in her garden, probably contaminated with animal faeces, supports acquisition. Being intensely pruritic, bacterial superinfection is frequent, thus providing a portal of entry for pathogenic bacteria [1,4]. We did not find published literature on CLM acting as an entry lesion in filarial lymphedema. However, bacteria (endosymbionts) carried by the larva or secondary bacterial infections due *Streptococcus pyogenes* may cause cellulitis [4] and can lead to ADLA in patients with lymphoedema; this was prevented in this case by timely interventions.

Topical thiabendazole (crushed oral tablets) for small lesions [4] or single dose oral ivermectin for larger lesions are usual treatments of choice [1]. However, both are not licensed in Sri Lanka. Inefficient absorption and tissue penetration necessitate up to a 7-day course of oral albendazole [1]. Quick healing was necessary in this young, yet self-negligent patient to prevent complications. Coolant spray (contains pentane, butane and propane) used by sportspersons for acute injuries to prevent internal bleeding and oedema has been successfully used at FRTSU for CLM, and was found to be effective in this patient as well. The aerosol spray has the advantage of covering the entire lesion compared to liquid nitrogen which is only applied to the edge of the lesion [4]. Coolant spray is applied only till pain is felt compared to the specified time of application of cryotherapy, thereby preventing burns, which can act as entry lesions and cause ADLA.

Management of other entry lesions and follow up will be beneficial in the long run especially since prolonged standing aggravates her lymphoedema. This case reiterates the importance of footwear and proper management (in limited resource setting) of common, easily diagnosed, yet neglected parasitic dermatoses in patients with lymphoedema.

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PACEMAKER LEAD ENDOCARDITIS CAUSED BY *Pseudomonas aeruginosa*

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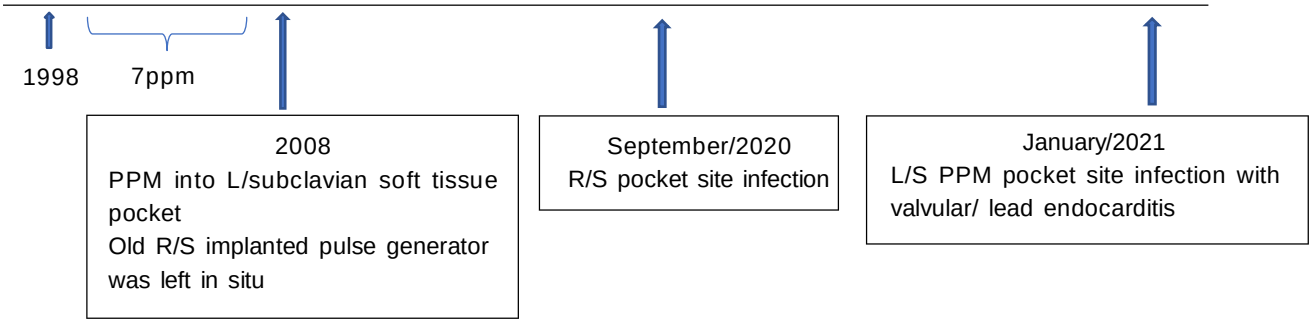
Introduction

With advancing medical technology cardiovascular implantable electronic devices (CIED) especially pace makers are being used more frequently for various clinical indications. Infections associated with CIED are recognized as serious complications resulting in increased mortality, morbidity and health care cost.

CIED infections present with bacteraemia, lead infection or endocarditis with or without generator pocket involvement. Incidence of infection depends on host defenses, microbial virulence factors and procedure related factors. Majority of CIED infections are caused by *Staphylococcus* spp. and other Gram-positive organisms [1]. Permanent pace maker (PPM) infection with endocarditis is rarely caused by Gram negative organisms [2].

We describe a case of PPM pocket site infection with valvular/lead endocarditis caused by *Pseudomonas* spp., diagnosed with the presence of local signs, positive blood cultures and lead/valvular vegetations [3].

Case Report



This 28-year-old female patient with congenital complete heart block had undergone 7 PPM implantations since 1993. The last implant was inserted in to L/pre-pectoral soft tissue pocket in 2008, but the old right sided (R/S) implanted pulse generator was left in-situ as it was deep inside the breast. She was asymptomatic until September 2020 when she presented with pus discharge from R/S PPM pocket site and eroding leads without other systemic features. Her blood cultures and TTE (Trans-Thoracic Echo) were negative. A swab culture from the pocket site grew methicillin resistant *Staphylococcus aureus.* This episode was managed with intra-venous vancomycin 1g 12 hourly for 14 days and a surgical intervention to excise both right side leads proximally.

She defaulted follow up and presented to a local hospital with intermittent fever for 2 months with left PPM pocket site inflammation. The single blood culture collected became positive for *Pseudomonas* spp. sensitive to all anti-pseudomonal antibiotics according to manual methods, however the TTE was negative. She was started on IV meropenem 1g 8 hourly and transferred to the cardio-electrophysiology unit, National Hospital of Sri Lanka (NHSL) for specialized care.

She was having fever with rigors at the time of admission to NHSL and out of the 4, 2 blood cultures became positive for *Pseudomonas aeruginosa* with sensitivity as above which was confirmed with automated identification and MIC was performed. Left PPM pocket site swab culture also yielded the same organism with similar sensitivity pattern. The TOE (Trans-Oesophageal Echo) showed a large vegetation (25mm x10mm) attached to the tricuspid valve and multiple vegetations attached to the lead and right ventricular free wall. Treatment was de-escalated to IV ceftazidime 2g 8 hourly and IV amikacin 15mg/kg daily combination therapy. The intracardiac and epicardial leads with bi-lateral pacemakers were removed and a new PPM to right pre-pectoral region was inserted. Vegetation tissue grew same organism as in blood cultures. Patient responded both clinically and biochemically with the dual antibiotic therapy which was continued up to 4 weeks. However, considering the static clinical condition towards the end of the therapy IV meropenem was started and continued for 2 more weeks under expert opinion. The patient was discharged and planned to follow up in the routine cardiac-electrophysiology clinic.

Discussion

Rate of PPM infection varies from 0.13 to 19.9% depending on host and procedure related factors. Lead extraction rate for CIED infection has increased over time [1]. Implementing preventive measures and early diagnosis are therefore crucial in improving the quality of care.

Though this case represents a late CIED infection, it is more likely to be pocket infection disseminating through blood stream rather than a primary bacteraemic infection with generator pocket involvement, since Gram negative bacteraemia rarely causes secondary seeding of PPM site [4]. Repeated CIED implantations probably with repeated infections could be a predisposing condition in this patient. Two blood cultures became positive despite effective antibiotic therapy until removal of the infected device. Presence of vegetations and foreign material leading to biofilm formation would have impaired the access of antibiotics to pathogenic bacteria and contributed to poor clearance of bacteraemia [1].

Treating Gram negative endocarditis in particular pseudomonas endocarditis is difficult and the recommendation is to use 2 anti-pseudomonal antibiotics [5] which have been used to treat this patient. In spite of 2 weeks of appropriate antibiotics, surgical samples became positive and we had to recalculate the antibiotic duration from the date of surgery. A new device had to be implanted to contralateral side on the same day since there was no alternative option.

Adhering to basic steps like drawing blood cultures before starting empirical antibiotics, Gram stain and culture of generator pocket site tissue and cardiac imaging aided in early accurate diagnosis, targeted management and the improved outcome in this patient.

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TEACHING AND TRAINING IN MEDICAL MICROBIOLOGY – FLAVOURS OF TWO COUNTRIES

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Having returned from post-MD overseas training at the Aberdeen Royal Infirmary, Scotland, UK, and realising the differences in teaching and training in the two countries, this attempt is to share my experiences with the Microbiology community in Sri Lanka. I reflected on the differences in teaching and training in Medical Microbiology in view of betterment of our local setting.

Undergraduate training in Medical Microbiology in Sri Lanka is based on a conventional curriculum (subject-based curriculum) in some universities and an integrated curriculum in others, while in Scotland; it is an integrated curriculum throughout. In a medical education point of view, the latter is more beneficial.

Postgraduate training in Medical Microbiology in Sri Lanka is of different paths. To become a fully-fledged Medical Microbiologist, basic MBBS degree and a MD or PhD is essential, and as per the training, one can specialise in any of the sub-specialities: Medical Virology/ Medical Parasitology/Medical Mycology/Medical Immunology. In Scotland, the basic medical degree is MBChB and passing through foundation years, one can undergo Core Medical Training [1]. This opens up a registrarship when furthering postgraduate studies in Medical Microbiology (Specialty Training) where either Microbiology or Combined Infectious Diseases and Microbiology could be chosen, and FRCPath Part I and II exams undertaken. Next, a Certificate of Completion of Training needs to be obtained after which an appointment as a Consultant in a NHS Trust can be pursued [1]. Ongoing continuous professional development activities and appraisals done in a systematic manner are required for General Medical Council (GMC) revalidation and the continuation of license to practice [2].

I was an International Medical Training Fellow in Microbiology as a Medical Training Initiative of Royal College of Pathologists, UK which was the pathway merging international trainees into the UK postgraduate system. My training was overseen by an Educational/ Clinical Supervisor and I was given a lab/corporate induction which was followed by shadowing, i.e. one-on-one learning. I was given laboratory bench training which introduced me to the state-of-art technology. Soon, they included me into Clinical Microbiology and Virology rosters. I was also trained at some centres away from the main centre (Health Protection Team Scotland, Centre for Sexually Transmitted Diseases, National Mycology Reference Centres in Bristol and Manchester and was an Honorary Clinical Fellow of the University of Aberdeen and was involved in teaching medical students, dental students and Physician Associates.

The expected key areas of outcomes of training are namely subject expertise, teaching, research, ethics and professionalism, information technology, life-long learning and reflective practice. As an eye-opener for the local trainees who have not yet ventured on overseas training, a few notes on experience in subject expertise gained from UK would be noteworthy. State-of-art technology, streamlined laboratory and patient information management systems and documentation processes, quality control/assurance systems, health and safety, laboratory management, laboratory accreditation which included clinical assessors assessing microbiologists, methodology for handling lab errors and strict analysing/ reporting of results and the cascade of investigations and transparency in them are to name some. Scotland has a well-structured free health care system. Multi-disciplinary approach is well practised in patient management. Communication skills are essential to survive in such a systematic setting. Antibiotic stewardship is implemented in an exemplary way in Scotland. Data protection is taken very seriously. Multisource feedback reports and appraisals are essential prerequisites for GMC revalidation.

However, despite the systems and infrastructure being in place, UK too has issues in infection prevention and control (IPC), e.g. compliance in adhering to IPC measures, financial cut downs. Overwhelming workload due to shortage of staff, way too many protocols/ procedures/ mandatory training and working with personnel diverse in training/ experience / knowledge are some challenges a medical microbiologist would face in the Scottish healthcare system.

UK training made me realise that a Microbiologist in Sri Lanka has to be a Jack of all trades. Positive aspects in

Medical Microbiology teaching/training in Sri Lanka I experienced were the taught course and bench training in the PG Diploma course, enormous clinical wealth and structured clinical rotations.

As for a take-home, I strongly believe that we in Sri Lanka need more emphasis on communication, data protection, document control, quality control, hospital/lab information management systems, antibiotic stewardship streamlined in teaching and training. As for a way forward in teaching/training; adaptation of novel teaching techniques (e.g. blended learning, ePortfolios which stress on personal development plans), effective feedback systems for teaching and training (e.g. online feedback platforms, multi-source feedback), more problem-based learning and to continue the momentum, a revalidation scheme for the consultants could be adopted in our setting too.

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SOME RECENT TRENDS IN PARASITIC ZOONOSES

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Introduction

Zoonoses are defined as infections that are naturally transmitted between humans and other vertebrate animals. Over 200 parasitic zoonoses have been documented. Transmission may be via direct contact with animals (animal bites) or animal products (contaminated hides, wool, or fur), or indirectly via contaminated food and water or arthropod vectors [1].

Humans are accidental dead-end hosts for most of these zoonotic parasites that cannot reach sexual maturity in humans. However, some zoonotic parasites can attain sexual maturity and produce progeny [1].

Case 1

A 70-year-old female from Veyangoda, presented with epigastric pain and abdominal discomfort. Haematological investigations were unremarkable apart from a low-grade anaemia (Hb- 11.4g/dl). The faecal examination was negative for occult blood and parasites. Upper Gastro intestinal endoscopy revealed a live worm within the duodenum. The worm was extracted and sent for identification to the Department of Parasitology, Medical Research Institute (MRI).

The worm was cylindrical, creamy white, 9 mm long and 48µm wide at the centre. The buccal cavity was 12µm in diameter with two clearly visible teeth on one side and on the other side the teeth were twisted medially. The lateral teeth were longer than the medial ones (Figure 1). The cuticle was thick with transverse striation. The width of the transverse striations was 5µm. A stumpy mucron, 7µm long was observed at the posterior end (Figure 2). The worm was identified as a female *Ancylostoma ceylonicum.*

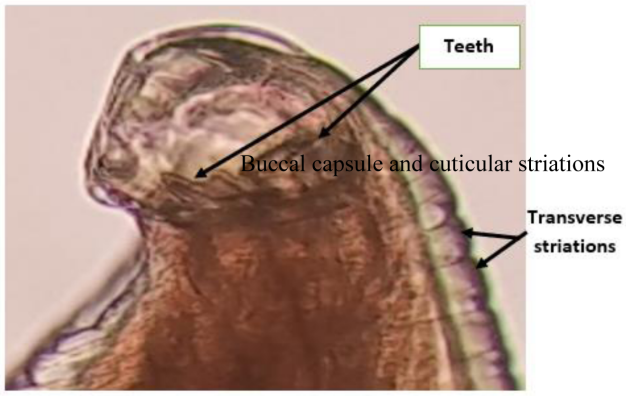

Figure 1. Buccal capsule and cuticular striations.

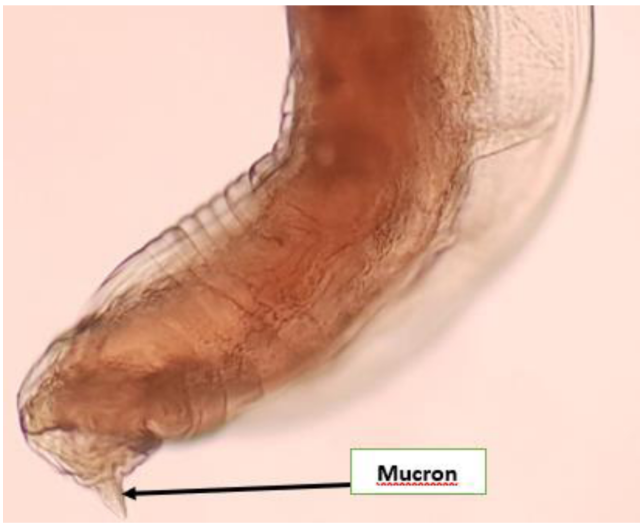

Figure 2. Poster end of the worm.

The patient lived with her husband and two daughters. The family used a water-sealed latrine. She was in the habit of walking bare-foot in the neighbourhood to collect firewood and cow-dung. Stray dogs and cats were abundan in the area. She had no history of foreign travel but one of her daughters was employed abroad and visited Sri Lanka occasionally. She had not been dewormed in the recent past (five years).

Management

A single dose of Albendazole (500mg) was administered after endoscopy and a repeat dose after two weeks with which her clinical symptoms subsided.

A faecal survey performed among the members of the index household and neighbouring houses after anthelmintic treatment using direct-saline and Kato-katz smears were negative for parasitic stages.

Case 2

A two-year-old boy from Weligama, presented with a non-painful, non-itchy, migrating lump on the left chest wall of two days duration. The child often stayed bare-chested during the day and slept under a mosquito net. No other anti-mosquito measures were practised. The family-owned two pet dogs who were regularly vaccinated for rabies. There was no known occurrence of similar lesions in the vicinity.

A non-tender, round, mobile, lump, 2cm in diameter was situated subcutaneously on the antero-lateral aspect of the left thoracic wall detected on palpation. The overlying skin was normal. Haematological investigations revealed a mild eosinophilia and on ultrasonography a worm granuloma containing a live worm was reported.

The lump was excised under local anaesthesia and the extracted live worm was transported in normal saline to the Department of Parasitology, Faculty of Medicine, Karapitiya for identification.

The worm was cylindrical, creamy white, 160mm long and 600µm wide (Figure 3). Microscopic examination after 48 hours in a clearing solution revealed a thick cuticle with longitudinal striae. The uterine pore was situated close to the anterior end. The worm was identified as a female *Dirofilaria repens*.

Figure 3. Longitudinal striae.

Case 3

A night blood survey done in the Thirappane Medical Officer of Health (MOH) area has detected microfilariae in a 25-year-old long-term resident of the Mooriya-kadawala PHI area.

Microfilariae were identified as *Brugia malayi* by microscopy based on kinky lie at x10 magnification, short length (mean length 200µm), a column of thick over-lapping body nuclei, pinkish-purple stained sheath with Giemsa and the presence of two nuclei at the tip of tail (Figure 4). His blood was positive for anti-Brugia IgG4 antibodies by the Brugia® Rapid Test.

The targeted DNA region as amplified using the pan-filarial primers DIDR-F1 and DIDR-R1 that spanned the internal transcribed spacer region 2 (ITS2) of the ribosomal DNA. PCR yielded the expected band of 615 bp confirming the microfilariae as *B.malayi*.

Management

A 12-day regime of diethyl carbamazine citrate 6mg/kg body weight was administered which cleared the microfilaraemia with follow-up at three monthly intervals.

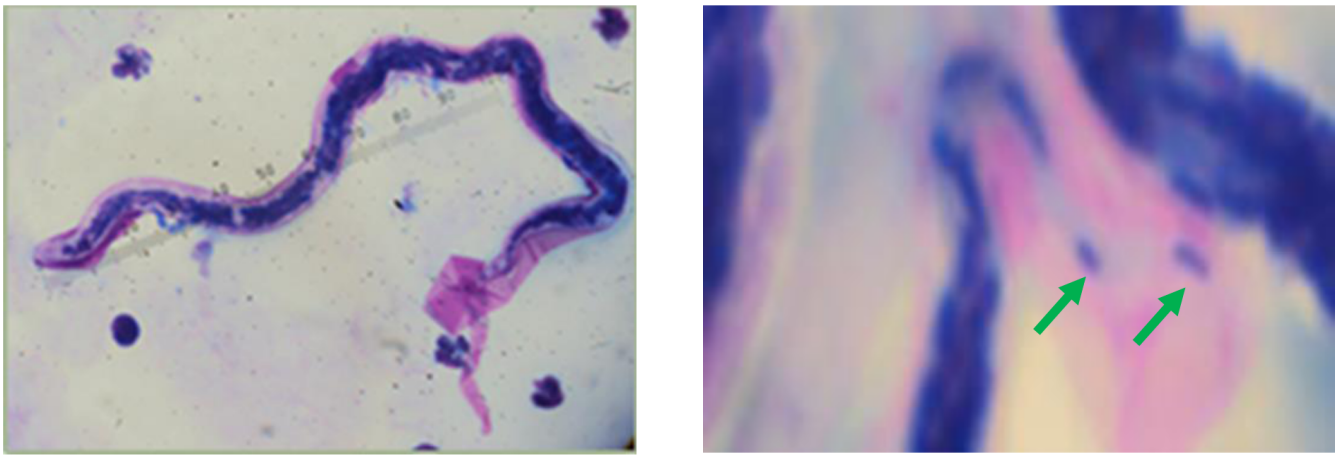

Figure 4. Microfilaria and tail end with nuclei.

Discussion

Hookworm infection is a soil-transmitted helminthiasis and is transmitted by the skin penetrating L3 infective larvae. *N.americanus* and *A.duodenale* are the two species causing human hookworm disease. *A.duodenale* has not been reported in Sri Lanka [2]. *A ceylanicum* was first described from a civet cat in Sri Lanka in 1970 and a high prevalence (92%) was reported among dogs [3]. Recent reports indicate that *A.ceylanicum* is an emerging public health risk in some communities in the Southeast Asian and West Pacific Ocean region countries with adult worms been detected in humans [4]. Due to the high population of dogs and cats in human habitations, soil contamination with animal excreta is unavoidable. People who work outdoors are invariably at risk of acquiring infections.

The negative faecal survey from the index case neighbourhood may be due to the low transmission potential of zoonotic infections, failure of the worms to reach sexual maturity in human intestines to produce ova and use of footwear. Although, this was the first report of an adult *A.ceylanicum* infection detected in humans, cases may be missed due to lack of suspicion.

Human dirofilariasis is caused mainly by two species, Dirofilaria repens and *D.immitis. D.repens* causes subcutaneous and ocular dirofilariasis while *D.immitis* causes pulmonary infection. *D.repens* has also been reported to affect the lungs, soft tissues, liver, intestine, lymphatic glands, and muscles [5,6].

Dogs are the principal definitive host of *D.repens* and *D.immitis*. Since Dirofilaria species demonstrate poor vertebrate host specificity they infect numerous mammalian species. Humans are less suitable hosts as worms do not mature sufficiently to produce micro-filaraemia (Accidental dead-end host) [5,7]. Transmission is via the bite of an infective mosquito of the Culicidae family [6].

According to recent reports, the dirofilariasis situation in Sri Lanka is on an upward trend even in the absence of human-to-human transmission [8]. A recent study reported both dogs (54.4%) and cats (34.33%) in Sri Lanka harboured *D.repens* [9]. Dogs were significantly more important as reservoirs for dirofilariasis ($p<0.05$).

Brugian filariasis has re-emerged in Sri Lanka after four decades. The re-emerged *B.malayi* exhibited nocturnal sub-periodicity suggesting a zoonotic origin [10]. Canine and feline surveys in Sri Lanka have shown that 51.6 % of dogs and 30.6 % of cats were infected with *B.malayi* [9].

A canine survey in Thirappane (Anuradhapura district) which is non-endemic for lymphatic filariasis reported 28.2% of dogs were carriers of *B.malayi* microfilariae [11]. The emergence of zoonotic *B.malayi* may pose a challenge to maintaining the filaria-free status in Sri Lanka particularly in a high carrier rate among animals.

Conclusions and Recommendations

The population of companion animals (pet cats and dogs) is rising with many stray animals. A recent survey has revealed the dog: human population ratio was 1:6.7 in Sri Lanka [12]. Emerging and re-emerging zoonotic infections of canine and feline origin is on an upward trend.

The One Health approach is recommended to address the complex issues of zoonoses. Active case detection, proper veterinary care for domestic pets, controlling the population of stray dogs and cats by mass sterilization, mosquito control and raising awareness among pet owners and general public by health education are recommended.

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RARE THINGS ARE THERE – AN ACCOUNT ON HISTOPLASMOSIS IN SRI LANKA

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Introduction

Histoplasmosis is an endemic fungal infection that can cause a range of disease spectrum. It is reported from various countries around the world and several cases have been reported from Sri Lanka. Lack of knowledge about its existence in Sri Lanka, its unusual clinical presentation and lack of awareness regarding the diagnostics may lead to miss or delayed diagnosis of this curable infection. This article aims at enlightening the reader about histoplasmosis in Sri Lanka, to increase vigilance among clinicians to ensure timely diagnosis in order to achieve a favourable treatment outcome.

Epidemiology and pathogenesis

Histoplasmosis is caused by the thermally dimorphic fungus, *Histoplasma capsulatum*. There are two varieties: var. *capsulatum* and var. *duboisii* [1]. Warm and humid environment, rich with organic compounds such as soil enriched with bat and bird excreta provide a good medium for sporulation and hyphal growth of *Histoplasma* sp. [1].

Hyphal form exists in the environment and spores are inhaled to the host. Spores convert to yeast upon reaching alveoli. Histoplasma is an intracellular fungus and innate

immune cells and T lymphocytes provide the main defense against it. Therefore, patients living with HIV and those who are on immunosuppressive medication are at a higher risk of disseminated histoplasmosis [1].

Histoplasmosis is recognized as a rare, systemic fungal infection typically endemic to Midwestern, Southeastern and Central America. But it has a worldwide distribution and South East Asia was identified as hyper-endemic for histoplasmosis [1,2].

Clinical presentation

Histoplasma is the most common fungal pathogen of respiratory tract [1]. Majority of the infected patients have mild respiratory symptoms. Some patients may manifest as acute pulmonary histoplasmosis with influenza like illness [1]. Chronic pulmonary histoplasmosis mimics pulmonary tuberculosis due to the symptoms of fever, night sweats, fatigue, loss of weight, dry cough and haemoptysis etc. [3,4]. Pulmonary nodules, cavities and fibrosis may be seen in chest radiographs further raising the suspicion of tuberculosis or a malignancy [1,4]. Systemic infection may occur in about 5% of the patients and is characterized by generalized lymphadenopathy, hepatosplenomegaly, fever and loss of weight [4]. Although it is commoner in immunocompromised population, immunocompetent people are not totally out of the risk [1].

Seven case reports have been published from Sri Lanka so far since 1975 [5-11]. Literature survey was performed using google scholar and pub med search engines using 'histoplasmosis', '*Histoplasma capsulatum*' and Sri Lanka. Bulletins of Sri Lanka College of Microbiologists were also referred. Mean age of the cases was 46 years and the majority (six patients) were males. Although HIV is a major risk factor for histoplasmosis, none of the Sri Lankan histoplasmosis patients was positive for HIV. One patient was a diagnosed patient with Non-Hodgkin lymphoma and three were diabetics. Betel chewing and smoking were noted in two patients who presented with oral ulcers [5-7]. Surprisingly, a 24-year-old apparently healthy female of European origin and a 35-year-old otherwise healthy farmer were diagnosed with disseminated histoplasmosis [8,11]. Importantly, the majority (5 patients) revealed no history of foreign travel indicating indigenous infection [5-7,9,11]. A significant history of exposure to bats in a cave was reported in one patient and two of the other patients were farmers, probably indicating the significance of soil contact in the pathogenesis, while the other patients revealed no significant predisposing factors [7,9,11].

Can histoplasmosis present as oral ulcers without dissemination?

More than 60% of patients with chronic disseminated histoplasmosis manifest mucosal ulceration [4]. But, a localized oral lesion without dissemination is an uncommon presentation and it may occur in irrespective of immune status [4]. Therefore, if an oral lesion is suspected as histoplasmosis, disseminated disease has to be excluded. A 66-year-old Sri Lankan male with diabetes and smoking who presented with oral ulcers was later diagnosed as disseminated histoplasmosis [5].

However, case series of localized oral histoplasmosis have been published in the recent past from several countries and most of the patients did not reveal pulmonary involvement [3]. Three patients reported from Sri Lanka had oral lesions without the involvement of other systems [6,7,9]. Nevertheless, due to the similarity of clinical symptoms, there is a possibility of misdiagnosing pulmonary histoplasmosis as pulmonary tuberculosis, especially if the latter is not microbiologically confirmed. Therefore, previous self-limiting pulmonary histoplasmosis cannot be excluded as Sri Lanka is hyper-endemic for tuberculosis [2].

Oral lesions may appear in any part of oral mucosa and the commonest sites are tongue, buccal mucosa and palate [2]. Lesions could be nodular, ulcerative, verrucous, or plaque-like. Oral histoplasmosis mimics other oral ulcerative lesions like chronic traumatic ulcers, squamous cell carcinoma, lymphomas, ulcerative necrotic gingivitis, stomatitis and ulcers of Crohn's disease and tuberculosis etc.[23]. It is important to be aware about this presentation, as it might be easily missed without a sound knowledge.

Diagnosis

Clinicians' lack of awareness about the available mycological facilities in the country leads to limited utilization of available resources, underestimation of the incidence of histoplasmosis in the country and importantly the incorrect diagnosis of the patient depriving the proper treatment.

Type of specimen suitable for diagnosis depends on the clinical presentation [4]. Biopsy of oral ulcer should be sent to histopathology laboratory as well as to mycology laboratory for direct microscopy and culture which is the gold standard test for diagnosis. Prolonged incubation is necessary to recover *Histoplasma* sp. [4]. Urinary antigen test and serum *Histoplasma* antibody test by immunodiffusion are also available in the Mycology Reference Laboratory at Medical Research Institute, Colombo.

In view of the diagnosis of the cases reported from Sri Lanka, incisional biopsies of the oral ulcers in two patients became positive in fungal studies [5,6]. Both revealed yeast cells in direct KOH smears and fungal cultures grew *Histoplasma capsulatum* which was confirmed by the demonstration of thermal dimorphism [5,6]. Pus and tissue from excisional biopsy of submandibular gland in a patient with oral ulcers and generalized lymphadenopathy revealed yeast cells in the direct smear and yielded *Histoplasma capsulatum* from the enriched culture after three weeks of incubation. Histopathology of the same biopsy specimen reported intracellular yeast cells with budding [10]. The diagnosis was confirmed in another patient by histopathological examination of an incisional biopsy of oral ulcer [7]. Grocott's Methenamine Silver stain of a bone marrow biopsy specimen of a patient with disseminated histoplasmosis lead to the diagnosis [8].

Treatment

Antifungal therapy is indicated in severe and moderately severe histoplasmosis whereas patients with mild disease of less than one month duration may recover without treatment [12]. Mild to moderate acute infection and chronic cavitatory histoplasmosis could be treated with oral itraconazole while severe and moderately severe acute pulmonary histoplasmosis and progressive disseminated disease warrants treatment with amphotericin B [4]. Duration of therapy depends on the severity of the infection and the immune status of the patient [12].

When considering the treatment delivered to the cases reported from Sri Lanka, a 24-year-old otherwise healthy female patient with disseminated histoplasmosis was successfully treated with intravenous amphotericin B for seven weeks followed by itraconazole for four months until all the clinical symptoms disappears [8]. Amphotericin B therapy for four weeks and subsequent two weeks of oral itraconazole lead to successful outcome in a 35-year-old male patient with disseminated histoplasmosis [11]. Oral ulcers caused by *Histoplasma* were cured with six weeks of itraconazole in a 66-year-old male [5]. Despite the initiation of antifungal therapy, four patients expired probably due to causes not related to histoplasmosis [5-7] .

Conclusion

Indigenous cases of histoplasmosis may be found in Sri Lanka. The patients could be immunocompetent and may not reveal a significant exposure history either. To further complicate the matter, they could present with atypical clinical features such as oral ulcers, without the involvement of respiratory tract or other systems. A high degree of suspicion and the knowledge about the available diagnostic tests will facilitate the diagnosis and proper treatment of histoplasmosis in Sri Lanka.

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The Bulletin of the Sri Lanka College of Microbiologists

The Bulletin of the Sri Lanka College of Microbiologists is the annual publication of the Sri Lanka College of Microbiologists issued along with the Annual Scientific Sessions of the College. The Bulletin includes the summaries of the speeches/lectures/symposia and abstracts of oral/ poster presentations to be made during the Annual Scientific Sessions in addition to reviews, research articles and case reports relevant to microbiology and infectious diseases sent by the membership. The aims of the bulletin are to encourage the membership to conduct and publish good quality research to support and improve the practice of microbiology in Sri Lanka and to share experiences to enrich and upgrade the professional standards.

All manuscripts will be subjected to review before acceptance and will be accepted with the understanding that the work is not being submitted simultaneously to another journal and has not been already published / accepted for publication elsewhere.

TYPES OF CONTRIBUTIONS

Review articles

Editorial board selects one or more from the articles submitted as review articles. This should contain less than 2000 words and address a microbiologically significant topic of current interest. This article should be supported by no more than 20 key references.

Research (original) articles

These should be in the format of introduction/background including the purpose of the study, materials and methods, results, discussion and conclusions. Each manuscript must have a structured abstract of 200 words giving the background, materials and methods, results and conclusions. The text should be limited to less than 2000 words and 15 references. Discussion should be clear and limited to matters arising directly from the results.

Articles

These articles should be limited to 1500 words and 12 references. Journal will give priority to articles dealing with topics of interest and importance in microbiology and infectious diseases in Sri Lanka.

Case reports

These should not exceed 750 words and 5 references and should be structured as Introduction, Case report and Discussion. Abstract is not required. Editorial board will be paying attention to the significance of the case report to the practice of microbiology in Sri Lanka.

Abstracts of presentations to be made at Annual Scientific Sessions

These should be limited to 350 words.

Photo quiz

This should be accompanied by a clear photograph and text. Limit your references to three for the answer. (Those submitted without references may be accepted if editors decide as suitable for publication).

Abstracts of research presentations (oral / poster) at Annual Scientific Sessions

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- Manuscripts should be submitted with **a cover letter** stating:
  - that the contents have not been published or accepted for publication elsewhere.
  - that the paper has not been submitted simultaneously to another journal.
- Cover letter should include a declaration signed by the principal author and co-authors to certify
  - the originality of the article.
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  - abide by the decision of the Editorial Board.
- The name, full mailing address, e-mail address and telephone number of the corresponding author should also be included.

Previous publication of some content of a paper does not necessarily mean that the paper will not be considered for publication in the Bulletin, but the Editorial Board should be made aware of this in the cover letter that accompanies the manuscript.

Authors should include all those who have contributed to the work described, including supervisors and if applicable, those interpreting and analysing data used in the study to be presented. Authors should meet all of the following criteria, and be able to take public responsibility for the content of the paper:

1. Conceived and planned the work that led to the paper, or interpreted the evidence it presents, or both.

2. Wrote the paper or reviewed successive versions, and took part in revising them.
3. Approved the final version.
4. Each author should have contributed sufficiently to the work to take public responsibility for the content.
5. Contributed to the intellectual content of the paper.
6. At least one of the authors of the paper should be a member of SLCM.

Collecting and assembling data reported in a paper and performing routine investigations are not, by themselves, criteria for authorship.

PREPARATION OF MANUSCRIPTS

All parts of the manuscript, including references, tables and figure legends should be typed with double-spacing and formatted in Times New Roman font (size 14 for the title and 12 for the rest of the article) for A4 sized paper. All pages of the manuscript should be numbered consecutively, starting with the title page.

The **title page** should contain the following:

1. Main title and subtitle (if any): capital letters should be used only for the first letter in the first word in the title and proper nouns. (Use Times New Roman font size 14, bold).
2. Name(s) of the author(s) should be given below the title. The author's surname should be preceded by the initial(s) or forename(s) but not by prefixes such as Mr. or Dr. or Prof. See above for guidelines regarding authorship. The name of the principal author should be stated first. Authors' names will be published in the order submitted by the principal author.
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Units/ abbreviations

Authors should follow the SI system of units (except for blood pressure which will continue to be expressed in mmHg). Abbreviations if used should be consistent throughout the text.

Photographs

All photographs of the patients will be published with covered eyes. Photo-micrographs should have scale markers that indicate the degree of magnification.

Tables

All tables must be double-spaced and numbered with Arabic numerals in the order in which they are cited in the text. The title should describe the contents of the table briefly and concisely. Explain all abbreviations and symbols as footnotes to the table.

Acknowledgements

Acknowledge only persons / organizations who have contributed to the scientific content and provided financial or technical support.

References

These should conform to the Vancouver style. The reference in the text should be numbered consecutively in Arabic numerals in parenthesis in the same line of the text in the order in which they appear in the text. The first five authors should be listed. If there are more than five then the first three should be listed followed by *et al*. An example is given below.

1. Dellit TH, Owens RC, McGowan JE et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clinical Infectious Diseases* 2007; **44**: 159-77.

PROOF READING

- The manuscript must be proof read by the author prior to submission.
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