

JOURNAL OF HEALTH AND TRANSLATIONAL MEDICINE
(formerly known as *Journal of the University of Malaya Medical Centre*)

JUMMEC

CONTENTS

Foreword

Plenary Lecture

Global Health Issues And Research Priorities In Middle Income Countries	1
<i>Frederick Altice</i>	
HIV Prevention And Treatment Strategies For Criminal Justice Populations – Evidence That Works	2
<i>Frederick Altice</i>	
Ethical Challenges In Stem Cell Research And Treatment	3
<i>Jeremy Sugarman</i>	

Research Colloquium

Addiction

Anxiety, Depression And Alcohol Use Among Clients Seeking Treatment In Government Drug Rehabilitation Centre, Malaysia	4
<i>R. Rashid, R. Ramli, W. A. Wan Mahmud, M. M. Ahmad Zahari, M. Maisarah, W.H Wan Azlinda Irnee, T. Seghatoleslam, M. N. Mohamed, M. H. Habil</i>	

Ageing and Regeneration

Nasogastric Feeding In Hospitalized Older Patients	5
<i>Nordin N, Tan MP</i>	
Mortality And Morbidity Associated With Falls In Older Patients Attending An Emergency Room In Malaysia	7
<i>Tan Maw Pin, Shahrul B. Kamaruzzaman, Philip J. H. Poi</i>	

HIV and Infectious Diseases

Implementation Science in HIV Research	8
<i>Frederick Altice</i>	
Ethics, Evidence and HIV Prevention	9
<i>Jeremy Sugarman</i>	
Molecular Epidemiology of HIV-1	10
<i>Tee Kok Keng.</i>	
Identifying novel determinants of immune recovery in HIV-infected individuals	11
<i>Reena Rajasuriar</i>	
The social determinants of HIV among fishermen in Kuantan, Malaysia	12
<i>Martin Choo</i>	
HIV health services in Malaysia's correctional system: The use of innovative diagnostic tools in tackling TB among this population	13
<i>Haider Al-Darraj, Joseph Bick</i>	

Medical Imaging

Retrograde degeneration of optic nerve and visual pathway in open angle glaucoma: a morphologic evaluation using 3T MRI	14
<i>S. Sidek, F. A. Rahman, K. Rahmat, N. Mohd Ramli, N. Mohd Ramli</i>	

Differentiating multiple system atrophy and Parkinson's disease on 3 T MRI: A novel use of decision tree	15
<i>Shalini Rajandran Nair, Tan Li Kuo, Norlisah Mohd Ramli, Lim Shen Yang, Kartini Rahmat, Hazman Mohd Nor</i>	

Microbiology and Parasitology

Comparison of Real Time Reverse Transcription-Polymerase Chain Reaction Assays for the Detection of Dengue Virus	16
<i>Tan KK, Johari J, Abdul-Jamil J, Zulkifle NI, Sulaiman S, Zainal N, Ab.Rahman HA, Sam SS, Teoh BT, AbuBakar S.</i>	

Permissiveness and Survivability Studies of Nipah Virus Infection of Human Monocytic THP-1 Cells Suggest a Role in Virus Spread	17
<i>Vunjia Tiong, Sazaly AbuBakar, Li-Yen Chang</i>	

Epidemiology and seasonality of respiratory viral infections in hospitalised children in Kuala Lumpur, Malaysia	18
<i>Chee-Sieng Khor, I-Ching Sam, Yoke-Fun Chan</i>	

Molecular characterisation of Chikungunya viruses from Malaysia	19
<i>Sam IC, Chan YF, Chan SY, Loong SK.</i>	

Insights into Bacterial Pathogenesis	21
<i>Jamuna Vadivelu</i>	

Respiratory Viral Infections in Children: An Overview	23
<i>Zamberi Sekawi</i>	

Isolation and characterisation of environmental phages of <i>Burkholderia pseudomallei</i>	24
<i>Ong, G.H., Chang L.Y., Vadivelu J.</i>	

Antiviral Effects of a Malaysia Medicinal Plant (<i>Phyllanthus</i>)	25
<i>Tan WC, Lee SH, Tang YQ, Sekaran SD</i>	

<i>Phyllanthus</i> , a broad spectrum anti-cancer agent: Properties and mechanisms of activities	26
<i>Lee SH, Tang YQ, Indu Bala Jaganath, Sekaran SD</i>	

Dengue Virus and the Vascular Endothelium	27
<i>Rathakrishnan A, Rajendran P, Alhoot MA, Manikam R, Sekaran SD</i>	

Immune Responses Involvement in Dengue Patients at Different Levels of Severity	28
<i>Rathakrishnan A, Yeo SL, Rajendran P, Alhoot MA, Lee SH, Manikam R, Sekaran SD</i>	

Novel Synthetic Antimicrobial Peptides With Potent <i>In Vitro</i> And <i>In Vivo</i> Antimicrobial Activities Against <i>Streptococcus Pneumoniae</i>	29
<i>Le CF, Mohd Yusof MY, Sekaran SD</i>	

Occupational and Environmental Health

Serum Cortisol and Cardiovascular Effects	30
<i>Marzuki Isahak, Azlan Darus, Moy Foong Ming, Retneswari Masilamani.</i>	

A cross sectional study on hand arm vibration syndrome among a group of tree fellers in a tropical environment	31
<i>Anselm Ting Su, Setsuo Maeda, Jin Fukumoto, Nobuyuki Miyai, Marzuki Isahak, Atsushi Yoshioka, Ryuichi Nakajima, Awang Bulgiba, Kazuhisa Miyashita</i>	

Symptoms of Sick Building Syndrome , Occupational Impact and Quality of Indoor Air in an Office Environment in Kuala Lumpur	33
<i>Azlan Darus, Fatin Syakira Abdul Manab</i>	
Prevalence and associated factors of stress in the Malaysian Police Force	35
<i>Retneswari Masilamani, Awang Bulgiba, Karuthan Chinna, Azlan Darus, Marzuki Isahak, Shathanapriya Kandiben, David Koh</i>	
A prospective study of work ability and multisite musculoskeletal pain among hospital based nurses	36
<i>Victor Hoe, Helen Kelsall, Donna Urquhart, Malcolm Sim</i>	
Physical and Psychosocial Factors Associated with Musculoskeletal Disorders Among Hospital Based Nurses in Australia	37
<i>Hoe VCW, Kelsall HL, Urquhart DM, Sim MR</i>	
Ophthalmology	
Congenital Rubella Syndrome In An Infant Despite Maternal Vaccination	38
<i>Florence Santiagu, Choo May May</i>	
Correlation of macula thickness with visual acuity and stage of retinopathy using Optical Coherence Tomography (OCT) in Diabetic patients	39
<i>N Ramli, Z Mimiwati, A Fauzi</i>	
Green tea and soybean flavonoids exert differential effects on the survival of RGC-5 cells exposed to various types of oxidative stress	40
<i>TA Kamalden, NN Osborne</i>	
Orthopaedics	
A Rare Presentation of Subacute Ipsilateral Neuropathic Arthropathy Involving Multiple Joints due to Syringomelia and Type-1 Arnold-Chiari Malformation	41
<i>Norazian Kamisan, T Ravi, Tunku Kamarul</i>	
A New Method of Measuring Gastrocnemius Tightness: Intra-and Inter-Observer Reliability	42
<i>Y P Chua, A Saw, S R Kanthan</i>	
Multiple ligament injury with common peroneal nerve palsy after traumatic dislocation of the knee	43
<i>M. Zubair, M. Razif Bin M. Ali, Ng Wuey Min, Shamsul Iskandar</i>	
The Effect of Growth Differentiation Factor-5 (GDF-5) on the Proliferation and Tenogenic Differentiation Potential of Human mesenchymal Stem Cells In Vitro	45
<i>Tan SL, Selvaratnam L, Ahmad RE, Ahmad TS, Merican AM, Abbas AA, Ng WM, Kamarul T</i>	
Chronic Osteomyelitis Of The Rib Mimicking A Sarcoma: A Case Report	46
<i>Chew Chin Seong, Azura Mansor, Vivek Ajit Singh</i>	
Paediatrics	
Genetic Analyses of Myotonic Dystrophy Type 1 in Malaysia	47
<i>Kaitlin K Ambrose, Mohd Taufik I, Lian LH, Goh KJ, Wong KT, Thong MK</i>	
Aetiology Of Pneumonia In Children And Usefulness Of C-reactive Protein In The Management Of Childhood Pneumonia	48
<i>Fairuz Rani, Rachel Jiun, Anna Nathan, Caroline Westerhout, I-Ching Sam, Jessie de Bruyne</i>	
Autoimmune Liver Disease in Malaysian Children	49
<i>Su Han Lum, Ruey Terng Ng, Benjamin TY Lim, Kim Mum Khoh, Christopher CM Boey, Way Seah Lee</i>	
Conjoined Twins	50
<i>K Somasundaram</i>	

Crohn Disease – a Clinico-epidemiology Study from Malaysia	51
<i>Alvin Kim Mun Khoh, Darren Tan, Ruey Terng Ng, Pei Fan Chai, Christopher CM Boey, Way Seah Lee</i>	
One in Five Overweight / Obese Adolescents in the Community Has Metabolic Syndrome	52
<i>Muhammad Yazid Jalaludin, Aisha Fadhilah Abang Abdullah, Noorasekin Saiman, Nurshadia Samingan, Zahurin Mohame², Fatimah Harun</i>	
Appropriateness and Contributive Yield of Pediatric Gastrointestinal Endoscopy: A Single-centre Audit Study	54
<i>Hafiah Zainuddin, Christopher CM Boey, Way Seah Lee</i>	
Paediatric Research in Malaysia in the Last 50 Years	56
<i>Boo Nem Yun</i>	
Population Health	
Malaysian Breast Cancer Survivorship Cohort (MyBCC) study	58
<i>Nur Aishah Mohd Taib, Tin Tin Su, Nabilla Al Sadat, Maznah Dahlui, Hazreen Abdul Majid, Nirmla Bhoo Pathy, Shamsinah Hussain, Mohd Nahar Azmi Mohamed, Yip Cheng Har and MyBCC team</i>	
MyHEARTS - Risk Factors For Chronic Non-Communicable Diseases Among Adolescents	59
<i>Nabilla Al Sadat, Muhammad Yazid Bin Jalaluddin, Hazreen Abdul Majid, Nowrozy Kamar, Tin Tin Su and MyHeARTs team</i>	
“PARTNER (Participatory Action Research Through Negotiation and Empowerment of Residents)” for low income urban community.....	61
<i>Awang Bulgiba, Rusdi bin AbdRashid, Nasruddin Jaafar, Adeeba Kamarulzaman, KhooEeMing, Liam Murray</i>	
Proteomics Research	
Proteomic Approaches For Mushroom Protein Profiling: Proteinchip And SELDI-ToF Complement Electrophoretic Analysis	63
<i>Lau Beng Fye, Noorlidah Abdullah, Norhaniza Aminudin, Amy Tan Bee Bee</i>	
Identification Of ACE Inhibitory Peptides From <i>Pleurotus Cystidiosus</i> O.K. Miller And <i>Agaricus Bisporus</i> (J.E. Lange) Imbach By LC-MS/MS	64
<i>Lau Ching Ching, Noorlidah Abdullah, Adawiyah Suriza Shuib</i>	
Sandwich Enzyme-Linked Lectin Assay: A Simple Method For Detection Of Total O-Glycans In Biological Samples	65
<i>Lee Cheng Siang, Puteri Shafinaz AbdulRahman, Veer Bhavanandan, Onn Haji Hashim</i>	
Proteomics Identification Of Differentially Expressed Proteins In HT-29 Cell Post-Treatment With <i>Pereskia Bleo</i> Extracts	66
<i>Lum Ai Theng, Norhaniza Aminudin, Puteri Shafinaz Abdul Rahman</i>	
Comparative SELDI-ToF/MS Analysis Of Antihypertensive Proteins From <i>Termitomyces Heimii</i> Natarajan And <i>Ganoderma Lucidum</i> Karst	67
<i>Noor Hasni Mohd Fadzil, Cahaya Fariza Misnan, Norhaniza Aminudin, Noorlidah Abdullah</i>	
Proteomic Profiling of Milk Fat Globule Membrane Associated Proteins of Ruminants And Humans	68
<i>Thaneswari Juvarajah, Onn Haji Hashim, Fung Shin Yee, Puteri Shafinaz Abdul Rahman</i>	
Serum Proteomic Analysis Of Patients With Bone Tumour	69
<i>Wan Izlina Wan Ibrahim, Vivek Ajit Singh, Onn Haji Hashim, Puteri Shafinaz Akmar Abdul Rahman</i>	
Rehabilitation Medicine	
Research in Non invasive brain stimulation to enhance neuroplasticity and recovery in Stroke rehabilitation	70
<i>Lydia Abdul Latif</i>	

Social and Preventive Medicine

The Application of Intra-Class Correlation Coefficient (ICC) in Assessing the Reliability of Medical Instruments Measuring Continuous Outcomes	71
<i>Rafdzah Zaki, Awang Bulgiba, Noor Azina Ismail</i>	
Patterns of health service utilization among Malaysian elderly with chronic pain	72
<i>Lily Rafidah Mohamed Zaki, Noran Naqiah Hairi</i>	
Cost Effective Analysis of Different Types of Recall on Patients' Response Rate in a Pap Smear Screening Program	73
<i>Rima Marhayu Abdul Rashid, Maznah Dahlui</i>	
Exploring factors associated with physical activity among adolescents in Sarawak: A grounded theory approach	74
<i>Saimon Rosalia, Choo Wan Yuen and Bulgiba Awang</i>	
The different smoking stages among adolescents and its associated factors	75
<i>Premila Devi, Noran N. Hairi, Nabilla Al Sadat</i>	
Health Related Quality Of Life In Malaysian Thalassaemia Patients Treated With Iron Chelation	76
<i>Jenifer John Kidi, Maznah Dahlui, Hishamshah Mohd.Ibrahim</i>	
Surgery	
The Detection Rate Of Prostate Cancer Using Prostate Specific Antigen (Psa) And Digital Rectal Examination (DRE) In Sabah	77
<i>Siang Lin Foo, Jasmine Lim, TeckMeng Tham, Teck Boon Wong, TengAik Ong</i>	
A grounded explanation on why women present with advanced breast cancer	79
<i>Taib NA, Yip CH, Low WY</i>	
Perforator Flaps in UMMC	81
<i>Magaret Leow Poh Gaik</i>	
Gene Expression Signatures For Early And Advanced Stage CRC	82
<i>Tze Pheng Lau, April Camilla Roslani, Lay Hoong Lian, Kek Heng Chua</i>	
Latissimus Dorsi Flap as a closure method in locally advanced breast cancer	83
<i>Ng CH, Teh YC, Taib NA, Yip CH</i>	
Tumour necrosis factor receptor-associated factor 1 (TRAF1) has a functional role in renal carcinoma (RCC) apoptosis, has decreased expression in RCC samples, and may have potential for targeted therapy	84
<i>Retnagowri Rajandram, Nigel C. Bennett, Zhiqiang Wang, Joanna Perry-Keene, David A. Vesey, David W. Johnson, Glenda C. Gobe</i>	
Genetic predisposition to breast cancer in Malaysian Breast Cancer Patients: Update from the Malaysian Breast Cancer Genetic Study (MyBrCa)	86
<i>Soo Hwang Teo, Yoon Sook-Yee, Thong Meow Keong, Phuah Sze Yee, Peter Kang, Kang In Nee, Norhashimah Hassan, Hanis Hasmad, Kavitta Sivanandan, Shivaani Mariapun, Woo Yin Ling, Cheng Har Yip, Nur Aishah Mohd Taib</i>	
Polymorphism in the APOE gene and promoter in the functional outcome of traumatic brain injury in the Malaysian population	89
<i>Poovindran A. R., Ganesan D., Wong K. T.</i>	
Association between ethnicity and survival after breast cancer in a multi-ethnic Asian setting: results from the Singapore-Malaysia hospital-based breast cancer registry	90
<i>Bhoo Pathy N, Verkooijen HM, Taib NA, Lee SC, Saxena N, lau P, Yip CH, Hartman M.</i>	

Shifting paradigms in surgical training – Initial experience with the University Malaya Neurosurgical simulation system	91
<i>V Waran, V Narayanan, Owen SLF, Aziz TZ</i>	
Women’s Health	
Evaluation of human papillomavirus (HPV) infection among women in UMMC – comparison between thin prep and fournier’s self sampling	92
<i>Hamzah H; Aziz A, Lim BK, Woo YL, Omar SZ</i>	
Induction of labour with Foley’s catheter in women with previous caesarean section	93
<i>Nuryuziliana D, Sofiah S, Vijeandreh S</i>	
The impact of postpartum haemorrhage (PPH) on maternal morbidity	94
<i>Mackeen A, Khong SY</i>	
The effect of knowledge on the desire for multiple pregnancies among patients with subfertility	96
<i>Razali N, Latar IL</i>	
The effectiveness and acceptability of self-sampling against conventional Pap smear in University Malaya Medical Centre (UMMC)	97
<i>Aziz A, Hamzah H, Lim BK, Woo YL, Omar SZ</i>	



FOREWORD by the editor-in-chief of JUMMEC

In conjunction with the celebration of the 50th anniversary of the Faculty of Medicine, University of Malaya, it is with great pleasure that a special issue of JUMMEC entitled **“JUMMEC-RESFOM 50TH ANNIVERSARY EDITION”** is now published to commemorate this special occasion. The theme of the event, which was held on the 21st till the 23rd of January 2013, has been titled **“Building on Heritage, Research Week, Faculty of Medicine”**. The 3-day event was held in the Faculty of Medicine, UM and conducted by the research centers under the Health and Translational Medicine Cluster (HTMC).

This issue contains the scientific abstracts of the talks/presentations related to research in the medical and dental disciplines by distinguished speakers who have excelled in their respective fields. Lectures were delivered from overseas and local universities/institutions are presented at the Research Colloquium as part of the activities of the Research Week. Many of the contents of the lectures and talks can be found on the FOM research website which is available at www.resfom.com.

It is an honour and a privilege for me to be the editor-in- chief of JUMMEC, whilst the faculty is in its 50th year and it is my sincere hope that the faculty will continue to strive in research for many years to come. JUMMEC having existed since 1996, and since then JUMMEC has been a great supporter of good research undertakings and outputs. It is hoped that following this celebration, academics everywhere will continue to show their support for JUMMEC, being part of the faculty of Medicine’s scientific support initiative to further enhance the research outreach of this journal.

Happy 50th Anniversary FOM!

With Best Wishes,

Professor Dr. Tunku Kamarul Zaman Tunku Zainol Abidin
Editor-in-Chief
JUMMEC

GLOBAL HEALTH ISSUES AND RESEARCH PRIORITIES IN MIDDLE INCOME COUNTRIES

Frederick Altice

Yale University

Developing a research agenda and setting priorities for medical and public health research requires a careful assessment of the magnitude and severity of a number of diseases that impact an effected population. It is well known that the global burden of diseases (GBD) differs dramatically for low-, middle- and high-income countries. A review of the GBD of over 220 diseases and injuries and more than 43 risk factors for 21 regions of the world provides insight for setting research priorities. Some diseases and injuries, however, disproportionately are age or gender specific and contribute differentially to morbidity rather than mortality. Research priorities should include the biological basis of disease, translation from bench to bedside and direct clinical care, including biological and behavioral interventions. From a larger perspective, research priorities should have high impact, transform science or clinical care and be scalable and translatable on a population basis using scientific approaches that incorporate implementation science techniques. Improving the health and well-being of the world's population is a moral imperative and is essential for global stability, reducing health disparities and progress. The vast energies, technologies, and resources that are pouring into global health have given us the capacity to fight disease, remedy disability, and address the deep inequalities in health between populations.

HIV PREVENTION AND TREATMENT STRATEGIES FOR CRIMINAL JUSTICE POPULATIONS - EVIDENCE THAT WORKS

Frederick Altice

Yale University

The proportion of people cycling through criminal justice settings (CJS) is staggering and increasing. Increases in incarceration over the past few decades have been in response to harsh laws and policies that target people who use drugs (PWUDs) and favor incarceration over treatment. As a result, there has been a concentration of infectious diseases, including HIV infection, among those involved in the CJS. In this presentation, the epidemiology of incarceration, substance abuse and HIV will be reviewed, followed by a review of evidence-based interventions that are effective in community settings. Last, a review of what is known about implementing evidence-based interventions within CJS that targets both substance abuse and HIV treatment outcomes, including medication-assisted therapies (MAT) will be reviewed. Studies that implement MAT such as the use of methadone, buprenorphine and extended-release naltrexone (XR-NTX) in CJS for treating opioid dependence and the use of XR-NTX for treating alcohol use disorders will be reviewed. Last, released prisoners with HIV and substance use disorders have poor post-release treatment outcomes and a review of other social and environmental factors that facilitate improved outcomes will be reviewed.

ETHICAL CHALLENGES IN STEM CELL RESEARCH AND TREATMENT

Jeremy Sugarman

Johns Hopkins University

Despite considerable scientific advances, a range of ethical issues are associated with stem cell research and treatment. Understanding these issues is important for patients, clinicians, scientists and policy-makers.

ANXIETY, DEPRESSION AND ALCOHOL USE AMONG CLIENTS SEEKING TREATMENT IN GOVERNMENT DRUG REHABILITATION CENTRE, MALAYSIA

R. Rashid¹, R. Ramli², W. A. Wan Mahmud¹, M. M. Ahmad Zahari¹, M. Maisarah¹, W.H Wan Azlinda Irnee¹, T. Seghatoleslam¹, M. N. Mohamed², M. H. Habil¹

¹University of Malaya Centre for Addiction Science (UMCAS), University of Malaya, Kuala Lumpur, Malaysia

²National Anti Drug Agency (NADA), Kuala Lumpur, Malaysia

Introduction

Excessive alcohol use and related problems are commonly being observed among clients in methadone maintenance treatment (MMT), yet relatively little is known about the psychological and social determinants of alcohol-related attitudes and behaviours during treatment.

Objectives

To investigate the prevalence of psychiatric morbidity, alcohol use and psychosocial correlates among the clients.

Methods

Cross-sectional study involving 201 inmates age 18 years and above with written consent who currently seeking treatment on volunteer basis under the government run rehabilitation centre, Kuala Lumpur. The study was conducted in December 2011 with approval from the Ethic committee board from the university hospital. The psychiatric morbidity measured by MINI Neuropsychiatric Inventory (MINI ver 5.0) and alcohol use measured by AUDIT and ASSIST.

Results

The current prevalence of anxiety and depression are 27.9% and 39.8% respectively. The lifetime prevalence for depression is 21.9%. We also found that lifetime and current prevalence of alcohol use are 77% and 37% respectively. Univariate analysis showed significant association between psychiatric morbidity and alcohol use (Odd ratio=1.9, P<0.05). However, no significance association found between alcohol use with age, gender, ethnicity, marital status and religion.

Conclusion

There is a need for specialised psychiatric and dual diagnosis services in Cure and Care 1-Malaysia clinic.

References

National Health and Morbidity Survey 1996. Institute of Public Health, Ministry of Health, Malaysia, 1997. In: Advocacy in action. *The Globe Issue 1*. Global Alcohol Policy Alliance, 2003.

NASOGASTRIC FEEDING IN HOSPITALIZED OLDER PATIENTS

Nordin N, Tan MP

Department of Medicine, Faculty of Medicine, University Malaya Medical Centre, Kuala Lumpur

Introduction

Older individuals are at increased risk for dysphagia due to changes in the swallowing mechanism due to various disorders associated with ageing, including stroke, neurodegenerative disorders and local upper gastrointestinal tract disorders. One of the consequences of dysphagia is aspiration pneumonia. Physiologically, oropharyngeal colonization by pathogenic organisms is prevented by the mechanical clearance provided by chewing and swallowing. In tube fed patients, the oropharynx is devoid of this protective effect. Therefore, oral feeding is believed to prevent aspiration, improve function, promote physical comfort and prolong life. However, the above assumptions have not been supported by clinical evidence.

Objectives

1. To determine the characteristics of individuals who receive tube feeding in our geriatric ward
2. To determine the frequency and types of complication associated with tube feeding in our older patients

Methods

Consecutive patients admitted to the geriatric ward at the University of Malaya Medical Centre with nasogastric feeding either inserted earlier or during the current admission were recruited into the study. All patients will have a swallowing test done by trained doctors on the ward; to confirm the indications for nasogastric feeding. Data was collected at baseline and prior to discharge.

Results

Thirty-five subjects, mean age 80 years, were recruited to the study. The main indications for NG tube feeding were reduced conscious level or coma (65.7%), dysphagia (28.6%) and stroke (22.9%). 71.42% of patients had at least one complication. Complication reported included gastroparesis (42.9%), aspiration pneumonia (34.3%) and electrolyte imbalance (22.9%).

Mechanical complications, e.g. mucosal ulceration, perforation and tube dislodgement was low. 28% had no complications. 14 (40 %) had died during their admission.

Conclusion

Complication rates are high among patients receiving NG feeding on our acute geriatric ward. It is important that carers receive adequate training about gastroparesis and feeding techniques to reduce the complications of aspiration. As this was a pilot study further research will now focus on factors leading to increased complications as well as the acceptability and burden of NG feeding to patients and carers.

MORTALITY AND MORBIDITY ASSOCIATED WITH FALLS IN OLDER PATIENTS ATTENDING AN EMERGENCY ROOM IN MALAYSIA

Tan Maw Pin, Shahrul B. Kamaruzzaman, Philip J. H. Poi

Division of Geriatric Medicine, Department of Medicine, Faculty of Medicine, University of Malaya

Background

Injuries resulting from falls in older people incur large economic, social and psychological burdens to individuals, careers and the society. The consequences of falls in the older population in Malaysia have not been defined previously.

Objective

To determine the effects of falls in terms of injury rate, activities of daily living and mortality in older fallers attending the Accident and Emergency (A&E) department at the University of Malaya Medical Centre.

Method

Consecutive patients over the age of 65 years presenting to A&E over a 6 month period were included in the study. Activities of daily living (ADLs) were assessed at presentation and one-year follow-up, using the Barthel Index. Injury rates at presentation were recorded. Vital status was determined at one-year.

Results

72/198 (37%) sustained fractures, 32/72 (44%) of which were hip fractures. Mortality data was available in 168 patients. 41/168 (24%) had died at 12-month follow-up, with 41% of deaths occurring in the first 4 weeks. Survivors showed reductions in all ADL domains at one year, with a significant reduction in total Barthel score (20 vs 18, $p < 0.001$).

Conclusion

The older fallers presenting to our A&E department had a 16% hip fracture rate and a 24% one-year mortality rate, while survivors experienced significantly increased dependency. Studies to develop effective interventions for this highly vulnerable group of patients are urgently required as the number of older fallers are likely to increase with our rapidly ageing population.

IMPLEMENTATION SCIENCE IN HIV RESEARCH

Frederick Altice
Yale University

Health care providers and public health authorities are increasingly aware that findings from promising research studies do not easily translate into improved human health. The science of implementation and dissemination comprises a multidisciplinary set of theories and methods aimed at improving this process of translation from research evidence to everyday health-related practices. Implementation research, in particular, examines how interventions can be better integrated into diverse practice settings, and emphasizes direct engagement with the institutions and communities where health interventions are introduced. In this presentation, we will provide definitions and research strategies that involve implementation science, review some evidence-based practices that favor improved HIV treatment outcomes found in either clinical trials or in clinical care settings, and provide examples of implementation science strategies that impact change and apply it to a real-world setting. Last, we will examine the HIV prevention and treatment situation in a middle-income, specifically Ukraine, where HIV is fueled primarily among people who inject drugs and where HIV treatment outcomes have worsened while global HIV treatment outcomes have generally improved.

ETHICS, EVIDENCE AND HIV PREVENTION

Jeremy Sugarman

Johns Hopkins University

The global burden of HIV infection supports a broad moral claim for developing effective means of prevention and treatment. Nevertheless, conducting this research inevitably encounters ethical challenges. Evidence-based practices can help to appropriately navigate them.

MOLECULAR EPIDEMIOLOGY OF HIV-1

Tee Kok Keng

Centre of Excellence for Research in Aids, Faculty of Medicine, University of Malaya

Advances in molecular genetics in the recent decades have greatly enhanced our knowledge on the breadth and diversity of microbial world. Although the availability of pathogen genetic information is essential, especially where Malaysia and other Southeast Asian countries are widely thought to be the geographical “melting pot” for various emerging and re-emerging infectious diseases, such information are usually sporadic or lack explanatory power. In order to obtain and integrate population and exposure information i.e. molecular genetic data, a comprehensive pathogen surveillance initiative is therefore essential. Here, we describe the molecular epidemiological surveillance of the human immunodeficiency virus type 1 (HIV-1) conducted in Malaysia and show tremendous genetic complexities of the virus, that includes the discovery of at least five novel HIV-1 strains during the last decade.

IDENTIFYING NOVEL DETERMINANTS OF IMMUNE RECOVERY IN HIV-INFECTED INDIVIDUALS

Reena Rajasuriar

Centre of Excellence for Research in Aids/Department of Pharmacy, Faculty of Medicine, University of Malaya

Combination antiretroviral therapy (cART) has led to a dramatic improvement in the mortality of patients with HIV infection however, long-term outcome is dependent on the adequate recovery of CD4 T-cells which is highly variable following cART. In developing countries like Malaysia where treatment in HIV-infected patients is started late (average baseline CD4 T-cell count at initiation of cART is $<200\text{cells}/\mu\text{l}$), up to 40% of patients fail to achieve a normal CD4 T-cell count (defined as $>500\text{cells}/\mu\text{l}$) despite years of suppressive therapy. There is now growing evidence that patients failing to reach counts $>500\text{cells}/\mu\text{l}$ are at increased risk of AIDS and more importantly non-AIDS defining illnesses including cardiovascular and liver disease and bone-related abnormalities. In these patients, alternative immune based therapies might be important to boost CD4 T-cell recovery apart from standard cART regimens currently available. This presentation will cover current efforts by CERiA researchers to understand the functional significance of key single nucleotide polymorphisms (SNPs) on immune recovery in HIV-infected patients. The presentation will focus on a genetic SNP in the interleukin-7 receptor (IL-7R) gene which has been shown to affect T-cell homeostasis and survival. We will present preliminary data on the influence of this SNP on immune reconstitution among HIV-infected patients receiving suppressive cART.

THE SOCIAL DETERMINANTS OF HIV AMONG FISHERMEN IN KUANTAN, MALAYSIA

Martin Choo

Centre of Excellence for Research in Aids, Faculty of Medicine, University of Malaya

Since the late 1980's, HIV has infected more than 30 million people worldwide. However, we now acknowledge that some populations are more at risk for HIV than others. Among those most at risk are fishermen. Since 2008, CERiA has been studying HIV among fishermen in Malaysia under Project Waves. In our 2011 survey conducted in Kuantan, Pahang, more than one in every 10 fishermen was infected with HIV. The majority of infections stem from injection drug use, and more than one-third of Kuantan fishermen injected drugs. Further analysis on data obtained from Kuantan suggests that HIV risk among fishermen have social determinants, and drug use among fishermen serves particular occupational and social functions. In this presentation, we will explore the social determinants of HIV and occupational functions of drug use among fishermen in Kuantan. These factors contribute to a better understanding of the high prevalence of HIV found in this population.

HIV HEALTH SERVICES IN MALAYSIA'S CORRECTIONAL SYSTEM: THE USE OF INNOVATIVE DIAGNOSTIC TOOLS IN TACKLING TB AMONG THIS POPULATION

Haider Al-Darraj, Joseph Bick

Centre of Excellence for Research in Aids, Faculty of Medicine, University of Malaya

Tuberculosis (TB) remains a major cause of morbidity and mortality in the correctional facilities of the low- to middle-income countries. Delay in TB diagnosis and treatment initiation, particularly among HIV-infected inmates, contributes largely to the increasing individual mortality and transmission of the diseases to other inmates. Lack of accurate and fast diagnostic tools represent one of the major factors to cause this delay. In a study of HIV infected inmates in Kajang prison, the new GeneXpert MTB/RIF technology was employed to screen for TB. Among 131 participants, the majority was male, under 40-years old and had injected drugs prior to current incarceration. GeneXpert MTB/RIF managed to detect an additional eight (6%) TB cases, with an increase of 35% in current TB case detection rate. This presentation establishes the urgent need for regular TB screening program in Malaysia's correctional facilities. Our study shows the importance of utilizing new technologies to increase case detection and proper management of infectious cases to ultimately reduce TB transmission in these settings.

RETROGRADE DEGENERATION OF OPTIC NERVE AND VISUAL PATHWAY IN OPEN ANGLE GLAUCOMA: A MORPHOLOGIC EVALUATION USING 3T MRI

S. Sidek, F. A. Rahman, K. Rahmat, N. Mohd Ramli, N. Mohd Ramli

Department of Biomedical Imaging, University Malaya Research Imaging Centre

Purpose

To assess glaucoma disease and the severity causing retrograde degeneration and atrophy of the optic nerve and optic radiation by using volumetric assessment and diffusion tensor imaging with 3T MRI. To measure the optic nerve volume, fractional anisotropy (FA) and mean diffusivity (MD) for optic nerve and optic radiation in patients with bilateral mild and severe glaucoma and comparison made with normal subjects.

Methods and Materials

90 subjects with ages ranging from 40 to 80 years old (30 normal subjects, 30 mild glaucoma, 30 severe glaucoma) underwent 3T MRI. Images were acquired with AX FSPGR 3D sequence (TE 1.868; TR 6.824 1.2mm) and DTI. The acquired images were post-processed using NIFTI (Neuroimaging Informatics Technology Initiative) format. Using NeuRoi software, each optic nerve volume was measured. Using Functool GE DTI software, the FA and MD values were obtained

from each optic nerve and optic radiation. We evaluated 180 optic nerves and 180 optic radiations.

Results

Multiple comparisons show significant difference of the optic nerve volume and FA and MD of the optic nerve and optic radiation, between normal subject and mild glaucoma group ($p \leq 0.001$), between normal subject and severe glaucoma group ($p \leq 0.001$) and between mild glaucoma group and severe glaucoma group ($p \leq 0.001$).

Conclusion

Retrograde degeneration of optic nerve and optic radiation occurs in glaucoma and the volume loss, reduction of the FA values and increasing MD values correlates with disease severity.

These findings highlight the importance of aggressive therapy for those patients at highest risk.

DIFFERENTIATING MULTIPLE SYSTEM ATROPHY AND PARKINSON'S DISEASE ON 3 T MRI: A NOVEL USE OF DECISION TREE

Shalini Rajandran Nair¹, Tan Li Kuo¹, Norlisah Mohd Ramli¹, Lim Shen Yang², Kartini Rahmat¹, Hazman Mohd Nor¹

¹Department of Biomedical Imaging, University Malaya Research Imaging Centre

²Neurology Unit, Department of Medicine, University Malaya

Purpose

Differentiation of multiple system atrophy (MSA) and Parkinson's disease (PD) remains a clinical challenge. The purpose of this study was to develop a decision tree using parameters obtained from standard MRI and diffusion tensor imaging (DTI) to distinguish these clinical entities.

Methods

We performed standard MRI brain and DTI at 3.0T on 26 PD and 13 MSA patients. Linear, volumetry and DTI (fractional anisotropy and mean diffusivity) of putamen, substantia nigra, pons, middle cerebellar peduncles (MCP) and cerebellum were measured. A three-node decision tree was developed, with the aim of 100% specificity at node 1, 100% sensitivity at node 2 and highest combined sensitivity and specificity at node 3.

Results

Mean MCP width, anteroposterior diameter of pons and mean FA MCP with cut-off values of 14.6 mm, 21.8 mm and 0.55 respectively, were selected for the decision tree from nine parameters (mean width, FA and MD of MCP; anteroposterior diameter of pons; cerebellar FA and volume; pons and mean putamen volume; mean FA substantia nigra compacta-rostral) that showed statistically significant ($P < 0.05$) differences between MSA and PD. The decision tree accurately classified 12 out of 13 MSA patients with an overall 92% sensitivity, 96% specificity, 92% PPV and 96% NPV.

Conclusion

The decision tree could be used as a diagnostic algorithm in the differentiation of MSA and PD.

COMPARISON OF REAL TIME REVERSE TRANSCRIPTION-POLYMERASE CHAIN REACTION ASSAYS FOR THE DETECTION OF DENGUE VIRUS

Tan KK, Johari J, Abdul-Jamil J, Zulkifle NI, Sulaiman S, Zainal N, Ab.Rahman HA, Sam SS, Teoh BT, AbuBakar S

Tropical Infectious Diseases Research & Education Centre, Department of Medical Microbiology, University of Malaya, Malaysia.

Globally, dengue has emerged as a major public health problem. Prompt diagnosis, especially during the acute phase of illness is essential for immediate and appropriate disease management. In the present study, we evaluated two dengue real time reverse transcription-polymerase chain reaction (RT-PCR) kits (in-house and PrimerDesign™ Genesig) for the detection of dengue virus serotypes 1, 2, 3 and 4 against in-house developed 2-step multiplex RT-PCR assay.

In order to assess the ability of the real time RT-PCR kits to detect all major circulating dengue strains in Malaysia, a total of 14 dengue subtypes comprising of serotypes 1, 2, 3 and 4 were used. These isolates represent the current and past circulating dengue virus genotypes in the country. The viruses were propagated through one passage in cell culture prior to the testing. The overall analytical reactivity is 100% (14/14) for both real time RT-PCR kits.

The performance of both real time RT-PCR assays was examined in comparison to the in-house 2-step multiplex RT-PCR assay. A total of 74 acute dengue-suspected samples were obtained from the Diagnostic Virology Repository at University Malaya Medical Center. All samples were tested negative by IgM capture ELISA. The percentage of positive samples by in-house real time RT-PCR, commercial real time RT-PCR and conventional in-house RT-PCR assays were 27.02% (20/74), 33.78 % (25/74) and 32.74% (24/74), respectively.

Findings from the study suggest both the in-house and commercial real time RT-PCR kits were able to detect all the major circulating dengue strains in Malaysia. The performance of commercial real time RT-PCR kits is comparable to that of the conventional in-house RT-PCR method.

PERMISSIVENESS AND SURVIVABILITY STUDIES OF NIPAH VIRUS INFECTION OF HUMAN MONOCYTIC THP-1 CELLS SUGGEST A ROLE IN VIRUS SPREAD

Vunjia Tiong, Sazaly AbuBakar, Li-Yen Chang*

Tropical Infectious Diseases Research and Education Centre (TIDREC), Department of Medical Microbiology, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia.

**Corresponding author email: changliyen@um.edu.my*

Nipah virus is an emergent infectious agent that causes severe diseases in humans and animals. First identified in an outbreak in Malaysia in 1998/1999, the zoonotic paramyxovirus has also caused outbreaks almost annually in Bangladesh and India resulting in mortality rates much higher than in Malaysia. Pathologic findings of NiV infection in human patients have shown a multi-organ involvement including the lungs, spleen, kidney and heart as well as a major involvement of the central nervous system. How NiV is able to efficiently spread and disseminate throughout the body is as yet unknown. A possible route of virus spread may involve circulating monocytes, a mechanism that has been implicated in the spread of other viruses. Through the process of extravasation, monocytes are able to exit the circulatory system to enter the surrounding tissues. We have found that following NiV infection, the human monocytic THP-1 cells were not rapidly destroyed, unlike more susceptible cells such as epithelial and fibroblast cells. There was also a general lack of cytopathic effect and the infected cells were able to sustain virus replication over several days. The survivability of the infected THP-1 is important as this would allow time for the infected monocytes to circulate the body. Additionally, NiV-infected and non-infected monocytes were examined for their transmigration ability across an endothelial monolayer. Our findings suggest a role for circulating infected monocytes that may aid the spread of virus throughout the body.

EPIDEMIOLOGY AND SEASONALITY OF RESPIRATORY VIRAL INFECTIONS IN HOSPITALISED CHILDREN IN KUALA LUMPUR, MALAYSIA

Chee-Sieng Khor, I-Ching Sam, Yoke-Fun Chan

Department of Medical Microbiology, Faculty of Medicine, University Malaya, Kuala Lumpur, Malaysia

Viral respiratory tract infections (RTI) are relatively understudied in tropical countries such as Malaysia. A retrospective study was performed from 1982-2008 to investigate viral RTIs in hospitalized children <13 years old in Kuala Lumpur, Malaysia. Of 2818 laboratory-confirmed cases, the most commonly detected respiratory viruses in children (<13 yrs old) were human respiratory syncytial virus (RSV, 1955, 69.4%), parainfluenza (385, 13.7%), influenza (328, 11.6%), and adenovirus (150, 5.3%). Children infected with RSV were significantly younger ($P < 0.001$), and were predominantly <1 year old whereas children infected with influenza were significantly older ($P < 0.001$). Viral RTIs is an important cause of hospitalization among children, and accounted for an average 1.9% of paediatric discharges, with the highest rate of 4.5% recorded in 2007. The four main viruses caused disease throughout the year but seasonal epidemics were observed. RSV activity peaked at the year-end (September-December), and was lowest in the mid-year (April-June). Parainfluenza virus peaked around March-May and October-November. No clear peak can be detected in influenza and adenovirus. Further analysis of RSV with climatic factors showed that rain days were positively correlated, while relative humidity and temperature were inversely correlated with monthly RSV cases.

MOLECULAR CHARACTERISATION OF CHIKUNGUNYA VIRUSES FROM MALAYSIA

Sam IC, Chan YF, Chan SY, Loong SK

Department of Medical Microbiology, Faculty of Medicine, University Malaya, 50603 Kuala Lumpur, Malaysia

Introduction

Chikungunya virus (CHIKV) is a mosquito-borne alphavirus causing fever, rash, and arthralgia. Since 2005, outbreaks of CHIKV of the East/Central/South African (ECSA) genotype have occurred worldwide. CHIKV isolates from Malaysia have not been studied in detail.

Objective

To characterise Malaysian CHIKV isolates from the recent nationwide outbreak (2008-2010), and a limited outbreak in Bagan Panchor (2006).

Methods

Near-complete genome sequences (11,166 nucleotide CDS regions) were amplified from 3 CHIKV isolates (2 from Bagan Panchor, 1 from the current outbreak). Partial E1 sequences (837 nucleotides) were obtained from 13 CHIKV isolates spanning 8 months of the current outbreak. Sequences were edited and aligned using Geneious, with 30 other full genomes and 64 partial E1 sequences. Sequence identities were calculated using BioEdit. Phylogenetic trees were drawn using neighbour-joining (ClustalX) and maximum-likelihood methods (PhyML), with reproducibility tested using 1,000 bootstrap samplings.

Results

Phylogenetic analysis divided CHIKV into West African, Asian, and ECSA genotypes. Within the ECSA genotype, isolates from the Indian Ocean islands clustered separately from Indian isolates, with 100% bootstrap support. Bagan Panchor strains were of the Asian genotype, and had an unusual 21-nucleotide deletion in the nsP3 gene. The current Malaysian outbreak strains are from the ECSA genotype (Indian subgroup), with 5 unique amino acid substitutions, and 2 unique nucleotide substitutions in E1 over time. Separate analyses of 4 of the 9 genes (nsP2, C, E2, and E1) gave tree topologies similar to using whole genome. Amino acid similarities ranged from 94.5-97.9% between genotypes, and were <2% within ECSA strains.

Conclusions

E1 phylogeny reflects that of the whole genome, and its current widespread use is appropriate. Both Asian and ECSA genotypes are now present in Malaysia. The presence of unique substitutions in current Malaysian ECSA strains suggests local microevolution, which warrants further study.

INSIGHTS INTO BACTERIAL PATHOGENESIS

Jamuna Vadivelu

Tropical Infectious Diseases Research and Education Centre (TIDREC), Department of Medical Microbiology, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur

Numerous approaches have been utilised to dissect the enigma of the pathogenesis of various pathogenic bacteria; from the genetic makeup to the transcriptional level, proteomics level and eventually up to the phenotypic expression. In our laboratory, we focus on two important Gram-negative bacteria, *Helicobacter pylori* and *Burkholderia pseudomallei*, which cause chronic and latent infections. *Burkholderia pseudomallei*, known as the “great mimicker” or the “Vietnam time bomb” by the clinicians and the U.S. Military, respectively, is the causative agent of melioidosis. It is one of the potential bacterium for the development of bioweapon. *Helicobacter pylori* is the main bacterial causative agent of various gastroduodenal disorders. *H. pylori* is also a risk factor in the development of gastric adenocarcinoma and MALT lymphoma. Despite been successfully cultured in the lab 30 years ago, many aspects of this bacterium remains a mystery.

Various approaches have been utilised in our laboratory to understand the mechanism(s) of how *B. pseudomallei* develop melioidosis. At the genetic level, targeted gene knockout approaches have been used to study the functional role of the genes of interest in the pathogenesis. The extracellular secretory proteins, which are important virulence factors, have also been extensively studied at the proteomic level with the aid of two-dimensional electrophoresis. In addition *in vitro* models such as human cancer cell lines and *in vivo* model such as in-breed mice were exploited to measure the virulence between *B. pseudomallei* clinical strains and/or genetically engineered strains. To understand the complexity of host responses towards *B. pseudomallei* infection or to the extracellular secretory proteins of the bacteria, high throughput microarray technology was employed to elucidate the interaction of the bacteria and its secretory proteins with the host at the transcription level.

In our lab, research on *Helicobacter pylori*-associated pathogenesis is studied using two different approaches. Firstly, we are committed to the understanding of the relationships between *H. pylori*, other microbial members of the human gut and the host. In turn, how this may lead to pathogenesis in some individuals while protecting others against seemingly unrelated disorders (e.g. metabolic disorders and immunological complications). Secondly, it is of our interest to unveil the mechanism behind the way this bacterium is able to keep its level of virulence factors (e.g. CagA and VacA) and pathogenesis in check in order to maintain a life-

long relationship with its host. Our research group adopts a multi-dimensional molecular approach comprising of various genomic, genetic, proteomic and metabolic techniques to answer our research questions.

RESPIRATORY VIRAL INFECTIONS IN CHILDREN: AN OVERVIEW

Zamberi Sekawi

Deputy Dean (Research and Internationalization), Consultant Clinical Microbiologist, Faculty of Medicine and Health Sciences, University Putra Malaysia

Respiratory infections are the commonest infections found in children, which are conveniently classified as upper respiratory tract infections (URTI) and lower respiratory tract infections (LRTI). URTI is often considered trivial but it poses significant morbidity to children and also has a great impact on economic burden. It is also proven that it has an effect on trends of antibiotic prescriptions among general practitioners, of which antibiotics had been probably overprescribed. This indirectly contributes to the antibiotic resistance particularly in the community. LRTI which commonly presented as bronchiolitis, pneumonia and croup, had of course, significant morbidity and mortality, particularly among high risk children, namely those with heart and/ or pulmonary problems. There are more than 200 viruses that can infect children. For many years, the most commonly encountered viral agent is respiratory syncytial virus (RSV). The other viruses include influenza viruses, parainfluenza viruses, adenovirus and rhinovirus. With the latest diagnostic tools, 'newer' viruses are detected; bocavirus and metapneumovirus, however, their impact is still unknown. Molecular epidemiology had also able to map out and predict certain outbreaks worldwide and in the region. There is evidence of seasonal association on certain respiratory viruses in Malaysia. This information is useful in terms of planning preventive approach and predicting future outbreaks.

ISOLATION AND CHARACTERISATION OF ENVIRONMENTAL PHAGES OF *BURKHOLDERIA PSEUDOMALLEI*

Ong GH, Chang LY, Vadivelu J

Department of Medical Microbiology, Faculty of Medicine, University of Malaya, 50603, Kuala Lumpur, Malaysia

Corresponding author email: ongguanghan@gmail.com

Infections due to *Burkholderia pseudomallei*, a Gram-negative soil bacterium which is the causative agent for melioidosis, is difficult to treat due to its intrinsic resistance to multiple antibiotics and high risk of relapse. Bacteriophage therapy may be an alternative treatment against this infection. In this study, three bacteriophages namely C34, C38 and K43 were isolated and purified. Observation under electron microscopy revealed that all three bacteriophages resembled members of the *Myoviridae*, a family of the viruses with icosometric head and contractile tail. These bacteriophages were proved to be three different bacteriophages on the basis of their host range and restriction fragment length polymorphisms. C38 was found to have the broadest host range, being able to lyse 51.2% tested *B. pseudomallei* clinical isolates. This was followed by C34 (39.5%) and K43 (27.5%). The ability of these bacteriophages to treat infected cells *in vivo* and genomic characterisation have also been performed.

ANTIVIRAL EFFECTS OF A MALAYSIA MEDICINAL PLANT (*PHYLLANTHUS*)

Tan WC, Lee SH, Tang YQ, Sekaran SD

Department of Medical Microbiology, Faculty of Medicine, University of Malaya, 50603, Kuala Lumpur, Malaysia

Introduction

Virus infections remain as one of the major health threat worldwide. For instance, the recurrent dengue cases in Malaysia and the ability of virus to establish lifelong infection such as infection by the herpes simplex virus (HSV) in immune-compromised patients that resulted in the emergence of mutant drug-resistant strain. With the lack of effective vaccines, development of broad spectrum antiviral drug becomes an urgent need. With the abundance of natural flora in Malaysia, plants could be an ideal source for drug development. The aim of this study is to evaluate the opportunities in the development of broad spectrum antiviral drugs from the *Phyllanthus* against both DNA viruses (HSV1 and HSV2) and RNA virus (DENV2).

Methodology and Result

Cocktail (aqueous and methanolic) extracts were prepared from four species of *Phyllanthus* (*P.amarus*, *P.niruri*, *P.urinaria*, and *P.watsonii*). A wide variety of active polyphenolics, including gallic acid, geraniin, flavonoids, and quercetin have been identified by HPLC-PDA and LC-MS-MS analysis. The maximum non-toxic dose (MNTD) on Vero cells determined using MTS assay for both aqueous and methanolic extracts were 250µg/ml and 15.63µg/ml, respectively. *In vitro* antiviral activity of aqueous *Phyllanthus* cocktail extracts against DENV2, HSV1 and HSV2 was screened by means of different modes of treatment (pre-, simultaneous and post-) using RT-PCR whereby strongest inhibitory activity against the viruses was observed in simultaneous treatment with more than 90% of virus reduction. 2D-gel electrophoresis results suggest that the extracts most probably target viral entry and replication. Aqueous cocktail extract was shown to be non-lethal below 10g/kg. Preliminary efficacy showed virus reduction in dengue-infected mice.

Conclusion

Phyllanthus could potentially be a source for development of broad spectrum antiviral drug, particularly against DENV2 and HSV.

PHYLLANTHUS, A BROAD SPECTRUM ANTI-CANCER AGENT: PROPERTIES AND MECHANISMS OF ACTIVITIES

Lee SH, Tang YQ, Indu Bala Jaganath, Sekaran SD

Department of Medical Microbiology, Faculty of Medicine, University of Malaya, Malaysia

Corresponding author: Prof. Dr. Shamala Devi, Department of Medical Microbiology, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia

Introduction

Cancer is one of the leading causes of human deaths worldwide. Although the current chemotherapeutic drugs improved overall survival rate of the patients, the outcome remains poor due to development of drug resistance and a wide range of side effects. Thus, alternative treatments founded using a 'back-to-nature' approach might yield improved treatment avenues with fewer or no undesirable effects. Our present work investigates the use of a natural product *Phyllanthus* as a potential broad spectrum anti-cancer agent.

Results and Discussion

Phyllanthus plant extracts was found to selectively inhibit lung (A549), breast (MCF-7), melanoma (MeWo) and prostate (PC-3) cancer cells. *Phyllanthus* extracts also exhibited anti-metastatic effects by effectively reducing invasion, migration, and adhesion of the cancer cells in a dose-dependent manner. In addition, *Phyllanthus* was also shown to be anti-angiogenic as it suppressed the micro-capillary tube formation. These anti-angiogenic and anti-metastatic effects of *Phyllanthus* were associated with the reduction of proteolytic enzymes, MMP-2, -7 and -9. Besides that, *Phyllanthus* induced apoptosis with more than threefold increase of caspases-3 and -7, the presence of DNA-fragmentation and TUNEL-positive cells. The underlying mechanism of these observations was mostly attributed to the disruption of five pathways in treated cancer cells, including MAPK/ERK, MAPK/JNK, Hypoxia, Myc/Max, and NFκB. Proteomic analysis revealed that the affected proteins were involved in various metabolic and cellular processes, including tumor cell adhesion, invasion, migration, apoptosis, angiogenesis, glucogenesis and glycolysis. In a preliminary *in vivo* study, *Phyllanthus* was shown to be non-toxic at 10g/kg.

Conclusion

This study provides insights into the mechanisms by which *Phyllanthus* inhibited major cancer pathways in lung, breast, melanoma, and prostate cancer cells and might offer further application as a broad spectrum anti-cancer agent. Hence this plant extract has potential use as an oral anti-cancer agent, having minimal or no toxicity.

DENGUE VIRUS AND THE VASCULAR ENDOTHELIUM

Rathakrishnan A, Rajendran P, Alhoot MA, Manikam R, Sekaran SD

Department of Medical Microbiology, Faculty of Medicine, University of Malaya, Malaysia

Dengue despite its high prevalence lacks effective vaccine and antiviral drugs this due to the incomplete and poorly understood pathogenesis of dengue. The hallmark of severe dengue is vascular leakage. The HLA association provides a likely model to determine the risk of developing severe dengue whereas a better understanding of the immune response was obtained by the HLA-restricted peptides ELISpot assay. The cytokine profiling of these patients has indicated cytokines may actually have roles in not only progression of the dengue severity but also seem to be protective and this may be useful with the current advancement of cytokine adjuvant and anti-cytokine therapies. The gene profiling study may be involved in preventing the development of clinical symptoms during infections. The aberrant immune responses not only impair the immune response to clear the virus, but also result in overproduction of cytokines that affect endothelial cells. In our study we note that endothelial cells from various sources (splenic, liver and dermal) were easily infected with dengue viruses. Reactive oxygen and nitric oxide species, for example superoxide, nitric oxide (NO), play a pivotal role in controlling the endothelial function and vascular tone. Also apocynin effectively inhibits the NADPH oxidase concentration and decrease the concentration of ROS, Nitric oxide and iNOS. In our studies it is observed that apocynin effectively reduced vascular leakage in dengue infected endothelial cells. These effects implicate responses of the infected endothelium in dengue pathogenesis and rationalize therapeutic targeting of the endothelium and EC responses as a means of reducing the severity of dengue virus disease. Presently our group is focused on the molecular mechanisms of endothelial dysfunction during dengue particularly the tight junctions.

IMMUNE RESPONSES INVOLVEMENT IN DENGUE PATIENTS AT DIFFERENT LEVELS OF SEVERITY

Rathakrishnan A, Yeo SL, Rajendran P, Alhoot MA, Lee SH, Manikam R, Sekaran SD

Department of Medical Microbiology, Faculty of Medicine, University of Malaya, Malaysia

Dengue despite its high prevalence lacks effective vaccine and antiviral drugs this due to the incomplete and poorly understood pathogenesis of dengue. The hallmark of severe dengue is vascular leakage. With this in mind our study our aimed to determine the HLA alleles in dengue susceptibility, dengue specific T cell response evoking peptides as well as profiling of cytokine response and its effect on the endothelium. Dengue patients (segregated ethnically and by dengue severity) were typed for their HLA-A and –B molecules and we found two alleles (A*24 and B*35) detected from patients that were significantly associated with increased dengue severity where as another two alleles (A*2 and A*3) seemed to have protectiveness against developing dengue. Further thirty-six peptide antigen designed using MHC-peptide binders predictive algorithms were used in an IFN- γ ELISpot assay and here 28 patients were found to have T cell responses towards one or more of the pooled peptides. Individual peptide analysis revealed that the NS1 and NS2A region to be multiple immunodominant epitopes. Multiple cytokines were detected via a multiplex bead-based assays and were shown to have roles with differing dynamism in patients with varying dengue severity and 4 of these cytokines (MCP-1, IP-10, MIP-1 β and G-GSF) were significantly different in dengue patients when compared with the controls at various time point of infection. Microarray studies on their asymptomatic household members (who had high neutralizing dengue antibodies) revealed several genes involved in macrophages initiated inflammatory response, T cell signaling pathway and B cell signaling pathways. The HLA association provides a likely model to determine the risk of developing severe dengue whereas a better understand on the immune response was obtained by the HLA-restricted peptides ELISpot assay. The cytokine profiling of these patients has indicated cytokine may actually have roles in not only progression of the dengue severity but also seem to be protective and this may be useful with the current advancement of cytokine adjuvant and anti-cytokine therapies. Besides that, the gene profiling study elucidate the immune responses involved during asymptomatic dengue infection and the genes that might play a protective role in preventing the development of clinical symptoms during a dengue infection.

NOVEL SYNTHETIC ANTIMICROBIAL PEPTIDES WITH POTENT *IN VITRO* AND *IN VIVO* ANTIMICROBIAL ACTIVITIES AGAINST *STREPTOCOCCUS PNEUMONIAE*

Le CF, Mohd Yusof MY, Sekaran SD

Department of Medical Microbiology, Faculty of Medicine, University of Malaya, Malaysia

Streptococcus pneumoniae is a major human bacterial pathogen causing significant morbidity and mortality worldwide. The increasing reports of antibiotic-resistant pneumococci have prompted the imperative search for novel antimicrobial agents. We have generated a series of synthetic antimicrobial peptides and found that five peptides (DM1-5) showed potent antipneumococcal activities and rapid killing rates irrespective of the penicillin resistance of the pneumococcal strains. These peptides induced overwhelming pneumococcal cell wall and cell membrane damages which eventually lead to cell death as observed using Transmission Electron Microscopy. The DMs were able to produce synergism in combination with the conventional antibiotic penicillin. Interestingly, DMs also displayed broad spectrum antibacterial activity against other common clinically-encountered bacterial pathogens such as *Staphylococcus aureus*, methicillin-resistant *S. aureus*, *E. coli*, *Pseudomonas aeruginosa*, and others. The hemolytic activities were low while cytotoxicities against two human lung cell lines varied among the DMs. Further testing of these peptides in mouse infection model found that intraperitoneal treatment with DM3 (40mg/kg) for three doses at 2hrs, 12hrs, and 24hrs protected 50% of mice from lethal pneumococcal infection by a penicillin-resistant strain. Mice treated with this DM3 regimen have no major abnormalities in blood haematogram and serum biochemistry parameters as well as histopathology of five major organs (spleen, liver, lung, kidney, brain). Interestingly, combination treatments using DM3 and penicillin produced *in vivo* therapeutic synergism. While DM3 (20mg/kg) and penicillin (20mg/kg) conferred 20% and 50% protection to the mice, all mice (100%) treated with this DM3-penicillin combination survived from the lethal pneumococcal challenge. Antimicrobial peptides represent the promising novel antimicrobial agent and here we have developed DM3 showing great potential as antimicrobial candidate in standalone form or to be formulated in combination with conventional antibiotics to enhance pneumococcal infections treatment outcome especially those involving pneumococcal-resistant strains.

SERUM CORTISOL AND CARDIOVASCULAR EFFECTS

Marzuki Isahak^{1*}, Azlan Darus¹, Moy Foong Ming², Retneswari Masilamani¹

¹Centre for Occupational and Environmental Health, University of Malaya. Kuala Lumpur.

²Julius Centre University Malaya, University of Malaya, Kuala Lumpur.

*Corresponding author

Introduction

Cortisol is a steroid hormone produced in the adrenal glands in response to stress. In the working population, stress had become part of their routine life and this can lead to multiple cardiovascular diseases. This study was conducted to determine the association between serum cortisol levels with cardiovascular indicators.

Methods

A cross-sectional study was done among 544 randomly selected staff in University of Malaya, Kuala Lumpur. Physical examinations (blood pressure, waist and hip circumference, height and weight) were carried out and blood investigations (fasting serum lipid, fasting blood sugar and serum cortisol) were taken between 7.30 am and 9.30 am.

Results

The median level of serum cortisol was 303 nmol/L. Male has higher median cortisol level (334 nmol/L) compared to female (288 nmol/L). Older age group (above 60 years old) has the highest median cortisol (394 nmol/L) compared to the others. Chinese participants have lowest median cortisol (296 nmol/L) compared to Malay (302 nmol/L), Indian (301 nmol/L) and others (425 nmol/L). The cardiovascular indicators that are significantly associated with serum cortisol level are systolic blood pressure (p value < 0.01), diastolic blood pressure (p value < 0.01) and fasting blood glucose (p value 0.04).

Conclusion

We conclude that staff with higher serum cortisol level will have higher risk of getting hypertension and diabetes mellitus. Thus, a comprehensive program on cortisol reduction (stress management, nutrition and exercise) can be introduced targeting into specific group of people.

Keywords: Metabolic disease, stress hormone, university workers

A CROSS SECTIONAL STUDY ON HAND ARM VIBRATION SYNDROME AMONG A GROUP OF TREE FELLERS IN A TROPICAL ENVIRONMENT

Anselm Ting Su^{1,2*}, Setsuo Maeda³, Jin Fukumoto², Nobuyuki Miyai⁴, Marzuki Isahak¹, Atsushi Yoshioka⁵, Ryuichi Nakajima⁶, Awang Bulgiba⁷, Kazuhisa Miyashita²

¹Centre for Occupational and Environmental Health, University of Malaya, Kuala Lumpur, Malaysia,

²Department of Hygiene, School of Medicine, Wakayama Medical University, Wakayama, Japan

³Faculty of Applied Sociology, Kinki University, Osaka, Japan

⁴School of Health and Nursing Science, Wakayama Medical University, Wakayama, Japan

⁵TEAC Corporation, Tokyo, Japan

⁶Rion Co. Ltd., Tokyo, Japan

⁷Julius Centre University Malaya, University of Malaya, Kuala Lumpur, Malaysia

*Corresponding author

Background

This study aimed to explore the clinical characteristics of hand arm vibration syndrome (HAVS) in a group of tree fellers in a tropical environment.

Methods

A total of 33 tree fellers and 15 control subjects working in a logging camp of central Sarawak were interviewed for history of vibration exposure and presence of HAVS symptoms, and examined for the effects of hand transmitted vibration exposure including the cold water provocation test.

Results

None of the subjects reported white finger. The tree fellers reported significantly higher prevalence of finger coldness as compared to the control subjects (OR = 10.32, 95%CI = 1.21 – 87.94). A lower finger skin temperature, longer fingernail capillary return time and higher vibrotactile perception threshold (VPT) were observed among the tree fellers as compared to the control subjects in all fingers (effect size > 0.5). The VPT following cold water provocation test of the tree fellers was significantly higher (repeated measures ANOVA $p = 0.002$, partial eta squared = 0.196) than the control subjects after adjusting for weight and height. The A(8) level was associated with finger tingling, numbness and dullness (effect size = 0.983) and cold finger symptoms (effect size = 0.524) among the tree fellers. The cut-off value of A(8) to differentiate the subjects with neurological symptoms from those without was 4.08 ms^{-2} (area under the ROC curve = 0.754, 95%CI = 0.584 – 0.924).

Conclusions

The VPT test may serve as an important confirmatory test for HAVS in tropical environments. Finger coldness has a great potential to become the surrogate symptom for vascular damage in HAVS in tropical environments. A(8) is associated with the neurological symptoms and finger coldness in tropical environments.

Keywords: HAVS, hand transmitted vibration, warm environment, forestry, cold provocation test

SYMPTOMS OF SICK BUILDING SYNDROME, OCCUPATIONAL IMPACT AND QUALITY OF INDOOR AIR IN AN OFFICE ENVIRONMENT IN KUALA LUMPUR

Azlan Darus¹, Fatin Syakira Abdul Manab²

¹*Centre for Occupational and Environmental Health, University of Malaya, Kuala Lumpur*

²*Faculty of Engineering, University of Malaya, Kuala Lumpur*

Background

The effect of non-industrial indoor air pollutant on the health of employees had been widely reported over the last two decades. Reports of symptoms suffered had raised concerns by employees who are worried about their health, and by employers who are concerned about the wellbeing of their employees and their business. In a warm climate country such as Malaysia, the climate control in an office environment relies heavily on the air-condition system, where the control of fresh air intake and circulation relies solely on the centralised ventilation system. Several reports had indicated employees complaining of symptoms due to indoor air pollution. This has led to deterioration in health, sick leaves and poor productivity. The objectives of this study are to determine the prevalence of symptoms of sick building syndrome among workers in an office with a floor exhaust ventilation system. We also seek to determine the relationship between the symptoms and measured indoor air parameters, and the impact on work absenteeism due to the symptoms suffered.

Methods

A universal sample of 300 employees in an office was invited to join the study. Participants are required to fill in a symptom survey on sick building syndrome. This was followed by an indoor air quality measurement. The parameters measured are temperature, relative humidity, formaldehyde and volatile organic compound level, particulate matter, carbon dioxide, carbon monoxide, total bacterial and fungal growth, and air movement. Indoor air quality measurement was entered as group level according to work area. Data was entered and analyzed using SPSS version 15.0.

Results

Two hundred and two (202) employees returned the questionnaire. Only 14.9% reported no symptoms at all, compared to 85.1% who complained of at least one symptom. Almost 50% of participants complained of suffering of more than 3 symptoms due to indoor air at the

workplace. The most common symptoms were headache (54%), rhinorhea (48%) and cough (47%). Twenty three percent (23%) of the employees had taken at least one sick leave due to the symptoms, while 20% had taken 2 days or more. Prevalence of symptoms is associated with areas of higher temperature, relative humidity, total bacterial and fungal growth.

Conclusions

The study showed high prevalence of symptoms of sick building syndrome, despite working in a modern high rise office with comprehensive ventilation system. The impact of the symptoms on work absenteeism was found to be high, which may also impact the morale of the employees. The symptoms were found to be related to the measured indoor air parameters, which strongly indicate the dependant nature of the symptoms on indoor air quality. This study necessitates action to be taken to improve indoor air quality in offices. Based on the results, we also recommend a periodic indoor air quality measurement to be conducted to mitigate sick building syndrome to the benefit of both the employees and the employer.

Keywords: Indoor Air Quality, Sick Building Syndrome

PREVALENCE AND ASSOCIATED FACTORS OF STRESS IN THE MALAYSIAN POLICE FORCE

Retneswari Masilamani¹, Awang Bulgiba², Karuthan Chinna², Azlan Darus¹, Marzuki Isahak¹, Shathanapriya Kandiben¹, David Koh³

¹*Centre for Occupational and Environmental Health, University of Malaya, Kuala Lumpur, Malaysia*

²*Julius Centre University Malaya, University of Malaya, Kuala Lumpur, Malaysia*

³*PAPRSB Institute of Health Sciences, Universiti Brunei Darussalam*

Objective

To determine the prevalence of stress and the associated socio-demographic and work factors among police personnel in Metropolitan Kuala Lumpur, Malaysia.

Method

A cross-sectional study was conducted in two randomly selected police districts in Kuala Lumpur from 2009-2011. A total of 579 police officers from 11 police stations and two headquarters participated in this study. The Depression, Anxiety and Stress 21-item questionnaire was used. Multinomial logistic regression analyses were carried out to examine the effect of socio-demographic and work factors on stress.

Results

The overall prevalence of stress was 39% (95% CI 34.2, 43.6) with 5.9% (3.9, 8.8), 14.9% (11.6, 18.8) and 18% (14.5, 22.2) for severe, moderate and mild stress, respectively. Inspectors were more likely to suffer from severe stress (aOR 10.68, 95% CI 3.51, 32.53) compared to junior officers. Those who complained that their salaries were not commensurate with their jobs were more likely to suffer from moderate levels of stress (aOR 2.73, 95% CI 1.43, 5.22) compared to those who were happy with their salaries.

Conclusions

This study strengthens the findings that police job is stressful. Special attention needs to be paid to Inspector-level ranks and the remuneration structure of police officers to address this issue.

Keywords: Police stress, police officers, stressors, job characteristics, income, police rank

A PROSPECTIVE STUDY OF WORK ABILITY AND MULTISITE MUSCULOSKELETAL PAIN AMONG HOSPITAL BASED NURSES

Victor Hoe^{1,2}, Helen Kelsall¹, Donna Urquhart¹, Malcolm Sim¹

¹ Department of Epidemiology and Preventive Medicine, Monash University, Victoria

² Department of Social and Preventive Medicine, Faculty of Medicine, University of Malaya, Malaysia

Objective:

To investigate the relationship between musculoskeletal pain, sociodemographic, individual and work place factors, and self-perceived work ability among hospital based nurses in Melbourne, Australia, as part of the international CUPID study.

Methods

Nurses working across three major hospitals who were first surveyed 12 months ago were included. Information on demographic, lifestyle, mental and physical health and wellbeing (SF-12), workplace physical and psychosocial factors, musculoskeletal pain at several body sites for seven days or more in the previous 12 months, and a modified Work Ability Index were collected. The association between risk factors and work ability was investigated using an ordinal logistic regression model.

Results

Of 1,111 baseline participants, 839 nurses (response rate 75.5%) completed the questionnaire. 768 nurses who had continued working in the study hospitals in the previous 12 months were included in the analysis. The majority (66.4%) reported excellent work ability, while 25.1% reported good, 7.3% moderate and 1.2% poor work ability. The independent factors associated with decreasing work ability were pain at any site (OR 1.86; 95%CI 1.08-3.19), pain at three or more sites (OR 1.99; 1.01-3.93), high job strain (OR 2.22; 1.27-3.88), female gender (OR 2.45; 1.04-5.75), part-time/casual employment (OR 1.69; 1.08-2.64), better mental (OR 0.86; 0.84-0.88) and physical (OR 0.86; 0.83-0.88) health and wellbeing.

Conclusion

Whilst the majority of nurses reported excellent or good work ability, efforts to retain the current workforce and improve their work ability should include the management of musculoskeletal pain, reducing job strain and improvement in general mental and physical health and wellbeing.

PHYSICAL AND PSYCHOSOCIAL FACTORS ASSOCIATED WITH MUSCULOSKELETAL DISORDERS AMONG HOSPITAL BASED NURSES IN AUSTRALIA

Hoe VCW^{1,2,3}, Kelsall HL², Urquhart DM², Sim MR²

¹ Centre for Occupational and Environmental Health, University of Malaya

² Department of Epidemiology and Preventive Medicine, School of Public Health and Preventive Medicine, Monash University, Australia

³ Department of Social and Preventive Medicine, Faculty of Medicine, University of Malaya

Objectives

To assess the demographic, employment, and workplace physical and psychosocial factors associated with musculoskeletal pain in Australian hospital-based nurses.

Methods

Information on low back, neck, shoulder, elbow, wrist/hand and knee pain, associated disability and sickness absence, demographic, and workplace physical and psychosocial factors among nurses working for three public hospitals in Melbourne, Australia was collected in a cross-sectional study. Association between the risk factor and musculoskeletal pain in the past 12 months was determined using a modified Poisson Regression Model to estimate the prevalence ratio (PR) with 95% confidence interval (95% CI).

Results

1,111 participants (response rate 38.6%) completed the questionnaire. The most common site of pain in the past 12 months was the low back (55.8%), neck (48.2%) shoulder (36.5%), knee (26.8%), hand/wrist (22.6%) and elbow (11.8%). The independent associated physical factors for low back pain was lifting =25 kg (PR 1.18; 95% CI 1.06-1.34) and kneeling/squatting for =1 hr/day (PR 1.17; 95% CI 1.02-1.34), neck pain was associated with keyboard use of =4 hrs/day (PR 1.21; 95% CI 1.04-1.39), hand/wrist pain with repeated movement of the hand/wrist =4 hrs/day (PR 1.74; 95% CI 1.31-2.30), and knee pain was lifting =25 kg (PR 1.49; 95% CI 1.19-1.86). The most consistent independent psychosocial factors that were associated with MSD at all sites are low job control and high job demand.

Conclusion

This study found that workplace physical and psychosocial factors were associated with musculoskeletal pain. Measure to reduce musculoskeletal disorder needs to consider both workplace physical and psychosocial factors.

Keyword: job control, job demand, workplace risk factors, prevalence

CONGENITAL RUBELLA SYNDROME IN AN INFANT DESPITE MATERNAL VACCINATION

Florence Santiago^{1,2}, Choo May May^{1,2}

¹University of Malaya Eye Research Centre

²Department of Ophthalmology, Faculty of Medicine University of Malaya

Objective

To report a case of an infant with congenital rubella syndrome, despite proper maternal vaccinations.

Method

Report of a case observation

Results

This infant was delivered via emergency Caesarean section due to fetal distress at term. Initially treated as presumed sepsis until clinical examination and investigations revealed that the infant had congenital rubella syndrome. Infant has bilateral white cataract, microphthalmos, bilateral hearing loss, congenital heart defect, chronic lung disease with persistent pulmonary hypertension of newborn. The infant underwent bilateral lensectomy and currently wearing aphakic glasses. Infant's mother received proper vaccinations since she was born. Despite that, Rubella IgM serology had tested positive. Mother had history of rashes and fever during gestation and was treated as viral fever. Antenatally, no obvious abnormalities was noted in the fetus.

Conclusion

Few case reports have been reported of similar incidences. Compulsory Rubella vaccinations are administered to all girls aged 15 years in Malaysia. Whether a need for repeat Rubella vaccination for Malaysian women planning for pregnancies must be considered, and if yes, when should this vaccination be repeated needs to be studied.

CORRELATION OF MACULA THICKNESS WITH VISUAL ACUITY AND STAGE OF RETINOPATHY USING OPTICAL COHERENCE TOMOGRAPHY (OCT) IN DIABETIC PATIENTS

N Ramli^{1,2}, Z Mimiwati^{1,2} A Fauzi^{1,2}

¹University of Malaya Eye Research Centre

²Department of Ophthalmology, Faculty of Medicine University of Malaya

Objective

To quantitatively analyse the macula in diabetic eyes using Stratus OCT and determine correlation of macula thickness with severity of diabetic retinopathy and visual acuity.

Methods

131 eyes from 73 consecutive diabetic patients attending UMMC Ophthalmology clinic over a 2 month period were clinically assessed underwent OCT macula scan. Cut off value for OCT macula oedema was determined by the ROC curve and set at 210 microns for the diabetic patients. Macula oedema was seen in 56 eyes (43%). Correlation between Log MAR visual acuity and foveal thickness was done using bivariate analysis. Independent samples t-test was used to determine whether central foveal thickness was significantly different between the different stages of retinopathy.

Results

For the cut off point of 210 microns the sensitivity was 85.1% and specificity was 97.0%. Analysis of the correlation between central foveal thickness and Log MAR visual acuity in all subjects shows a moderate degree of correlation. Visual acuity correlated with in diabetics with OCT defined macula oedema ($p=0.325$; $p=0.019$). The presence of macula oedema was found to have a low degree of correlation with more advanced stages of retinopathy ($r=0.310$; $p<0.001$). There was no significant difference between height of central foveal thickness in the severe NPDR group and mild NPDR ($p=0.195$), moderate NPDR group ($p=0.506$) or proliferative retinopathy group ($p=0.200$). There was however a significant difference in between the severe NPDR and no retinopathy group ($p=0.041$).

Conclusion

Height of macula oedema measured with OCT correlates with visual acuity and severity of diabetic retinopathy.

GREEN TEA AND SOYBEAN FLAVONOIDS EXERT DIFFERENTIAL EFFECTS ON THE SURVIVAL OF RGC-5 CELLS EXPOSED TO VARIOUS TYPES OF OXIDATIVE STRESS

TA Kamalden^{1,2}, NN Osborne³

¹*University of Malaya Eye Research Centre*

²*Department of Ophthalmology, Faculty of Medicine University of Malaya*

³*Nuffield Laboratory of Ophthalmology, University of Oxford, UK*

Purpose

To investigate the neuroprotective properties of three different flavonoids.

Methods

Lipid peroxidation studies were conducted to determine the anti-oxidative properties of the selected flavonoids. Immortalized retinal ganglion cells (RGC-5 cells) in culture were exposed hydrogen peroxide (H₂O₂), glutamate and serum deprivation in the presence or absence of green tea flavonoids (epicatechin gallate, EC and epigallocatechin gallate, EGCG) and soybean isoflavonoid, genistein. Cell cultures were analysed by viability assays, immunocytochemistry, western blot, stimulation of reactive oxygen species (ROS) and staining for apoptosis.

Results

All three selected flavonoids demonstrate good antioxidant properties against lipid peroxidation. Insults of H₂O₂, glutamate and serum deprivation resulted in a time and dose-dependent stimulation of ROS associated with an apoptotic type of cell death of RGC-5 cells. Importantly, EG blunted cell death induced by H₂O₂ and glutamate, whereas EGCG only attenuated H₂O₂ effects

Conclusion

The results suggest the idea that defined insults can be attenuated by specific flavonoids.

A RARE PRESENTATION OF SUBACUTE IPSILATERAL NEUROPATHIC ARTHROPATHY INVOLVING MULTIPLE JOINTS DUE TO SYRINGOMELIA AND TYPE-1 ARNOLD-CHIARI MALFORMATION

Norazian Kamisan¹, T Ravi², Tunku Kamaru²

¹*Hospital Tuanku Jaafar, Seremban Malaysia*

²*University Malaya Medical Centre, Kuala Lumpur, Malaysia*

Neuropathic arthropathy (NA) is a chronic condition that ultimately leads to joint destruction as a result of loss of joint sensation. This condition is usually secondary to an underlying cause such as tabes dorsalis, diabetes mellitus and peripheral nerve disease. Syringomelia can also result in NA involving a number of joints which commonly includes the shoulder, elbow, knee and ankle. This condition rarely involves the wrist or more than one joint. The disease is said to have a slow progression. In this article, we report a case of NA secondary to syringomelia that was presented to us subacutely with symptoms described similar to the symptoms of carpal tunnel syndrome. Upon further investigation, it was found that there was multiple joint destruction including the wrist, which in turn resulted in compromise of the carpal tunnel space, thus causing median nerve compressive neuropathy.

A NEW METHOD OF MEASURING GASTROCNEMIUS TIGHTNESS: INTRA-AND INTER-OBSERVER RELIABILITY

Y P Chua, A Saw, S R Kanthan

Department of Orthopaedic Surgery, University of Malaya, Kuala Lumpur, Malaysia

Background

Isolated Gastrocnemius tightness has been demonstrated to be associated with the development of a variety of chronic problems of the foot and ankle in neurologically normal people. The Silverskoid test allows the clinician to differentiate between calf tightness due to tricep surae and that due to isolated gastrocnemius. However, the severity of the tightness cannot be determined objectively.

Objective

The study aims to develop a reliable procedure for measuring gastrocnemius tightness objectively in clinical settings.

Method and Result

A new electronic patient self-operated inclination device is invented for this purpose. Thirty subjects with a mean age of 27 years were included in the study. Also recruited were, four observers from different orthopaedic experience who were responsible for measuring the 30 subjects on three difference occasions to determine intra-and inter-observer reliability using the intraclass correlation coefficient <ICC>. Results showed that intra-rater ICC ranged from 0.974 to 0.986 with a confidence interval of 95% and the overall ICC of the four observers was 0.946 with a confidence interval of 95%.

Conclusion

This newly developed method is reliable in helping the clinician to measure gastrocnemius tightness objectively and subsequently helps in grading the level of severity. In addition, it also facilitates the monitoring of the progress of patients' treatment at the time of follow up at the clinic.

MULTIPLE LIGAMENT INJURY WITH COMMON PERONEAL NERVE PALSY AFTER TRAUMATIC DISLOCATION OF THE KNEE

M. Zubair, M. Razif Bin M. Ali, Ng Wuey Min, Shamsul Iskandar

Orthopaedic Sport Unit, Department of Orthopaedic Surgery, University of Malaya Medical Centre, Kuala Lumpur, Malaysia.

Introduction

Traumatic dislocation of the knee is uncommon representing less than 0.2% of all orthopaedic injuries. It is usually caused by high-energy sport injuries or motor-vehicle accidents. It is always associated with considerable ligamentous disruption, but the pattern of injury varies considerably. The most common pattern of injury is a bicruciate disruption with associated disruption of the MCL or posterolateral corner depending upon the direction of the deforming force. Complete disruption of all four major ligament stabilizers is less common. The risk of vascular damage in association with dislocation of the knee is well known. Damage to the common peroneal nerve is less well recognised than vascular injury, the incidence is more in the presence of disruption of the PCL and posterolateral corner.

Case Report

A 28 yrs junior doctor was involved in a motor-vehicle accident in July 2011. He had left knee dislocation and was treated primarily in a local hospital. He was referred for the significant instability his left knee which is associated with foot drop. Physical examination showed grade 3 laxity of ACL, PCL and PLC which was confirmed by MRI findings. NCS showed common peroneal nerve axonal neuropathy. Reconstruction of the cruciate ligaments and the posterolateral corner had been performed using autogenous grafts. Exploration of the common peroneal nerve showed a neuroma in continuity. Therefore, neurolysis done for the nerve and tibialis posterior tendon transfer performed to restore the dorsiflexion of the foot. The patient was assessed according to tegner activity level scale, Lysholm and IKDC scoring system pre and post-operatively.

Conclusion

Dislocation of the knee results in severe soft tissue disruption. The common peroneal nerve is susceptible to injury because of its fixed attachment at the region of neck of fibula. It is usually associated with PCL and posterolateral corner injury during the hyperextension and varus stress of the knee which put the nerve on traction.

In general, traction injuries to the common peroneal nerve have a poor outcome due to the extensive damage to the nerve. Lesions in continuity can be observed for signs of spontaneous recovery, nerve grafting is reserved for patients with short segment involvement while the transfer of the tendon of tibialis posterior may be a useful alternative procedure to restore dorsiflexion of the foot.

THE EFFECT OF GROWTH DIFFERENTIATION FACTOR-5 (GDF-5) ON THE PROLIFERATION AND TENOGENIC DIFFERENTIATION POTENTIAL OF HUMAN MESENCHYMAL STEM CELLS IN VITRO

Tan S.L.¹, Selvaratnam L.², Ahmad R.E.³, Ahmad T.S.¹, Merican, A.M.¹, Abbas A.A.¹; Ng, W.M.¹, Kamarul, T.¹

¹Tissue Engineering Group (TEG), National Orthopaedic Centre of Excellence for Research and Learning (NOCERAL), Department of Orthopaedic Surgery, Faculty of Medicine, University of Malaya, Pantai Valley, Kuala Lumpur, 50603, Malaysia.

²School of Medicine & Health Sciences, Monash University, Sunway Campus, Selangor, Malaysia.

³Department of Physiology, Faculty of Medicine, University of Malaya, Pantai Valley, Kuala Lumpur, 50603, Malaysia.

Background

Growth differentiation factor-5 (GDF-5) has been shown to increase tendon neo-formation when used in tendon repair. We hypothesized that similar effects would be observed when applied in human mesenchymal stem cells (hMSC) differentiation, in other words, it could induce tenogenic differentiation in hMSCs. However, this effect has not been previously elucidated. The objective of this study was to investigate the effect of GDF-5 on hMSC proliferation and tenogenic differentiation.

Methods

In this study, human bone marrow derived MSCs were isolated, cultured and expanded in vitro. Cell proliferation, total collagen expression and selected gene expressions (Scleraxis (Scx), type-I collagen (Col-I), type-III collagen (Col-III), decorin (Dec) and nucleostemin (Nst)) in hMSCs, subjected to varying concentrations of GDF-5 (0, 5, 25, 50, 100 and 500ng/ml) measured at different time points (day 4, 7 and 10) were performed.

Results

It was found that GDF-5 does not cause significant change in cell proliferation rate. However, at 100ng/ml of GDF-5, total collagen expression was significantly elevated after 4 days of cell cultures as compared to lower concentrations of GDF-5 (0, 5 and 25ng/ml). Higher concentration did not provide significant change in collagen expression. At 100ng/ml, there was also significant up-regulation of Scx, Col-I, Col-III but not for Dec. Interestingly, Nst gene was persistently expressed in tenogenic differentiated hMSCs.

Conclusions

The use of GDF-5 does not alter the proliferation rates of hMSCs but provide optimal tenogenic differentiation response at 100 ng/ml concentrations.

CHRONIC OSTEOMYELITIS OF THE RIB MIMICKING A SARCOMA: A CASE REPORT

Chew Chin Seong, Azura Mansor, Vivek Ajit Singh

Orthopaedic Oncology Unit, Department of Orthopaedic, University of Malaya, Kuala Lumpur Malaysia

Chronic osteomyelitis is an infrequent cause of soft tissue mass. It is almost impossible to differentiate from bony or soft tissue sarcoma based on clinical grounds alone. This report highlights the importance of histological examination and tissue culture in the diagnostic of such cases. We present a 60 year old man, with a history of diabetes who came to us with left chest wall swelling of a 4-month duration. There was no history to suggest infection but he had experienced significant weight loss in the past months. Imaging studies showed a destructive lesion of the left 7th rib with soft tissue involvement. A preliminary was treated with long term antibiotics and the symptoms resolved. Infection should always be considered as one of the differentials when dealing with tumours.

GENETIC ANALYSES OF MYOTONIC DYSTROPHY TYPE 1 IN MALAYSIA

Kaitlin K Ambrose¹, Mohd Taufik I², Lian LH¹, Goh KJ³, Wong KT⁴, Thong MK²

¹Department of Molecular Medicine

²Department of Paediatrics

³Department of Medicine

⁴Department of Pathology

Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

Introduction

Myotonic Dystrophy (DM1) is an autosomal dominant, neuromuscular disorder. It is caused by an expansion of the trinucleotide repeat sequence, CTG, located within the 3' Untranslated Region of the *DMPK* gene on chromosome 19q13.3. The frequency of CTG>18 alleles has been used to predict the prevalence of DM1 in populations world-wide.

Objective

To determine the frequency of DM1 in the Malay, Chinese and Indian sub-populations, and to establish a suitable genetic diagnostic test for DM1.

Methodology

377 DNA samples from healthy individuals were subjected to the Polymerase Chain Reaction (PCR) technique. PCR products were sequenced to determine the exact number of CTG repeats. Chi-squared test was performed on the data.

18 DM1 patients were also recruited for this study. The PCR-Southern Blot technique was used to estimate the expanded CTG repeat sizes.

Results

We observed a total of 19 alleles, ranging from 5 to 29 in the normal control. The frequency of CTG>18 was 3.20%, 1.57% and 4.00% in the Malay, Chinese and Indian sub-populations respectively. The frequency pattern of CTG>18 was similar between the three sub-populations and also showed similarities with frequency patterns of the Thai and Taiwanese populations, where incidences of DM1 are low. All three sub-populations also showed significant difference in CTG>18 with the European population, where DM1 incidences are common.

The PCR-Southern Blot technique was able to detect expanded alleles of up to 690 CTG repeats.

Conclusion

DM1 incidence is low in Malaysia and the PCR-Southern Blot technique can be used as standard confirmatory diagnostic test for DM1.

AETIOLOGY OF PNEUMONIA IN CHILDREN AND USEFULNESS OF C-REACTIVE PROTEIN IN THE MANAGEMENT OF CHILDHOOD PNEUMONIA

Fairuz Rani,¹ Rachel Jiun, Anna Nathan², Caroline Westerhout, I-Ching Sam, Jessie de Bruyne²

¹ Medical Student, University of Malaya, Kuala Lumpur, Malaysia

² Department of Paediatrics, University Malaya Medical Centre, Kuala Lumpur, Malaysia

Aim

To determine i) the aetiology ii) the sensitivity patterns of bacteria isolated and iii) the usefulness of the CRP in differentiating between viral and bacterial causes of lower respiratory tract infections in children.

Methods

This was a retrospective study where case-notes of all children, aged less than 18 years, admitted from 1st November 2010 till 31st October 2011, were reviewed. Children diagnosed with asthma or multiple trigger wheeze were excluded. A significant bacterial pathogen was defined as the presence of a single organism isolated with pus to epithelial ratio > 10:1 or if there were no epithelial cells and a single organism was cultured with significant fever and high neutrophil count. This was based on a modification of the Bacterial Pneumonia Score (BPS) by *Moreno et al.* Direct immuno-fluorescence assays on viral antigens or viral PCR was done to detect common viruses in nasopharyngeal aspirates.

Results

Four hundred and sixty-three case-notes were reviewed. The median age was 8 months (IQR 4-14 months). A bacterial aetiology was suspected in 8.9% of cases, a viral cause in 47.5% and mixed (virus + bacteria) in 4.1%. In 39% of children, no definite aetiology could be found. The commonest virus isolated was respiratory syncytial virus (20.7%) followed by *Parainfluenza 3* (1.9%) and Adenovirus 1.7% (8 cases). The commonest bacteria isolated were *Haemophilus influenzae* (9.7%), *Staph aureus* (8.0%) and *Streptococcus pneumoniae* (4.3%). Only 6.9% of *Haemophilus influenzae* (2 out of 29) were resistant to ampicillin. CRP was significantly higher in children presumed to have a bacterial infection ($p = 0.002$).

Conclusion

Viruses are a common cause of lower respiratory tract infections in children. Most bacteria isolated in our study could be treated with first line antibiotics.

AUTOIMMUNE LIVER DISEASE IN MALAYSIAN CHILDREN

Su Han Lum, Ruey Terng Ng, Benjamin TY Lim, Kim Mum Khoh, Christopher CM Boey, Way Seah Lee

Department of Paediatrics, University of Malaya Medical Centre, Kuala Lumpur, Malaysia

Background and aims

Autoimmune liver disease (AILD) in children is a potentially treatable autoimmune hepatobiliary disease including autoimmune hepatitis type 1 and 2 (AIH1, AIH2), autoimmune sclerosing cholangitis (AISC) and primary sclerosing cholangitis (PSC). It is not commonly described among Asian children. We reviewed the features, subtypes and outcome of children diagnosed with AILD referred to a single centre in Malaysia.

Methods

Retrospective chart review of all children referred to the paediatric hepatology unit, University Malaya Medical Centre, Malaysia.

Results

A total of 23 children (males=12, 52%; median age at presentation 7.4 years, range 1.8-15.5 years) with AILD from 1999 to 2012 were referred during the study period. AIH1 was the commonest form (n=12, 51%), followed by AISC (n=6, 26.1%) and AIH type 2 (n=2, 8.7%), while no patient with PSC was diagnosed in our study. The median duration of symptoms before referral was 2 months (range 0.01-92.0 months). Pattern of presentations was: 8 (35%) had insidious onset, 7 (30%) had acute hepatitis, 3 (13%) presented with complications of chronic liver failure and/or liver cirrhosis, and 5 (22%) had incidental findings of deranged liver enzymes during investigations or follow up for other medical illnesses. The commonest presenting features were jaundice (n=14, 61%) and hepatomegaly (n=15, 65%). Associated autoimmune diseases and family history of autoimmune diseases were present in 5 (22%) and 2 (9%) patients respectively. Two patients with acute hepatitis progressed to acute liver failure. Portal tract inflammation, lymphocytic aggregation, periportal/periseptal necrosis and lobular/nodular activity were common histological features. 81% of patients were steroid responsive, with 50% of patients remained in clinical and biochemical remission after first induction. Two patients underwent liver transplantation. The overall mortality was 13%.

Conclusions

AILD in this cohort were similar to those described in the literature. Lack of timely liver transplant in those with liver failure adversely affected the outcome.

CONJOINED TWINS

K Somasundaram

Consultant General and Paediatric Surgeon

We at the University Malaya Medical Centre were the first in Malaysia to successfully operate to separate and reconstruct conjoined twins. This was done in March 1981 and again in another set in April 1982.

They were ischiopagus twins which is the most complex of the five varieties of conjoined twins.

The procedure required a team effort of Surgeons, Paediatricians, Anaesthesiologists and Radiologists to evaluate and prepare for the operative procedure. We were fortunate that the babies survived for 6 months without the need for an emergency operative separation which carries a high operative mortality. It is a credit to the Paediatric team for the pre and post operative care.

It was our intention that the operative technique for separation be planned to enable the reconstruction also to be done at one single operation. This required weeks of preparation and detailed anatomical studies to work out the procedures that hitherto had not been reported in the medical literature. The shared internal organs had to be separated into two sets of viable functional internal organs. The operative time for the first set of twins was 12 hours and for the second set 11 hours. The long period of anaesthesia for small babies was a major challenge to the anaesthesiologists. Intra operative monitoring machines that are available today were not in existence 30 years ago.

Radiological investigations were limited because scans such as CT and MRI were not available. The internal anatomical complexities including the shared pelvic floor muscle and the fused pelvic girdle had to be worked out without the benefit of imaging techniques and were based entirely on the knowledge of anatomy and embryology.

It was planned that colostomies be avoided and anal and rectal reconstruction be done at the same time. Life without abdominal colostomies gave them normal lifestyle. This has not been done in the six previous operations for the separation and reconstruction of ischiopagus conjoined twins.

It needs to be recorded that none of the four twins had the need for any further operative procedures and are leading normal lives except for one of the first pair that passed away at about 10 years of age from renal failure due to under development of the kidneys at birth.

CROHN DISEASE – A CLINICO-EPIDEMIOLOGY STUDY FROM MALAYSIA

Alvin Kim Mun Khoh, Darren Tan, Ruey Terng Ng, Pei Fan Chai, Christopher CM Boey, Way Seah Lee

Department of Paediatrics, University Malaya Medical Centre, 50603 Kuala Lumpur, Malaysia

Background and Aims

Crohn Disease (CD) is a chronic inflammatory condition affecting the gastrointestinal tract. It is most prevalent among children from Europe, United States and Australia. Its epidemiology, clinical features and disease behavior are not well described in Asian children. We aimed to describe the epidemiology, presenting features and disease behavior of CD in Malaysian children.

Methods

Retrospective chart review of all children with CD seen at the pediatric gastroenterology and hepatology unit, University Malaya Medical Centre from January 1997 till December 2011.

Results

A total of 25 children (median age at diagnosis 7 years, range 10 months – 14 years) with CD were referred during the study period. There was an increasing trend in the incidence of CD in the recent years: an average of 2.3 new cases/year from 2005 to 2011, compared to 1.1 cases/year from 1997 to 2004 ($p=0.08$). There were more boys than girls (ratio of 2:1). The most common symptoms at presentation were abdominal pain (80%) and diarrhoea (68%). Ileocolonic disease accounted for 72% of patients, followed by colonic disease (20%). Majority of the patients had non-stricturing, non-penetrating disease ($n=18$, 72%); another 20% ($n=5$) had stricturing disease, one had penetrating disease, while another had both penetrating and stricturing disease. Forty-eight percent ($n=12$) of patients required surgical intervention. At the most recent review, majority ($n=19$, 76%) was in clinical remission. One patient died from a disease unrelated to CD.

Conclusion

Childhood CD is not uncommon in Malaysia, and there was increasing incidence over the last six years. The disease behavior and outcome is similar to that seen among Caucasian population.

ONE IN FIVE OVERWEIGHT / OBESE ADOLESCENTS IN THE COMMUNITY HAS METABOLIC SYNDROME

Muhammad Yazid Jalaludin¹, Aisha Fadhilah Abang Abdullah¹, Noorasekin Saiman¹, Nurshadia Samingan¹, Zahurin Mohamed², Fatimah Harun¹

¹Department of Paediatrics, Faculty of Medicine, University Malaya, Kuala Lumpur, Malaysia

²Department of Pharmacology, Faculty of Medicine, University Malaya, Kuala Lumpur, Malaysia

Introduction

Childhood obesity is on the rise globally, and Malaysia is of no exception. The major concern of childhood obesity is that it is highly associated with metabolic syndrome which predispose an early risk of cardiovascular disease and type 2 diabetes mellitus.

Objective

To determine the rate of metabolic syndrome in overweight/obese adolescents in the community.

Methodology

Overweight (OW) and obese (OB) adolescents who have never seek medical attention, were identified from schools in a local township and invited to attend a one-day obesity workshop. Anthropometric and waist measurements, together with fasting bloods were taken. Metabolic syndrome was defined using International Diabetes Federation (IDF) 2007 Guidelines i.e presence of abdominal adiposity (WC >90th centile for age and gender) plus two/more clinical features (i.e high fasting plasma glucose (FPG > 5.6mmol/L), hypertension (BP >130/85 mm Hg), elevated triglyceride (TG > 1.7mmol/L) and low HDL-cholesterol (<1.03mmol/L).

Results

A total of 172 adolescents (19.7% OW, 80.3% OB) attended the workshop; with 96 (55.8%) were males and mean age 14.2 years (ranges 12 to 17 years). Abnormal WC was documented in 157 (91.3%); 18 (10.4%) had high FPG and 61 (35.5%) had hypertension. Nineteen (11.0%) had high TG while 43 (25.0%) had low HDL. Thirty three (19.2%) fulfilled metabolic syndrome criteria (30.7% were OW, 59.3% were OB).

Conclusion

The prevalence of metabolic syndrome among the overweight/obese adolescents in this community was high. Routine screening by the school health authority is highly recommended to help reduce the risk of complications.

References

1. Ismail MN et al. *Prevalence and Trends of Overweight and Obesity in Two Cross-sectional Studies of Malaysian Children, 2002-2008. Symposium 2, MASO Scientific Conference on Obesity, 12-13 August.*
2. Poh BK, et al. Waist circumference percentile curves for Malaysian children and adolescents aged 6.0 – 16.9 years, *Int J Pediatr Obesit*, 2011;6: 229–235.
3. Poh BK, et al. Metabolic Syndrome Based on IDF Criteria in a Sample of Normal Weight and Obese School Children. *Malaysia J Nutr* 2010;16:207 – 217.

APPROPRIATENESS AND CONTRIBUTIVE YIELD OF PEDIATRIC GASTROINTESTINAL ENDOSCOPY: A SINGLE-CENTRE AUDIT STUDY

Hafiah Zainuddin, Christopher CM Boey, Way Seah Lee

Department of Paediatrics, University Malaya Medical Centre, Kuala Lumpur, Malaysia

Background

North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) and American Society for Gastrointestinal Endoscopy (ASGE) guideline in endoscopic practice for children helps clinicians in selecting appropriate patients for endoscopy. Little is known on its predictability on positive endoscopic finding or contributive yield in clinical outcome.

Objective

To determine the predictability of the NASPGHAN and ASGE guideline on positive endoscopic finding and contributive yield in clinical practice in children.

Design

Descriptive, retrospective analysis.

Setting

Department of Paediatrics, University Malaya Medical Centre, Malaysia.

Patients

All children who had esophagogastroduodenoscopy (EGE) and colonoscopy from January 2008 to June 2011.

Interventions

None

Main outcome measurement

An endoscopy was considered appropriate when its indication complied with the NASPGHAN and ASGE guideline. All endoscopic finding was classified as either positive (presence of any endoscopic or histologic abnormality) or negative (no or minor abnormality, normal histology); effecting a positive contributive (a change in therapeutic decisions or prognostic consequences) or non-contributive yield (no therapeutic or prognostic consequences).

Results

99.7% of the 345 procedures studied were considered appropriate. Overall, 76% had a positive finding. The overall positive contributive yield for a change in diagnosis and/or management was

44%. The presence of a positive endoscopic finding was more likely to effect a change in the therapeutic plan than in the initial diagnosis.

Limitations

Retrospective review.

Conclusions

The NASPGHAN and ASGE guideline is more likely to predict a positive endoscopic finding but less sensitive to effect a change in the initial clinical diagnosis or the subsequent therapeutic plan.

PAEDIATRIC RESEARCH IN MALAYSIA IN THE LAST 50 YEARS

Boo Nem Yun

Faculty of Medicine and Health Sciences, Universiti Tunku Abdul Rahman

Paediatricians in Malaysia have been involved in research at various levels of intensity since the 1960's

In the 1960's to 1970's, the majority of the paediatric research output in Malaysia were carried out by paediatricians from the Department of Paediatrics of Universiti Malaya, the first university in the country. They were later joined by those from Universiti Kebangsaan Malaysia (UKM) and Universiti Sains Malaysia (USM) when Departments of Paediatrics were set up and where research has since been viewed as an important part of academic activities. In recent decades, other public universities such as Universiti Putra Malaysia and private universities such as the International Medical Universiti and Universiti Tunku Abdul Rahman began actively promote research in their respective institutions.

In the early days, there was no career path for full time paediatric researchers. Almost all research output by our senior paediatric colleagues were carried out on the side-line, as teaching and service provision were their primary responsibilities. Research grants were very scarce and limited in amount, particularly in the 1960s to the 1970's. Securing grants to carry out research with the help of research assistants was unheard of in the early days. Despite these limitations, many of our senior pioneers did research out of interest and, probably, curiosity to find the truth. Many of them published high quality research output in a number of internationally reputable journals such as the Archives of Diseases in Child Health, the World Health Organisation Bulletin, Journal of Paediatrics, Australian Paediatric Journal, and Pediatric Research.

Initially, most of the paediatrics researches were of the observational type. Later, case control studies began to be reported in the 1990's and findings of randomised controlled trials were published during the last two decades by some investigators.

Many fields of paediatrics were studied. The most widely published findings in the 1970's and 1980's were viral infections, childhood leukaemia, renal diseases in children, neonatal infections, cow's milk protein enteropathy, and nutritional status of children in Malaysia. Some of the research findings which have made an impact on our practice even to these days. These include cow's milk protein enteropathy by Professor Lynkaran N and his colleagues, the discovery of the link between margosa oil and Reye's syndrome by Professor Sinniah D and his collaborators, Flavobacterium meningitis and respiratory syncytial virus infection reported by

Dr Lee Eng Lam and his colleagues, and identification of Gilbert's disease as an important cause by severe neonatal jaundice in Malaysia by the UKM and USM groups.

With the establishment of postgraduate courses in Paediatrics in the 1980's and 1990's in the three universities mentioned above, the number of paediatric research increased, as each postgraduate student had to complete a research project to graduate. However, the number of published findings initially was low until recent years when the need to meet key performance index by the university lecturers provides an impetus to get these findings published.

To help the postgraduates to do research, a number of steps have been put in place by the universities. In UKM, for instance, all paediatric postgraduates have to undergo a training course in research methodology before they begin their research project. Regular journal critique sessions of published paediatric research are carried out. Since its inception in the 1980's, all research dissertation of the paediatric postgraduates in UKM are evaluated by external examiners to determine whether are of reasonable standard to graduate.

Besides the universities, research has also been encouraged by the Ministry of Health in recent years. Collaborative studies with national and international bodies are promoted by both the MOH and the universities. Publications of such joint efforts have begun to appear. However, compared with other disciplines, such collaborations are still very few, even among the universities.

In summary, our senior paediatric colleagues showed us that it is possible to do good quality research in Malaysia. To take us to the next level, we need to create a career path in paediatric research with appropriate rewards for output of international standards. Furthermore, we need to raise the level of collaboration between basic scientists and clinicians, and also inter-institutional collaboration to maximise the use of all expertise and facilities.

MALAYSIAN BREAST CANCER SURVIVORSHIP COHORT (MYBCC) STUDY

Nur Aishah Mohd Taib², Tin Tin Su¹, Nabilla Al Sadat¹, Maznah Dahlui¹, Hazreen Abdul Majid¹, Nirmala Bhoo Pathy¹, Shamsinah Hussain¹, Mohd Nahar Azmi Mohamed³, Yip Cheng Har² and MyBCC team

¹Centre for Population Health (CePH), Department of Social and Preventive Medicine Faculty of Medicine, University of Malaya

²Department of Surgery, Faculty of Medicine, University of Malaya

³Department of Sports Medicine, Faculty of Medicine, University of Malaya

Background

Breast cancer is the most common cancer among Malaysian women. Previous studies reported there is disparity of breast cancer survivorship among Malaysian patients. Breast cancer is a multifactorial disease- that is due to complex combination and interaction of different factors such as disease clinic-pathological features, ethnicity, health behaviors, lifestyle, genes and environment. However, the study about its interaction and impact on patient survivor is still inadequate.

The Malaysian Breast Cancer Cohort (MyBCC) is a prospective cohort study which aims to identify the association between genetics, lifestyle and nutrition on overall survival and quality of life of Malaysian Breast Cancer patients. It is a collaboration project with Queens University of Belfast, United of Kingdom and funded by Ministry of Higher Education, Malaysia since 2011.

Methods

In MyBCC, detailed information about each patient including clinic-pathological features, quality of life, psycho-social support, physical activity, complementary and alternative medicine used, occupation and finance will be collected along with tissue, blood and urine samples. Patients will be followed up routinely up to 3 years. The participations of the breast cancer patients will be voluntary. The project aims to recruit at least 1000 Malaysian Breast Cancer patients who visit to University of Malaya Medical Centre and representing various ethnic groups, cultures, occupation and lifestyles.

Discussion

The UM Cancer Research Institute (UMCRI) biobank served as key infrastructure in MyBCC. Biobank would support long-term storage of blood, serum, plasma, tissue and urine for future potential researches. MyBCC, therefore, represents the resource and opportunity to investigate the factors that affecting the patients' survivor by analyzing the answers, measurements, and biospecimen collected from patients.

MyHEARTS - RISK FACTORS FOR CHRONIC NON-COMMUNICABLE DISEASES AMONG ADOLESCENTS

Nabilla Al Sadat¹, Muhammad Yazid Bin Jalaluddin², Hazreen Abdul Majid¹, Nowrozy Kamar¹, Tin Tin Su¹ and MyHeARTs team

¹*Centre for Population Health (CePH), Department of Social and Preventive Medicine Faculty of Medicine, University of Malaya*

²*Department of Pediatrics, Faculty of Medicine, University of Malaya*

Background

One of the public health concerns in the country is the dramatic increase in the number of obese children among Malaysian population. It was noted from the National Health & Morbidity Survey III (2006) that the prevalence of overweight among children aged less than 18 years in Malaysia had more than doubled in the last ten years; from 2.0% in 1996 to 5.4% in 2006¹. This observation is of public health importance with the identification of overweight/obesity as a risk factor for exposing individuals to chronic diseases such as type2 diabetes mellitus (T2DM), heart disease and certain types of cancers, and increased mortality. Thus, a prospective cohort study of schoolchildren attending Secondary One (aged 13) in Malaysia is done to gather primary data.

Methods

The method of sampling is a cluster, multistage sampling design. The sampling frame will be all the students from all government schools, except boarding, religious and vernacular schools. This cohort study involved initial recruitment and health screening of approximately 1361 adolescents from 15 schools from Perak, Selangor and Wilayah Persekutuan Kuala Lumpur (WPKL). They were interviewed, using a standardized pre-tested questionnaire on demographic, socio-economic, behavioral and gestational variables.

Results

According to preliminary analysis, prevalence of overweight and obese among the study participants were 13% and 14.7% respectively. 4.3% of the adolescents have high blood cholesterol and 0.7% has high blood glucose. High prevalence of vitamin D deficiency was found in the study population.

Discussion

The cohort of children would be followed again at later age. This longitudinal cohort study, the first of its kind among adolescents in Malaysia, will result in information upon which effective health care prevention strategies can be designed to prevent chronic non-communicable

diseases in the future. The analysis of the determinants in high risk behaviors as well as chronic diseases will create innovative approaches in the generation of healthy adults and a healthy nation.

“PARTNER (PARTICIPATORY ACTION RESEARCH THROUGH NEGOTIATION AND EMPOWERMENT OF RESIDENTS)” FOR LOW INCOME URBAN COMMUNITY

Tin Tin Su¹, Hazreen Abd Majid¹, Wong Li Ping¹, Maznah Dahlui¹, Farizah Hairi¹, Nithiah Thangiah¹, Awang Bulgiba², Rusdi bin AbdRashid³, Nasruddin Jaafar⁴, Adeeba Kamarulzaman⁵, KhooEeMing⁶, Liam Murray⁷

¹Centre for Population Health (CePH), Department of Social & Preventive Medicine, Faculty of Medicine, University of Malaya

²JCUM, Department of Social & Preventive Medicine, Faculty of Medicine, University of Malaya

³UMCAS, Faculty of Medicine, University of Malaya

⁴Community Oral Health Research Group (COHRG), Faculty of Dental Medicine, University of Malaya

⁵CERIA, Faculty of Medicine, University of Malaya

⁶Department of Primary Care Medicine, Faculty of Medicine, University of Malaya

⁷Centre for Public Health, Queens University of Belfast

Contact: tstin@ummc.edu.my

Background

The prevalence of non-communicable diseases (NCD) in Malaysia has almost doubled over the last decade. The rapid rise of non-communicable diseases predominantly affects the lower socio-economic groups living in urban areas. Realizing this, a group of researchers from the University of Malaya (UM) took an initiative to improve the general wellbeing and health status of the urban population involving lower socio-economic group by conducting a community based participatory action research project.

This research project is funded by the Research University Grant from the Ministry of Higher Education as UM is on the 5 Research Universities identified. This is one of the Flagship Projects identified by UM and headed by the Centre for Population Health in conjunction with other centres under the Health and Translational Medicine Research Cluster.

Objectives

Among the objectives of this study were to explore the health and social needs, life style factors and health risk behaviour of urban population from lower socioeconomic groups in Kuala Lumpur so that a tailor-made intervention programme can be carried out according to the health and social needs of the community.

Methods

Altogether 800 households from four *Projek Perumahan Rakyat: Community Housing Project (PPR)* which are PPR Kerinchi, PPR Pantai Ria, PPR Seri Cempaka and PPR Seri Pantai were selected using multistage proportionate simple random sampling. The project will be carried out in three phases of exploratory (household survey and medical screening), intervention (health

promotion campaign, self-management and therapeutic life style changes) and post-intervention (cost effectiveness of intervention programme) within five years.

Results

Preliminary analysis of the household survey data showed that 88% of the study population are Malay and 56% of households have monthly income less than RM 2,000. The result of medical screening showed high prevalence of obesity, and non-communicable diseases such as hypertension, diabetes and hyperlipidemia.

Discussion

Among the expected outcome are increased awareness of individual health status and lifestyle factors in relation to NCD, improvement of healthy diet intake and level of physical activities, reduction of health risk behavior, community empowerment of health promotion and self-management of NCD and enhanced health status and self-reliance of the general well-being of the community.

As the ultimate goal of the project is to focus on research that may be translated directly in improving the healthcare and wellbeing of the community, through the implementation of this project, the public especially communities in the proximity of the university would equally benefit from it.

PROTEOMIC APPROACHES FOR MUSHROOM PROTEIN PROFILING: PROTEINCHIP AND SELDI-TOF COMPLEMENT ELECTROPHORETIC ANALYSIS

Lau Beng Fye¹, *Noorlidah Abdullah¹, Norhaniza Aminudin^{1,2}, Amy Tan Bee Bee¹

¹Institute of Biological Sciences, Faculty of Science and Mushroom Research Centre,

²University of Malaya Centre for Proteomic Research, Faculty of Medicine,
University of Malaya, 50603 Kuala Lumpur, Malaysia

*Corresponding author e-mail address: noorlidah@um.edu.my

Proteins from mushrooms are valued for their nutritional and medicinal attributes but systematic profiling of the proteins received little attention. Proteomic approaches were used for profiling and characterization of water-soluble proteins in aqueous extracts of an indigenous mushroom—the tiger's milk fungus or *Lignosus rhinocerus*. Taken into consideration the high abundance of low-molecular-mass proteins (< 20 kDa), proteinchip and SELDI-ToF were used to complement results from one- and two-dimensional gel electrophoresis. Preliminary findings indicated that protein profiles of *L. rhinocerus* from various developmental stages, cultivation techniques, growth conditions, mushroom parts and processing methods were significantly different. Protein profiles of cultivated and wild strains were found to be fairly similar nevertheless. Use of statistical tools aids in identification of potential marker(s) which might be useful when distinguishing aqueous extracts of different origin. With regards to that, several proteins of interest will be identified via mass spectrometry. Findings from this study might provide insights into physiological role of the proteins as well as their potential therapeutic and/or toxicity effects.

IDENTIFICATION OF ACE INHIBITORY PEPTIDES FROM *PLEUROTUS CYSTIDIOSUS* O.K. MILLER AND *AGARICUS BISPORUS* (J.E. LANGE) IMBACH BY LC-MS/MS

Lau Ching Ching¹, *Noorlidah Abdullah¹, Adawiyah Suriza Shuib^{1,2}

¹Mushroom Research Centre, Institute of Biological Sciences, Faculty of Science,

²University of Malaya Centre for Proteomic Research, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia

*Corresponding author e-mail address: noorlidah@um.edu.my

Hypertension is one of the major health problems worldwide. Bioactive peptides that inhibit Angiotensin I-Converting Enzyme (ACE) in the blood pressure regulation system (renin-angiotensin system) can contribute to the prevention and treatment of hypertension. Mushrooms are high in protein content, which makes them a potentially good source of antihypertensive peptides. Protein extracts from *Pleurotus cystidiosus* and *Agaricus bisporus* having high levels of antihypertensive activity were further purified by reverse-phase high performance liquid chromatography and size exclusion chromatography. LC-MS/MS analysis of the active protein had identified nine peptide sequences with potential ACE inhibitory activity. These peptides have common characteristics of potent ACE inhibitory peptides, which usually consist of less than six amino acids in length, high content of hydrophobic amino acid with aromatic and branched aliphatic amino acid at the C and N-termini, respectively. The IC₅₀ values of the synthesized peptides were in the range of 42.69 to 435.86 µg/ml. The nine peptides exhibited enhanced antihypertensive activity after gastrointestinal digestion. These peptides are from food source hence should have no side effects.

SANDWICH ENZYME-LINKED LECTIN ASSAY: A SIMPLE METHOD FOR DETECTION OF TOTAL O-GLYCANS IN BIOLOGICAL SAMPLES

Lee Cheng Siang¹, Puteri Shafinaz AbdulRahman^{1,2}, Veer Bhavanandan³, *Onn Haji Hashim^{1,2}

¹Department of Molecular Medicine, ²University of Malaya Centre for Proteomic Research, Faculty of Medicine, University Of Malaya, 50603, Kuala Lumpur

³Department of Biochemistry and Molecular Biology, Penn State College of Medicine, USA

*Corresponding author e-mail address: onnhashim@um.edu.my

Changes in O-glycosylation are often implicated in numerous diseases including malignancy. Alteration in the O-glycan structures is difficult to be quantified because of the lack of a method that could detect all structures. We have attempted to develop a simple, sensitive and reliable assay to analyse total O-glycans in complex biological fluid samples. The developed assay was based on the binding of lectins to the unique and consistent GalNAc-Ser/Thr structure in O-glycosylated proteins. Our first strategy was to maximize the exposure of GalNAc-Ser/Thr linkage by subjecting the test glycoproteins to acid desialylation and Smith degradation. Next, the levels of the O-glycans were assessed by enzyme-linked lectin assay (ELLA). Desialylation of the glycoprotein greatly improved the binding of the lectins but treatment with Smith degradation did not improve binding. Of the three lectins tested, jacalin showed the highest detection sensitivity followed by champedak galactose binding (CGB) lectin and *Vicia villosa* agglutinin. The sensitivity was further improved when CGB lectin was pre-coated on plate to specifically capture the O-glycoconjugates. The developed sandwich ELLA was applicable to analyse trace amounts of O-glycans in serum samples that were subjected to acid desialylation.

PROTEOMICS IDENTIFICATION OF DIFFERENTIALLY EXPRESSED PROTEINS IN HT-29 CELL POST-TREATMENT WITH *PERESKIA BLEO* EXTRACTS

Lum Ai Theng¹, *Norhaniza Aminudin^{1,2}, Puteri Shafinaz Abdul Rahman^{1,2}

¹Institute of Biological Sciences, Faculty of Science and Mushroom Research Centre,

²University of Malaya Centre for Proteomic Research, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia

*Corresponding author e-mail address: hanizaaminudin@um.edu.my

Pereskia bleo or locally known as Bunga Jarum Tujuh Bilah, has been claimed to have various medicinal capabilities, including anti-cancer activity. The aim of this study was to investigate the anti-cancer effect of *P. bleo* in selected human cancer cell lines through proteomics approaches. Cytotoxic activities of the crude hot water extract and fractions (water and ethyl acetate) of *P. bleo* against HT-29, Ca Ski and HepG2 were tested using MTT assays. *P. bleo* was found to exert highest cytotoxic effect against HT-29 cells. DNA fragmentation assay showed that apoptosis was induced in HT-29 cells treated with water and ethyl acetate fractions, but not with crude hot water extract. Treated and untreated HT-29 cell lysates were subjected to 2D PAGE for protein expression profiling. Silver stained gels were scanned and analysed using Progenesis SameSpot software. More than 1500 protein spots were detected in each gel, however for the post-treatment analysis, only spots that showed a fold change of at least 2, *p*-value (ANOVA) <0.05 and *q*-value (a FDR adjusted *p*-value) <0.05 were considered differentially expressed. Following treatment with ethyl acetate fraction, eleven proteins were found to be differentially expressed, whereby three proteins were down-regulated and eight proteins were up-regulated. Treatment using water fraction on the other hand, showed that one protein was down-regulated whilst six proteins were up-regulated. No differentially expressed protein was found upon treatment with crude extract. Differentially expressed proteins of interest were identified using MALDI-ToF/ToF mass spectrometry analysis.

COMPARATIVE SELDI-TOF/MS ANALYSIS OF ANTIHYPERTENSIVE PROTEINS FROM *TERMITOMYCES HEIMII* NATARAJAN AND *GANODERMA LUCIDUM* KARST

Noor Hasni Mohd Fadzil¹, Cahaya Fariza Misnan¹, Norhaniza Aminudin^{1,2}, *Noorlidah Abdullah¹

¹Institute of Biological Sciences, Faculty of Science and Mushroom Research Centre

²University of Malaya Centre for Proteomic Research, Faculty of Medicine
University of Malaya, 50603 Kuala Lumpur, Malaysia

*Corresponding Author Email: noorlidah@um.edu.my

Bioactive compounds from mushrooms have been known as a source of beneficial medicine and also as functional food. In this study, the antihypertensive effect of *Termitomyces heimii* (Termite mushroom) and *Ganoderma lucidum* (Lingzhi) was investigated by looking at the inhibition of angiotensin I-converting enzyme (ACE). Dialysed protein fractions consisting of F30, F60 and F90 prepared by ammonium sulphate precipitation were subjected to ACE assay and profiled by SELDI-ToF/MS. *Termitomyces heimii's* protein fraction F30, F60 and F90 inhibited ACE at 57.38 %, 65.08 % and 63.06 % respectively. Expression differential mapping analysis showed F30 contains one peak, F60 having four peaks and F90 two peaks ($p < 0.001$) with m/z values of 3.21 kDa; 9.07, 9.58, 18.14 and 19.16 kDa and 11.86 and 12.86 kDa respectively. Protein fraction F30 from *G. lucidum* exhibited highest ACE inhibition of 58.2% and contains protein peaks m/z 6.75 and 7.59 kDa while another two protein fractions of *G. lucidum*, F60 and F90 exhibited lower ACE inhibitions of 44.7% and 21.9% respectively. Comparing SELDI profiles of potent fractions; F60 from *T. heimii* and F30 from *G. lucidum* showed different protein peaks and molecular weights. Both mushroom species may be a potential source for the antihypertensive proteins.

PROTEOMIC PROFILING OF MILK FAT GLOBULE MEMBRANE ASSOCIATED PROTEINS OF RUMINANTS AND HUMANS

Thaneswari Juvarajah¹, Onn Haji Hashim^{1,2}, Fung Shin Yee^{1,2}, *Puteri Shafinaz Abdul Rahman^{1,2}

¹Department of Molecular Medicine

²University of Malaya Centre for Proteomic Research
Faculty of Medicine, University Of Malaya, 50603, Kuala Lumpur

*Corresponding author e-mail address: terisar@um.edu.my

The milk fat globule membrane (MFGM) which is derived from the apical membrane of lactating cells is highly complex in structure and composed of different proteins and lipid components which are nutritionally beneficial to young offspring. These proteins are distributed between the intracellular and extracellular matrix and some are membrane-associated proteins. Identification of the proteins found on MFGM is highly informative and may reveal unknown pathways that are involved in the mammary glands. Recent studies have reported numerous bioactive proteins on MFGM that play significant roles in cell signaling and defence mechanisms. The present study aims to compare the MFGM proteome profiles in the milk of ruminants and human. MFGM protein extracts were subjected to two-dimensional gel electrophoresis (2-DE) and subsequently developed using silver staining. The respective 2-DE profiles were analysed using Image master 2D Platinum software 7 and the resolved proteins were identified using mass spectrometry and database search. Our results demonstrated that the 2-DE profiles of bovine and caprine MFGM were comparable but markedly different from those of the humans. Immunoglobulin alpha-1 which was exclusively detected in the human MFGM proteome profiles was not detected in the ruminant milk proteome profiles. In contrast, beta lactoglobulin, a potential milk causing allergen was only detected in the ruminant milk proteome profile. Our data suggest the difference in the proteins components found on the 2-DE proteome profiles reflects the variation in the nutritional value as well as immunity influence of different milk sources.

SERUM PROTEOMIC ANALYSIS OF PATIENTS WITH BONE TUMOUR

Wan Izlina Wan Ibrahim¹, Vivek Ajit Singh², Onn Haji Hashim^{1,3}, *Puteri Shafinaz Akmar Abdul Rahman^{1,3}

¹Department of Molecular Medicine

²Department of Orthopaedic Surgery

³University of Malaya Centre for Proteomics Research

Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur

*Corresponding author e-mail address: terisar@um.edu.my

Bone tumour refers to a neoplastic growth which originates from various types of bone tissues, the surrounding soft tissues, muscles and ligaments. In this study, the expression of serum proteins was analysed using the proteomic approach. The method has been widely utilised by researchers to elucidate biomarkers from numerous types of cancers. Five types of bone tumour were analysed, namely osteosarcoma, Ewing's sarcoma, pleomorphic sarcoma, chondrosarcoma and giant cell tumour of bone. Two-dimensional electrophoresis was carried out to profile proteins from sera of newly diagnosed patients with age-matched normal healthy individuals as control group. The data were analysed using Image Master Platinum version 7.0 and protein spots with different altered expression were detected and identified using mass spectrometry. The aberrantly expressed serum proteins offer tremendous potential for use as biomarkers to aid early diagnosis of these tumours.

RESEARCH IN NON INVASIVE BRAIN STIMULATION TO ENHANCE NEUROPLASTICITY AND RECOVERY IN STROKE REHABILITATION

Lydia Abdul Latif

Department of Rehabilitation Medicine, Faculty of Medicine, University of Malaya

Functional recovery after stroke is dependent on the plasticity of both the cerebral cortex and the other unaffected parts of functional neural network. The human brain has the potential to adapt to change following injury based on the concept of neuroplasticity. The field of neurorehabilitation is now embarking on a new period of discoveries with a lot of advances and technologies to facilitate plasticity and functional recovery. Over the last 20 years, new technologies have evolved to support stroke rehabilitation including neuromodulation using transcranial direct current stimulation (TDCS) and transcranial magnetic stimulation. The lecture will focus on discussing research work done in UM using invasive brain stimulation, specifically using TDCS in stroke rehabilitation for motor and speech recovery.

THE APPLICATION OF INTRA-CLASS CORRELATION COEFFICIENT (ICC) IN ASSESSING THE RELIABILITY OF MEDICAL INSTRUMENTS MEASURING CONTINUOUS OUTCOMES

Rafdzah Zaki^{1*}, Awang Bulgiba², Noor Azina Ismail³

¹⁻²Julius Centre University of Malaya, Department of Social & Preventive Medicine, Faculty of Medicine, University of Malaya, 50603, Kuala Lumpur, Malaysia.

³Department of Applied Statistics, Faculty of Economics & Administration, University of Malaya, 50603, Kuala Lumpur, Malaysia

*Corresponding author

Background

The Intra-Class Correlation Coefficient (ICC) is the most popular method used to test for reliability but there are different types of ICC. The objective of this study was to evaluate the application of ICC for consistency (ICC_C) and ICC for absolute agreement (ICC_A) in testing the reliability of medical instruments measuring continuous outcomes.

Method

Comparisons were carried out using both clinical data and simulated data. A cross-sectional study with a sample size of 300 was conducted to obtain clinical data. Variables collected were systolic blood pressure, diastolic blood pressure, heart rate, body temperature, peak expiratory flow rate and carbon monoxide level. Measurements for each variable were repeated three times. All instruments were validated by their manufacturer and should be reliable. Five sets of simulated data were then produced for each variable to represent measurements from unreliable instruments. Analyses were performed using SPSS 17 software.

Result

The analysis of clinical data showed that both the ICC_C and ICC_A correctly predicted that all the instruments tested were reliable. The analysis of simulated data showed that the ICC_C failed to provide correct prediction of reliability for all simulated data. In contrast, the ICC_A correctly predicted the poor reliability in all the simulated data. However, interpretations based on the ICC_A point estimate (not the confidence interval) failed to provide correct prediction in half of the cases.

Conclusion

The ICC_A rather than the ICC_C should be the choice of statistical test for testing the reliability of instruments measuring continuous outcomes. The interpretation of ICC should be based on the confidence intervals, not on a single ICC value.

PATTERNS OF HEALTH SERVICE UTILIZATION AMONG MALAYSIAN ELDERLY WITH CHRONIC PAIN

Lily Rafidah Mohamed Zaki¹, Noran Naqiah Hairi²

¹ *Department of Social and Preventive Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia*

² *Julius Centre University of Malaya, Department of Social and Preventive Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia*

Objective

The aim of the study was to analyze pattern of health care utilization in elderly with chronic pain and predictors of hospitalization and type of facilities used.

Methods

We used data from The Third National Health and Morbidity Survey (NHMS III) conducted in 2006 on all elderly aged 60 and above (N=4954).

Results

Prevalence of chronic pain among Malaysian elderly was 15.2%. Elderly with chronic pain were more likely to be hospitalized and frequent users of health services. The multivariate result showed educational status ($p=0.013$), chronic pain status ($p=0.004$), level of interference of pain ($p=0.046$) and present of chronic diseases ($p<0.001$) were the significant predictors of hospitalization among the elderly. Among those hospitalized, majority (88.9%) prefer Public hospital admission compared to Private hospital (11.1%). A quarter (25.0%) of public hospital attendees were from household with average income less than RM1,000. More than half (75.0%) were from the group with income of more than RM 1,000. The multivariate analysis showed ethnicity ($p <0.001$) and income level ($p=0.04$) were associated with the choice of facilities, but not for chronic pain ($p=0.795$), chronic diseases (0.109) and level of interference of chronic pain (0.602).

Conclusions

The findings revealed a high rate of utilization of health services by Malaysian elderly, especially when chronic pain and chronic diseases were present.

COST EFFECTIVE ANALYSIS OF DIFFERENT TYPES OF RECALL ON PATIENTS' RESPONSE RATE IN A PAP SMEAR SCREENING PROGRAM

Rima Marhayu Abdul Rashid¹, Maznah Dahlui²

¹ *Department of Social and Preventive Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia*

² *Julius Centre University of Malaya, Department of Social and Preventive Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia*

The objective of this study was to determine the patients' response rates between different types of recall used i.e. postal letter, registered letter, short message services (sms) or a phone call and the cost effective analysis between different types of recall used in the population based cervical cancer screening in Klang.

A Randomized Control Trial study was carried out from May, 2011 to November, 2011. A total of 1108 samples were selected among women who fulfilled the inclusion and exclusion criteria. These participants were then allocated equally into four different groups. The participants were recall by a postal letter, registered letter, phone call or sms according to the respective group they were assigned to for a repeat smear.

Our findings showed that there was a significant increase in the proportion of patients who return for a repeat smear in the intervention groups compared to the conventional letters (control group) (18.8% vs 20%, 21.6% and 32.8% for registered letters, sms and phone call respectively, $p=0.001$). The cost per outcome for a registered letter is highest among all the interventions, followed by postal letter, sms and a phone call (RM14.84 \pm 0.13 vs RM6.79 \pm 0.11, RM3.55 \pm 0.12 and RM 3.32 \pm 0.15 respectively).

In conclusion, the recall methods using phone calls significantly improved the continuity of care for a repeat smear among patients who had normal findings on the previous smear. It is the most cost effective method among other intervention used.

EXPLORING FACTORS ASSOCIATED WITH PHYSICAL ACTIVITY AMONG ADOLESCENTS IN SARAWAK: A GROUNDED THEORY APPROACH

Saimon Rosalia*^{1,2,3}, Choo Wan Yuen^{1,2}, Bulgiba, Awang^{1,2}

¹Julius Centre University of Malaya, Kuala Lumpur, Malaysia

²Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

³Faculty of Medicine and Health Sciences, Universiti Malaysia Sarawak, Sarawak, Malaysia

*Corresponding author

Background

Physical inactivity equates to as many deaths as tobacco causes globally. Currently about 80.3% inactive adolescents worldwide is exposed to various chronic diseases. Unfortunately the existing health promotion programs are still ineffective to overcome this problem. Evidence from developing countries is scarce.

Objective

This study aimed to explore the factors of physical activity among adolescents in Sarawak.

Design

The approach of grounded theory was followed to systematically collect and analyze data. Triangulation of data and methods (*photovoice*, focus groups, and depth interviews) was applied.

Results

A total of 151 photographs were discussed by the adolescents (n=22) in four focus groups and in-depth interview with parents (n=8). Factors influencing adolescent physical activity include; physical and social environment (e.g crime, road safety, aesthetics, weather); parent's supportive and restrictive role, peer influence, leisure time; transportation mode; and ethnic segregation of play space. Positive perceptions about the environment (e.g. recreation facilities) prop adolescent's self-efficacy, parent's supportive role, and peer support. Negative perceptions of the environment (e.g crime, traffic safety) induce parent restriction, perceived barrier, and induce screen time. Parent's fear of their children to be the victim of crime must not belittle. Parents used scare tactics (e.g. ghost stories) and electronic entertainment to limit adolescents' routine outdoor activities.

Conclusion

Programmes that improve the neighbourhood environment to promote physical activity may be more effective where efforts are made to enhance psychosocial support and self-efficacy.

THE DIFFERENT SMOKING STAGES AMONG ADOLESCENTS AND ITS ASSOCIATED FACTORS

Premila Devi^{1,2,3}, **Noran N Hairi**^{1,4}, **Nabilla Al Sadat**^{1,2}

¹ *Department of Social and Preventive Medicine, Faculty of Medicine, University of Malaya*

² *Centre for Population Health, Faculty of Medicine, University of Malaya*

³ *Ministry of Health, Malaysia*

⁴ *Julius Centre University of Malaya, Faculty of Medicine, University of Malaya*

Objective

To estimate the size and demographic characteristics of the smoking stages among adolescents and to identify if similar factors are associated with all the stages.

Method

A total of 2550 form one students across 15 secondary schools in Kinta, Perak were assessed using a self-administered questionnaire. Participants were categorized as never smokers, susceptible never smokers, experimenters, current smokers or ex-smokers. Complex sample analyses were used to derive population estimates and confidence intervals.

Results

There were 55.1% male participants. Thirteen to fifteen percent of the participants in the experimenter, current smoker and ex-smokers stages came from families with single parents. Results showed 19.3% of the adolescent population to be susceptible never smokers. This study also estimated 6.0%, 5.5% and 3.1% of the population to be experimenters, current smokers and ex-smokers respectively. Gender, ethnicity, best friends' smoking status and smoking refusal self-efficacy were significantly associated with all four stages of smoking when compared to never smokers. Excluding the ex-smokers, the remaining three stages were found to be associated with siblings' smoking status. Sensation seeking characteristics was not associated with being a current smoker but was associated with the rest of the stages. Participants who admitted to having conflicts with their parents had higher odds of being an experimental smoker. Surprisingly parents' smoking status was not significantly associated with any stages.

Conclusions

This study included only form one students, thus the lower percentage of current smokers. The findings suggest that though there were some similarities, the factors associated with adolescent' smoking also depends on the smoking stages.

Keywords: adolescent, smoking stages

HEALTH RELATED QUALITY OF LIFE IN MALAYSIAN THALASSAEMIA PATIENTS TREATED WITH IRON CHELATION

Jenifer John Kidi¹, Maznah Dahlui², Hishamshah Mohd.Ibrahim

¹ *Department of Social and Preventive Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia*

² *Julius Centre University of Malaya, Department of Social and Preventive Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia*

Thalassemia, a chronic hereditary disease needs lifelong blood transfusion for survival. Iron chelation is crucial to avert the risk of developing iron overload complications resulted from lifesaving blood transfusion. The injective desferrioxamine was the sole iron chelator accessible for the past five decades and only in recent years the oral iron chelators were made available. The aim of the study was to compare the health related quality of life (HRQoL) of thalassaemia children between the iron chelation therapies. A Cross-sectional study was conducted on all transfusion dependent patients on iron chelation in Hospital Kuala Lumpur in 2010. HRQoL scores were measured using the translated PedsQL 4.0 Generic Core Scale, while disease related to iron overload complications and medications were obtained from the medical records and interview with patients. Eighty-seven thalassemia patients were enrolled with mean (SD) age of 13.0 years (3.70). Twenty-one thalassemia patients were treated with desferrioxamine, 20 with combine treatment of desferrioxamine with deferiprone and 46 with deferasirox. The HRQoL results showed the mean (SD) total summary score was 76.9 (13.0). The physical health summary score was 78.3 (15.0) and psychosocial health summary score was 75.8 (15.1). The HRQoL scores of the patients who received desferrioxamine, combine treatment and deferasirox were 80.5 (12.1), 79.5 (15.3) and 74.1 (11.9), respectively ($p = 0.097$). The HRQoL had no significant differences by age, gender, type of thalassemia or serum ferritin level. The three iron chelation therapy showed no differences in impact on the HRQoL of thalassaemia children in this study.

THE DETECTION RATE OF PROSTATE CANCER USING PROSTATE SPECIFIC ANTIGEN (PSA) AND DIGITAL RECTAL EXAMINATION (DRE) IN SABAH

Siang Lin Foo¹, Jasmine Lim¹, TeckMeng Tham², Teck Boon Wong², TengAik Ong¹

¹Department of Surgery, University Malaya Medical Centre, Kuala Lumpur, Malaysia.

²Urology Unit, Department of General Surgery, Queen Elizabeth Hospital, Kota Kinabalu, Malaysia.

Background

The number of false positives is high for TRUS guided prostate biopsy based on the current PSA cut off point, leading to numerous negative biopsies. No comprehensive analysis of various variables stratified with the PSA level has been reported for patients in Sabah.

Objectives

To study the detection rate for prostate cancer based on TRUS biopsies taken according to serum PSA level and DRE and the correlation between these parameters.

Methods

Patients who underwent TRUS guided prostate biopsy in the Urology Unit, Queen Elizabeth Hospital from the 1st of January 2008 to the 31st of June 2012 were selected. 12 core biopsies were done in Queen Elizabeth Hospital by urologists. The type of data collected were date of procedure, hospital registration number of the patients, age, ethnic, and digital rectal examination (DRE) findings of the prostate gland, measured volume of the prostate gland with the ultrasound machine, and PSA level.

Results

A total of 342 patients were recruited in our study. Amongst these, prostate cancer was detected in 111 patients (32.46%). In terms of ethnic groups distribution, the highest detection rate was found in Sabah Native (46/99, 46.46%), followed by Malay (33/87, 37.93%) and Chinese (31/148, 20.95%). We identified a positive association between age-adjusted PSA to prostate cancer which is statistically significant (p value = 0.002; fisher's exact test). In addition, the DRE results is significantly associated with the identification of prostate cancer cases ($p=0.0001$; fisher's exact test) in which prostate cancer was detected in 76/120 (63.33%) patients with a DRE suspicious of cancer.

Conclusion

The detection rate of prostate cancer with TRUS biopsy based on serum PSA level and DRE in Queen Elizabeth Hospital (tertiary hospital in Sabah) is high, at 32.46% and 63.33% respectively. Our data suggests the presence of ethnic differences with regard to detection rates of prostate cancer.

Keywords

PSA (Prostate-Specific Antigen), Prostate Cancer, TRUS biopsy, DRE (Digital Rectal Examination)

A GROUNDED EXPLANATION ON WHY WOMEN PRESENT WITH ADVANCED BREAST CANCER

Taib NA¹, Yip CH¹, Low WY²

¹*Department of Surgery, University of Malaya*

²*Dean's Office, Faculty of Medicine, University of Malaya*

Purpose and relevance

The prevalence of advanced presentation remains a large obstacle to achieving lower mortality rates in low and middle resource countries. Research on the reasons for late presentation is scarce in the Asia Pacific region. This study aims to provide clarity in the reasons why women present their breast cancer at an advanced stage.

Method

Purposive sampling of 19 breast cancer patients presenting with delayed treatment and/or advanced cancer diagnosed within two years at the University Malaya Medical Centre (UMMC), Kuala Lumpur. In-depth interviews were conducted using a topic guide. The audio-recordings were transcribed verbatim. NVivo 8 qualitative software was utilised for data management. Triangulation with patients' medical notes was done. The sample size was determined by theoretical sufficiency a constructivist grounded theory method was utilised. Reflexively the main researcher is a breast surgeon who was not involved in the medical care of the patients.

Results

The constructs were derived from the journey of the patients. Through an iterative process, evidenced by thick description, two models emerged. The first was the stages of breast cancer delay (SBCD) model where four concepts emerged :- i) pluralistic health systems; ii) stages or points of delay; iii) presence of patient or system delays and lastly iv) patient decision making at each stage. Eight points or stages of delay were found :- (i) Appraisal delay; (ii) Disclosure delay; (iii) Illness delay; (iv) Behavioural/ Referral Delay; (v) Scheduling delay; (vi) Diagnostic delay and (vii) Treatment decision delay and (viii) Treatment delay. At each stage, a patient decision making model emerged, the breast cancer delay explanatory (BCDE) model, which was the process of assessing severity, knowing options and choosing options. Four main constructs found to be operational here were; i) knowledge on disease and disease outcomes, ii) knowledge on treatment and treatment outcomes, iii) psychological and physical resources and support and lastly iv) roles in patient and medical decision making.

Conclusion

The theoretical framework on why women present to medical authorities with advanced disease emerged from the constructivist grounded theory. Deconstructing this complex phenomenon, and understanding the breast cancer patients allows for clarity of the issues and opportunities for interventions.

Ethical clearance was obtained from the Medical Ethical Committee of University Malaya Medical Centre MEC 655.7. The study was funded by Vote F FS2252008 Ministry of Higher Education.

PERFORATOR FLAPS IN UMMC

Magaret Leow Poh Gaik

Department of Surgery, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

Perforator flaps have become increasingly popular in reconstructive microsurgery. Plastic surgeons are using them more widely now due to better outcomes with less donor morbidity. Perforator flaps provide a good technique of reconstructing a challenging wound. This poster shows the outcomes of 3 different types of perforator flaps for different indications performed by a single surgeon in a unit during the period of one year.

This poster was presented at the 1st Asia-Pacific Perforator and Supermicrosurgery Course in May 2007 in Singapore.

GENE EXPRESSION SIGNATURES FOR EARLY AND ADVANCED STAGE CRC

Tze Pheng Lau¹, April Camilla Roslani², Lay Hoong Lian¹, Kek Heng Chua¹

¹Department of Molecular Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

²Department of Surgery, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

Background

Colorectal Cancer (CRC) is one of the most frequent cancer types worldwide. In Malaysia, it is ranked as the second most frequent cancer in men, and third in women. CRC is the fourth most common cause of global cancer death and has accounted for approximately 8% of cancer mortalities worldwide. Currently, the clinicopathological parameters used are insufficient for accurate cancer staging, individual prognostic prediction and therapeutic intervention, owing to the great biologic and genetic heterogeneity of this disease. Hence, a new classification scheme based on molecular biomarkers is needed to improve management of CRC.

Methodology

A combination of ACP-based PCR and RT-qPCR was used to identify differentially expressed genes (DEGs) associated with early and advanced stage sporadic CRC. Initially, early stage CRC patients (Stage I - II) were recruited for the preliminary differential expression study. Subsequently, the confirmatory test via RT-qPCR was performed with a total of 27 paired samples, ranging from CRC Stages I – IV.

Results

We have successfully identified distinctive gene expression signatures based on cancer stage and site of tumours. The *RPL35*, *RPS23* and *TIMP1* genes were found to be over-expressed in both early and advanced stage CRC ($p < 0.05$). It is noteworthy that the *ARPC2* gene was under-expressed in early stage CRC tumours while the *C6orf173* gene was over-expressed in late stage CRC tumours only ($p < 0.05$). On the other hand, the *C6orf173*, *RPL35* and *TIMP1* genes were over-expressed in both right- and left-sided CRC tumours ($p < 0.05$). Remarkably, the left-sided CRC tumours have an additional over-expressed gene ($p < 0.05$), i.e., *RPS23* gene.

Conclusion

It is anticipated that these distinctive molecular signatures might complement current histopathological and biochemical parameters in aiding CRC staging. This might then promise a more accurate prognosis prediction and effective therapeutic intervention in future.

LATISSMUS DORSI FLAP AS A CLOSURE METHOD IN LOCALLY ADVANCED BREAST CANCER

Ng CH, Teh YC, Taib NA, Yip CH

Department of Surgery, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

In Malaysia, about 25% of patients with breast cancer present with either locally advanced or metastatic disease. In the management of these patients, the dilemma that most surgeons have is whether to do a toilet mastectomy or primary chemotherapy/ occasionally, these patients have infected fungating lesions and the concern exists for development of sepsis during primary chemotherapy, or disease progression during treatment. It is also not uncommon for patients with benign phyllodes to present with large tumours.

In University Malaya Medical Centre, we will excise these lesions with clear gross margin and cover the large defect using local abdominal advancement flap in combination with a latissimus dorsi flap to cover the defect. Mastectomy and axillary clearance and harvesting of the flap are performed concurrently by two separate surgeons with the patient in the lateral position.

The median size of tumour excised was 11 cm. Clear microscopic margins were obtained in 64% of the patients, close in 9% and involved margins in 27%. One patients (9%) developed local recurrence around the flap as she refused radiotherapy post-operatively.

We conclude that this technique is simple and safe to be performed by a general surgeon and improves the quality of life of these patients and allows them to proceed with chemotherapy and radiotherapy.

TUMOUR NECROSIS FACTOR RECEPTOR-ASSOCIATED FACTOR 1 (TRAF1) HAS A FUNCTIONAL ROLE IN RENAL CARCINOMA (RCC) APOPTOSIS, HAS DECREASED EXPRESSION IN RCC SAMPLES, AND MAY HAVE POTENTIAL FOR TARGETED THERAPY

Retnagowri Rajandram^{1,2}, Nigel C. Bennett¹, Zhiqiang Wang³, Joanna Perry-Keene⁴, David A. Vesey^{1,5}, David W. Johnson^{1,5}, Glenda C. Gobe¹

¹Centre for Kidney Disease Research, School of Medicine, The University of Queensland, Brisbane, Australia

²Department of Surgery, University of Malaya, Kuala Lumpur, Malaysia

³Centre for Chronic Disease, School of Medicine, The University of Queensland, Brisbane, Australia

⁴Department of Anatomical Pathology, Royal Brisbane and Women's Hospital, Brisbane, Australia

⁵Department of Nephrology, Princess Alexandra Hospital, Brisbane, Australia

Background and aims

Renal cell carcinoma (RCC) is the most widespread and lethal among the renal neoplasms.¹ Its resistance to therapy-induced apoptosis^{2,3} impacts on the success of RCC treatments⁴ and needs definition. The tumour necrosis factor (TNF) receptor-associated factor (TRAF) family of proteins links the TNF receptor superfamily to cell signalling cascades.⁵ TRAF1 is involved in regulation of apoptosis, proliferation, differentiation and stress responses. It has a role in development of numerous malignancies; however it has not been investigated in RCC to date.⁶ The aims of this study were to develop expression profiles for TRAF1, apoptosis and mitosis in human RCC of varying classification sub-types, and to investigate the functional role of TRAF1 in therapy-treated RCC *in vitro*.

Methods

121 samples of human RCC of different sub-types plus paired normal kidney were prepared in tissue microarrays. Expression profiles for TRAF1 (immunohistochemistry and morphometry), apoptosis (ApopTag) and mitosis (proliferating cell nuclear antigen/PCNA) were investigated. TRAF1 function was analysed *in vitro* in ACHN RCC cells. TRAF1 short interfering RNA (siRNA) was used to inhibit TRAF1 expression in cancer therapy-treated cells (20Gy X-irradiation and/or 500IU/mL interferon-alpha) and apoptosis and mitosis were quantified.

Results

In patient samples, TRAF1 localised to proximal tubular epithelium in normal kidney and was significantly decreased in clear cell RCC ($P < 0.01$) and all other RCC sub-classifications grouped together ($P < 0.05$) compared with normal kidney. There was little apoptosis or mitosis

identified in any RCC samples. *In vitro*, TRAF1 siRNA caused a significant reduction in therapy-induced RCC apoptosis and restored mitosis (both $P < 0.05$) in treated cells.

Conclusions

TRAF1 may have a pro-apoptotic, anti-mitotic role in RCC. The reduced TRAF1 expression in RCC patient samples compared with normal kidney and localisation of TRAF1 to the proximal tubular epithelium, from which many RCC originate, may demonstrate a potential for targeted therapy in RCC.

References

1. World Health Organisation Pathology & Genetics: Tumours of the Urinary System and Male Genital Organs (2004) Eds Eble JN, Sauter G, Epstein JI, Sesterhenn IA. IARC Press, Lyon, pp 12-31.
2. Sfoungaristos S, Giannitsas K, Perimenis P. Present and future therapeutic options for locally advanced and metastatic renal cell carcinoma. *Expert Opin Pharmacother* 2001; 12: 533-47.
3. Gobe G, Rubin M, Williams G, Sawczuk I, Buttyan R. Apoptosis and expression of Bcl-2, Bcl-X-L, and Bax in renal cell carcinomas. *Cancer Invest* 2002; 20: 324-32.
4. Hutson TE. Targeted therapies for the treatment of metastatic renal cell carcinoma: clinical evidence. *Oncologist* 2001; 16(Suppl 2): 14-22.
5. Zapata JM, Llobet D, Krajewska M, Lefebvre S, Kress CL, Reed JC. Lymphocyte-specific TRAF3 transgenic mice have enhanced humoral responses and develop plasmacytosis, autoimmunity, inflammation, and cancer. *Blood* 2009; 113: 4595-603.
6. Zhang B, Wang Z, Li T, Tsitsikov EN, Ding HF. NF-kappaB2 mutation targets TRAF1 to induce lymphomagenesis. *Blood* 2007; 110: 743-51.

GENETIC PREDISPOSITION TO BREAST CANCER IN MALAYSIAN BREAST CANCER PATIENTS: UPDATE FROM THE MALAYSIAN BREAST CANCER GENETIC STUDY (MyBrCa)

Soo Hwang Teo^{1,2}, Yoon Sook-Yee¹, Thong Meow Keong³, Phuah Sze Yee^{1,2}, Peter Kang², Kang In Nee², Norhashimah Hassan², Hanis Hasmad², Kavitta Sivanandan², Shivaani Mariapun^{1,2}, Woo Yin Ling^{1,4}, Cheng Har Yip^{2,5}, Nur Aishah Mohd Taib²

¹Cancer Research Initiatives Foundation, Sime Darby Medical Centre, Subang Jaya, Selangor, Malaysia

²Breast Cancer Research Unit, University Malaya Cancer Research Institute, Faculty of Medicine, University Malaya Medical Centre, University Malaya, Kuala Lumpur, Malaysia

³Department of Paediatrics, Faculty of Medicine, University Malaya Medical Centre, University Malaya, Kuala Lumpur, Malaysia

⁴Department of Obstetrics and Gynaecology, Faculty of Medicine, University Malaya Medical Centre, University Malaya, Malaysia

⁵Sime Darby Medical Centre, Subang Jaya, Malaysia

Introduction

To date, more than 20 genes and 65 genetic loci have been proposed to cause an increased risk to breast cancer. However, although Asians constitute more than 60% of the world's populations, relatively little is known about the prevalence and penetrance of *BRCA* mutations or mutations in other breast cancer predisposition genes, and the uptake and utility of genetic testing in Asian populations, particularly in low and middle income Asian countries. For *BRCA1* and *BRCA2*, this is in large part because the cost of genetic testing has limited its availability in medium- and low-resource countries, and to date, the majority of testing has been funded through research and charitable funding. Here, we report an update of the results of genetic testing and clinical management of patients for *BRCA1* and *BRCA2*, and the results of testing other breast cancer predisposition genes in the Malaysian Breast Cancer Genetic Study [MyBrCa] and describe the clinical presentation of individuals high-risk for *BRCA* mutations.

Methodology

Since January 2003, a cohort of incident and prevalent breast cancer patients treated at the Breast Cancer Unit at the University Malaya Faculty of Medicine has been established. As of December 2012, a total of 1741 patients have been recruited, of whom 487 patients with early-onset breast cancer and/or a personal and/or family history of breast or ovarian cancer have been fully analysed for *BRCA1* and *BRCA2* mutations. Mutations identified in this and other Asian studies were subsequently tested in a population-based cohort of ~1,500 Chinese, Malay and Indian patients with invasive breast cancer cases and ~1,500 non-cancer controls by

genotyping. Free genetic counseling and genetic testing was offered to all index and 1° and 2° relatives.

Main findings:

1. We have shown that similar to that in other populations, *BRCA1* and *BRCA2* mutations are associated with early age of onset and family history of breast and ovarian cancer [Toh et al., PlosOne 2008]. However, although there is strong association with age and family history, the risk assessment models which were built on Caucasian populations based on these variables severely under predicted the number of carriers in Asians, suggesting that there is a strong need to develop or calibrate risk assessment models for Asians [Thirthagiri et al., Breast Cancer Research 2008].
2. We reported that *BRCA1* carriers are more likely to develop ER- breast cancer and the majority develop triple negative breast cancer [Yip et al., World J Surgery 2009]. More recently, we have shown that triple negative breast cancer is a significant predictor of BRCA mutations in early onset breast cancer patients and in those with significant family history, but may have limited utility in patients with isolated late-onset breast cancer [Phuah et al., Breast Cancer Res 2012].
3. Of the mutations we have detected, we find that a small proportion are recurrent [including the *BRCA1* 185delAG mutation, Laitman et al., 2012] and we have used this information to develop a rapid and cost-effective genotyping strategy for detection of mutations [Kang et al., in prep]. In addition to point mutations and small insertions/deletions, we have found that large genomic rearrangements in both *BRCA1* and *BRCA2* constitute ~10% of the mutations found [Kang et al., Breast Cancer Res Treat 2010].
4. Notably, a significant proportion of mutations identified are novel and many are variants for which there is little functional or genetic studies to determine whether they are clinically relevant. We have analysed the clinical relevant of Malaysian and other Asian mutations in a case control study [Kang et al., in prep] and in collaboration with the ENIGMA consortium, are developing methodologies for the classification of other variants [Spurdle et al., Human Mut 2012]. Notably, functional analysis of one of the *BRCA1* variants conducted in collaboration with the National Cancer Institute USA uncovered a novel function for *BRCA1* [Chang et al., Nature Medicine 2011].

5. We reported that genetic counseling and genetic testing for *BRCA1* and *BRCA2* are generally acceptable to Asian patients, although there is a gap in the provision of such services throughout Asia [Yoon et al., Familial Cancer 2010]. All patients and their relatives with clinically significant mutations are offered clinical follow up and a significant proportion take up screening or risk-reducing surgery [Nur Aishah et al., in prep].
6. In collaboration with the IMPACT international collaborative group, we have shown that men with *BRCA1* and *BRCA2* mutations are at increased risk to prostate cancer and furthermore, that PSA is a sensitive and specific screening tool [Mitra et al., BJU Int 2011].
7. In collaboration with CIMBA, an international consortium of investigators of modifiers of *BRCA1* and *BRCA2* penetrance, we have determined the lifestyle and genetic modifiers of *BRCA1* and *BRCA2* [Antoniou et al., Hum Mol Genetics 2011; Ramus et al., Human Mutation 2012; Antoniou et al., Breast Cancer Res 2012; Couch et al., Cancer Epi Prevention Biomarkers 2012]. More recently, this Consortium has conducted a larger genome-wide study and the results are being reviewed [Antoniou et al., submitted; Zheng et al., submitted].
8. In collaboration with the Breast Cancer Association Consortium, we have identified 42 new loci that contribute to an increased risk to breast cancer [Garcia-Closas et al., Nature Genetics 2013; Michailidou et al., Nature Genetics 2013], and 11 new loci that contribute to an increased risk to ovarian cancer [Pharoah et al., Nature Genetics 2013].
9. In addition to *BRCA1* and *BRCA2*, we have studied the significance of germline mutations in other genes, including CHEK2 [Thirthagiri et al., Familial Cancer 2009], TP53 [Lee et al., Breast Cancer Res 2012], PALB2 [Phuah et al., in prep], and ATM [Mariapun et al., in prep]. More recently, we have embarked on a pilot study to determine the mutations of 20 genes in 1,000 individuals [Sivanandan et al., in prep] and to use whole genome sequencing to identify novel breast cancer genes in families with 4 or more cases of breast cancer but do not have mutations in *BRCA1* or *BRCA2*.

Conclusion

In summary, since 2003, the Malaysian Breast Cancer Genetic Study, a collaborative effort between the Breast Cancer Research Unit at University Malaya and Cancer Research Initiatives Foundation, has uncovered the genes that contribute to an increased risk to breast cancer and the team has begun to use translate this information to the clinic to benefit breast cancer patients and their families.

POLYMORPHISM IN THE *APOE* GENE AND PROMOTER IN THE FUNCTIONAL OUTCOME OF TRAUMATIC BRAIN INJURY IN THE MALAYSIAN POPULATION

Poovindran A. R.¹, Ganesan D.¹, Wong K. T.²

¹Department of Surgery, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia

²Department of Pathology, Faculty of Medicine, University of Malaya, 50603, Kuala Lumpur, Malaysia

Email: anadaraj2001@yahoo.com

Introduction

The variability in outcome following traumatic brain injury (TBI) is only partly explained by prognostic factors such as age and estimated damage. Genetic factors that may influence the brain's susceptibility to brain injury and the capacity for repair and regeneration may also aid in predicting outcome. The *APOE* gene and its promoter region that is responsible for the production of apolipoprotein E (apoE) is an attractive candidate for predicting outcome after TBI. The possession of at least one *APOE*-e4 allele may be linked to poor outcome in patients following TBI.

Aim

To determine whether single nucleotide polymorphisms in the *APOE* gene and promoter region influence the outcome of patients following TBI in Malaysian population.

Method

A total of 209 subjects with TBI who were admitted in Neuro Intensive Care Unit of University Malaya Medical Centre enrolled. Demographic and clinical data collected upon admission. DNA extracted from collected EDTA blood using phenol- chloroform extraction method. The region of interest is amplified using PCR and genotyped by direct PCR sequencing. Glasgow Outcome Scores were determined at six months via telephone. Logistic regression analyses were done using STATA version 10 adjusting for patients' age, gender and Glasgow Coma Scale.

Result

The findings explain the role of single nucleotide polymorphisms in the *APOE* gene and promoter region, in the outcome of patients following TBI in Malaysian population.

ASSOCIATION BETWEEN ETHNICITY AND SURVIVAL AFTER BREAST CANCER IN A MULTI-ETHNIC ASIAN SETTING: RESULTS FROM THE SINGAPORE-MALAYSIA HOSPITAL-BASED BREAST CANCER REGISTRY

*Bhoo Pathy N, Verkooijen HM, Taib NA, Lee SC, Saxena N, Iau P, Yip CH, Hartman M
Singapore-Malaysia Breast Cancer Working Group

Background

Little is known on the impact of ethnicity on survival after breast cancer in the multi-ethnic Asian setting.

Methods

Using the multi-institutional Singapore-Malaysia hospital-based breast cancer registry, we investigated the association between ethnicity and risk of mortality after breast cancer in 3,366 patients diagnosed between 1990 and 2007 (Chinese: 77%, Malay: 15%, Indian: 8%). Kaplan-Meier analysis was used to estimate overall cumulative survival (OS). Multivariable hazard ratios (HR) adjusted for tumor and treatment characteristics were computed using Cox regression analysis after splitting follow-up time along the age-axis and calendar-*time* axis.

Results

Malay patients presented at younger age compared to Chinese and Indians (47years vs 52years vs 53years, respectively, $p < 0.001$) with larger tumors (35mm vs 24mm vs 30mm, respectively, $p < 0.001$), and at later stages (TNM stage III or IV) (37% vs 23% vs 25%, respectively, $p < 0.001$). Malay women were least likely to have undergone surgery, and most likely to receive chemotherapy. Five-year OS was 71.9 (95% CI: 69.7-74.1) in Chinese, 47.2% (95%CI: 41.9-52.5) in Malays and 62.7 (56.0-69.4) in Indians. After adjustment for stage, tumor characteristics and treatment, Malays patients had approximately 60% higher risk of death than the Chinese (HR:1.57; 95%CI:1.40-1.77). Indian ethnicity was not significantly associated with risk of mortality after breast cancer compared to Chinese (HR:1.12; 95%CI: 0.98-1.30).

Conclusion

In the Asian setting, Malay ethnicity seems to be associated with significantly poorer survival after breast cancer, independent of stage, tumor and treatment profile. The underlying reasons for this association are unclear but may be explained by variations in susceptibility to treatment, co-morbidity and lifestyle after diagnosis of breast cancer.

SHIFTING PARADIGMS IN SURGICAL TRAINING – INITIAL EXPERIENCE WITH THE UNIVERSITY MALAYA NEUROSURGICAL SIMULATION SYSTEM

V Waran¹, V Narayanan¹, Owen SLF², Aziz TZ³

¹*Department of Neurosurgery, University of Malaya Medical Centre, Kuala Lumpur*

²*Department of Health Sciences, University of Portsmouth*

³*Nuffield Department of Surgical Sciences, University of Oxford*

In the past, neurosurgical training was essentially “See one, do one and teach one”. In the current environment with reduction in training hours, less exposure to real operating environment and unusual surgical cases, the need for hands on training in a realistic environment is critical for surgeons and theatre staff. With modern technology using scanned images and 3-D laser printing techniques, it is possible to create near realistic surgical models for trainees to develop surgical skills. This technique also allows assessment of surgical competency by objective scoring to quantify training. We present our early experience in the use of such techniques at the University of Malaya in training residents in image guided neurosurgery.

Keywords: Neurosurgery, Simulation, Training

EVALUATION OF HUMAN PAPILLOMAVIRUS (HPV) INFECTION AMONG WOMEN IN UMMC – COMPARISON BETWEEN THIN PREP AND FOURNIER'S SELF SAMPLING

Hamzah H, Aziz A, Lim BK, Woo YL, Omar SZ

Department of Obstetrics and Gynaecology, Universiti Malaya Medical Centre, Kuala Lumpur, Malaysia

Background

Testing for high-risk human papillomavirus (HPV) in primary screening for cervical cancer is considered more sensitive, but less specific, in comparison with Pap smear cytology. Introduction of vaginal self-sampling for human papillomavirus (HPV) DNA testing could increase the rate of screening participation.

Methods

This is a cross sectional study which has been conducted in the period of 12 months from 1st October 2010 till 30th September 2011. A total of 345 patients were recruited. Two samples were taken from all patients by physician directed smear (Thin Prep) and vaginal self-sampling (Fournier's sampler). Both samples were tested for HPV DNA and cytology. Both results were then compared for its efficacy.

Results

The overall detection of the HPV DNA by Thin Prep among 345 patients was 11.3% (39 of 345 samples), whereas it was 9.9% (34 of 345 samples) by the Fournier's self-sampling. The absolute agreement between the ThinPrep and Fournier's self sampling was 93.3% with a Kappa value of 0.648 indicating good agreement with a P value of 0.405, thus it is not significantly different. Overall the prevalence of HPV infection among Malaysian women was 13.6%. The commonest high risk HPV DNA type detected were HPV 68 and 18, and for low risk type was HPV 42.

Conclusions

Self-sampling device compares favourably with physician directed sampling in terms of HPV detection. It also has high acceptability among Malaysian women. This might be the future screening tools for cervical cancer among Malaysian women.

INDUCTION OF LABOUR WITH FOLEY'S CATHETER IN WOMEN WITH PREVIOUS CAESAREAN SECTION

Nuryuziliana D, Sofiah S, Vijeandreh S

University of Malaya, Hospital Melaka

Induction of labour in women with previous caesarean section is a major concern because of increased risk 23 fold of uterine rupture compared to those without previous caesarean section. Mechanical induction with Foley's catheter had been shown less risk of uterine rupture and maternal morbidity with good success rate of vaginal delivery.

Objective

To review the outcome of induction of labour with Foley's catheter in women with previous caesarean section.

Design

A 1 year prospective observational study conducted in Hospital Melaka from January 2010 to December 2010.

Methods

Women with one previous caesarean section who consented for induction of labour and had their labour induced with Foley's catheter. All indication of IOL, initial cervical Bishop's score and labour outcome in these women were recorded and analysed. Main outcome measures: Labour outcome and incidence of any maternal morbidity such as uterine rupture.

Results

A total of 104 women with one previous caesarean section were included in this study. Sixty-six women had successful vaginal delivery (63.5%) and 38 had repeat caesarean section. Eighty-one (77.9%) women needed augmentation with oxytocin until delivery. Among these women, three of them had complication during labour with scar dehiscence or ruptured. No babies were admitted for any perinatal complications.

Conclusion

In women with one previous caesarean section, induction of labour using Foley's catheter is a safe option with good successful rate of vaginal delivery. However multiple factors play a role in determining the success of induction process with Foley's catheter.

THE IMPACT OF POSTPARTUM HAEMORRHAGE (PPH) ON MATERNAL MORBIDITY

Mackeen A, Khong SY

Department of Obstetrics & Gynaecology, University Malaya Medical Centre (UMMC) Malaysia

Background

PPH remains one of the most common causes of maternal mortality worldwide. Delay in diagnosis and suboptimal management are often significant contributing factors leading to maternal morbidity and mortality.

Objective:

To investigate the incidence and management of PPH and to identify its risk factors.

Study Design

Retrospective observational study.

Setting

Delivery Suite, UMMC.

Methods

Between September and November 2011, women who had vaginal blood loss more than 500 mL at vaginal delivery and more than 1000 mL in caesarean delivery within 24 h of delivery were identified. Data collected included ethnicity, age, parity, BMI, medical history, haemoglobin level, ultrasonographic findings, details of previous and current delivery such as induction, duration of labour, the mode and estimated blood loss. Types of medical and/or surgical management and the timing of these interventions noted.

Results

The incidence of PPH at UMMC was 3.0% (44/1448), comprising 65.9% Malays, 20.5% Chinese, 9.1% other Asians and 4.5% Indians. More than half (52.3%) were aged 20–30 years, while nearly half (47.7%) had BMI of 26–30 kg/m². 27.3% had haemoglobin (Hb) level of 10.1–11 g/dL whilst 11.3% had Hb of 8–10 g/dL. There were 93.2% singletons, 4.5% twins and 2.3% triplets. 31.8% had amniotic fluid index (AFI) >18 cm whilst 9.1% had AFI ≤ 8cm. Placental praevia existed in 13.6%. A quarter had one or more previous caesarean section. 4.5% had previous history of PPH. 31.8% had undergone induction of labour. Mode of delivery included spontaneous vaginal delivery (36.4%), emergency caesarean (31.8%), elective caesarean (25%) and instrumental delivery (6.8%). Placental tissue was retained in 6.8%. 18.2% were in

labour for more than 8 h. Women with estimated blood loss 500–999, 1000–2000 and >2000 mL were 36.4%, 54.5%, and 9.1% respectively. Blood transfusion was required in 31.8%. 45.5% were managed by medical means only while 54.5% also required surgical intervention. Oxytocin was the most commonly used drug (79.5%). The causes of PPH were uterine atony (43.2%), trauma (25%), tissue (11.3%), thrombin (3%) whilst 13.6% had more than one cause.

Conclusion

There was significant maternal morbidity but no mortality secondary to PPH. Generally, documentation of the management of PPH was poor. To optimise our clinical practice, we suggest increasing awareness of the guideline, running obstetric 'drills' and using a proforma for documentation.

THE EFFECT OF KNOWLEDGE ON THE DESIRE FOR MULTIPLE PREGNANCIES AMONG PATIENTS WITH SUBFERTILITY

Razali N, Latar IL

Department of Obstetrics and Gynaecology, Faculty of Medicine, University Malaya, Kuala Lumpur, Malaysia

Objective

To study the influence of informing patients regarding the risks associated with multiple pregnancies to both mother and fetus and their initial desire for multiple pregnancies.

Methods

A prospective study was carried out in the Infertility clinic of University Malaya Medical Center, Kuala Lumpur, Malaysia involving patients and their spouses. Couples attending the clinic were offered to fill up a questionnaire separately. Following this, they were handed a pamphlet with information regarding the risks associated with multiple pregnancies. The patients will then be required to answer again the question on the number of pregnancy desired that was previously asked. Univariate and Multivariate regression analysis was performed looking at predictors for desire for multiple pregnancy and also predictors of continuous desire for multiple pregnancies after provision of information.

Results

41% of patients desired multiple pregnancies. Patients older than 35 years old have increased while patients with preexisting knowledge of risks associated with multiple pregnancy and previous treatment for infertility have decreased desire for multiple pregnancies. However, for those patients who have preexisting knowledge of the increased risk, providing further information regarding the risks did not change their increased desire for multiple pregnancy. Similarly, patients who are older than 35 and with longer duration of infertility also did not change their desire after given information regarding the increased risk.

Conclusion

Providing and reinforcing knowledge on the risks to mother and fetus associated with multiple pregnancies did not decrease the preference for multiple pregnancies in patients.

THE EFFECTIVENESS AND ACCEPTABILITY OF SELF-SAMPLING AGAINST CONVENTIONAL PAP SMEAR IN UNIVERSITY MALAYA MEDICAL CENTRE (UMMC)

Aziz A, Hamzah H, Lim BK, Woo YL, Omar SZ

Department of Obstetrics and Gynaecology, Universiti Malaya Medical Centre, Kuala Lumpur, Malaysia

Introduction

The effectiveness of a device for the self-collection of cervical cells for the purpose of supplying a Pap test and for HPV testing has been previously demonstrated. This study expanded upon earlier studies to determine whether the use of a self-sampling device will be more acceptable to Malaysian women and it has acceptable analytic sensitivity to detect precancerous abnormalities.

Methology

This is a cross-sectional study which has been conducted in the period of 10 months from October 2010 till July 2011 with 293 subjects enrolled. Two samples were taken from all patients by physician directed smear (Thin Prep) and vaginal selfsampling (Fournier's sampler). Both samples were tested for cytology. A questionnaire was given to assess their acceptability.

Results

Of 293 women recruited, 289 agreed to participate in the study and performed the self-sampling. We evaluated the sensitivity and specificity of self-sampling by using CytoBrush(Thin Prep) as the comparing test. The sensitivity of cytology for self-sampling was 41% while the specificity of the test was high 73%. The positive predictive value for the test is 34% and negative predictive value is high of 79%. The acceptability of selfsampling was very good which generally it is more acceptable in patient age 35 years and above. 82% of the women considered self-sampling to be practically easy to perform. 77% of the women preferred self-sampling over gynaecological examination in the clinic. 78.2% of them may recommend the test to their female colleagues.

Conclusion

The usage of self-sampling device as a screening tool in the context of detection cervical premalignant cells is limited albeit well acceptable to the local community.