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SMJ

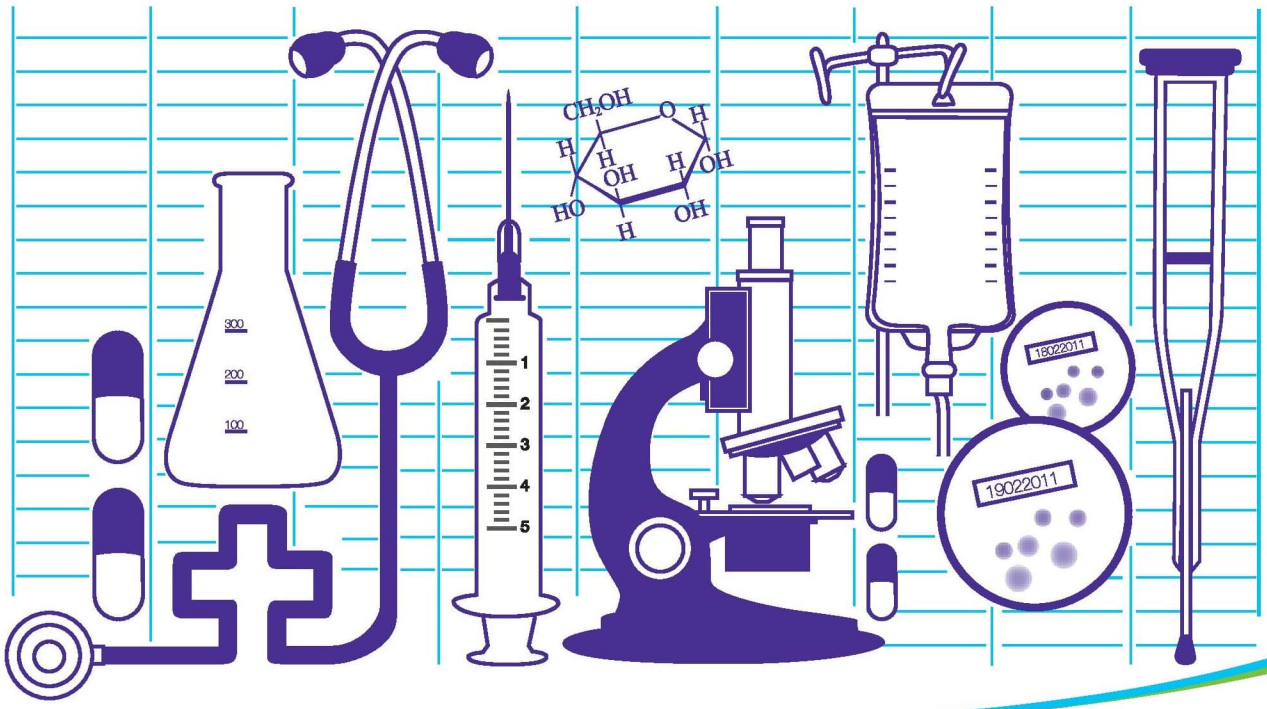
SINGAPORE MEDICAL JOURNAL

ALEXANDRA HEALTH RESEARCH FORUM 2011: New Frontiers

Translating research into clinical practice

18 & 19 Feb 2011

Khoo Teck Puat Hospital
Auditorium (Learning Centre), Level 1, Tower B



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Journal of the Singapore Medical Association

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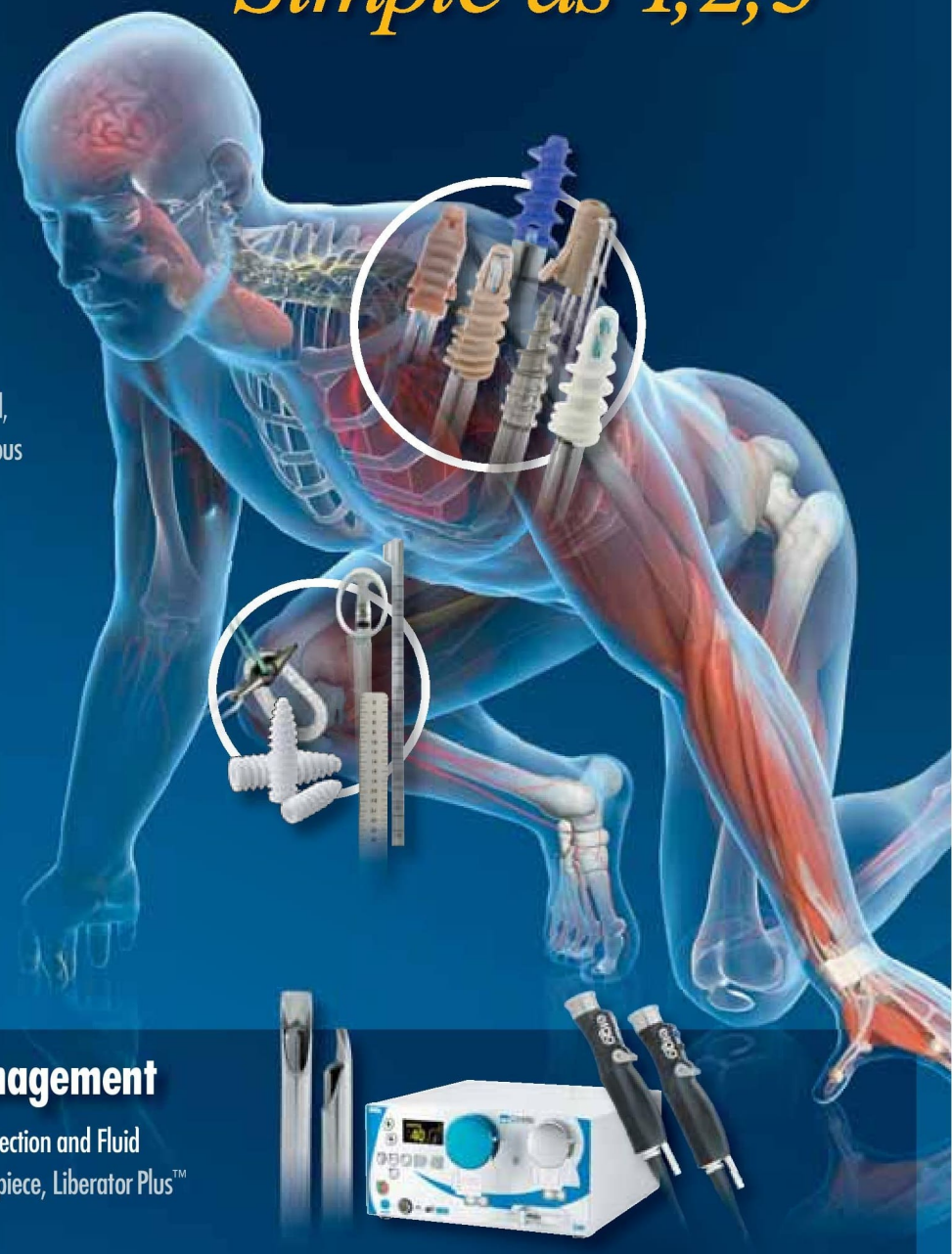

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Welcome Message by the Organising Chairman, Alexandra Health Research Forum 2011 – New Frontiers

It gives me great pleasure in welcoming everyone to the first Alexandra Health Research Forum at Khoo Teck Puat Hospital. The theme "New Frontiers" not only emphasises the new challenges that we face as a brand new hospital in Singapore, but also the need to break old boundaries and redefine new ones in the quest for excellent patient care.

This Research Forum aims to provide a platform for discussion among healthcare workers on how patient care can be enhanced through research and innovation, and in doing so, facilitate transdisciplinary cooperation. At this Forum, we are extremely privileged and excited to have participation from the Genome Institute of Singapore, Nanyang Technological University, Yishun Polyclinic and Jurong General Hospital who will be presenting some of their work. There are in total 87 abstracts to be presented in oral or poster format.

The event will also be graced by a clinician respected by the community, Dr Lim Wee Kiak, our Guest of Honour, and two leading researchers of Singapore: Professor Lee Eng Hin, Executive Director of Biomedical Research Council, A*STAR and Professor Edison Liu, Executive Director of Genome Institute of Singapore, who will be giving plenary lectures.

The organising committee hopes that this Forum will bring about fruitful sharing and discussions for future cooperations, leading to new frontiers in medical science. Lastly, I would like to thank the organising committee for their hard work in making this a memorable event and also our Chairman, Medical Board, A/Prof Pang Weng Sun and Chief Executive Officer, Mr Liak Teng Lit for their unconditional support.

Dr Tan Kok Yang
Organising Chairman
Alexandra Health Research Forum 2011 – New Frontiers

Message from the Guest of Honour

In current times, with an ageing population, coupled with an exponential surge in medical technology, knowledge and discovery in diagnostic and therapeutic options and devices, healthcare systems worldwide face challenging times, and Singapore too is not spared. As has been in the past, we continue to need to deliver healthcare in most timely, appropriate and cost-efficient ways. Only through constant innovation and redefinition of current boundaries can advancements into new frontiers in medicine be made.

It is with this understanding that I am very excited about the research works of our latest hospital in Singapore. In addition to continuing with its aims of being not just a garden in a hospital but also a hospital in a garden, Khoo Teck Puat Hospital aims to deliver seamless and exciting models of healthcare through research innovation.

I look forward to the academic contributions and presentations by the staff of this hospital in their quest to be Singapore's premier hassle-free hospital.

Dr Lim Wee Kiak, PBM
Member of Parliament, Sembawang GRC
Vice-Chairman, Sembawang Town Council

Message from the Chief Executive Officer, Alexandra Health

Most of us are in healthcare because we find meaning in our work – to cure some time, to heal often and to comfort always. We would like to think that we are doing our best and achieving the best outcomes for our patients. But are we?

The truth is, we do not know unless we check.

When we look at outcomes across institutions and among individuals, we often see a bell-shaped distribution. The best is often many times better and safer than the average. As a professional, everyone of us would like to be among the best in our profession. Our patients expect us to be too. The hard truth is that most of us are probably delivering average care. Our complication rates may be three times or more than those of our best colleagues. If we want to provide safer and better care, we need to know where we are now before we can even start to improve.

Mark Twain said over a hundred years ago: *"It ain't what you don't know that gets you into trouble. It's what you know for sure that just ain't so."*

In this era of explosive growth in scientific knowledge, we have to be humble enough to acknowledge that we do not know many things. But with mobile phones, the Internet, Google and Wikipedia, we can find out soon enough.

We need to go about our work with the confidence that 'what we know for sure' is good for our patients. Otherwise, we would all be nervous wrecks and unable to function, even as human beings. Fortunately, most of the time, 'what we know for sure' has been right and has served us and our patients well.

But when 'what we know for sure' turns out to be wrong, we hurt our patients and waste their money, and sometimes, we kill them.

Unfortunately, it is also difficult for us to unlearn 'what we know for sure'. The greater the effort we make to learn something, the harder it is for us to question it. Our colleagues around us too reinforce our perspectives. The professional bodies that we belong to mandate that we conform to the norm. We therefore hang onto 'what we know for sure', long after evidence clearly points the other way.

We need to be inquisitive. Search the literature, attend conferences, look worldwide to seek out the people who are achieving the best results and study what they do. We need to examine what we are doing, and measure our outcomes and benchmark against the very best. We need to experiment, learn and apply what we learn.

Research is pivotal to keep us on track, ensuring that we are indeed doing our best and achieving the best outcomes for our patients. We need to make sure that what we know for sure is indeed so.

Mr Liak Teng Lit
Chief Executive Officer, Alexandra Health

Message from the Chairman, Medical Board, Khoo Teck Puat Hospital

It has been almost a year since Khoo Teck Puat Hospital opened its clinics in March 2010 and the wards and emergency services in June 2010. Within weeks, the wards were overflowing and we had to manage the flow of emergency ambulances. We are more settled now and the hospital was officially opened on 15 November 2010.

I am encouraged that despite the busy workload, our Clinical Research Committee is able to organise this Alexandra Health Research Forum, the first to be held in Khoo Teck Puat Hospital.

I recall that our first Research Forum was held in Alexandra Hospital in 2008. It was a modest one-day forum with several departments chipping in with poster presentations in the rehabilitation medicine gym. We repeated this in 2009 and had medical students participating as well.

We have made much progress since. While clinical service has been a major thrust of the hospital—the biggest wheel in the tricycle—there is a need to develop the two smaller wheels: education and research, without which there would be no breakthroughs or improvements in patient care.

As we settle into the northern community, we need to grow our expertise in research and build clinicians with enquiring minds, eager to find new answers to questions, new and old. We need to create a stimulating and supportive environment. This will be a constant challenge in the presence of a heavy clinical and teaching workload, but we must strive to make it possible.

My congratulations and thanks to the Organising Committee for making this Forum possible, to all who have contributed to the papers and posters, and to all of you for supporting and attending this forum. Have a fruitful time.

Clinical A/Prof Pang Weng Sun
Chairman, Medical Board, Khoo Teck Puat Hospital

Message from the Director, Clinical Research Unit, Khoo Teck Puat Hospital

The theme chosen for this year's Research Forum – New Frontiers – is a very appropriate one. Given the breathtaking pace of advances in science in recent decades, there is no better time for health professionals to exploit these advances for the purpose of setting new frontiers in healthcare. We now understand the pathobiology of diseases better, have better tools in diagnosing diseases and have rapidly expanding choices of preventive and interventional strategies.

However, setting new frontiers will not happen without directed effort. Leaving things to take its natural course of action is incompatible with this goal. To begin, it requires one to adopt a new mindset and thinking paradigm. Our colleagues in information technology call it a T-shaped expertise. I would like to phrase it as ***'embracing breadth and depth'*** – an extremely demanding but exciting challenge for all of us in this time of history. We are enabled but also challenged by the daily voluminous output of information. Therefore, there is a need to read widely. This, however, is not enough. We need to be able to 'connect the dots' in the midst of staring at a starry sky to see the constellation, i.e. to derive meaning and messages from the mass (mess) of information and data. To acquire this skill, one will need considerable training and thinking. Therefore, continual learning (i.e. maintaining 'teachability') is paramount.

We need to strive toward looking beyond boundaries. It is intuitive to call for avoidance of over-specialisation. It is less intuitive to call for avoidance of over-generalisation.

To set new frontiers, we need to embrace breadth and depth, because the stake is high (our patients' well-being) and the reward is great (a fulfilled life well lived in history).

May I congratulate the organising committee and secretariat for an outstanding Forum. May I also sincerely thank our guests, collaborators, sponsors and attendees, for without you, the Forum would not be a meaningful and successful one.

A/Prof Lim Su Chi
Director, Clinical Research Unit, Khoo Teck Puat Hospital

ALEXANDRA HEALTH RESEARCH FORUM 2011 - NEW FRONTIERS		
Day 1 : 18th February 2011		
Time	**Programme**	**Speaker**
0730 – 0800	Registration	
0800 – 0810	All to be seated	
0810 – 0820	Arrival of Guest of Honour - Dr Lim Wee Kiak, Member of Parliament, Sembawang GRC	
0820 – 0825	Welcome Address by the Organising Chairman	Dr Tan Kok Yang
0825 – 0840	Address by Guest of Honour	
0840 – 0855	Opening Address by the Chairman of Medical Board	A/Prof Pang Weng Sun
0855 – 0925	**Plenary Lecture 1** *"A Road Less Travelled: Chronicles of an Orthopaedic Clinician Researcher"*	Prof Lee Eng Hin
0925 – 1010	Research Oral Presentations – Doctors' Category I	
1010 – 1030	Tea Break	
1030 – 1140	Research Oral Presentations – Doctors' Category II	
1140 – 1315	Lunch Break	
1200 – 1300	Manuscript Writing Workshop	
1315 – 1455	Research Oral Presentations – Basic Science Category	
1455 – 1515	Tea Break (Launch of Clinical Research Unit website)	
1515 – 1645	**Combined Genome Institute of Singapore (GIS) – Alexandra Health Symposium**	
1515 – 1535	*"Comprehensive Paired-End-Tag Mapping Reveals Characteristic Patterns of Structural Variations with Mechanistic Implications in Epithelial Cancer Genomes"*	A/Prof Ruan Yijun, GIS
1535 – 1555	*"Genetic Dissection of Disease Susceptibility: GWAS and Beyond"*	A/Prof Liu Jianjun, GIS
1555 – 1615	*"A Genomic Understanding of Infectious Diseases, from Host and Pathogen Genomes to Transcriptomes"*	A/Prof Martin Hibberd, GIS
1615 – 1635	*"Genomic Medicine: A Clinician's Perspective"*	A/Prof Lim Su Chi, KTPH
1635 – 1645	*Panel Discussion*	
Day 2 : 19th February 2011		
0730 – 0830	Manuscript Writing Workshop	
0835 – 0840	All to be seated	
0845 – 0915	**Plenary Lecture 2** *"Personalised Medicine through Genomics"*	Prof Edison Liu
0915 – 1015	**Engineering Innovations & Medicine Symposium**	
0915 – 0935	*"Tissue Engineering – Using Engineered Materials to Grow Tissues"*	A/P Ng Kee Woei, NTU
0935 – 0955	*"Designer Particles – A Platform for Revolutionising Drug Delivery"*	A/P Loo Say Chye Joachim, NTU
0955 – 1015	*"Healthcare Innovation through Design Thinking"*	Dr Eugene Shum, KTPH
1015 – 1030	Tea Break	
1030 – 1210	Research Oral Presentations - Nursing and Allied Health Category	
1210 – 1220	Closing Speech by CEO, Alexandra Health	Mr Liak Teng Lit
1220 – 1255	Closing Ceremony and Prize Presentation	
1400 – 1600	GP Forum	

Professor Lee Eng Hin
Executive Director, Biomedical Research Council (BMRC), A*STAR
Emeritus Consultant, Department of Orthopaedic Surgery, National University Health System

*As the Executive Director of BMRC, A*STAR, Prof Lee's predominant role today is in research administration. Over the years, as Head of Department of Orthopaedic Surgery in NUS/NUH, and subsequently as Dean of Medicine and Director of Division of Graduate Medical Studies, he has played a crucial role in undergraduate medical education, postgraduate medical training as well as continuing medical education for the medical community. He joined NUS after finishing his orthopaedic training in Toronto, Canada, and has established himself as a leading paediatricorthopaedic surgeon, a respected teacher and mentor and a clinician researcher. His research on stem cells and musculoskeletal tissue engineering has won him many international and national awards. He has published over 150 peer-reviewed articles in clinical and basic science journals, delivered over 250 conference papers and written many book chapters. He has co-edited a book with Prof Ariff Bongso entitled "Stem Cells: from Bench to Bedside" which has been very well received internationally and is now in its second edition.*

A ROAD LESS TRAVELLED: CHRONICLES OF AN ORTHOPAEDIC CLINICIAN RESEARCHER

The research landscape has changed dramatically in the last 25 years. When I returned from my training in Canada in 1983, the research environment was still very nascent. Funding for research was limited and the clinical work load was immense. Protected time for research was unheard of. Research was mainly in the form of retrospective clinical reviews. However, with the support of NUS a small research infrastructure developed within the Orthopaedic Department. At that time, research funding by the National Medical Research Council was helpful but insufficient. The quantum leap in impactful research and publications came after A*STAR was set up and more sizeable competitive research funds were made available by the Biomedical Research Council. Today, there is also significant funding available from the National Research Foundation.

An academic orthopaedic surgeon has to juggle teaching and research with clinical practice which tends to take up a large proportion of his time. To be a credible clinician researcher, it is essential that physicians and surgeons stay relevant clinically. It is through patient contact that the right questions are asked which may lead to meaningful solutions for improvement of health outcomes. The clinician also plays a key role in helping to translate discoveries by basic scientists from the bench to the bedside. In this presentation, I will share my experience with you using relevant examples of my own basic, translational and clinical research on the musculoskeletal system.

The sustained commitment to biomedical research has led to an increase in the overall research budget for the biomedical sector by about 15% for the next five years. There is increased support to grow the number of clinician scientists and there is a call for more meaningful collaborations between scientists and clinicians to enhance translational and clinical research that will lead to better health outcomes and economic impact.

Professor Edison T Liu
Executive Director, Genome Institute of Singapore (Biomedical Sciences Institutes)
Professor of Medicine, National University of Singapore
President, Human Genome Organization (HUGO)
Chairman, Health Sciences Authority

*Prof Edison T Liu is the Executive Director, Genome Institute of Singapore, (A*STAR) and Professor of Medicine, National University of Singapore. He received his degrees at Stanford University. Prof Liu's research focus is on the functional genomics of human cancers, particularly breast cancer. He has authored over 260 scientific papers, reviews and books, and is the recipient of the following awards: Leukemia Society Scholar (1991–96); the Brinker International Award (1996); the Rosenthal Award from the American Association for Cancer Research (2000); the President's Public Service Medal (2003) and a Doctor of Medicine Sciences honoris causa, Queen's University, Belfast (2007). He was elected as a Foreign Associate Member of the European Molecular Biology Organization (EMBO) in 2008. Currently, Prof Liu is serving his second term as President of Human Genome Organization (HUGO). Prof Liu is also Chairman of Health Sciences Authority, a health regulatory and blood banking agency in Singapore.*

PERSONALISED MEDICINE THROUGH GENOMICS

Genomic medicine involves the provision of medical care that uses the power of genomic knowledge and technologies to resolve complex problems. The fundamental difference between this and older strategies in medicine research is the comprehensiveness and the precision of the analyses afforded by new genomic technologies, such as in sequencing, cloning, and genotyping. The new challenge will be the assembly and management of this high volume of data with dimensional complexity. Genomic medicine therefore means computational and systems medicine as well. Systems biology, as a discipline, seeks to explain biological phenomenon through the net interactions of all cellular and biochemical components within a cell or organism. Operationally, systems biology requires the digitalisation of biological output, the computational power to analyse comprehensive and massive datasets, and the capacity to integrate heterogeneous data into a usable knowledge format.

We will describe how genomic approaches are changing our understanding of cancer, as a model system. Our work, at Genome Institute of Singapore, in transcriptional profiling has led to transcription factor binding site dynamics and human variations in those binding sites. We employ a strategy of using genomic data to reconstruct systems maps of critical regulatory networks. This integrative approach permits modelling of complex interactions and allows us to quickly uncover complex mechanisms of drug action. Coupled with the dramatic expansion of disease gene discovery in population studies, we now find that rather than a few genes, hundreds of genes may be involved in the genesis of a single complex disease.

Combined Genome Institute of Singapore (GIS) – Alexandra Health Symposium

Associate Professor Ruan Yijun
Associate Director, Genomics Technology, Genome Institute of Singapore (GIS)
Senior Group Leader, Genomics Technology, GIS

A/Prof Ruan Yijun is currently the Senior Group Leader and Associate Director of Genomics Technology at GIS. His primary interest is to elucidate the structures and dynamics of all functional DNA elements in complex genomes through transcriptome characterisations and genome interrogation. To facilitate such understanding, A/Prof Ruan's lab has developed pair-end-tag (PET) based high-throughput and high-precision DNA sequencing and mapping methodologies. These sequencing-based measurements are used to address complex biological questions such as how cancer cells progress and how stem cells maintain their unique properties. Another major interest of A/Prof Ruan is to discover previously uncharacterised microbial genes and genomes that are relevant to human health. To this end, his lab has established a metagenome analysis capability that includes a filtration system for isolating uncultured microbes, shotgun and PET sequencing of metagenomes to uncover viral and bacterial genome sequences from a variety of environment settings and cavities of the human body.

COMPREHENSIVE PAIRED-END-TAG MAPPING REVEALS CHARACTERISTIC PATTERNS OF STRUCTURAL VARIATIONS WITH MECHANISTIC IMPLICATIONS IN EPITHELIAL CANCER GENOMES

Somatic genome rearrangements are thought to play important roles in cancer development. However, our ability for thorough characterisation of cancer genome structural variations is still limited. We optimised the paired-end-tag (PET) sequencing approach for analysing large genomic DNA fragments to study human genome structural variations, and have applied this approach to comprehensively characterise the structural variations of 15 cancer genomes and 2 non-cancer genomes as normal controls. Our analyses revealed that most inversions, deletions, and insertions are germ-line structural variations, whereas tandem duplications, unpaired inversions, inter-chromosomal translocations, and complex rearrangements are over represented among somatic rearrangements in cancer genomes. Large tandem duplications are probably among the initial rearrangements that trigger genome instability for extensive amplification in cancer genomes.

Associate Professor Liu Jianjun
Associate Director, Human Genetics, Genome Institute of Singapore (GIS)
Senior Group Leader, Human Genetics, GIS

A/Prof Liu obtained his PhD in genetics at Duke University and did his postdoctoral training in genetics of psychiatric disorders at Columbia University. A/Prof Liu joined GIS in 2002 and is currently leading its Human Genetics Programme. A/Prof Liu's main research interest is to understand the genetic basis of human diseases. Currently, the main focus of his lab is to identify genetic risk factors for human diseases by using large-scale genetic association analysis. More recently, the research effort has been expanded to include the identification of rare mutations by using next-generation sequencing technologies. In addition, his lab is also working on functional studies using various molecular techniques and animal models to understand the molecular mechanism underneath identified disease risk factors.

Combined Genome Institute of Singapore (GIS) – Alexandra Health Symposium

GENETIC DISSECTION OF DISEASE SUSCEPTIBILITY: GWAS AND BEYOND

Rapid development of large-scale genotyping technology and greatly expanded understanding of the genetic variation pattern of human genome has lead to a surge of genome-wide association study (GWAS) efforts around the world, which have discovered thousands of genetic variants that can influence the development of human diseases. However, for most of the diseases, only a small proportion of genetic risk or heritability of disease can be explained by these identified genetic variants, and there has been limited progress in revealing the 'biology' underlying these identified disease susceptibility genes through functional investigations. This has caused many to question whether GWAS has been 'over-sold' in terms of promises. Furthermore, the emergence of next-generation sequencing has also raised the question of whether current genotyping-based GWAS will soon be replaced by sequencing-based human genetic study, such as exome sequencing analysis. In this presentation, I will first introduce our efforts of GWAS in the Chinese population and some recent developments beyond the initial GWAS. I will then discuss the current concerns over GWAS as well as its future.

Associate Professor Martin Hibberd
Associate Director, Infectious Diseases, Genome Institute of Singapore (GIS)
Senior Group Leader, Infectious Diseases, GIS
Associate Professor, Epidemiology and Public Health, National University of Singapore

A/Prof Martin Hibberd is the Senior Group Leader and Associate Director of Infectious Diseases at GIS, and has adjunct positions at the National University of Singapore and Imperial College (London, UK). A/Prof Hibberd graduated with Honours from Brunel University in 1985 (West London, UK) and received his Doctorate on the immune-genetics of the human T-cell antigen receptor from King's College, London. A/Prof Hibberd has a broad scientific background spanning both microbial and human determinants of infectious and inflammatory diseases. His previous appointments include WHO-funded Senior Microbiologist at UK's central Public Health Laboratories, and Lecturer and Senior Lecturer in Paediatric Infectious Diseases at Imperial College School of Medicine, a top-ranking British university, for seven years prior to his current appointment. A/Prof Hibberd's current research interests cover both pathogen and host aspects of infectious disease, understanding how microbial agents cause the observed disease (including pathogen identification and sequence characterisation) and why specific individuals are susceptible to the disease (using host genetics on a genomic scale). Approaching infectious disease from these two directions also allows specific host pathogen responses to be investigated (utilising RNA arrays or sequencing). This work aims to identify key host responses to specific pathogens that could be targeted by new therapies.

A GENOMIC UNDERSTANDING OF INFECTIOUS DISEASES, FROM HOST AND PATHOGEN GENOMES TO TRANSCRIPTOMES

Human infections can result in a wide variety of clinical outcomes, with severe disease usually being a rare occurrence. For example, in areas with endemic dengue disease, such as Vietnam, seroprevalence studies have shown that infection occurrs in over 88% of children by the age of 15 and yet hospitalised disease occurs in less than 0.1%. The cause of this variation in clinical outcome is unclear. Using whole-genome unbiased approaches, we have investigated this problem from the pathogen, host and host response perspectives to look for synergistic effects that might explain and predict outcome.

In dengue, this has lead to the identification of the interferon pathway as a key player, and interferon response molecules as potential biomarkers for outcome. In an initial study of 200 patients, a clinical algorithm using just one biomarker together with clinical signs, showed 87.5% sensitivity and 84.7% specificity for clinically severe disease three days before hospitalisation (at 42 hours of undifferentiated fever). This work aims to build up a molecular understanding of the host-pathogen interaction that may also point the way to novel therapeutic interventions.

Combined Genome Institute of Singapore (GIS) – Alexandra Health Symposium

Associate Professor Lim Su Chi
Senior Consultant, Department of Medicine, Khoo Teck Puat Hospital (KTPH)
Deputy Director, Diabetes Centre, KTPH
Clinical Director, Clinical Research Unit, KTPH
Adj Associate Professor, Epidemiology & Public Health Department, Yong Loo Lin School of Medicine
Adj Associate Professor, Duke-National University of Singapore (Duke-NUS) Graduate Medical School

A/Prof Lim Su Chi is a Senior Consultant general physician cum endocrinologist at KTPH. His other responsibilities and appointments include: Deputy Director of Diabetes Centre and Clinical Director of Clinical Research Unit at KTPH. He is also an Adjunct Associate Professor at the Department of Epidemiology and Public Health, Yong Loo Lin School of Medicine, National University of Singapore. A/Prof Lim sits on the Ministry of Health's Clinical Management Guidelines Development Committee for Diabetes Mellitus. His present research interests include in vivo endothelial function in diabetes mellitus, genetics of diabetic nephropathy and adipocytes biology in bariatric surgical interventions.

GENOMIC MEDICINE: A CLINICIAN'S PERSPECTIVE

Genomic medicine refers to using genetic information for the diagnosis, prevention and treatment of disorders. Several powerful enabling tools have empowered the spectacular development of genomic medicine. Just to name a few: network information technology, super-computing resources, creative biostatistical approaches and revolutionary molecular genetics platforms, such as microarray and next-generation sequencing.

The dazzling success of Genome Wide Association Study (GWAS) in shedding light on the pathogenetic basis of complex diseases have stretched our minds that 'impossible is nothing'. Better understanding of the pathophysiology of diseases promises to usher in better diagnostic, preventive and therapeutic measures. However, the horizon charted by GWAS has also revealed our deficiency in understanding the functional significance of these genetic variants associated with disease. The journey to unravel the biology of these variants has only just begun.

The ability of genetic information to predict complex disease susceptibility is a little frustrating. This is largely due to the underlying intricate genetic architecture of such diseases and perhaps the near-limitless combination and permutation of gene-gene and gene-environment interactions. Our ability to identify rare variants with moderate-to-large effect size may improve our predictive power. However, it is obvious that more needs to be done to realise our dream of complex disease susceptibility prediction.

Pharmacogenomics is probably one of the most promising fields whereby genetic information may guide therapeutic options. One good recent example is the emerging data that genetic variations in cytochrome P450 enzymes (CYP2C19) and efflux pump P-glycoportein (ABCB1) may affect therapeutic responses to platelet inhibition by certain thienopyridine during acute ischaemic events. Such individuals may do better on alternative antiplatelet agents.

Ethical and regulatory framework needs to keep pace with the above developments, so that we will not lose our souls in the midst of technical advances.

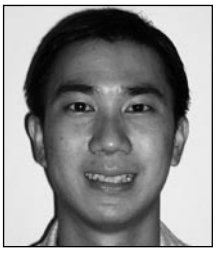
Engineering Innovations & Medicine Symposium

Assistant Professor Ng Kee Woei
Assistant Professor, School of Materials Science and Engineering, Nanyang Technological University

*A/P Ng Kee Woei was one of the first recipients of the A*STAR Graduate Scholarship. A mechanical engineer by training, he completed his PhD at Yong Loo Lin School of Medicine, National University of Singapore, in 2005. A/P Ng underwent postdoctoral training at Institute of Molecular and Cell Biology and at Institute of Medical Biology, A*STAR. He has worked on a number of projects on tissue engineering of skin, bone and cartilage. More recently, he has extended his research to fundamental understanding of stem cell biology and cell-material interactions. He is currently Assistant Professor at the School of Materials Science and Engineering, Nanyang Technological University.*

TISSUE ENGINEERING: USING ENGINEERED MATERIALS TO GROW TISSUES

The acute shortage of human tissues and organs for transplantation led to the birth of tissue engineering, a field that was officially conceptualised at a National Science Foundation workshop in 1988. In essence, tissue engineers strive to grow functional tissues and organs in a laboratory setup. In the last two decades, encouraging results have been obtained for several tissues including skin, cartilage, bone, nerve, muscle, bladder and liver. Some successes have resulted in commercially available products today but widespread clinical use of tissue engineered products is still unlikely in the near future. A few examples of tissue engineering projects will be discussed in this talk, demonstrating how engineered materials can potentially be used to provide clinicians with transplantable tissues. The limitations and possible pitfalls of current technologies will also be discussed.



Assistant Professor Loo Say Chye Joachim
Assistant Professor, School of Materials Science and Engineering, Nanyang Technological University
Secretary, Materials Research Society of Singapore

*A/P Joachim Loo graduated with a Bachelors degree in Applied Science (Materials Engineering) and received his PhD (recipient of the A*STAR Graduate Scholarship) from Nanyang Technological University (NTU). He did his postdoctoral fellowship in Mayo Clinic (MN, USA) before joining NTU as a faculty staff in 2006. His research interests include particulate drug delivery systems, drug-eluting balloons (DEB) and nanotoxicology. He has published more than 40 papers and has filed 6 patents. A/P Loo is currently a Principal Investigator, as well as a collaborator, for several local and international research grants amounting to more than S$10M. He is currently an Assistant Professor at the School of Materials Science and Engineering, NTU. He is also currently serving as Secretary of Materials Research Society of Singapore (MRS-S).*

"DESIGNER" PARTICLES: A PLATFORM FOR REVOLUTIONISING DRUG DELIVERY

Particulate systems, in the form of micro- or nano-sized particles, have tremendous potential to achieve controlled release and targeted delivery of drugs. However, single-layered polymeric particles have several inherent limitations, including initial burst release of drugs, a lack of time-delayed or pulsatile release of drugs and the inability to achieve constant drug release. Multi-layered particles have shown huge potential in overcoming these disadvantages. Herein, we show how to exploit the use of a simple, reliable and economical one-step solvent evaporation technique to fabricate drug-loaded multilayered biodegradable microparticles, with selective drug localisation in different layers. This fabrication process can therefore be used to tailor microparticle designs, allowing such "designer" particulate drug delivery systems to function across a wide range of applications.

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Engineering Innovations & Medicine Symposium

Dr Eugene Shum
Director, Medical Affairs & Innovation, Khoo Teck Puat Hospital (KTPH)
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HEALTHCARE INNOVATION THROUGH DESIGN THINKING

The ageing of the population and the rising prevalence of chronic diseases will lead to increasing demand for healthcare services. The growth of healthcare infrastructure and medical manpower to meet this demand is not sustainable due to limited resources. There is a need to transform the delivery of healthcare.

Healthcare organisations, such as Mayo Clinic and Kaiser Permanente, have applied design thinking to transform the delivery of healthcare. Using design as a strategy, they have observed and studied the needs of users, and carried out many iterative prototypes before reaching the final solutions.

This presentation will explore the use of design thinking in healthcare. We will describe the set-up of the Innovation Unit at Alexandra Health and how it has facilitated innovation in the organisation. We will also share our experience in setting up the Dream Room in Ward 82 in Khoo Teck Puat Hospital. The Dream Room is the first of its kind in Singapore and allows a patient to control his environment from his bed.

Doctors' Category: D01

A collaborative geriatric surgery team ensures consistent successful outcomes in elderly colorectal surgery patients

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Introduction: We hypothesised that a dedicated collaborative transdisciplinary geriatric surgery team (GST) would improve care and outcomes in elderly colorectal surgery patients.

Methods: Patients over 75 years old who were undergoing major colorectal surgery were included. The GST employed a transdisciplinary collaborative model of care. There were frequent quality reviews and a patient-centred culture was ensured. Prospective data from the GST were compared to similar patients not managed by them.

Results: 29 patients managed by the GST were compared to 52 patients who underwent standard treatment. The median age in the GST group was higher, but there was no difference in ASA (American Society of Anesthesiologists) scores and predicted POSSUM (Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity) morbidity scores. The GST achieved lower rates for mortality and major complications. 84.6% of patients managed by the GST returned to preoperative functional status by six weeks. The GST attained a trend of successive desired outcomes, which is evident from the downward sloping CuSum (Cumulative Summation) curve. This was in contrast to patients not managed by the GST.

Conclusion: The GST, through its transdisciplinary collaborative care practices, was able to achieve sustained superior outcomes in elderly colorectal surgery patients when compared with the patient group provided standard treatment.

Doctors' Category: D02

How would the new diagnostic criteria for gestational diabetes mellitus affect us?

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Introduction: The International Association of Diabetes and Pregnancy Study Groups (IADPSG) recently recommended a revised diagnostic criteria for gestational diabetes mellitus (GDM). According to the new criteria, the recommended plasma glucose levels for fasting, one hour and two hours post 75 g oral glucose tolerance tests (OGTT) have become ≥ 5.1 mmol/L, 10.0 mmol/L and 8.5 mmol/L, respectively. This study aimed to investigate the implications of the new diagnostic criteria for GDM.

Methods: Demographic data and 75 g OGTT results were retrospectively collected from patients who visited the high-risk pregnancy clinic at Singapore General Hospital, Singapore, in 1999. Women with two-hour post 75 g OGTT plasma glucose values ≥ 7.8 mmol/L were diagnosed as GDM in this group.

Results: The mean age of the study population (n = 481) was 32 ± 5 years, with a racial distribution of 53.2% Chinese, 34.1% Malays, 10.0% Indians and 2.7% others. Prevalence of GDM by the old and new criteria differed minimally at 56.5% and 55.3%, respectively, with a similar distribution by age and ethnicity. However, the degree of agreement between the two diagnostic criteria (κ = 0.60) was moderate, with approximately one in five patients being reclassified – about 20% of women with GDM according to the old criteria would become normal under the new criteria; similarly, about 20% of women who were earlier adjudjed normal according to the old criteria would now be reclassified as GDM under the new criteria ($p < 0.001$).

Conclusion: In an Asian population at high risk for GDM, the revised IADPSG diagnostic criteria for GDM would reclassify approximately 20% of pregnant women into different diagnostic categories.

Doctors' Category: D03

Accuracy of ProSeal™ laryngeal mask airway intracuff pressure estimation by the finger palpation technique

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Introduction: The incidence of pharyngolaryngeal adverse events after general anaesthesia with laryngeal mask airways (LMAs) can be more than 40%. These adverse outcomes can be reduced by 70% if manometry is used to limit LMA intracuff pressure (< 60 cmH_2O). Routine monitoring of intracuff pressure using manometry has not been widely adopted as the standard of care amongst anaesthesiologists, with many still estimating LMA intracuff pressures by finger palpation of the valve pilot balloon. In this study, we determine the accuracy of finger palpation technique in different anaesthesia personnel against actual readings obtained from a handheld manometer.

Methods: 80 patients undergoing general anaesthesia with LMA were prospectively recruited. After induction with propofol and fentanyl, LMA ProSeal™ was inserted and the cuff inflated with a standard volume of air as per manufacturer's recommendation. The LMA intracuff pressure of every patient was then independently estimated and recorded by finger palpation of the pilot balloon by two anaesthesiologists (one senior and one junior) and one anaesthetic nurse assistant. The actual intracuff pressure was then obtained using a manometer and adjusted to 60 cmH_2O. Estimated vs. actual intracuff pressures were correlated using the Pearson's test. A p-value of less than 0.05 was considered significant.

Results: A scatter plot correlation was plotted for the pressure readings recorded by the anaesthesia nurse assistant, junior anaesthesiologist and senior anaesthesiologist. The strength of association, that is, R values were 0.21 (weak), 0.35 (moderate) and 0.78 (strong), respectively, for the anaesthesia nurse assistant, junior anaesthesiologist and senior anaesthesiologist, while the mean difference between the actual and estimated intracuff pressures was 15.6 ± 25.4, 12.8 ± 24.4 and 2.5 ± 16.2, respectively, for these personnel. Subgroup analysis showed that anaesthesiologists with more than three years experience were more accurate than those with less than three years experience. The mean difference between the actual and estimated intracuff pressures for senior and junior anaesthesiologists was 3.7 ± 17.4 and 19.1 ± 26.9 ($p < 0.001$). In all groups, the palpation technique underestimated the actual intracuff pressure by a mean pressure of 10.3 cmH_2O. Accuracy of the palpation technique correlated poorly when actual intracuff pressures were more than 80 cmH_2O.

Conclusion: Senior anaesthesiologists are more accurate at estimating LMA ProSeal™ intracuff pressures than nurses and junior anaesthesiologists. Medical personnel tend to underestimate intracuff pressures, especially when the pressures are more than 80 cmH_2O, putting patients at risk of postoperative pharyngolaryngeal adverse events. Manometry should be recommended as a standard of care for use with LMAs.

Doctors' Category: D04

Safety, efficacy and postoperative pharyngolaryngeal adverse events of laryngeal mask airway Supreme™ at different intracuff pressures: a randomised controlled trial

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Introduction: Higher oropharyngeal leak pressure (OLP) is a marker of the efficacy and safety of laryngeal mask airways (LMAs), as it indicates airway protection and feasibility for positive pressure ventilation under general anaesthesia. The new disposable polyvinylchloride single-cuffed LMA Supreme™ (LMA-S) has lower OLP compared to the silicone-based

double-cuffed ProSeal™. Increased LMA intracuff pressure may improve the glottic seal, but may also result in more postoperative pharyngolaryngeal adverse events. This study was designed to compare OLP of LMA-S at varying intracuff pressures.

Methods: Approval for the study was obtained from the hospital ethics committee. 104 patients consented to the study and were randomly allocated to three LMA-S intracuff pressure groups of 40 cmH_2O, 60 cmH_2O and 80 cmH_2O. The method for general anaesthesia was standardised with propofol-fentanyl induction and desflurane in air-oxygen for maintenance. Experienced anaesthesiologists performed all LMA-S insertions. Intracuff pressures were calibrated at 40 cmH_2O, 60 cmH_2O and 80 cmH_2O according to the patient's group allocation. The primary outcome was OLP. Secondary outcomes were postoperative pharyngolaryngeal adverse events, and patient and anaesthesiologists satisfaction scores. OLP was compared between the groups using Bonferroni and Scheffe tests. A p-value less than 0.05 was considered significant.

Results: 104 patients were analysed for the primary outcome according to the intention-to-treat. Baseline demographic data for all groups were comparable. The mean OLP in the 80 cmH_2O group (25.9 ± 5.8 cmH_2O) was significantly higher when compared to that in the 40 cmH_2O (18.0 ± 4.8 cmH_2O) and 60 cmH_2O (20.5 ± 5.9 cmH_2O) groups ($p < 0.001$). The incidence of postoperative pharyngolaryngeal adverse events ($p = 0.52$), patient satisfaction scores ($p = 0.16$) and anaesthesiologist satisfaction scores ($p = 0.80$) were comparable between the three groups. No complications of aspiration or nerve injuries were encountered.

Conclusion: For LMA-S, a higher intracuff pressure of 80 cmH_2O gave higher OLP than lower intracuff pressures of 40 cmH_2O or 60 cmH_2O without resulting in more postoperative pharyngolaryngeal adverse events or nerve injuries. As the LMA-S design for cuff and material is different from that of LMA ProSeal™, we recommend an intracuff pressure of 80 cmH_2O when using LMA-S in order to achieve a higher OLP and a superior glottis seal.

Doctors' Category: D05

Risk factors associated with arterial stiffness in type 2 diabetes mellitus

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Introduction: Emerging evidence indicates that arterial stiffness may be an intermediate step in linking type 2 diabetes mellitus (T2DM) to cardiovascular disease (CVD). There is limited data on arterial stiffness in Asian patients with T2DM. We hypothesise that arterial stiffness may be predicted by metabolic parameters associated with the development of CVD.

Methods: 211 patients with T2DM from a hospital-based diabetes clinic consented to enrolment in the study. Anthropometric parameters, and fasting venous blood and urine samples were obtained. Central aortic systolic pressure (CASP), measured using a BPro™ device, was used to estimate arterial stiffness. Factors significantly associated with CASP in bivariate correlation analysis ($p < 0.05$) were analysed using linear regression.

Results: The group consisted of 72% Chinese, 16% Malay and 10% Indians. Majority of the population were men (65%). Study parameters included age (60 ± 11 years), body mass index (27.1 ± 4.5 kg/m^2), systolic blood pressure (137 ± 19 mmHg), diastolic blood pressure (77 ± 10 mmHg), glycated haemoglobin (8.2 ± 1.5%), high-density lipoprotein cholesterol (HDL-C; 1.2 ± 0.3 mmol/L), low-density lipoprotein cholesterol (2.6 ± 0.8 mmol/L) and triglyceride (1.9 ± 1.7 mmol/L), median CASP (124 mmHg, 5th–95th percentile 98–159), estimated glomerular filtration rate (eGFR; 76 ml/minute/1.73 m^2, range 12–142 ml/minute/1.73 m^2), and urine albumin-creatinine ratio (UACR; 46 μg/mg, range 0–3,831 μg/mg). Univariate analysis suggested age, UACR, eGFR and HDL-C were significantly correlated with CASP ($p < 0.05$). Multivariate analyses indicated that these four factors collectively accounted for approximately 97% variation in CASP ($p < 0.001$).

Conclusion: Arterial stiffness is almost exclusively defined by increasing age, HDL-C levels, UACR and diminishing eGFR. Results of the present study may shed light on the pathogenic mechanisms underlying variation in CASP among patients with T2DM.

Doctors' Category: D06

Effect of the treatment of hyperthyroidism on body composition and its correlation with ghrelin levels

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Introduction: Disturbances in thyroid function are associated with changes in body composition, energy expenditure and food intake, with weight loss being a key feature of hyperthyroidism. Ghrelin, an orexigenic hormone, is associated with food intake and energy balance. This study aims to observe the relationship between the treatment of hyperthyroidism, changes in body composition and its correlation with ghrelin levels.

Methods: Patients with Graves' hyperthyroidism were enrolled in the study (n = 10). The mean age of patients was 42 (range 21–75) years. Study parameters included free thyroxine (fT4), thyroid stimulating hormone (TSH) and total triiodothyronine (T3) levels as well as body weight, fat mass (FM), fat free mass (FFM) and ghrelin levels which were measured before and after treatment.

Results: The mean value observed for fT4 was 48.3 (range 29.7–100; normal range 11.8–24.6) pmol/L and T3 was 5.21 (range 2.90–9.78; normal range 1.60–2.60) nmol/L. TSH ranged from <0.005–0.013 (normal range 0.270–4.20) mIU/L. Mean treatment duration to euthyroidism was 118 days. Nine patients gained weight, with a mean weight gain of 3.3 (range 0.9–9.1) kg. Mean change in FM was 1.87 ± 1.73 kg and FFM was 1.43 ± 1.98 kg. Linear regression analysis showed a positive correlation between the level of T3 and weight gain ($p = 0.031$). Ghrelin levels increased during the course of treatment, with a mean ghrelin level of 17.17 (range 11.01–27.57) pg/ml at hyperthyroidism and 35.47 (range 13.31–95.16) pg/ml at euthyroidism; the mean change in ghrelin levels was 18.3 ± 26.31 pg/ml. This rise in ghrelin levels post-treatment reached near significance ($p = 0.051$) and was significantly associated with pre-treatment ($p = 0.003$) and post-treatment ($p = 0.007$) FM. No correlation was found between ghrelin levels, weight change and FFM.

Conclusion: In hyperthyroidism, ghrelin levels increased upon achieving euthyroidism. This rise in ghrelin was associated with an increase in FM. Results also suggest that baseline T3 may be a useful predictor of weight gain.

Doctors' Category: D07

Effect of fasting during the month of Ramadan on body composition and glycaemic control in Muslims with type 2 diabetes mellitus

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Introduction: Millions of diabetic Muslims worldwide fast during the month of Ramadan. However, little is known about the metabolic impact of Ramadan on individuals with type 2 diabetes mellitus (T2DM). With a hypothesis that fasting would bring about favourable changes in glycaemic control and body composition, the study aimed to investigate the effects of fasting on body weight, composition and glycaemic control in Muslims with T2DM.

Methods: Ten T2DM patients from a secondary-care diabetes centre were recruited for the study. The mean age of patients was 54 (range 44–72) years. Parameters measured before and after the fasting month of Ramadan were glycated haemoglobin (HbA1c) levels, body mass index (BMI), waist-hip-ratio (WHR) and body composition, which included skeletal muscle mass (SMM), body fat mass (BFM) and percentage body fat (PBF). Self-monitoring of blood glucose

was mandated for three consecutive days of fasting. Body composition was measured using the multifrequency bioimpedence method. These patients were treated according to the Ramadan-management guidelines recommended by the American Diabetes Association.

Results: Mild hypoglycaemia, self-aborted by food intake, was seen in three patients. Two of these patients required medication adjustment. Two patients did not complete the full 30 days of fasting. Changes in the measured parameters were significant for HbA1c (pre-Ramadan 9.01 ± 2.41%, post-Ramadan 7.86 ± 1.58%; p = 0.011), BFM (pre-Ramadan 31.7 ± 12.8 kg, post-Ramadan 29.1 ± 11.9 kg; p = 0.011) and PBF (pre-Ramadan 38.2 ± 11.4%, post-Ramadan 35.8 ± 11.0%; p = 0.026), but not significant for body weight (pre-Ramadan 81.0 ± 11.8 kg, post-Ramadan 79.5 ± 11.4 kg; p > 0.05), BMI (pre-Ramadan 31.7 ± 6.4 kg/m^2, post-Ramadan 31.2 ± 6.2 kg/m^2; p = 0.067), WHR (pre-Ramadan 0.99 ± 0.08, post-Ramadan 0.99 ± 0.08; p > 0.05) and SMM (pre-Ramadan 26.6 ± 4.8 kg, post-Ramadan 27.2 ± 4.9 kg; p > 0.05).

Conclusion: Fasting during Ramadan brings about improvement in glycaemia, body weight and composition with a seemingly low risk of hypoglycaemia. Determinants for these improvements, if identified, may be helpful in guiding future T2DM management. Future larger studies with more detailed metabolic assessment may uncover factors useful in guiding T2DM interventions in this group of patients.

Doctors' Category: D08

Is minimally invasive video-assisted thyroidectomy feasible in Graves' disease?

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Introduction: Although the safety and advantages of minimally invasive video-assisted thyroidectomy (MIVAT) are well documented in nodular thyroid disease, its use in Graves' disease remains controversial. We compared the outcomes of patients undergoing MIVAT with those undergoing conventional thyroidectomy for Graves' disease.

Methods: Of the 497 patients with Graves' disease referred for surgery between 1999 and 2009, 157 (31.6%) patients underwent the MIVAT procedure (VA-group). The control group consisted of the remaining 340 patients who underwent a conventional thyroidectomy (CT-group). MIVAT was proposed if the thyroid volume was ≤ 30 ml. Data was gathered through a prospectively maintained surgical database.

Results: A majority of patients in both groups underwent total thyroidectomy (VA-group 98%, CT-group 96.5%). Three conversions to open surgery (1.9%) occurred in the VA-group. Hospital stay was significantly shorter in the VA-group (2.1 ± 0.4 days) compared to the CT-group (2.4 ± 1.4 days, p = 0.008). The mean operative time was shorter for the VA-group (84 ± 29 minutes, range 15–240 minutes) compared to the CT-group (94 ± 43 minutes, range 20–360 minutes) although not statistically significant (p = 0.05). A comparison of the incidence of postoperative transient hypocalcaemia (VA-group 14 [8.9%], CT-group 23 [6.8%]), transient recurrent laryngeal nerve palsy (VA-group 2 [1.3%], CT-group 11 [3.2%]) and postoperative haematoma (VA-group 5 [3.2%], CT-group 8 [2.3%]) between the two groups showed no statistical significance.

Conclusion: MIVAT was feasible for the patients with Graves' disease who were selected for this study. MIVAT can be performed safely for such patients, with results being comparable to those of open surgery.

Doctors' Category: D09

Multivariate analysis of poor outcome predictors of perianal fistula surgery

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Introduction: We hypothesised that expertise of the operating surgeon and complexity of the pathology may have an impact on patient outcomes following perianal fistula surgery in a general surgery department setting.

Methods: A retrospective review of all patients who underwent surgery for anal fistula from January 1, 2006 to December 31, 2009 was performed. Patient demographics, fistula pathology, surgical management, surgeons involved and outcomes of the first surgery were recorded. Outcome measure was defined as cases subjected to repeat unplanned definitive reoperation. A multivariate regression model was used to evaluate the effects of operating surgeons and complexity of the fistula as independent predictors of surgical outcome.

Results: Of 228 patients analysed, seven (3.1%) patients needed unplanned reoperation within 30 days of the surgery and 30 (13.2%) patients required unplanned definitive operation subsequently. The first surgeries were performed by registrars (47.6%), medical officers (27.6%), consultants (17.5%) and associate consultants (7.5%). Compared with surgeries done by surgeons of the rank registrar and above, patients first operated by a surgical medical officer were at a higher risk of requiring subsequent definitive unplanned operations (OR 4.00, 95% CI 1.81–8.83). On multivariate analyses, independent predictors for patients requiring unplanned definitive surgery were initial operation by a junior staff (OR 3.47, 95% CI 1.46–8.25), complex fistula (OR 3.33, 95% CI 1.21–9.16) and presentation as abscess rather than fistula (OR 8.84, 95% CI 2.52–31.01). Factors such as surgery performed by colorectal surgeons, age, gender and diabetes mellitus were not associated with unplanned reoperation.

Conclusion: Study findings clearly show that perianal fistula surgery by junior surgeons has a significant impact on patient outcome, with an associated higher risk of reoperation. It is suggested that surgeries done by junior surgeons be supervised by more experienced surgeons, especially for patients with more complex fistulae.

Doctors' Category: D10

Predictors for extracorporeal shockwave lithotripsy outcome

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Introduction: Extracorporeal shockwave lithotripsy (ESWL) is a well-established treatment for renal and ureteric calculi. Although several studies abroad have evaluated predictors for ESWL outcome, their conclusions remain conflicting. This study aimed to determine the predictors of ESWL outcome from local patient data using a multivariate analysis approach.

Methods: We reviewed our database for patients who underwent ESWL within an 18-month period. Patient variables and stone variables that were potential predictors of ESWL outcome were analysed. These variables were correlated to outcome at two weeks using the chi-square and Pearson correlation tests. After preliminary univariate analyses, all variables with a significant effect on ESWL outcome were further analysed to determine independent predictors using simultaneous regression analyses. As the presence of hydronephrosis has been commonly associated with either neutral or negative effects on ESWL outcome in previous studies, a hierarchical regression analysis was performed to determine if the effect of hydronephrosis on outcome was moderated by stone location, while controlling for stone size and number. Patients with lower pole renal stones were excluded to minimise any confounding effects from anatomical factors.

Results: Results from preliminary analyses showed stone location, size, number and presence of hydronephrosis as significant predictors of ESWL outcome. Simultaneous regression analyses showed larger stone size ($p = 0.009$) and the presence of

multiple stones (p = 0.012) to adversely affect ESWL outcome; the presence of hydronephrosis positively affected outcome (p = 0.046). Patients with ureteric stones had better outcomes than those with renal stones (p = 0.09). Hydronephrosis was found to have no significant effect on ESWL outcome for ureteric stones, but maintained a positive effect for renal stones (p = 0.046).

Conclusion: This study showed that stone size and number are independent predictors for ESWL outcome at two weeks. ESWL for ureteric stones may have a marginally better outcome than renal stones. Hydronephrosis has no effect on ESWL outcome for ureteric stones, but may improve outcome for renal stones.

Doctors' Category: D11

Transanal radical endoscopic resection of the rectum on swine model: surviving model

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Introduction: A novel technique of transanal endoscopic radical resection of the rectum (TRRR) was reported in 2009 by this research group. In this present study, we hypothesised that this procedure is not only technically feasible but also safe, and can be performed with survival of the animal model.

Methods: This procedure was performed on two swines as a surviving model. The project was approved by Innoheart Institutional Animal Care and Use Committee (IACUC). After radical resection of the rectum and primary anastomosis, the two swines were monitored in an animal holding area for a period of one week, following which the anastomoses were inspected.

Results: Both swines had good postoperative outcomes and intact anastomoses at one week after the procedure. Both could eat and had bowel action within three days of surgery. The postoperative period was captured in a multimedia video presentation.

Conclusion: We conclude that TRRR is not only technically feasible but also safe for swine. The procedure can be performed with good postoperative outcomes for the animal model.

Doctors' Category: D12

Use of complementary and alternative medicine in head and neck cancer patients in Singapore

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Introduction: A cross-sectional survey was conducted to determine the use and prevalence of complementary and alternative medicine (CAM) by a cohort of patients with head and neck cancer in Singapore.

Methods: 55 consecutive patients with head and neck cancer attending the Otorhinolaryngology Head and Neck Surgery Clinic at Alexandra Hospital, Singapore, between May 2008 and November 2009 were surveyed using a questionnaire via telephone interview.

Results: The prevalence of CAM use was 49.1%. The most commonly used CAMs were traditional Chinese medicine (66.7%), vitamins (14.8%) and cod liver oil (11.1%). Patients used CAM mostly for physical health and well-being (48.1%) or to provide symptomatic relief for the cancer or its treatment (29.6%). 55.6% of patients failed to inform their primary physician of their CAM usage. 63% of patients perceived their CAM therapies to be effective. Information about CAM was obtained most commonly from friends (40.7%), family (33.3%) and CAM practitioners (14.8%).

Conclusion: The high prevalence of CAM usage among patients with head and neck cancer emphasises the need for otolaryngologists to educate themselves on CAM and its interactions. Physicians should routinely ask patients about their use of CAM in order to facilitate communication and provide appropriate advice regarding the use of such therapies.

Doctors' Category: D13

Pitfalls in the management of traumatic haemothoraces and tension pneumothoraces

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Thoracostomy tube insertion is a common procedure performed for patients with chest trauma. However, it is not without its dangers. Minor complications include subcutaneous emphysema, haematoma and pain at the insertion site. Major complications include vascular and visceral injuries, infection, re-expansion pulmonary oedema and malpositioning. We report a case of traumatic bilateral occult haemopneumothoraces from blunt injury in a middle-aged man. Soon after insertion of bilateral thoracostomy tubes and tracheal intubation, the patient developed haemodynamic instability and respiratory distress. The clinical impression was that of a unilateral tension pneumothorax. Diagnosis based on frontal chest radiographs was difficult. Repositioning of the thoracostomy tube lead to the ventilatory and haemodynamic stabilisation of the patient. Computed tomography showed a malpositioned thoracostomy tube with a large left-sided tension pneumothorax with mediastinal shift. This report highlights the fact that classical signs that are commonly used for a clinical diagnosis of tension pneumothoraces can often be absent. Diagnosis based on supine anteroposterior chest radiographs can also be difficult, especially in the context of concurrent injuries, such as rib fractures, haemothoraces and pulmonary contusions. Although tube thoracostomies are accepted as life-saving management for tension pneumothoraces, up to 30% of these may be malpositioned. Tension pneumothorax must be suspected even with a tube thoracostomy *in situ* in the face of sudden clinical deterioration. This highlights the need for vigilance and rapid action by physicians involved in the care of trauma patients.

Doctors' Category: D14

Lateral lymph node dissection in the management of lower rectal cancer

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Introduction: The aims of this study were to elucidate the oncological and functional outcomes of total mesorectal excision (TME) in combination with lateral lymph node dissection (LLND; TME + LLND) for the management of low rectal cancers as given in the literature and to compare these outcomes to those achieved using the more standard approach of TME combined with adjuvant radiotherapy (RT; TME + RT).

Methods: A review of the literature was performed. Outcome measures selected were five-year local recurrence, overall survival and disease free survival, urinary dysfunction, sexual dysfunction and bowel dysfunction rates.

Results: The overall five-year survival rates for TME + LLND and TME + RT were reported to be 30.8%–83.2% and 43.0%–79.5%, respectively. The oncological outcomes for TME + LLND were comparable with those of TME + RT. Functional outcomes varied; some studies showed no significant difference between mortality following the two treatment modalities; others reflected a difference of over 27%–76% for patients having urinary and sexual dysfunction following TME + LLND. Superior results were seen in nerve-sparing lymph dissection. However, the quality of literature in this area is far from ideal. With poor standardisation of definitions and criteria, it is nearly impossible to compare the assorted treatment modalities across these studies.

Conclusion: There is an urgent need for well-organised studies comparing the modalities of TME + LLND against TME + RT for the management of low rectal cancers, with an emphasis on standardised classification of tumours and definition of outcomes.

Doctors' Category: D15

Outcome studies on geriatric surgery patients are missing the mark

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Introduction: With a rapidly ageing population, surgeries on geriatric patients have become more prevalent. Although the traditional outcome measures of morbidity and mortality remain important for such surgeries, an additional dimension of functional outcome after surgery should be included for elderly patients. This study reviewed the literature for data on postoperative functional outcomes in elderly patients following major abdominal surgery.

Methods: A review of the literature was performed for all studies with outcome reports of patients over 70 years of age who underwent major abdominal surgery. A prospectively collected database of patients over 75 years old who underwent colorectal resection at Alexandra Health, Singapore, was also performed.

Results: Our review found a paucity of studies that reported the functional outcomes of patients who had undergone major surgery. 13 out of 16 studies did not include functional outcome data. Only 35.8% of elderly patients had documentation of measurable functional outcome data.

Conclusion: Although functional outcomes are far more important as outcome measures for elderly surgical patients than mortality and morbidity, inadequate attention appears to have been given to these in the literature. There is an urgent need to redefine suitable outcome measures for elderly patients undergoing surgery, so that all efforts can be directed toward ensuring their optimal well-being after surgery.

Doctors' Category: D16

Choroidal neovascularisation following laser *in situ* keratomileusis for high myopia: a case-series

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Introduction: The study reports three patients who developed unilateral choroidal neovascularisation (CNV) following laser *in situ* keratomileusis (LASIK) for high myopia.

Methods: Data was retrospectively reviewed for these patients.

Results: Two women and one man (mean age 34 ± 2.8 years) underwent LASIK for high myopia in both eyes. The mean spherical equivalent was –9.92 (range –6.75 to –18.00) D. The mean time interval between LASIK and the appearance of symptoms was 9.3 ± 8.5 weeks. One patient developed a recurrent juxtafoveal CNV, one developed a new subfoveal CNV and one developed a new juxtafoveal CNV. The mean best-corrected visual acuity (BCVA) at the time of CNV presentation was 0.44 (range 0.10–0.70) logMAR. All patients were treated with a combination of intravitreal ranibizumab and photodynamic therapy with verteporfin. Following treatment, the mean BCVA improved to 0.17 logMAR, with complete resolution of CNV in two patients.

Conclusion: CNV is a rare but potentially blinding complication following LASIK. Short-term good visual outcome can be achieved with timely intervention using current treatment modalities.

Doctors' Category: D17

Spatial profile of macular pigment in Singaporean Chinese

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Introduction: This study aimed to measure the spatial profile of macular pigment (MP) in Singaporean Chinese and to examine its relationship with serum levels of lutein (L) and zeaxanthin (Z).

Methods: 80 patients were recruited for the study. Data collected included demographic data, lifestyle information, anthropometric measurements, spatial profile of MP using a macular densitometer, and blood sample for serum analysis of L and Z.

Results: The mean age of the study population was 44.7 ± 12.0 (range 21–68) years. There were 56 women (70%) and 24 men (30%) in the group. The mean MP at 0.25°, 0.50°, 1.0° and 1.75° of retinal eccentricity was 0.63 ± 0.19, 0.53 ± 0.19, 0.35 ± 0.16 and 0.17 ± 0.11, respectively. MP levels were lower in patients aged ≥ 40 years (MP 0.52) than in younger patients (MP 0.56), but the difference was not statistically significant. 71% of patients within the lowest tertile of MP (< 0.25) were aged ≥ 40 years. The difference in the mean MPs of women (MP women, 0.504) and men (MP men, 0.605) was statistically significant (p = 0.04). MP and serum levels of L (serum L 0.14; p = 0.20) and Z (serum Z 0.25; p = 0.02) were positively correlated, but the only relation that reached statistical significance was that between MP and Z.

Conclusion: Study results suggest that old age and female gender, the two known risk factors for age-related macular degeneration (AMD), are associated with a relative lack of MP. Furthermore, a positive relationship between MP and serum levels of L and Z suggests that dietary modification and/or nutritional supplementation may augment MP in people at risk for developing AMD. Future studies with larger sample sizes are warranted to confirm these findings.

Doctors' Category: D18

Preoperative dexamethasone for postoperative analgesia and recovery after laparoscopic cholecystectomy: a qualitative systematic review

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Introduction: Laparoscopic cholecystectomies are increasingly common as the procedure is the gold standard surgical treatment for cholelithiasis. Postoperative pain, fatigue, nausea and vomiting may delay recovery and hospital discharge. Opioid analgesics have conventionally been used despite evidence of their manifold adverse effects. Dexamethasone is a long-acting, anti-inflammatory glucocorticoid with antinocioceptive and antiemetic action. It has been recognised to be useful for the prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy. We postulate that preoperative dexamethasone may also be used as an adjunct to ameliorate pain, decrease analgesic consumption and hasten postoperative recovery in laparoscopic cholecystectomy patients.

Methods: A systematic online literature search was performed for the keywords laparoscopic cholecystectomy, gallbladder, pain, analgesia and dexamethasone on PubMed, MEDLINE and Google Scholar. Additional studies were identified by manually searching references from published articles. Only randomised clinical trials involving human studies in the English language were shortlisted for review. A qualitative analysis of the 16 trials was carried out based on systematic review questions.

Results: Of the 16 trials included in our review, five of 13 trials showed a reduction in pain scores, while six of 13 trials showed a reduction in analgesic consumption. Five of seven trials, where pain was the primary outcome, had positive findings for dexamethasone as an analgesic adjunct. Negative results were mainly found in trials where pain outcomes were secondary measures. Five of seven trials showed faster postoperative recovery, with a shorter length of hospital stay, less fatigue and better quality of recovery scores. A dose of dexamethasone of ≥ 8 mg was associated with positive outcomes. Dexamethasone was also associated with more favourable patient satisfaction scores. There were no reported adverse effects from a single dose administration.

Conclusion: Patients treated with preoperative dexamethasone showed a trend toward less pain, analgesic-sparing effect and faster recovery in the postoperative period without the risk of adverse effects. Dexamethasone may be recommended as an analgesic and antiemetic in laparoscopic cholecystectomy patients.

Doctors' Category: D19

In-plane short-axis approach to femoral catheter insertion works well for postoperative pain management for total knee replacement

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Introduction: Use of continuous femoral nerve catheters and perineural local anaesthetic infusions for postoperative pain management in patients undergoing total knee replacement (TKR) has been shown to achieve significant reduction in pain scores, need for rescue analgesics, better patient satisfaction and early rehabilitation. Traditionally, catheters have been inserted along the long axis of the nerve to facilitate catheter migration along the nerve. This has necessitated the use of an out-of-plane (OOP) approach for ultrasonography. We hypothesised that in-plane (IP) techniques may be safer as the needle and its trajectory remain visible along the whole length during insertion.

Methods: The acute pain services provided on catheter insertion to 37 patients who underwent TKR surgery at Khoo Teck Puat Hospital, Singapore, were reviewed. The technique of catheter insertion, pain scores at rest and on movement on postoperative Days 1, 2 and 3, patient satisfaction scores and any complications observed in these patients were noted.

Results: The IP technique was used for catheter insertion in 22 patients while the OOP technique was used for 15 patients. 48% of the catheters were tunnelled. Pain scores on postoperative Days 1, 2 and 3 were comparable. More patients had pain scores greater than 6 in the OOP group (0.00% vs. 6.67%), but the difference was not significant. On postoperative Day 2, 63.6% of patients in the IP group had no pain at rest vs. 33.0% in the OOP group. Overall, patient satisfaction scores for the IP or OOP groups were similar. In the OOP group, three of 15 catheters (20%) slipped out before their time, but no such instances were seen in the IP group.

Conclusion: Femoral catheter insertion, via either the IP or OOP technique, is a good analgesic option for patients undergoing TKR. The benefit of being able to view the needle shaft in its entirety while using the IP short-axis view for femoral catheter insertion and its attendant advantages make the IP technique safer when compared to the traditional OOP short-axis view for catheter insertion.

Doctors' Category: D20

Novel uses for the new laryngeal mask airway Classic Excel™

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Laryngeal mask airways (LMAs) have been used in the clinical practice of anaesthesia since the prototype was invented by Dr Archie Brain in 1981. It has gained worldwide recognition and popularity among anaesthesiologists and is used routinely as an airway management device in more than 50% of routine general anaesthetics. A new LMA Classic Excel™ was introduced in 2009, which has improved features including an epiglottic elevating bar and a removable airway connector that facilitates intubation via the LMA. We report a novel diagnostic surgical use for the new LMA Classic Excel™. A 61-year-old woman, with a long-standing history of Graves' disease, presented with an enlarged 4 cm × 5 cm thyroid mass and a histological diagnosis of papillary carcinoma. Computed tomography of the neck showed a heterogeneous thyroid mass with multiple cystic areas and focal calcification. Clinically, there were no compressive symptoms associated with the thyroid carcinoma. Fibreoptic brochoscopy was requested prior to surgery by the otolaryngology surgeons to assess for tracheal invasion. The patient was induced with inhaled sevoflurane, intravenous propofol and remifentanil. The LMA Classic Excel™ was inserted and hand ventilation was assessed to be adequate. The patient was allowed to breath spontaneously on the supraglottic airway device. Bronchoscopic assessment of the trachea was performed through a 15-mm fibreoptic bronchoscope swivel connector while the patient was maintained under general anaesthesia. The patient was subsequently paralysed and intubated via the LMA Classic Excel™. Surgery proceeded uneventfully. En bloc dissection and removal of the thyroid gland with overlying strap muscles, and excision of the tumour adherent on the first tracheal cartilage was performed. The patient was extubated successfully at the end of the operation. Newer modifications of the original LMA, such as LMA Fastrach™, have been used to aid diagnostic and therapeutic laryngeal surgical procedures. Novel uses for the LMA Classic Excel™ may include facilitating various diagnostic procedures, such as bronchoscopic tracheal assessment of malignant thyroid tumours.

Doctors' Category: D21

Clarithromycin-induced depression during *Helicobacter pylori* eradication therapy

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With the discovery of *Helicobacter (H.) pylori* as the main causative agent of peptic ulcer disease, the use of triple therapy has become its mainstay eradication treatment in recent years. Clarithromycin has been reported to cause psychiatric complications in patients on triple therapy and patients receiving this treatment must be monitored. This report describes a 56-year-old man who developed depression, insomnia and suicidal intent after consuming clarithromycin for *H. pylori* eradication. Literature searches were conducted on PubMed and MEDLINE for articles published from 1990 through October 2010 using the search terms peptic ulcer, *Helicobacter pylori*, clarithromycin, psychiatric and triple therapy. Relevant articles were retrieved and referenced in this report. Patients on triple therapy with no past psychiatric history who present with new onset psychiatric symptoms should prompt the surgeon to investigate for drug-related causes. Surgeons must be cognisant of the possible psychiatric problems that may arise from the use of clarithromycin with triple therapy.

Doctors' Category: D23

Ocular manifestations of spitting cobras: a report of two patients

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Spitting cobras have a strangely modified venom apparatus that enables them to spit venom across a distance of metres into the eyes of their predators or enemies. The resulting venom ophthalmia can have a host of clinical presentations. Most literature reports are about incidents seen in the rural milieu. We hereby report two patients who were victims to the spitting cobra in urban Singapore. A retrospective study of the two patients was carried out. Two men were exposed to the spitting cobra while at work. Both patients had conjunctival injection and corneal involvement in the form of punctuate epithelial erosions. One patient had chemosis of pre-existing pterygium as well as anterior uveitis. Irrigation of the eyes with tap water was done as first aid for both the patients by coworkers. Both the patients were treated with topical antibiotics and lubricants and had a good visual outcome after a week of treatment without any permanent sequelae. Early treatment of the venom ophthalmia can minimise complications and result in a good clinical outcome.

Doctors' Category: D24

Knowledge and attitudes of Singaporean women toward breast cancer

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Introduction: Breast cancer is the most common cancer among women in Singapore, with three being diagnosed everyday and as many dying every four days. Participation in the screening programme is, however, subject to patient knowledge and attitudes toward the disease, with many still harbouring misconceptions about its diagnosis and treatment. This study aimed to identify related false beliefs shared by symptomatic and asymptomatic women, so that clinicians are able to conduct more purpose-led consultations in addressing them. By correcting these misconceptions, it is hoped that more women will attend screening, thereby reducing morbidity and mortality.

Methods: A questionnaire study was conducted with 55 randomly selected respondents from Northern Singapore. Respondents were grouped by age into those above and below 40 years, as mammogram screening is recommended for women older than 40 years in Singapore.

Results: 10% of respondents thought all breast lumps were cancerous. 36% of respondents felt mammograms were painful, nearly half of who were aged < 40 years and had not yet taken a mammogram. This latter finding highlights the damaging preconceived notions that could be harboured in the target group even in the absence of first-hand experience. Those aged > 40 years were generally less informed and more pessimistic about the prognosis of breast cancer and its treatment. 51% of respondents aged > 40 years believed that a complete mastectomy was unavoidable in the course of treatment and 40% believed that breast cancer was incurable. This finding suggests that some women may view screening as a futile exercise that leaves one with a diagnosis and, at best, a quiescent disease.

Conclusion: Study results highlight the possibility of women harbouring misconceptions regarding breast cancer and its treatment. In view of the rising incidence of breast cancer among Singaporean women, this study calls attention to an urgent need for efforts aimed at correcting prevalent false beliefs and encouraging women to participate in the screening programme, enabling the medical fraternity to effectively address the disease.

Doctors' Category: D26

Providing acupuncture for patients with chronic knee pain at Yishun Polyclinic

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Introduction: Acupuncture, which is one of the best known complementary and alternative therapies, originated more than 3,000 years ago in China. It is part of the therapeutic methods used in traditional Chinese medicine (TCM), with its theories based on the doctrine of channels. In recent years, acupuncture has gained popularity and wide usage locally, especially in the management of acute and chronic pain. On October 13, 2008, Yishun Polyclinic started its acupuncture clinic, which offers acupuncture therapy as a complementary modality to patients with painful musculoskeletal conditions.

Methods: 23 patients with chronic knee pain for more than six months were referred to the acupuncture clinic by the polyclinic doctors with a diagnosis of osteoarthritis of the knees. All the patients were treated with eight sessions of acupuncture at intervals of 4–7 days, by the same acupuncturist who used similar acupuncture points.

Results: Using the Wong-Baker Faces Pain Rating Scale, 55% of the patients achieved a 50% improvement in the pain score at completion of all the sessions.

Conclusion: This unique complementary health model utilising both scientific medicine and acupuncture is set to be highly popular in the evolving model of integrative medicine. This is especially important in polyclinics, which provide both primary healthcare services and pain management.

Doctors' Category: D28

Incision and drainage versus saucerisation in the treatment of cutaneous abscesses: a randomised controlled trial

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Introduction: Cutaneous abscesses are mostly treated by saucerisation in Singapore, although they result in a large skin defect and have long healing times. Incision and drainage (ID) is considered inferior as an alternative because of the recurrent suppuration caused by the perceived premature closure of the drainage wound. However, historic data suggests that ID is equally effective in draining such abscesses. This randomised control study aimed to establish that ID is not inferior to saucerisation as a treatment option for cutaneous abscesses, but has instead the advantage of faster healing and better cosmesis.

Methods: Approval for the study was obtained from the institutional review board. 98 patients who required drainage of cutaneous abscesses at Alexandra Hospital, Singapore, between December 2007 to October 2009 were recruited for the study and randomised into two treatment arms, ID and saucerisation, after obtaining informed consent. Randomisation was carried out using a sealed envelope and assignment of treatment was carried out using a computer programme. The procedures were performed by on-duty surgical teams at Alexandra Hospital using predetermined protocols. The patients were followed up after operation and data was collected on wound closure and complications. The primary endpoint of the study was the time taken for complete healing of the surgical wound.

Results: 49 patients were recruited in each treatment group. Patient characteristics, such as age, gender distribution and presence of comorbidities, were comparable between the two groups. The mean healing time for the ID and saucerisation groups was 24.34 days and 45.84 days, respectively. One patient from each group required reoperation. Statistically, the ID group healed significantly faster without any increase in the abscess recurrence rates.

Conclusion: This study provides level 1 evidence that ID is a superior surgical option for treatment of abscesses when compared to saucerisation.

Doctors' Category: D29

Influence of injury characteristics and timing of primary surgical repair on visual outcome of open globe injury

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Introduction: This study was conducted to determine the influence of injury characteristics and timing of primary surgical repair on the visual outcome of open globe injury.

Methods: 75 consecutive patients with open globe injury that were repaired surgically over a period of one year were retrospectively analysed. Data collected included demographic details, nature of injury and the initial and final best-corrected visual acuities (BCVA). The BCVA was graded as > 20/40, 20/50 to 20/100, 19/100 to 5/200, 4/200 to light perception (PL), and no light perception (NPL). The zone of injury was defined as isolated to cornea including the corneoscleral limbus (zone I), limbus to a point 5 mm posterior to the sclera (zone II), and posterior to the anterior 5 mm of the sclera (zone III). All patients were classified as either positive or negative for relative afferent pupillary defect (RAPD) in the affected eye. In addition, the patients were categorised into three groups based on the time interval from injury to primary surgical intervention as group I (< 24 hours), group II (24–36 hours), and group III (> 36 hours). The groups were compared with each other with respect to the various parameters studied. The chi-square test was used for comparison of categorical data. A p-value of less than 0.05 was considered significant.

Results: On analyses, statistically significant associations were found between final visual outcome and the presenting BCVA ($p < 0.05$), zone of injury ($p < 0.05$) and presence of RAPD ($p < 0.001$). No significant difference in the postoperative BCVA was found between the early and late repair groups ($p > 0.05$).

Conclusion: The presenting BCVA, zone of injury and RAPD were associated with a better final visual outcome following surgical repair in patients with open globe injury. The timing of intervention did not significantly alter the visual outcome in these patients.

Doctors' Category: D31

Uncommon benign breast tumours

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Pseudoangiomatous stromal hyperplasia (PASH) is a benign tumour arising from myoepithelial cells of unknown aetiology and pathogenesis. Reports have suggested an association between PASH and the hormonal fluxes occurring during the perimenopausal period in women. PASH is usually managed by wide local excision (WLE), with a reported recurrence of 15%–22%. Adenosis tumour is not associated with increased risks of developing breast cancer. Similarly, fibrocystic changes without atypical epithelial components are not associated with any oncologic risks. However, studies have reported patients with adenosis tumour along with non-infiltrating carcinoma. Most breast tumours in adolescents are fibroadenomas, with juvenile fibroadenomas typically being 1–10 cm in size and occurring at age 10–18 years. Fibroadenomas less than 5 cm are managed conservatively due to the low malignant risk in this age group. In this report, we present four uncommon benign breast tumours that were diagnosed accurately on core biopsy. Case A was a 53-year-old postmenopausal Chinese woman who underwent WLE of a 2.3 cm solitary breast lump. Histology showed benign mesenchymal proliferation consistent with nodular PASH, with positive CD34 staining. Case B was a 56-year-old postmenopausal Malay woman who presented with a 8 cm left breast mass and a 7 cm left axillary mass over a five-month period. Ultrasonography of the breast and axilla showed well-circumscribed and homogeneous hypoechoic masses measuring 8 cm and 6 cm, respectively. The patient underwent mastectomy with excision of the axillary lump. Histology showed PASH with fibroadenomatoid features positive for CD34 and CD31. Case C was a 17-year-old Malay girl who presented with a 5 cm mass in the left breast. She underwent WLE and histology showed juvenile fibroadenoma. Case D was a 41-year-old premenopausal Chinese woman who underwent WLE of a 2 cm solitary breast lump. Histology showed adenosis tumour with fibrocystic changes.

Doctors' Category: D32

Correlation between the integrity of the plantar arch and the number of runoffs and amputation rates in patients with peripheral vascular disease

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Introduction: This study aimed to determine the effect of the integrity of the plantar arch and the number of runoffs in legs on amputation rates in patients with peripheral vascular disease (PVD). We hypothesised that a good plantar arch or higher number of runoffs may be associated with a lower amputation rate.

Methods: This was a retrospective study of all patients who underwent angiographic study of the lower limb from June 1, 2008 to January 22, 2010.

Results: The study group (n = 90) had 48 men and 42 women. 19 patients had bilateral disease while 71 patients had unilateral disease. 156 angiograms were performed. Indications included PVD (89.9%), acute limb thrombosis (9.2%) and Raynaud's disease (0.9%). Average age was 68 (range 36–97) years. Common comorbidities included hypertension (76.7%), diabetes mellitus (87.8%) and hyperlipidaemia (65.6%). The plantar arch was good in 15 patients, moderate in 28 patients and poor in 60 patients. Among patients with a good plantar arch, 11 patients did not need any amputation, two required ray amputations (RA) and two needed below-knee amputations (BKA). Among patients with moderate arches, 18 patients did not need an amputation, five underwent RA, one had transmetatarsal amputation (TM) and four underwent BKA. In those with poor arches, 43 patients did not need an amputation, eight had RA, four needed TM, four underwent BKAs and one needed an above-knee amputation (AKA) [$p > 0.05$]. There were no runoffs in four patients, one runoff in 56 patients, two runoffs in 31 patients and three runoffs in 18 patients. In patients with three runoffs, 14 needed no surgery, two underwent RA, one had TM and one needed BKA. In those with two runoffs, 21 patients needed no amputation, six had RA, one required TM and three needed BKAs. Among patients with one runoff, 39 patients did not need surgery, seven had RA, four needed TM, five underwent BKAs and one had AKA ($p > 0.05$).

Conclusion: Study results suggest that the integrity of the plantar arch and the number of runoffs do not influence the level or rate of amputation in patients with PVD.

Doctors' Category: D33

Use of radioisotope and blue dye for sentinel lymph node identification: a single surgeon's results

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Introduction: The blue dye method and radioisotope technique are used to reduce routine axillary clearance (AC) during sentinel lymph node (SLN) identification. Our aim was to determine whether the blue dye alone could satisfactorily achieve SLN identification when compared with the radioisotope technique or dual studies.

Methods: This was a single-surgeon prospective study of 74 consecutive patients from July 1, 2006 to October 30, 2009. SLN was detected preoperatively by injecting 2 MBq radioisotope into the subareolar region and performing an axillary scan. Intraoperatively, 2 ml methylene blue was injected into the subareolar region with a five-minute massage. Dye staining was scored as negative when there was no uptake (0), and positively stained for light uptake (1+), moderate uptake (2+) and strong uptake (3+). A gamma probe radioisotope counter was used to pick up radioactivity in the periareolar region and background. This was then used to locate SLN in the axilla to settle the place of incision over an area of maximal count. The SLN with the highest count was taken as the first SLN using a ten-second count. The other SLNs were required to be 10% of the highest node or blue stain positive.

Results: 138 SLNs were identified in total. 73 SLNs were identified in 53 (71.6%) patients using the dye technique while radioisotope helped identify 122 SLNs in 71 (95.9%) patients. The two methods had a 100% combined identification rate. Mean time taken for SLN biopsy was 31.61 minutes. The average number of SLNs harvested was 1.85. 21 patients had positive SLN on immunohistochemistry; 19 (90.4%) were detected by the dye and 21 (100%) by the radioisotope. 19 patients went on to have AC while two did not. Seven patients had positive SLN and AC. 14 patients had positive SLN but negative AC. Three (4.1%) patients underwent mastectomy and 95.9% of patients underwent wide local excision.

Conclusion: Study results indicate that the blue dye method is less effective than the radioisotope technique for SLN identification. Although radioisotopes can be used alone, best results are achieved following dual localisation.

Doctors' Category: D34

Metaplastic breast carcinoma: a case report

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Metaplastic breast carcinoma (MBC) is a rare form of breast cancer, occurring in less than 1% of patients. MBC is heterogeneous and characterised by epithelial or mesenchymal cells with adenocarcinoma. Although Wargotz et al originally divided MBC into five histological subtypes, more subtypes have since been identified. Clinically, it presents with larger tumour size and few lymph node metastases, with frequent systemic metastases to the lungs. A high proportion of these tumours are triple-negative. A large tumour size and triple-negative status have implications for both treatment and prognosis, as such patients do not benefit from hormone or targeted therapy and chemotherapy is often needed. Preoperative histology of MBC could, however, allow for a mastectomy without axillary nodal clearance (ANC). MBC displays more aggressive behaviour than typical breast cancer, with almost all tumours showing recurrence in the first five years. Long-term follow up is necessary for this tumour regardless of hormone receptor status. We report a 54-year-old woman who presented with a painless left breast lump noticed three weeks ago. Menstrual and family histories were unremarkable. Medical history revealed a benign mass in the left breast that was excised 23 years ago. On clinical examination, a 5 cm × 5 cm central breast lesion was found with skin tethering and nipple retraction. No palpable axillary lymph nodes were found. Ultrasonography and mammogram showed a lobulated partially defined non-homogeneous hypoechoic mass measuring 52 mm × 50 mm × 32 mm with irregular cystic foci (BIRADS 4). Core biopsy showed grade invasive ductal carcinoma with negative estrogen receptor, progesterone receptor and HER-2 status. Liver ultrasonography and bone scintiscan were unremarkable. The patient underwent a left simple mastectomy with ANC. A retroareolar tumour measuring 4.5 cm was also observed. Histology showed a 60 mm × 41 mm × 37 mm matrix-producing poorly differentiated carcinoma with chondroid mesenchymal differentiation (Grade 3) but no lymphovascular invasion. Hormone receptor status was triple-negative. Axillary lymph nodes were negative.

Doctors' Category: D35

Does home cycloplegia for children help in turnaround times in busy ophthalmic practice?

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Introduction: Cycloplegic refraction is carried out in children to paralyse the ciliary muscles in order to eliminate accommodation, which can otherwise mask hyperopia. Patients currently undergoing such refraction need to wait for the cycloplegic eye drops to work after they have been instilled when they are in the eye clinic. This study aimed to determine whether home cyclopegia could help reduce waiting time for patients undergoing such refraction.

Methods: Patients requiring cycloplegia on arrival at Jurong Medical Centre, Singapore, from August to September 2010 were identified by looking through the appointment schedule. These patients were randomly assigned into two groups; the home cycloplegia group and the cycloplegia on arrival group. Waiting times before patients saw the eye doctor were recorded and compared.

Results: 14 patients underwent home cycloplegia and 20 underwent cycloplegia on arrival. The two groups were comparable for age ($p = 0.102$). The home cycloplegia group showed an improvement in waiting time ($p < 0.001$) and a reduction in the total number of eye drops instilled ($p < 0.05$).

Conclusion: Home cycloplegia showed an improved waiting time for patients requiring cycloplegic refraction and their parents. This will also help improve patient and parent satisfaction at the clinic.

Doctors' Category: D36

Laparoscopic fingeroscopic appendicectomy aids dissection in complicated acute appendicitis

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Introduction: Laparoscopic fingeroscopic appendicectomy was described in 1999 by Katkhouda to reduce conversion rates to open surgery for patients requiring complicated appendicectomy. We describe our experience with this procedure with a video segment.

Methods: When a difficult appendicectomy is anticipated on initial evaluation by laparoscopy, an additional 10 mm port is placed in the right iliac fossa (RIF) just below or caudal to the appendix instead of at the suprapubic port. The index finger replaces the RIF port and is then used to gently dissect the appendix from adhesions similar to the open method. This gives tactile feedback that is lost in the standard laparoscopic approach.

Results: Four patients with appendiceal phlegmon underwent appendicectomy; three procedures were successfully completed laparoscopically and one required conversion to open surgery following perforation in the pelvis by the fingertip during finger dissection.

Conclusion: Fingerscopy has several benefits. It does not require any additional instruments, as all instruments are available in the standard laparoscopic set, there is no learning curve for surgeons as it borrows on techniques from the open method, and it reduces conversion to open surgery even for patients with complicated appendicitis.

Doctors' Category: D37

A multimodality approach for the treatment of Dialysis-access Steal Syndrome with preservation of vascular access

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Introduction: Dialysis-access Steal Syndrome (DASS) is a devastating complication of vascular access surgery that results in ischaemia of the limb. Although simple ligation of the fistula is the simplest method of treating Steal Syndrome, the problem of dialysis access persists in this approach. Moreover, DASS could recur during the subsequent dialysis access procedure. We report the outcome of a multimodality approach that treats renal failure patients with DASS but preserves the vascular access at the same time.

Methods: A retrospective review was conducted of all patients with DASS who were treated at a tertiary institution over one year by the same surgeon. Upper limb arterial duplex was performed immediately for all DASS patients with no immediate risk of limb loss. Arteriogram was performed if the duplex study suggested suspicion of radial or ulnar artery disease. Angioplasty was performed in the same session if a treatable lesion was identified. For patients with arteriovenous fistula and large size outflow vein, banding or refashioning of the anastomoses was the first line of treatment. Proximal brachial artery to distal vessel bypass with or without interval ligation was performed for those with failed first-line treatment. Intraoperative duplex was used to help assessment of the fistula and native arterial flow condition. Data collected included patient demographics, type of procedure, outcome in terms of resolution of ischaemia and preservation of vascular access and complications, if any.

Results: Seven of 76 (9.2%) patients with vascular access operations developed DASS. Majority were women (male-to-female ratio 2:5). Median age of the group was 62 years. All patients had upper arm arteriovenous fistulae or grafts that required brachial artery inflow (three brachiocephalic, three brachiobasilic and one brachioaxillary). Nine procedures were performed in total for the seven DASS patients, including one angioplasty of the radial artery, three bandings, two refashioning of fistula anastomosis, two bypasses without interval ligation and one distal revascularisation interval ligation. Two of three patients who underwent banding needed further procedures (one refashioning and one bypass) to alleviate their ischaemic symptoms. One patient died in the early postoperative period due to acute myocardial infarction and one patient had wound infection. None of the DASS patients had tissue loss or persistent deformity or disability of the hand and finger after treatment. Dialysis access was successfully preserved in all patients.

Conclusion: A multimodality approach to DASS can achieve the aim of ischaemia correction while preserving the vascular access at the same time.

Doctors' Category: D38

Acute kidney injury secondary to focal renal cortical necrosis

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Renal cortical necrosis is an unusual presentation in adults, with involved mechanisms being vascular spasm, microvascular injury, or intravascular coagulation. However, there is also a possibility for thromboembolic phenomena, as in the patient reported here. We report a 27-year-old previously healthy Indian man, who presented with non-oliguric acute kidney injury and a one-week history of acute gastroenteritis. The patient was a smoker, and appeared dehydrated clinically

although no hypotension was documented. Serum creatinine and blood urea levels were 1,544 umol/L and 43 mmol/L, respectively. Metabolic acidosis, microscopic haematuria and proteinuria of 0.5 g/dl were noted. There was no evidence of haemolysis. Although ultrasonography of the kidney was unremarkable, a renal biopsy was performed in view of persistent elevated urea and creatinine levels despite rehydration. Histology revealed focal cortical necrosis and acute tubular injury without features of thrombotic microangiopathy. The patient's serum creatinine gradually improved to 374 umol/L. Ultrasonography of the renal artery was unsuccessful. However, the patient returned three weeks later with acute left lower limb ischaemia, and underwent embolectomy for femoral artery thrombi. A thrombophilia screen was negative except for raised homocysteine levels (49.3 umol/L), which was of uncertain significance. Transthoracic echocardiogram revealed left ventricular thrombus. The patient was started on anticoagulant therapy. The serum creatinine at discharge was 249 umol/L. It is possible that the history of diarrhoea in this patient might have precipitated a hypercoagulable state. The presence of left ventricular thrombus could also have contributed to thromboembolic events in the kidneys and lower limb. Epidemiological studies have suggested that mild hyperhomocysteinemia is associated with thrombotic risk in the absence of renal disease. Further studies are needed to confirm this association, as homocysteine levels are known to be elevated in renal failure.

Doctors' Category: D39

Early experience of laparoscopy-assisted distal gastrectomy for gastric cancer in Singapore: a case control study and cost analysis

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Introduction: This study investigated the short-term outcomes of the initial experience with laparoscopy-assisted distal gastrectomy (LADG) for early gastric cancer and compared the economic cost of LADG with open surgery.

Methods: Clinical and pathological data were prospectively collected for patients who underwent LADG with nodal dissection for stage I or II gastric cancer. 21 patients treated between 2005 and 2009 were included in the LADG group. Patients who underwent conventional open distal gastrectomy (CODG) during the same period were matched to the LADG group for demographics and clinical and pathological variables. Perioperative data, short-term postoperative outcomes, patient satisfaction and economic cost were compared between the LADG and CODG groups.

Results: LADG was associated with longer operation time (295 ± 83 vs. 241 ± 62 minutes, p = 0.001), reduced blood loss (239 ± 125 ml vs. 335 ± 143 ml, p = 0.008), less postoperative pain (pain score on postoperative Day [POD] 1: 2 vs. 3, p = 0.001; score on POD 2: 1 vs. 2, p = 0.003), less requirement for analgesics (morphine: 52 ± 47 mg vs. 62 ± 14 mg, p < 0.001), faster recovery of bowel function (5 [range 4–8] days vs. 6 [range 4–10] days, p = 0.001), early ambulation (4 [range 3–7] days vs. 7 [range 4–11] days, p ≤ 0.001) and shorter hospital stay (7 [range 5–103] days vs. 9 [range 5–66] days, p = 0.011) when compared to CODG. Complication rates were similar between the two groups. The number of resected lymph nodes was comparable (24 ± 10.40 vs. 25 ± 15.16, p = 0.364). LADG achieved a higher degree of patient satisfaction. Total hospitalisation bills were similar for both groups (US$8,946 ± US$30,127 vs. US$9,256 ± US$11,112, p = 0.653).

Conclusion: LADG with lymph node dissection is a safe treatment option for early gastric cancer. Recovery is faster in patients undergoing LADG although the technique is comparable to open resection for radicality. In addition, LADG ensures increased patient satisfaction, without inviting an appreciable increase in the costs incurred.

Nursing and Allied Health Category: NA01

Assessment for frailty is useful for predicting morbidity in elderly patients undergoing colorectal cancer resection whose comorbidities are already optimised

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Introduction: Elderly patients undergoing major colorectal surgery have a relatively higher morbidity rate. This happens even when the comorbidities have been adequately optimised. We hypothesised that frailty is useful in predicting adverse outcomes in optimised elective elderly patients undergoing colorectal surgery.

Methods: A prospective study was conducted at two centres, Singapore and Japan. All patients over 75 years undergoing colorectal resection were assessed for the presence of frailty based on assessment of weight loss, physical exhaustion, physical activity level, grip strength and walking speed. All assessments were performed by a nurse clinician in Singapore. Frailty was classified as positive when three of five criteria were satisfied. All patients had already had their comorbidities optimised for surgery. Outcome measures were major postoperative complications. The study was approved by ethics committees in both Singapore and Japan.

Results: 75 patients were studied from February 2008 to April 2010. Mean age was 81.5 (range 75–96) years. Mean comorbidity index was 3.2 (range 0–11). 19 (24.4%) patients were ASA 3 and above. Chi-square analysis revealed that the odds ratio of major postoperative complications was 7.05 (95% CI 2.288–21.721) when the patient satisfied the criteria for frailty. Albumin < 35, ASA > 3, comorbidity index > 5 and POSSUM scores were not predictive of major postoperative complications.

Conclusion: Preliminary findings show that the assessment of frailty by a trained nurse is a potent adjunctive tool for predicting postoperative morbidity. Frailty can be used to identify elderly patients needing further optimisation prior to major surgery.

Nursing and Allied Health Category: NA02

A dedicated nurse clinician has a positive impact on elderly colorectal surgery patients

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Introduction: We hypothesised that a dedicated nurse clinician (NC) plays an important role in improving the outcomes of elderly patients undergoing colorectal surgery.

Methods: We studied the nursing care of 81 patients aged over 75 years who underwent major colorectal resections from January 2007 to July 2010. A review of the prospectively collected database was performed. Nursing failures identified included inaccurate documentation, delayed recognition of deterioration, non-compliance of orders and improper discharge planning. Statistical analyses were performed using chi-square and *t*-tests. Cumulative Summation (CuSum) methodology was used to plot sequential performance of nursing care, with the minimum standard set at 70% success. Sequential performance of the Geriatric Surgery Service (GSS), Khoo Teck Puat Hospital, Singapore, which introduced a NC to their management protocol, was compared to the performance of standard service.

Results: 22 patients managed perioperatively by a NC were compared to 59 patients who were managed without one. There were no significant differences in the mean age, ASA scores, comorbidity index and POSSUM model predicted morbidity and mortality rates in both groups. Patients not managed perioperatively by a NC had five times the

risk of major complications (OR 5.34, 95% CI 1.43–20.02). Overall nursing failures were lower in the NC group at 13.3% compared to 33.9% in the group without NC, although the difference was not statistically significant (p = 0.07). CuSum curve indicated that sequentially consistent good nursing care was rendered to the patients after inclusion of a NC, which was in contrast to patients managed without a NC.

Conclusion: Results support the premise that a dedicated NC has a positive impact on the nursing standard and outcome of elderly patients undergoing colorectal surgery.

Nursing and Allied Health Category: NA03

Peripheral intravenous catheter-related complications from routine replacement versus clinically indicated replacement: a systematic review

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Introduction: Communicable Diseases Centre (CDC), Singapore, and Ministry of Health (MOH), Singapore, guidelines advocate the routine replacement of peripheral intravenous catheters (PICs) every 72 hours. However, both guidelines have not been reviewed since 2002. This systematic review aimed to evaluate the relationship between PIC indwell time and the incidence of catheter-related complications, as well as to investigate the efficacy of routine replacement vs. clinically indicated replacement of PICs for preventing complications in adult patients in an acute inpatient local setting.

Methods: An exhaustive literature search was conducted on 15 databases including hospital databases, the Internet, MOH Clinical Practice Guidelines, and Local Hospital Standard of Practice from 1998 to February 2009 using keywords, such as nursing, systematic review, adult patients, peripheral intravenous catheter, intravenous cannula, duration, indwell time, catheter/cannula-related, infection, complications, obstruction, phlebitis, infiltration and extravasations. The review included randomised controlled trials (RCTs) and cohort studies related to PIC indwell time and complications in an adult inpatient setting. Five reviewers assessed the data found to satisfy predetermined criteria. Outcome measures considered were phlebitis, catheter-related infections, catheter-related complications, obstruction of the catheter, infiltration and extravasations. Studies were analysed utilising the Scottish Intercollegiate Guidelines Network (SIGN 50) methodological appraisal checklist. The CDC and MOH practice guidelines were evaluated using the Appraisal of Guidelines for Research & Evaluation (AGREE) Instrument assessment tool.

Results: Eight studies were selected for review, of which two were RCTs and six were cohort studies. All articles suggested that clinically indicated replacement of PICs reduce the incidence of phlebitis and severity of complications when compared to routine replacement as per MOH guidelines.

Conclusion: An assessment of available evidence did not reveal any conclusive evidence supporting a relationship between PIC indwell time and the incidence of catheter-related complications. Study results highlight the need for a reexamination of current guidelines in view of recent evidence challenging the need for routine replacement of PICs in an inpatient setting.

Nursing and Allied Health Category: NA04

Predictors of progression of moderately advanced diabetic nephropathy secondary to type 2 diabetes mellitus

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Introduction: Diabetic nephropathy (DN) secondary to type 2 diabetes mellitus (T2DM) is a leading cause of end-stage renal disease. The natural history of DN is heterogenous. KDOQI (Kidney Disease Outcomes Quality Initiative) recommends the control of certain factors for retardation of DN progression. We examined these factors in patients attending the DN clinic at Khoo Teck Puat Hospital, Singapore, to determine whether they correlated with the likelihood of worsening renal function.

Methods: Among 257 DN patients attending the clinic over a two-year follow-up period, 70 patients were identified as progressors, with serum creatinine levels elevated ≥ 50%, and 89 patients were identified as non-progressors, with serum creatinine levels either improving or increasing by < 10%. Univariate (Student's *t*-test) and multivariate (binary logistic regression) analyses were performed. Area under the receiver-operator-curve (ROC; C statistics) was used to explore the parameter test for discriminating progressors from non-progressors.

Results: At baseline, progressors and non-progressors showed similar distribution for gender (men 55% vs. women 53%, p = 0.71), age (59 ± 11 years vs. 59 ± 11 years, p = 0.89), duration of diabetes mellitus (14 ± 8 years vs. 12 ± 8 years, p = 0.27), HbA1c (8.4 ± 2.2% vs. 8.0 ± 2.0%, p = 0.34) and serum creatinine (166 ± 84 uM vs. 156 ± 88 uM, p = 0.48). However, baseline systolic blood pressure (SBP; 159 ± 23 mmHg vs. 144 ± 20 mmHg, p < 0.01), diastolic blood pressure (DBP; 83 ± 13 mmHg vs. 79 ± 11 mmHg, p = 0.027) and urinary albumin-creatinine ratio (ACR; 2,562 ± 1,864 mg/g vs. 858 ± 1,022 mg/g, p < 0.01) were significantly higher among progressors. Multivariate analysis revealed baseline SBP, DBP and urinary ACR as strong independent predictors of DN progression (p < 0.01). SBP had the best discriminative performance (C statistics 0.823, 95% CI 0.73–0.91; p < 0.01). SBP of approximately 146 mm Hg had ~80% sensitivity and specificity for identifying progressors.

Conclusion: Among the DN patients studied, clinical measurements, such as SBP, DBP and ACR, were strong and independent predictors of worsening renal function. These findings may be helpful in identifying individuals who require intensive renal retardation interventions.

Nursing and Allied Health Category: NA05

Inpatient diabetes training for nurses: using interactive sharing, case-scenario experiential learning and ground-practice observations to strengthen learning effectiveness

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Introduction: An inpatient diabetes training programme was recently initiated for nurses, with an emphasis and design that focuses on interactive sharing and experiential learning and highlights on-the-ground incidents. The objective was to encourage participation, enhance understanding and create awareness of current diabetes-related ward issues. This study aimed to assess the effectiveness of this training. A set of diabetes care assessment questionnaires was

instituted for use both before and after the training was conducted.

Methods: Two rounds of inpatient diabetes training were conducted for nurses in 2009. Training included ice-breaking sessions, a quick run-through of important must-know information, real scenario-based case discussions, hands-on sessions on hypoglycaemia treatment and insulin administration, sharing on specific ground situations and misses as well as difficulties faced on the ground. A set of 20 questions was administered immediately before and after the training. The paired *t*-test was used to compare pre- and post-training test scores.

Results: A total of 27 registered nurses and one principal assistant nurse from the inpatient wards of Alexandra Hospital, Singapore, participated in the training. Participants were from the medical, surgery, orthopaedic or geriatric wards, and had experience nursing patients with diabetes mellitus and its related comorbidities. The mean length of experience post registration was 9.75 years. The post-training assessment revealed an improvement in the mean correct answers given from 61.42% (pre-test) to 90.36% (post-test), with significant improvement ($p < 0.05$) on 17 paired questions; four were hypoglycaemia related, five were insulin related and eight were diabetes related.

Conclusion: Interactive group learning, experiential scenario sharing and realisation of current issues helps create better understanding and improves knowledge retention among nurses. Individual vigilant observation and care can contribute toward better care of patients with diabetes mellitus.

Nursing and Allied Health Category: NA06

Risk of raised serum creatinine and potassium levels in patients treated with ACEIs or ARBs among type 2 diabetes mellitus patients with albuminuria and/or hypertension

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Introduction: Angiotensin converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) are recommended as antihypertensive treatment for patients with diabetes mellitus and albuminuria. Hyperkalaemia and serum creatinine elevation are two common concerns. In our centre, for patients with Stage 1–3 chronic kidney disease (CKD), ACEIs or ARBs are titrated by diabetes nurse educators (DNEs) based on an algorithm that recommends lowering the dose or discontinuing these medications should serum creatinine level rise by more than 20% or when serum potassium rises above 5.2 mmol/L. This study evaluated the risk for raised serum creatinine and potassium among Stage 1–3 CKD diabetes patients with albuminuria and/or hypertension who were treated with ACEIs/ARBs.

Methods: Patients with diabetes mellitus who were prescribed ACEIs or ARBs for treatment of hypertension or albuminuria were assessed at baseline and within four weeks of initiation or uptitration for serum potassium, creatinine, estimated glomerular filtration rate (eGFR), and other clinical variables.

Results: 112 patients with type 2 diabetes mellitus (Stage 1 CKD 43.75%, Stage 2 CKD 36.60%, Stage 3 CKD 19.64%) who were treated with ACEIs/ARBs were included in the analysis. Mean age (55.9 years), HbA1c (8.1%), systolic blood pressure (137.7 mmHg) and diastolic blood pressure (73.6 mmHg) were noted. 36.6% patients were normoalbuminuric; 38.4% patients had microalbuminuria while 25% had macroalbuminuria. Only 4.46% patients (n = 5; Stage 1 CKD 1, Stage 2 CKD 4) had creatinine elevation of more than 20% after exposure/dose escalation of ACEI/ARBs. Similarly, only 3.57% patients had serum potassium more than 5.2 mmol/L (n = 4; Stage 1 CKD 2, Stage 2 CKD 2).

Conclusion: Study results indicated an approximate 4.5% risk of significant elevation of creatinine and 3.6% risk of elevation of potassium to be associated with the use of ACEIs/ARBs in diabetes patients with Stage 1–3 CKD. If confirmed by a larger study, the need for reevaluation of serum creatinine and potassium within four weeks of ACEI/ARB initiation/uptitration in early-stage CKD could be reviewed.

Nursing and Allied Health Category: NA08

Registered nurses' perceived competence in asthma care: a survey

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Introduction: Patient education improves outcomes in asthma. Besides the asthma nurse educator, ward registered nurses (RNs) must be prepared and confident to discuss asthma management with their patients under any setting. Locally, no study has evaluated the competence of nurses in asthma care. This study aimed to determine the perception of competence among RNs in asthma care.

Methods: A 26-question survey was developed, piloted and sent to all RNs across the wards. The questionnaire covered areas on asthma definition, causes/triggers, diagnosis, classification, control, management, use of inhaler techniques and patient education. All RNs were asked to answer questions based on honest self evaluation of competence in the subject matter as 'yes, I know', 'no, I don't know', or 'not sure'.

Results: 297 (82%) RNs responded to the survey. The proportion of 'yes' answers was 66%, 'no' was 8%, and 'not sure' was 26%. Chi-square analysis showed no association between RNs' perception of competence and designation or gender. An analysis of departmental affiliation showed a statistically significant association only for questions 23 and 24 ($p < 0.05$), where a significant number of nurses reported as 'not sure' what asthma exacerbation was and 'no' to confident enough to provide asthma education to patient/family/caregiver. RNs who had previous asthma training perceived more competence in asthma care across most questionnaires (chi-square, $p < 0.05$).

Conclusion: RNs perceived suboptimal competence in asthma care. Nurses who had previously received asthma training apparently felt more competent than those who were without such training. Survey results highlight the urgent need for in-house asthma training to ensure that every RN is confident of providing basic asthma education in the course of duty.

Nursing and Allied Health Category: NA09

Antidepressant treatment and psychosocial intervention improves depression, diabetes mellitus control and quality of life in diabetic patients

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Introduction: Patients with diabetes mellitus are at higher risk of developing depression than non-diabetics. However, the need to provide and evaluate appropriate intervention for depression or distress in these patients is under-recognised. This longitudinal study assesses the efficacy of antidepressant and psychosocial interventions in improving depression, HbA1c and quality of life in these patients.

Methods: 211 outpatients were screened using the Center for Epidemiologic Studies Depression Scale (CES-D), Problem Areas in Diabetes (PAID) and World Health Organization Quality of Life-Brief (WHOQOL-BREF). 39 (18.5%) patients screened had scores of CES-D ≥ 16 or PAID ≥ 40, reflecting high levels of depressive symptoms or diabetes-related distress, while 20 (9.5%) patients had both. Patients with CES-D ≥ 16 and diagnosed with depression were treated with antidepressants and received counselling, while the rest received counselling only. Within six months to one year, 23 patients completed the same instruments. Change in HbA1c was also recorded.

Results: Patients reported a significant decline in CES-D (t[22] = 6.68, p < 0.01) and PAID (t[22] = 4.07, p = 0.001). 70.6% of patients with initial CES-D ≥ 16 fell below the cutoff values, while 78.6% of patients with PAID ≥ 40 reported scores below the cutoff. There was significant increase in quality of life in the physical (t[22] = 5.18, p < 0.01) and psychological domains (t[22] = 2.59, p = 0.017), but not in the social and environmental domains. There was no significant change in HbA1c, but 60.9% of patients had lower HbA1c readings compared with baseline.

Conclusion: Antidepressant and psychosocial interventions were able to reduce depression and diabetes-related distress and improve quality of life in patients with diabetes mellitus. More than half of the patients showed improved diabetes control, although the mean improvement in HbA1c for the group was not significant. This could be due to the small sample size of the present study, limited range of values for HbA1c and the effect of patients who did not show improvement. However, study results demonstrate the importance of screening for depression and providing appropriate intervention.

Nursing and Allied Health Category: NA10

Patient medication list: improving patient's understanding and adherence to medication regime

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Introduction: Inadequate understanding of medication, their indications and adverse effects often leads to poor adherence among patients, resulting in negative patient health outcomes. This study aimed to determine the impact of a personalised patient medication list (PML) on patients' understanding of their medication and identify the patients who were more likely to benefit from the PML in a hospital setting.

Methods: Patients on three or more chronic medications were prospectively studied over four months. A drug database with names, corresponding images, pronunciation, common indications, side effects and patient advice was created along with a standard template. Upon recruitment, this template was personalised with the patient's medication and corresponding information from the drug database to generate the PML. Baseline understanding of medication was assessed at recruitment and follow-up appointment via direct interviews. Pearson's correlation and paired sample t-test were used for statistical analyses.

Results: 93 patients were recruited of which 41 completed the study. Overall understanding of medication (p = 0.000), administration (p = 0.005) and awareness of indication(s) (p = 0.015) were areas which showed statistically significant improvement after the provision of PML. Patients on more medications had poorer understanding, especially with regard to indication(s) (p = 0.001). Stratified analysis showed that patients on 5–8 medications (n = 24) had the most knowledge improvement, particularly in overall understanding (p = 0.002), knowledge of adverse effects (p = 0.015), indication(s) (p = 0.033) and administration (p = 0.047). More than 60% of patients strongly agreed that PML was useful in improving their understanding and in managing their medication regime and that they would like to continue receiving it.

Conclusion: PML significantly improves patients' overall understanding of medication, their administration and knowledge of their indication(s) in a hospital setting. Patients on 5–8 medications benefited most from provision of a PML.

Nursing and Allied Health Category: NA12

Gerontological care in nursing education programmes

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Introduction: While in recent years the average age of patients has increased, nurses do not always have the knowledge, competencies or attitudes necessary to care for older people. The complexities of caring for elderly patients are also not recognised. This report is of a study conducted to identify the coverage of gerontological care in diploma and degree nursing programmes.

Methods: A descriptive cross-sectional survey of three nursing education programmes in Singapore was conducted. The three institutions included in the study were Nanyang Polytechnic and Ngee Ann Polytechnic, which provide a three-year diploma in nursing, and National University of Singapore, which provides a three-year nursing degree programme.

Results: While there was great variability among nursing education programmes in terms of gerontology courses, clinical placements and number of experts, it was encouraging that most programmes had integrated gerontology content into non-gerontology courses, all programmes offered gerontology clinical placements, and many nursing educators and clinicians were considered to be experts in gerontology. Lack of interest in care for older people in general, lack of gerontology-related competencies within curricula, and a negative image of gerontological care were reported as the most frequently-encountered barriers to incorporating gerontological care aspects into curricula.

Conclusion: Gerontology content in basic nursing curricula should be increased in view of the rising trend in the average age of patients needing nursing care. A minimum standard curriculum and specific competencies for care of older people should be formulated for all diploma and degree nursing education programmes. Strengthening educators' expertise and investing in role models, such as clinicians in gerontology care, remain important priorities for the nursing profession.

Nursing and Allied Health Category: NA13

Registered nurses' knowledge of nursing documentation in geriatric wards

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Introduction: Registered nurses' (RNs) knowledge of nursing documentation is important, as its purpose is to communicate health information, facilitate quality assurance and research and demonstrate the nurses' accountability. This study investigated RNs' knowledge of the documentation used in two geriatric wards in Khoo Teck Puat Hospital, Singapore.

Methods: A cross-sectional retrospective study was conducted on a sample of 40 RNs in two geriatric wards using a modified version of Edelstein's questionnaire. Participants completed a questionnaire in which they identified factors that influence their knowledge and understanding of documentation.

Results: Participants reported that they have considerable knowledge of nursing documentation. They also indicated that they were most knowledgeable about policies on documentation and writing discharge instructions. However, their knowledge of nursing assessments ranked fifth and they were least knowledgeable about reading reports for each shift.

Conclusion: The modified Edelstein's questionnaire provided a valid and reliable instrument for measuring RNs' knowledge of nursing documentation. A factor analysis of the 16 items in the Knowledge scale showed excellent reliability. RNs in the two geriatric wards have high levels of knowledge about documentation. Specific recommendations relate to the implementation of comprehensive documentation education programmes that reflect the needs of organisations and the level of RNs' skills and knowledge concerning documentation.

Nursing and Allied Health Category: NA14

The use of glucometrics to evaluate quality of inpatient glycaemic control

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Introduction: While outpatient glycaemic control is easily assessed by the HbA1c test, no equivalent examination exists for inpatients. Glucometrics is a mathematical analytical process that permits objective comparisons of inpatient glycaemic control among hospitals and patient care units. It utilises time-averaged glucose readings from which the patient-day glucose (average glucose for each patient's hospital day) is used, as it is the most reasonable metric that allows for fair patient-to-patient comparison. The aim of this study was to show that glucometrics could be used as a tool to evaluate the quality of inpatient glycaemic control in a general medical ward.

Methods: Capillary blood glucose readings from a general medical ward over a two-month period were collected using the hospital Cobas-IT system. The readings were converted into patient-day average values using the glucometrics software developed at Yale University. The readings were benchmarked against the best patient care unit in the Yale-New Haven Hospital, which achieved a 65% patient-day mean of between 3.9 to 8.3 mmol/L.

Results: A total of 6,245 samples were collected over the study period with 324 patient-days. The median patient-day glucose was 7.3 mmol/L. 60.5% of patient-days had glucose readings within our defined target range of 3.9 to 8.3 mmol/L. 3.4% of patient-days had hypoglycaemia of < 3.9 mmol/L and 6.8% had severe hyperglycaemia of > 16.6 mmol/L. The median duration of glucose monitoring was 1.3 days.

Conclusion: We achieved 60.5% patient-days with glucose readings within the target range, which is lower than the Yale-New Haven figure of 65%. This study demonstrates that glucometrics can be used to compare inpatient diabetes management across institutions. It can also be used to help institutions benchmark their services against centres of excellence and act as a means for improvement.

Nursing and Allied Health Category: NA15

Nurses' perception of the benefits of patient education II

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Introduction: Patient education (PE) is a core responsibility of nurses. Nursing shortage and resource constraints have increased the challenges faced by nurses in coping with patient/family expectations as well as organisational needs to discharge patients quicker and sicker to optimise bed utilisation. Therefore, it has become crucial that nurses actively participate in PE to help patient/family make decisions for self-directed care. This study assessed nurses' perception of the importance of PE. Results were also compared against a similar 2004 study with an aim to promote, encourage and empower nurses to practice PE by exploring ways to overcome barriers.

Methods: A cross-sectional survey was conducted across the nursing workforce in Alexandra Hospital, Singapore. Questions were drawn from literature reviews. A convenience sample of 500 nurses from various disciplines participated in the study.

Results: The response rate was 93.6%. All participants rated PE as important vs. 93.6% in the 2004 survey, 97.4% agreed that health education was helpful to patients. 97.6% of respondents agreed that PE was a part of nursing. 83.2% participants were prepared to provide PE vs. 69% in the 2004 survey. 91.9% respondents felt that protected time would

encourage participation in PE vs. 80.5% in the 2004 survey. Barriers to PE were lack of communication skills (26%), knowledge (24.1%), teaching tools (16.2%), training (15.9%), insufficient time (17.8%) and distractions from other work. Patient factors that hindered effective education were language barrier (17.7%), emotional barriers (42.6%), low education level (14.1%), beliefs (13.9%) and pain (11.7%).

Conclusion: Participation in PE improved from 42.5% in year 2004 to 56.8% in the current study. More nurses viewed PE as important and expressed willingness to actively participate in PE if protected time and training were provided. However, significant barriers to effective PE still continue to exist and there is a need for concerted efforts to address these issues.

Nursing and Allied Health Category: NA16

Knowledge of asthma care among registered nurses: a survey study

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Introduction: Patient education improves the outcomes in asthma. Medical professionals, including ward registered nurses (RNs) require sound knowledge of asthma care in order to discuss asthma management with patients under any setting. To date, no local study has evaluated the knowledge level of asthma among ward nurses. This study was designed to determine the level of asthma knowledge of ward RNs.

Methods: A cross-sectional survey study was conducted among ward RNs using a purpose-designed and pilot-tested questionnaire. A total of 21 multiple-choice questions were developed based on patient education packages, such as definition, causes/triggers, diagnosis cum classification and control, treatment of asthma, inhaler techniques and patient education.

Results: 295 out of 361 RNs (82%) responded to the survey questionnaire. Many RNs were unable to participate in the survey due to busy work schedules. The responses included 63% correct answers, 25% incorrect answers, and 12% 'not sure' responses. The mean score among the RNs was 63.81 ± 13.9. When benchmarked against the hospital competency-based programme passing score of ≥ 80, only 37 (12.5%) RNs achieved the target while 258 (76.5%) failed to meet the target.

Conclusion: Study results point at insufficient knowledge of asthma care among RNs and highlight the need for asthma training. Nursing training institutions should consider incorporating additional asthma education modules, including inhaler techniques, into nursing skill curricula to bridge the gap between knowledge and service needs.

Nursing and Allied Health Category: NA17

Prevalence study of methicillin-resistant *Staphylococcus aureus* in Alexandra Hospital

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Introduction: Asymptomatic methicillin-resistant *Staphylococcus aureus* (MRSA) carriers are often not recognised. In 2003, a Society for Healthcare Epidemiology Association (SHEA) taskforce advocated a strategy of using active surveillance cultures to identify MRSA carriers. However, universal MRSA screening remains controversial. At Alexandra Hospital, Singapore, only patients classified as high risk for MRSA are screened on admission. This study aimed to investigate the prevalence of MRSA and assess the need for universal MRSA screening according to risk stratification.

Methods: Surveillance screening for MRSA was conducted on all adult inpatients on admission. MRSA surveillance swabs were taken from nasal, axilla, groins and wound, if present. Patients were stratified into high risk, moderate risk and low risk groups according to disease processes, history of

hospitalisation and nursing home stay. Prevalence of MRSA was tabulated according to the different risk groups.

Results: 377 patients were admitted to the hospital from April 27, 2010 to May 4, 2010. Prevalence of MRSA on admission was 10.3%. MRSA prevalence was 22% in the high risk group (n = 127), 5.5% in the moderate risk group, and 2.9% in the low risk group. Although the high risk group had the highest prevalence of MRSA, it represented only 34% of all inpatients, as 66% of patients admitted to the hospital belonged to either the moderate or low risk groups, which accounted for 28% of all MRSA on admission.

Conclusion: Screening of only the high risk group patients for MRSA would imply that 28% of patients with MRSA woud go undetected on admission. This would lead to poor MRSA control in the hospital due to ineffective contact precautions. Study findings support the need for universal MRSA screening on patient admission to enable successful control of MRSA transmission among hospitalised patients.

Nursing and Allied Health Category: NA18

Surveillance of *Enterobacteriaceae* producing extended spectrum β-lactmase in Alexandra Hospital from January 2009 to June 2010

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Introduction: The Alexandra Hospital Antibiogram 2008 and the Network for Antimicrobial Resistance Surveillance Singapore (NARSS) data revealed a high prevalence of extended spectrum β-lactmases (ESBLs) in Alexandra Hospital, Singapore. The infection prevention and control team at Alexandra Hospital investigated the factors associated with ESBL in order to put in place interventions that could arrest the trend as well as the disturbing sequelae associated with infections.

Methods: An 18-month prospective study was carried out on specimens sent for laboratory investigations in the hospital. Results of these examinations and patient biodata were collected and analysed. The criteria for community- and nosocomial-acquired infections were based on definitions from Centers for Disease Control and Prevention, United States.

Results: Urine (53.3%) accounted for majority of the specimens (223/418). Most urine samples (50.6%) were taken via urinary catheters (113/223). 11.4% urine specimens were from patients admitted from nursing homes. *Escherichia coli* (47.1%) and *Klebsiella* spp. (31.6%) accounted for 78.7% of ESBL-producing enterobacteria (329/418).

Conclusion: Findings suggest the need to focus on factors associated with the infection of ESBL-producing enterobacteria, such as care management of urinary catheter.

Nursing and Allied Health Category: NA19

Relatives accompanying PACS 2 and above patients in emergency department treatment areas: a literature review

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Introduction: Emergency departments (EDs) in Singapore, other than for paediatric patients, keep relatives of patients who are triaged as Patient Category Scale (PACS) 2 and above away from the designated treatment areas. Such access control raises anxiety levels, leading to complaints from these individuals, and also affects patients' psychological well-being. This study evaluates existing evidence supporting or opposing the concept of relatives accompanying patients in ED treatment areas.

Methods: Literature searches were conducted using EBSCOHost, MEDLINE, PsycINFO and CINAHL databases for the search terms relatives and emergency department, and family and emergency department. Searches were limited to studies reported in the English language. No predetermined year of publication was set. Related evidence was extracted and synthesised. Reports related to paediatric patients and relatives witnessing resuscitation or invasive procedures in the ED were excluded from the study.

Results: Most reports agree that family crisis and their needs must be considered while attending to patients in the ED. Several studies have suggested inventory lists to measure and manage the anxiety of relatives. Nevertheless, most studies also acknowledge the reluctance of medical staff to having relatives in the ED treatment areas. The leading worry of medical personnel in the ED was the possible misinterpretation of clinical situations by relatives and needless legal implications thereafter. There is inadequate evidence to draw any conclusive deduction, as most studies were carried out in the critical care setting and were cardiopulmonary resuscitation-related and did not involve acute treatment in the ED. The relevance of the present findings might consequently be applicable in a parallel manner at best.

Conclusion: Allaying the anxiety of relatives and patients is the cornerstone for customer service satisfaction initiatives in the ED. Further controlled prospective studies are warranted in the ED setting in Singapore to gather further evidence supporting or opposing the concept of relatives accompanying patients in treatment areas.

Nursing and Allied Health Category: NA20

Wetness Alert Diaper for assisting with timely diaper replacement among patients with dementia

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Introduction: Urinary incontinence is highly prevalent and diaper use is common among patients with dementia. Timely diaper replacement is necessary to avoid complications secondary to prolonged lying in soiled diapers for such patients. Current scheduled diaper change is labour intensive, inefficient and cannot guarantee immediate detection of diaper wetness, which is an important step toward timely diaper replacement. The Wetness Alert Diaper (WAD) system was developed to enable timely detection of diaper wetness and prompts for assistance through appropriate reminders for a diaper change once the diaper is soiled. The goal of this study was to explore the real needs, practical usability issues and their influence on functioning, and efficacy of WAD under institutional care settings.

Methods: A clinical trial with WAD was conducted on 6 patients with dementia at a local nursing home to test the effectiveness of the system in an institutional setting.

Results: Preliminary analysis of the data collected indicated 75% sensitivity and 96% specificity when using WAD for detecting soiled diapers.

Conclusion: Trial outcomes demonstrate promising results for the automated and timely detection of diaper wetness using WAD. Study findings are being used to effect improvements in WAD. With proper usage and functioning of the system, timely diaper replacement will become a reality with WAD. As the sample size of this study was small, a bigger clinical trial on 12 patients with dementia is planned.

Nursing and Allied Health Category: NA21

MRSA registry at Alexandra Hospital to identify risk for methicillin-resistant *Staphylococcus aureus*

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Introduction: The methicillin-resistant *Staphylococcus aureus* (MRSA) burdens are increasing in Singapore according to the Network for Antimicrobial Resistance Surveillance (Singapore). Alexandra Hospital, Singapore, reported high MRSA rates between January and June 2009, which suggests significant implications for patient outcomes and the hospital's infection control programme. This study was designed to identify patients at high risk for the pathogenic development of MRSA colonisation or infection.

Methods: A prospective study was conducted on MRSA positive screening results of patients admitted from April 2009. Biological data from over 200 patients were collated and studied in detail, with information including age, gender, site of specimen collection, preexisting risk factors such as premorbid conditions, wound type, and whether patients were admitted from their homes or nursing homes. MRSA colonisation was defined as MRSA positive within 48 hours of hospital admission (CA-MRSA). MRSA infection was defined as MRSA positive after 48 hours of hospital admission with signs and symptoms of infection. Multivariate analyses were performed.

Results: 65.6% of patients were men. A majority of the patients were aged above 65 years. 65% of patients had community-acquired MRSA (CA-MRSA), with a majority having one or more risk factors in the preceding 12 months. Wounds comprised 33% of specimens processed.

Conclusion: The increasing MRSA burden in Singapore calls for concerted efforts toward controlling and preventing the spread of infection in hospital patients. Decolonisation of carriers and careful use of antibiotics is the key to preventing, reducing and resisting antibiotic resistance. Therefore, stringent control over the use of antibiotics must be implemented. Wound care excellence should be developed, as it is critical to give patients the best treatment and care to ensure both a hassle-free hospital stay and rapid recovery.

Nursing and Allied Health Category: NA22

Hook-composite flexion and finger-wrist extension for the rehabilitation of flexor tendon repaired at zone 2: a case study

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The rehabilitation and repair of ruptured flexor tendons in the hand has been the subject of extensive research generating volumes of literature. This study presents the debut rehabilitation of zone 2 flexor tendon repair using the hook-composite flexion and full finger-wrist extension (HCFE) exercise regime to achieve maximal tendon excursion and differential gliding. HCFE differs from traditional rehabilitation techniques as it allows simultaneous full finger-wrist extension at postoperative Day 2. We report a man who sustained a left ring finger zone 2 flexor digitorium profundus and flexor digitorium superficialis tendon lacerations, and middle phalanx comminuted fracture. Both tendons were repaired, and the fracture treated conservatively. Following surgery, the patient was informed that he was unlikely to flex his distal interphalangeal joint (DIPJ), and to expect a 300–400 proximal interphalangeal joint (PIPJ) flexion contracture. To achieve maximal tendon excursion and reduce PIPJ flexion contracture, the HCFE exercise regime was used. The patient was instructed to exercise 6 × 10 repetitions daily. The traditional dorsal extension block splint was used in between exercises to prevent tendon rupture. Although instructed to exercise more often, the patient was able to only do 3 × 10 repetitions daily due to pain. The range of motion of the left ring finger at week three was 0°–75° for metacarpophalangeal joint (MCPJ), 0°–85° for PIPJ and 15°–15° for DIPJ. At week 5, the range of motion was 0°–80° for MCPJ, 0°–85° for PIPJ and 0°–0° for DIPJ. There

was no change in the range of motion at week 8 for MCPJ and DIPJ. However, the range of motion for PIPJ improved to 0°–95°. The patient achieved full PIPJ extension in spite of only exercising three times daily, and despite the possibility of PIPJ flexion contracture due to a failure to achieve full extension in the postoperative period; such flexion contracture would compromise any subsequent attempts at salvage by secondary tendon surgery. The key to preventing contracture of the repaired flexor tendons is to allow them a greater finger and wrist range of extension and maximal proximal tendon excursion. This simultaneous extension was achieved in the HCFE exercise regime. Furthermore, the synergistic pattern of the exercise regime, which allows for increased finger flexion with low flexion tension, is also an excellent alternative for achieving safe maximal tendon gliding without rupturing the repaired tendon.

Nursing and Allied Health Category: NA23

Factors influencing emergency department patient turnaround time

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Introduction: This study aimed to identify the impact of various factors on emergency department turnaround time (ED TAT) for acuity scale 3 (P3) patients who are ambulant with mild-to-moderate conditions that require acute treatment.

Methods: Patient data over four consecutive weeks were analysed from the administrative databases of Khoo Teck Puat Hospital, Singapore. ED TAT was calculated as the interval between patient registration time and case end time. A multivariate linear regression model was constructed with the presence of various ED subprocesses, such as admission, laboratory test, medication, point-of-care test, procedure, radiology investigation and referral, as dependent variables. The regression coefficients demonstrated the actual impact of each of these subprocesses on TAT after adjusting for patient arrival time, that is non-peak and various peak hours identified from historical arrival patterns.

Results: Based on a total of 4,438 ED visits, all subprocesses significantly affected ED TAT ($p < 0.001$). The presence of admission, medication, laboratory test, radiology investigation, referral, point-of-care test and procedure resulted in a TAT increase of 46.7, 45.5, 43.7, 22.7, 19.0, 13.7, 13.0 minutes, respectively. Different patient arrival times also had a statistically significant influence on TAT. Arrival during morning peak (10 am to 12 pm) timings, afternoon peak (12–1 pm and 3–4 pm) timings and night peak (8–10 pm) timings increased TAT by 7.4, 9.6 and 20.0 minutes, respectively, when compared with non-peak hours.

Conclusion: The presence of admission, medication and laboratory test resulted in greatest increases to ED TAT, which may be substantially shortened by more targeted efforts to streamline these subprocesses. Additional resources may also be deployed during night peak hours to reduce TAT.

Nursing and Allied Health Category: NA24

MONICA: toward a continuous non-intrusive monitoring system for the care of patients in hospitals

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Introduction: Current practices for monitoring patient health status and well-being in hospitals is tedious, time consuming and intrusive, as it typically involves manual periodic checks by medical professionals or requires the patients to wear specialised probes that cause at least some level of discomfort. Furthermore, such monitoring is infrequent and may miss the onset of crisis events. The aim of this study was to develop a non-intrusive intelligent monitoring system that can continuously monitor the health status of patients, including their vital signs, and evaluate events of interest that threaten their well-being in hospitals.

Methods: The proposed system uses Fiber Bragg Grating sensors that are placed beneath the bed to obtain an indicative spatial-temporal signature of signals for patient monitoring. It is non-intrusive as patients only need to lie on the bed. It allows continuous monitoring of patient's vital signs, such as respiratory and heart rate, in addition to monitoring for posture and movement from pressure points to prevent bedsore and bed occupancy. Wavelet transform-based processing techniques are used to separate the vital sign signals from other movement-related signals. In an emergency, such as weakening of the patient's vital signs, caregivers can be informed promptly through an alert system for immediate attention.

Results: Initial trials suggest that the system is stable and robust for continuous non-intrusive monitoring. The results are promising as it shows near 100% accuracy for respiratory monitoring, with a maximum estimated error of ± 2 breaths per minute. However, challenges remain for heart rate monitoring as the results obtained were not comparable to those achieved in the laboratory, where the maximum error was ± 3 beats per minute for heart rate.

Conclusion: The system is an innovative means of providing continuous monitoring of patients in an unobtrusive manner. It obviates the need for intrusive probes and minimises labour-intensive manual procedures.

Nursing and Allied Health Category: NA25

Depression and distress in patients with diabetes mellitus

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Introduction: Research has shown that patients with diabetes mellitus are twice as likely to develop depression as compared to the general population. Comorbid depression was also found to be associated with poor glycaemic control and quality of life. There is no known study on the effect of depression or diabetes-related distress on disease control and patient well-being among diabetic patients in Singapore. We hypothesised that patients with depressive symptoms or diabetes-related distress are more likely to have higher HbA1c and lower quality of life.

Methods: 445 outpatients attending full diabetes assessment were interviewed using the Center for Epidemiologic Studies Depression Scale (CES-D), Problem Areas in Diabetes (PAID), and World Health Organization Quality of Life Brief (WHOQOL-BREF). Their HbA1c readings were also recorded. Patients with CES-D ≥ 16 or PAID ≥ 40 were considered to have met the criteria for presence of depressive symptoms or diabetes-related distress.

Results: 62 (13.9%) patients were found to have depressive symptoms or diabetes-related distress. 33 (7.4%) patients had both depressive symptoms and diabetes-related distress. Compared with non-depressed and non-distressed diabetic controls, patients with depressive symptoms or diabetes-related distress had significantly higher HbA1c ($F[1,443] = 11.1$, $p = 0.001$), lower general quality of life ($F[1,436] = 55.6$, $p < 0.001$) and lower scores on all four domains (physical, psychological, social and environmental) of the WHOQOL-BREF.

Conclusion: This study shows that depressive symptoms or diabetes-related distress in diabetic patients affects their diabetes management and well-being. In addition to physical and laboratory assessment of diabetic patients, screening for psychological symptoms, such as depression, distress or coping difficulties, should be carried out as part of a holistic assessment.

Nursing and Allied Health Category: NA26

Improving the efficacy of nutritional supplementation in elderly patients

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Introduction: Protein-energy malnutrition delays wound healing, extends length of stay, and increases complications and readmission rates. Identification of patients at risk of malnutrition, together with early interventions, may prevent further deterioration in the nutritional status of elderly patients. The main objectives of this study were to investigate the efficacy of delivering nutritional supplements to malnourished elderly patients using a 'nutrition as medication' programme for improving consumption rates, and to ascertain the acceptance of this intervention and compliance with the programme among nursing staff.

Methods: 40 malnourished geriatric patients (10 male and 30 female) were recruited for the study. Data collected included age (82.4 ± 9.1 years), height (1.55 ± 0.08 m), weight (35.5 ± 5.9 kg), body mass index (14.8 ± 2.3 kg), and baseline albumin (32.6 ± 5.0 g/L). The patients were randomly divided into two groups, with Group 1 receiving mid-meal supplements (n = 20) and Group 2 receiving 60 ml of a 2 kcal/ml supplement given four times daily at medication rounds (n = 20). Outcome measures included comparison of supplements and changes in he consumption of hospital food. The patients' length of stay was also monitored. Nursing staff (n = 20) were surveyed using a short qualitative questionnaire midway through the study to assess their acceptance of the 'nutrition as medication' programme.

Results: Patient compliance with the programme was excellent compared with current practices. The consumption rate of 80% in the intervention group was significantly different from that of 53% in the control group (p = 0.002, 2-tailed *t*-test). The survey showed that none of the nurses found it difficult to dispense the 2 kcal/ml supplement. 75% of nurses felt that it was an effective means of supplementing patients, while the remaining 25% felt that it was the same as before.

Conclusion: The 'nutrition as medication' programme is an acceptable and effective means of delivering nutritional supplements to malnourished elderly patients, thereby attenuating deterioration in their nutritional status.

Nursing and Allied Health Category: NA27

Use of blister packs to improve medication adherence: a pilot study

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Introduction: Study aims included determining the impact of blister packs on medication adherence and associated objective outcome measurements in patients on chronic medications for diabetes mellitus (DM), hypertension (HT) and/or hyperlipidaemia (HL).

Methods: Patients deemed as non-adhering by physicians were recruited from outpatient clinics at baseline visit. Inpatients who did not obtain a full score using the medication transfers were likewise also recruited. Medications were packed into blister packs on the second outpatient visit or upon discharge. Adherence was assessed by pill count method. Systolic blood pressure (SBP), HbA1c and low-density lipoprotein cholesterol (LDL-C) were objective outcome measures employed. Measurements were obtained upon recruitment and during subsequent follow ups. Feedback on the blister pack was also collected via satisfaction surveys.

Results: 29 patients were recruited of which 14 completed the study. All patients had HT, with eight patients having DM and HL. Mean patient age was 65.4 ± 13.4 years. Outpatients (n = 2) showed an increase in compliance from 72.5% to 75.5% and from 77.5% to 111.7% at the second and third visits, respectively. Inpatients (n = 12) showed high adherence (97.8 ± 19.9%) at follow-up. Five (62.5%) patients had objective decreases in LDL-C (up to 2.6 mM, p = 0.86) and HbA1c (up to 0.9%, p = 0.31) over a mean duration of 53.8 ± 33.7 days and 55.9 ± 29.3 days, respectively. Five (41.7%)

patients had decrease in SBP (up to 19 mmHg, p = 0.27) over a mean duration of 46.9 ± 30.8 days. All patients reported that blister packs simplified their medication regime; 92.8% patients felt that blister packs improved adherence to medications. Most patients (78.6%) were keen to continue with this service.

Conclusion: Blister packs improved medication adherence in patients with DM, HT and/or HL, thus resulting in a potential decrease in HbA1c, SBP and LDL-C levels. As its use was well received among the study group, it is possible that it could prove helpful in optimising adherence and health outcomes in patients with chronic diseases.

Nursing and Allied Health Category: NA28

Pharmacoeconomic analysis of nursing home medication reviews by pharmacists

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Introduction: Elderly patients in nursing homes (NHs) are known to be on polypharmacy. Medication reviews by pharmacists have been shown to improve rational prescribing and effect cost savings for the NHs. This study analyses the interim results of direct cost savings from interventions made by pharmacists in four NHs from January 2008 to December 2010, while reporting on data from January 2008 to December 2008 only.

Methods: A retrospective evaluation of all NH reviews in 2008 was performed. Medication interventions were identified from the drug evaluation forms, which contained information on medication issues, recommendations from pharmacists and actions taken by doctors. Direct cost-saving interventions accepted by doctors were identified. Such interventions included overdose, over frequency, over duration and therapeutic duplication; drug use without indication, drug substitutions and better drug selection also lead to cost reduction. Direct cost savings from following such medication interventions were calculated based on a one-year projection.

Results: 235 direct cost-saving medication interventions were identified from 780 residents in the four NHs in 2008. Total cost savings for the four NHs amounted to S$27,380.94 per year. Top four direct cost-saving medication interventions were drug use without indication (61%; savings $16,005.82 per year), over frequency (29%; savings $7,736.34 per year), overdose (5%; savings $1,290.19 per year), and better drug selection leading to cost reduction (5%; savings $1,421.08 per year).

Conclusion: Interim analysis of this ongoing study showed that interventions suggested by pharmacists in the four NHs during 2008 resulted in direct medication cost savings amounting to S$27,380.94. Drug use without indication was the most common direct cost-saving medication intervention (61%; savings $16,005.82 per year). Further analysis of the data available when the study ends in December 2010 will help provide a clearer picture.

Nursing and Allied Health Category: NA29

Preventing falls in the elderly after discharge through follow-up home visits

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Introduction: Home visits (HVs) aim to promote and enhance independence and safety at home whereas phone calls (PCs) made two weeks after discharge ensure that instructions are being followed. However, such reports are based on the client's feedback alone. Reports in the literature indicate that frequent follow-up HV and PC can reduce falls in the elderly by nearly 80%. No studies have evaluated the effectiveness of HV by occupational therapists (OTs) in reducing falls in discharged elderly patients in Singapore. This study was designed to assess the effectiveness of an HV programme

being conducted by OTs. The programme included three HVs and three PCs by an OT, and addressed the physical, emotional and psychological needs of elderly people after a fall.

Methods: 65 participants were recruited based on the inclusion and exclusion criteria selected. An initial HV was made after discharge, which was followed up with PC at two weeks. At the 3rd and 6th month, follow-up HVs were conducted, and the programme was concluded with a PC at the 9th month. The Barthel Index (BI), Frenchay & Lawton Activities Index (FAI), Modified Fall Efficacy Scale (MFES), Falls Calendar and SF-12 were the outcome measures employed.

Results: 78.2% of the participants had improvement in their Basic Activity of Daily Living (ADL) with their BI score within the range of 0.2–8.0, and 76.1% of them experienced improvement in their Instrumental ADLs through their FAI. 78.2% had improvement in their MFES, showing a reduction in their fear of falling. 84.3% of the participants did not experience recurrent falls and 92.2% did not have any hospital readmission due to falls after the follow-up HV. Improvements in the average score of the emotional and physical components of SF-12 were also observed.

Conclusion: Follow-up HVs significantly prevent further falls and functional decline in elderly people. It also enhances their psychological, social and physical well-being.

Nursing and Allied Health Category: NA30

Nail resection with phenolisation is the treatment of choice for onychocryptosis

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Introduction: Onychocryptosis is a common presentation in podiatry clinic secondary to poor nail-trimming techniques or abnormal nail anatomy. These often lead to pain and risk of infections where conservative treatment requires frequent follow-up, which may not always relieve symptoms. Surgical treatment for such patients can offer a more permanent solution. We hypothesised that nail resection with phenolisation reduces recurrence of ingrown toenail-related problems in podiatry patients. A clinical audit was conducted for nail resection with phenolisation performed by podiatrists in the outpatient clinic.

Methods: A retrospective analysis of data collected from February 2009 to October 2010 was performed for all nail resections conducted by podiatrists at Alexandra Hospital (AH), Singapore, and Khoo Teck Puat Hospital (KTPH), Singapore. Data related to postsurgical infection and recurrence were reviewed. 80% phenol was used in all resections.

Results: Nail resections were performed for 46 (90.2%) toes in AH and five toes in KTPH. The mean age of patients was 32.3 ± 16.8 (range 17–87) years. 13 patients were women (25.5%). Six (11.8%) patients had type 2 diabetes mellitus and two had rheumatoid arthritis. Ten (19.6%) toes had previous total nail avulsions (TNA) and six had partial nail avulsions (PNAs) without phenolisation in the same affected toe. Four (7.8%) toes were infected prior to surgery. Six (11.8%) toes had acute ingrown toenails while 55 toes had chronic growth for over six months. 26 (51.0%) toes had unilateral PNAs, 22 (43.1%) had bilateral PNAs and three had TNAs. After surgery, four (7.8%) toes had infection and two (3.9%) toes had nail regrowth; mild pain was seen for three (5.9%) toes. Mean healing time was 2.43 ± 1.15 (range 1.0–6.0) weeks.

Conclusion: Nail resection with phenolisation is an easy, yet effective treatment for onychocryptosis. The low post-surgery infection and recurrence rates associated with the procedure are encouraging evidence for offering such options to patients with nail-related problems.

Nursing and Allied Health Category: NA31

A clinical framework for music therapy in palliative care: analysis of the Alexandra Hospital experience

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Introduction: Music therapy has been clinically accessible to patients receiving palliative care at an acute hospital since January 2008. A retrospective analysis was conducted for music therapy over one year (March 2009 to March 2010) to review the demographics, trends and efficacy of the modality. Data was based on the statistics and case notes collected by the author.

Methods: 177 patients (men 100, women 77) were referred to and assessed for music therapy by an overseas-trained board-certified clinician; 28 patients refused the offer. 188 sessions were conducted for the patients who accepted the therapy (n = 124) during which 65% patients engaged in the session passively, 13% patients actively played instruments or sang and engaged in entertainment experiences or song-writing, and 21% patients did both. Parameters tracked included pain, breathlessness, coping, sleep, relaxation, validation of feelings, and support of family, leisure and faith. Tools employed were the Visual Analogue Scale (VAS), DoloPlus-2 Scale, Body Colouring Tool, and patient or family self-reports.

Results: Of the 89 (72%) patients who experienced relaxation, 47 verbalised their relaxing music experience and 16 fell asleep. All 24 (19%) patients who were in acute pain experienced relief after music entertainment, and two patients refused pain medication following the session as they felt able to manage without it. 29 (23%) patients stated it as an effective coping strategy while 23 (19%) framed a positive statement about their hospitalisation. 33 patients and 21 families received psychosocial support. 12 family members were able to utilise music experiences to engage with the patients. 36 (29%) patients achieved deep relaxation toward sleep outcomes through music while 19 (15%) reported increased ease of breathing. 44 (35%) patients were not in acute distress and utilised music therapy services for leisure.

Conclusion: Music therapy interventions were useful in reducing acute symptoms of pain and breathlessness, and supported the coping strategies of patients and their families, with increased perceptions of relaxation or comfort as valuable outcomes. Future research will be focused toward the efficacy of various music interventions.

Basic Science Category: B01

Association of pigment epithelium-derived factor and insulin resistance

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Introduction: Pigment epithelium derived-factor (PEDF) is known as a multifunctional protein secreted by adipocytes that has antiangiogenic and neurotrophic functions. Recent studies in rodents suggest a relationship between PEDF and insulin resistance. The evidence of PEDF influencing insulin resistance in humans is scarce. We hypothesised that circulating PEDF levels are significantly different between healthy controls (CTL) and those with abnormal glucose tolerance (ABGLT).

Methods: 238 healthy adults (age 18–70 years), with no past history of type 2 diabetes mellitus (T2DM), who presented to Alexandra Hospital, Singapore, for health screening from July 2008 to July 2009 were enrolled. Based on their fasting glucose (FG) levels, these individuals were classified as T2DM (FG 7.0 mmol/L or greater), impaired fasting glucose (IFG; FG 6.1–6.9 mmol/L) or CTL (FG < 5.6 mmol/L). All participants with T2DM and IFG were shortlisted for further study along with 31 CTLs matched for age and gender. Demographic and anthropometric data and fasting lipids were measured. Serum PEDF was determined using enzyme-linked immunosorbent assay. Insulin and highly sensitive C-reactive protein (hs-CRP) were measured according to standard laboratory techniques. HOMA-IR was calculated from fasting glucose and insulin levels, as a marker of insulin resistance.

Results: Compared to CTLs, participants with ABGLT had higher PEDF levels (11.90 ± 2.889 μg/ml vs. 13.60 ± 3.079 μg/ml, $p < 0.05$), HOMA-IR (2.66 ± 2.38 vs. 8.21 ± 10.99, $p < 0.05$), waist circumference (86.57 ± 11.50 cm vs. 95.34 ± 15.10 cm, $p = 0.05$) and triglyceride levels (1.35 ± 0.59 mmol/L vs. 1.99 ± 1.54 mmol/L, $p < 0.05$). PEDF was positively associated with body mass index ($r = 0.270$, $p = 0.05$), diastolic blood pressure ($r = 0.340$, $p < 0.05$), waist circumference ($r = 0.384$, $p < 0.05$) and hs-CRP ($r = 0.292$, $p < 0.05$), but negatively associated with high-density lipoprotein ($r = –0.405$, $p < 0.05$). Women had significantly lower PEDF compared to men (12.1 ± 3.28 μg/ml vs. 13.51 ± 2.79 μg/ml, $p < 0.05$).

Conclusion: In this cross-sectional study, PEDF was found to be significantly increased in ABGLT. Further prospective and *in vitro* studies are warranted to better understand the mechanisms of association between PEDF and insulin resistance.

Basic Science Category: B02

Serum haemopexin and haptoglobin are differentially expressed in individuals with type 2 diabetes mellitus and impaired fasting glucose

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Introduction: Type 2 diabetes mellitus (T2DM) accounts for about 80% of all diabetes. Current understanding of the development of impaired fasting glucose (IFG) and T2DM is incomplete. We hypothesised that serum proteins in T2DM, IFG and healthy individuals are differentially expressed and may serve as potential early biomarkers, thus improving our understanding of the pathogenesis of glucose tolerance deterioration and producing potential therapeutic targets.

Methods: Previously healthy men (age 21–70 years) seen at Alexandra Hospital, Singapore, for health screening from July 2008 to March 2010 were recruited for the study. Individuals were categorised based on fasting glucose (FG) levels as T2DM (FG ≥ 7.0 mmol/L), IFG (FG 6.1–6.9 mmol/L), and control (CTL; FG < 5.6 mmol/L). Anthropometric data and fasting lipids were measured. Serum from T2DM and IFG individuals and CTLs were compared. CTLs were individuals

with normal blood pressure (BP) and desirable lipid profile, and were matched for age and body mass index (BMI). Albumins and immunoglobulins were depleted and protein analysis was performed by two-dimensional differential in-gel electrophoresis (2D-DiGE). Protein spots that showed significant differences were picked and digested in-gel. Mass spectrometry and database searching allowed spot identification.

Results: 181 men were enrolled in the study of whom 11.6% and 8.3% participants had T2DM and IFG, respectively. Seven men with T2DM, seven with IFG and six CTLs were selected. Mean age (48.50 ± 7.30 years), BMI (25.16 ± 3.89 kg/m^2) and FG (CTL 4.35 ± 0.49 mmol/L, IFG 6.33 ± 0.10 mmol/L, T2DM 10.83 ± 4.55 mmol/L) were significantly different ($p < 0.05$). BP, cholesterol and triglyceride levels were not significantly different. Ten protein spots were upregulated while 11 were downregulated in participants with T2DM and IFG compared to CTLs. Haemopexin was found to be significantly upregulated by 1.3 fold while haptoglobin was upregulated by 2.8 fold in individuals with IFG and T2DM ($p < 0.05$).

Conclusion: Results suggest that serum proteins are differentially expressed in individuals with T2DM and IFG compared to healthy CTLs. Haptoglobin binds to haemoglobin while haemopexin binds to haeme, and thereby prevent haemoglobin-induced oxidative tissue damage. Whether these proteins are causal or associated with abnormal blood glucose is unknown and remains to be elucidated.

Basic Science Category: B03

Blood microRNA profiles in women with impaired fasting glucose

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Introduction: Prediabetes is a state of abnormal glucose homeostasis that is characterised by the presence of impaired fasting glucose (IFG) and impaired glucose tolerance. These individuals are at risk for type 2 diabetes mellitus. Molecular understanding of the onset and progression of IFG remains incomplete. MicroRNAs (miRNAs) are a class of small non-coding RNAs functioning as translational modifiers, typically as repressors. Blood miRNA levels vary with disease states, and so represent an attractive class of potential biomarkers. We hypothesised that blood miRNAs in IFG were different from those in healthy controls (CTL), mainly at the pathways controlling glucose homeostasis.

Methods: Healthy adult women (age 21–70 years), seen at Alexandra Hospital, Singapore, for health screening from July 2008 to March 2009 were recruited for the study. Anthropometric data, fasting glucose (FG) and lipids were measured. Individuals were categorised based on FG levels as IFG (FG 6.1–6.9 mmol/L) or CTL (FG < 5.6 mmol/L). RNAs (including miRNAs) were isolated using the RiboPure-Blood kit. 1 μg of RNA was ^{3}H-labelled and hybridised on miRNA microarray. Data was quantified using the median fluorescence intensity of four spots for each miRNA and normalised using global LOWESS (locally weighted scatterplot smoothing). A 1.5-fold increase, 0.3-fold decrease, or p-value less than 0.05 was considered significant up/downregulation.

Results: 60 healthy women, not on any medications, were enrolled in the study; 16 women had IFG. Pooled RNA from nine randomly selected women with IFG was compared with nine CTLs, matched for body mass index, blood pressure and lipids. Mean FG was statistically different between CTLs (4.67 ± 0.78 mmol/L) and participants with IFG (6.47 ± 0.10 mmol/L) ($p < 0.05$). An upregulation of 114 miRNAs and a downregulation of 219 miRNAs was observed in women with IFG when compared to CTLs, with 39 miRNAs having ≥ 50% upregulation and 49 miRNAs showing ≥ 30% downregulation ($p < 0.05$). miR-519d which potentially targets PPAR-α (peroxisome proliferator-activated receptor α) expression was increased 115-fold in individuals with IFG. PPAR-α mediates the balance between fatty acid metabolism and glucose homeostasis.

Conclusion: Identification of differentially expressed miRNAs may provide new insights into the pathophysiology of abnormal glucose homeostasis. Future studies, including studies on the effects of a modified expression of miR-519d on PPAR-α expression, are planned.

Basic Science Category: B04

Validation of adipocytokine zinc alpha-2 glycoprotein as novel urinary biomarker for normoalbuminuria diabetic nephropathy using western blot analysis

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Introduction: A substantial proportion (up to 55%) of individuals with diabetic nephropathy (DN) has normal urinary albumin. These patients, at risk for progressive renal impairment and cardiovascular disease, cannot be identified using standard screening for urine albumin. Zinc alpha-2 glycoprotein (ZAG) was identified in previous experiments by this research group as a potential biomarker using two-dimensional differential in-gel electrophoresis (2D-DiGE). Using the results from previous 2D-DiGE protein profiling, this study aimed to validate the urinary biomarker ZAG in an independent cohort of patients with classical DN and non-albuminuric DN using western blot analysis.

Methods: Group 1 patients had classical DN (urinary albumin-creatinine ratio [ACR] > 1,000 mg/g, estimated glomerular filtration rate [eGFR] < 60 ml/minute/1.73 m^2) and group 2 patients had non-albuminuric DN (ACR < 30 mg/g, eGFR < 60 ml/minute/1.73 m^2). Urine proteins (10 μg/sample) were separated on 12.5% sodiumdodecyl sulphate–polyacrylamide gels at 90 V for 2.5 hours. Resolved proteins were blotted onto Hybond nitrocellulose membrane at 100 V for one hour. The membrane was rinsed with 0.05% phosphate buffered saline–Tween and blocked with 10% non-fat milk for two hours at room temperature. Membranes were probed overnight at 4°C with primary antibody (rabbit anti-human ZAG polyclonal, 1:2,000). The membranes were then incubated with a secondary antibody (horseradish peroxidase-labeled donkey anti-rabbit IgG) at room temperature for one hour. Detection was done using an enhanced chemilumiscence plus reaction kit. Band intensities were scanned using a Typhoon Trio scanner with appropriate lasers and filters and a photomultiplier tube voltage set between 500 and 600. Urinary creatinine was used to normalise ZAG protein expression.

Results: Using western blot analysis, the ZAG protein was confirmed and quantified to be upregulated 3-fold in men and 2.6-fold in women for the non-albuminuric vs. albuminuric cohorts. This finding is consistent with our earlier 2D-DiGE results suggesting that ZAG protein could be a robust biomarker for screening of non-albuminuric DN.

Conclusion: ZAG may be a novel target urinary biomarker for the screening of non-albuminuric DN.

Basic Science Category: B05

Association of MYH9 gene with diabetic nephropathy secondary to type 2 diabetes mellitus among Singapore Chinese

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Introduction: Diabetic nephropathy (DN) is a leading cause of end-stage renal disease (ESRD). Epidemiological evidence suggests that DN is strongly influenced by genetic determinants. Recent studies reported a novel candidate gene (non-muscle myosin heavy chain-9 [MYH9], and in particular, its E1 haplotype) that confers increased risk for focal segmental glomerulosclerosis and ESRD in non-diabetic individuals. Given the notion that aetiologically diverse renal injury,

such as hypertension, diabetes and autoimmunity, share a final common pathogenic pathway, the E1 haplotype of MYH9 may also be associated with DN. We hypothesised that the E1 haplotype of MYH9 was associated with DN among Singaporean Chinese adults.

Methods: A case-control study was carried out (n = 960). Patients were defined as individuals with spot urinary albumin-creatinine ratio (ACR) ≥ 1,000 μg/mg and/or serum creatinine > 113 μmol/L whereas controls were defined as those with ACR ≤ 30 μg/mg and serum creatinine < 113 μmol/L. Based on the Haploview database for Hans-Chinese-Beijing, 13 single nucleotide polymorphisms (SNPs) were selected to tag for the E1 haplotype region. Genotyping experiments were performed using the Illumina BeadXpress platform. Binary logistic regression and maximal likelihood ratio was used to estimate effect size and statistical significance.

Results: Patients and controls were comparable in distribution of gender, age, duration of diabetes and HBA1c levels. Single locus analysis revealed that an intronic SNP-rs735853G > C (MAF = 0.117, OR for G allele 1.465, 95% CI 1.105–1.941, p = 0.001) conferred increased susceptibility to DN, which was significant even after Bonferroni correction for multiple testings (0.05/13 = 0.0038). A 5' haplotype formed by the above SNP-rs735853 and rs735854 (D' 1.0, frequency 0.117) showed similar association with DN suggesting that the causal variant may reside within this gene region.

Conclusion: Our results suggest that the E1 haplotype of MYH9 gene conferred increased susceptibility to DN in Singaporean Chinese participants. Replicating these preliminary results in a larger cohort may further clarify the role of MYH9 in DN.

Basic Science Category: B06

Differential gene expression of angiogenic factors between human visceral and subcutaneous adipose tissue

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Introduction: Obesity is a medical condition characterised by enlarged adipocytes. The expansion of adipose tissue (AT) is linked functionally to active angiogenesis. It is believed that adipogenesis is associated with local microhypoxia in expanding AT, which induces angiogenesis to provide the needed oxygen. However, little is known about the differences in proangiogenic potential between subcutaneous and visceral adipocytes. Our preliminary observations based on SuperArray revealed possible differential gene expression between visceral and subcutaneous adipocytes. We sought to validate this observation using Lonza Human StellARray™ qPCR Array. As the normalisation procedure in the latter array is based on global gene expression patterns, no presuppositions were made regarding the constancy of expression of a particular normaliser. This is purported to provide better discriminative efficiency in deciphering differentially expressed candidate genes. We hypothesised that the gene expression of angiogenic factors differs between subcutaneous and visceral adipocytes.

Methods: Preadipocytes were isolated from paired human visceral and subcutaneous AT (n = 3) and cultured *in vitro*. Total RNA was extracted and reverse transcribed to cDNA with random primers. Real-time polymerase chain reaction (PCR) using Lonza Human StellARray™ qPCR was performed on three pairs of AT. A p-value less than 0.05 was considered statistically significant and fold change was calculated using the Global Pattern Recognition™ software.

Results: Our data revealed differential expression of angiogenic factors in visceral and subcutaneous adipocytes. Genes found to be upregulated in visceral adipocytes were pleiotrophin (18.6-fold, p < 0.01) and leptin (143.4-fold, p < 0.05). Genes that were downregulated in visceral adipocytes were HOXD3 (–108.6-fold, p < 0.02) and aminopeptidase N (–3.4-fold, p < 0.03). The panel of differentially expressed genes on SuperArray was different from that obtained via the StellARray platform probably due to erroneous assumptions that the level of expression of selected housekeeping normalisers is invariant.

Conclusion: Angiogenic potential differs between depot-specific adipocytes. This may contribute to site-dependent differential adipogenesis that is associated with visceral adiposity.

Basic Science Category: B07

Asian study of clopidogrel pharmacogenomics (ASCLOP)

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Introduction: The bioactivation of clopidogrel is highly influenced by genetic variations that require further characterisation. This study aimed to investigate the prevalence of such variations in our local population and the manner in which they correlate with platelet reactivity.

Methods: 53 patients on a stable dose of clopidogrel were recruited for genotyping. P2Y12 reaction units (PRU) were measured using a VerifyNow® meter. Patients with PRU > 235 were regarded as poor responders.

Results: Variations in CYP2C19*2 (49%) and CYP3A5*3 (37.3%) were most prevalent; 2C19*17 heterozygotic variations occurred in 11.8% of patients. There were less than 20% variations with CYP2C9*2, *3, CYP2C19*3 and CYP3A5*6. The poor responder CYP2C19*2 variations were seen more often in Malay patients (66.7%) than Chinese (42.3%) or Indians (45.5%). Similarly, more Malays (58.3%) displayed the CYP3A5*3 poor metaboliser homozygote variants than Chinese (33.3%) and Indian (35%) patients. The average PRU (avPRU) was 220 (range 54–432). 24 (45.3%) patients had PRU > 235 (poor responders). The avPRUs displayed by wild 2C19*2 status (51% patients) was 214 against 221 in heterozygotes variants (43% patients) and 258 in homozygotic variants (6% patients) (p = 0.686). The avPRUs of patients with preserved 3A5*3 function (63%) was 218 compared to 224 in patients with loss of function (37%) [p = 0.804]. Amongst 3A5*3 poor responder homozygote variants with wild 2C19*2 and *17 status, statistically more patients were non-responders (6 vs. 2, p = 0.019; Fischer's exact test), and this observation was clinically significant (avPRU 247 vs. 174, p = 0.051). Among 3A5*3 poor responders, patients on concurrent 3A4 inhibiting drugs had higher avPRU than those not on concurrent 3A4 inhibitors (275 vs. 194, p = 0.079).

Conclusion: Previous studies have shown significant relationships between 2C19*2 variations and poor response and/or increased adverse outcomes. Our findings suggest that 3A5*3 variations are more significant in the local population than 2C19*2 variations, with the latter being more common in Caucasians. Important trends were observed with patients who were 3A5*3 poor responders receiving concurrent 3A4 inhibitors, which is the most common drug interaction. We propose that a larger study be conducted to confirm the significance of these findings in the local population.

Basic Science Category: B08

Effects of α and β poly (vinylidene fluoride) phase conformations on cell attachment and proliferation

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Introduction: Membranes of poly (vinylidene fluoride) [PVDF] have good potential for use in biomedical applications due to their stability and biocompatibility. More interestingly, PVDF possesses variable piezoelectric properties depending on the polymorph conformations present. Although many reports have described PVDF as suitable biomaterial, few have considered the specific effects that different polymorph conformations exert on cellular behaviour. We hypothesised that different polymorphs, specifically α- and β-phase PVDF, would exert direct but different influences on cell attachment and proliferation.

Methods: PVDF films were fabricated using N, N dimethylformamide and hexamethylphosphoramide by solvent casting. Samples were characterised by differential scanning calorimetry, Fourier transform infrared spectroscopy and X-ray diffraction.

Results: Films containing 85% α-phase PVDF and predominant β-phase PVDF were produced and used to evaluate *in vitro* attachment and proliferation of L929 cells. Cell metabolic activity on both PVDF conformations increased by about 3-fold over the one-week culture period, with higher cell metabolic activity observed on α-phase dominant PVDF on Day 5 of culture compared to β-phase dominant PVDF. Cells grown on α-phase dominant PVDF were spindle shaped and well spread, expressing spotted paxillin in focal adhesion points mainly localised to perinuclear regions of the cells; a high proportion of cells on β-phase dominant PVDF were round and less spread, expressing relatively fewer paxillin spots.

Conclusion: Our results suggested that α- and β-phase PVDF conformations can evoke different cellular behaviour. Such variations can potentially be useful for different biomedical applications.

Basic Science Category: B09

Designing multilayered polymeric microparticles for drug delivery

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Introduction: Particulate systems have tremendous potential to achieve controlled release of drugs. However, single-layered polymeric microparticles have several inherent limitations, including initial burst release of drugs, a lack of time-delayed or pulsatile release of drugs and the inability to achieve constant drug release. Multilayered particles have the potential to overcome these disadvantages. Herein, we show how triple-layered microparticles comprising poly (D,L-lactide-co-glycolide, 50:50) [PLGA], poly (L-lactide) [PLLA] and poly (ethylene-co-vinyl acetate, 40 wt% vinyl acetate) [EVA] can be fabricated through a simple, economical, and versatile one-step solvent evaporation technique.

Methods: Multilayered microparticles were prepared by using an emulsion solvent evaporation method. The three polymers and a model drug, ibuprofen, were first dissolved in dichloromethane (DCM). The resultant polymer solution was subsequently added to a poly (vinyl alcohol) aqueous solution and emulsified using an overhead stirrer at room temperature (25°C). The evaporation of DCM results in the phase separation of PLLA, PLGA and EVA, yielding triple-layered microparticles. Finally, the microparticles were centrifuged, rinsed, lyophilised and stored in a desiccator. Processing parameters, such as the starting polymer solution concentration, stirring speed, oil-to-water ratio and polymer mass ratio, were carefully manipulated to form the multilayered structure. Particle morphologies, layer configurations and drug distribution were determined using scanning electron microscopy and Raman mapping.

Results: The particles exhibited a triple-layered PLGA (shell)/PLLA (middle layer)/EVA (core) morphology. A higher stirring speed resulted in smaller triple-layered particle sizes. Layer thickness and the layer inversion of these microparticles were altered by changing the polymer mass ratios — a higher mass polymer forms the outer layer. Strong affinity between hydrophobic long ethylene chains of EVA and hydrophobic ibuprofen drove the drug to be localised in the EVA core.

Conclusion: Triple-layered microparticles composed of PLGA, PLLA, and EVA with controllable layer thicknesses, configurations and localisation of drug were fabricated using a one-step solvent evaporation method.

Basic Science Category: B10

Bone-targeting drug delivery systems

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Introduction: Osteomyelitis is one of the most serious orthopaedic complications, especially following open fracture treatments and during post surgery follow-up of orthopaedic implants. The objective of this study was to develop a particulate system that both delivers the drug to the diseased site through surface modification and also promotes cell adhesion and bone regeneration, thus accelerating the healing process. Coating polymer particles with a calcium phosphate (CaP) layer provides them with similar properties to bone, thus increasing the bioactivity of these particles. Similarly, bisphosphonate (BP) tags have been used as bone targeting ligands to facilitate drug delivery to infection sites in the bone. BPs are a group of compounds that have a strong affinity to bone due to the strong bonding between Ca^{2+} from bone mineral and O^{-} from the phosphonate group in these compounds.

Methods: Poly (lactic-co-glycolic acid) [PLGA] particles were prepared by emulsion solvent evaporation method using the anionic surfactant poly (ethylene-alt-maleic anhydride). The CaP layer was deposited by a simple coprecipitation method and surface functionalisation of BP to the particles was achieved via conventional silane chemistry. Amine-terminated silane was first functionalised onto the surface to introduce amine groups and subsequently carbodiimide chemistry was employed to covalently attach an aliphatic chain containing the BP moiety.

Results: The presence of CaP coating was confirmed by electron microscopy, Fourier transform infrared spectroscopy (FTIR) and energy-dispersive X-ray spectroscopy (EDX). FTIR and EDX analyses showed the presence of both PLGA and CaP layer. For the functionalisation of silane, X-ray photoelectron spectroscopy survey analysis confirmed the presence of silane grafting and amide bonding.

Conclusion: Novel ceramic-polymer hybrid systems with bone ligand on the surface were synthesised in this study for bone targeting applications. In the long term, the delivery system of choice could be further explored for treating other bone-related diseases, such as osteosarcoma and osteoporosis.

Basic Science Category: B11

ncRNAs as novel theranostics in diseased contexts

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Introduction: RNA interference (RNAi) is triggered by double-stranded RNA (dsRNA) that results in the degradation of homologous mRNA or in the inhibition of mRNA translation. The selective recognition of regulatory DNA sequences is widely accepted as a basis for differential gene regulation in stem cells. Most transcription factor binding sites are, however, short, degenerate and have a strong affinity for homologous proteins, even ones with antagonistic effects, begging the question *'What is regulated in gene regulation?'*.

Methods: Genome-wide transcription factor binding site studies show that key regulators co-occupy many binding sites. Thus, the prediction of gene activities based on such data is poor. Our studies with embryonic stem cells, deficient for *Dicer (dcr–1–)* and targeted with either *dcr–1* or *dcr–2* from *Drosophila melanogaster*, give insight into the pathways that underlie the si- and miRNA networks in both wildtype and diseased contexts.

Results: Many of the non-coding transcripts show a differential expression in differentiation and disease and transcriptional interference plays an important role when transcripts compete for transcription. Typical ncRNAs appear to be spliced, polyadenylated, and exported just like regular mRNA and processed from longer precursors. Our experiments with *Dicer* give functional insights into the RNA mediated gene silencing pathways and provide novel cellular models for studying the individual effects of ncRNAs, for assay/drug development and biomarker identification.

Conclusion: At the interface of therapy and diagnostics (theranostics), interest has grown in combining both paradigms into clinically effective formulations. Our ncRNA profiling allows for the identification of specific signatures associated with diagnosis, prognosis and response to treatment of human diseases and, in particular, tumours. Our cellular models, which can be used for drug screening and biomarker identification, are a first step to bringing ncRNAs into the clinic.

Basic Science Category: B12

Influence of crystalline polyethylene glycol on paclitaxel drug release and mechanical properties of poly (lactic-co-glycolide) 53:47/polyethylene glycol formulated thin films

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Thin films of poly (lactic-co-glycolic acid) [PLGA] incorporating paclitaxel have typically had slow release rates of paclitaxel in the order of 1 μg/day.cm^2. For implementation in medical devices, a range of zero-order release rates, that is 1–15 μg/day.cm^2, is desirable for different tissues and pathologies. Polyethylene glycol (PEG) of 8 k and 35 k molecular weight was incorporated at 15%, 25%, and 50% weight ratios in PLGA containing 10% w/w paclitaxel. The mechanical properties were assessed for potential use in medical implants and the rates of release of paclitaxel were quantified in percent release and the more clinically useful μg/day.cm^2. Paclitaxel quantification was correlated to the release of PEG from PLGA to further understand its role in paclitaxel/PLGA release modulation. PEG release was found to correlate with paclitaxel release and the level of crystallinity of the PEG in the PLGA film, as measured by Raman spectra. This supports the concept of using a phase separating, partitioning compound to increase the release rates of hydrophobic drugs such as paclitaxel from PLGA films, where paclitaxel is normally homogenously distributed or dissolved. Two formulations could be promising for medical device thin films, when optimised for tensile strength, elongation, and drug release. Both slow and fast drug release were well controlled; an average of 3.8 μg/day.cm^2 using 15% 35 k PEG for > 30 days was achieved for slow rates of paclitaxel release, while a high 12 μg/day.cm^2 rate of drug release was maintained using 25% 8 k PEG for up to 12 days.

Basic Science Category: B13

Abnormalities in protein metabolism are associated with impaired fasting glucose and diabetes mellitus in previously healthy adults

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Introduction: Metabolic profiling of small molecules from body fluids gives a snapshot of physiological processes. We hypothesised that there exists in blood, apart from the well-known differences in glucose and fatty acids, differences in metabolic profiles between healthy controls (CTL) and those with abnormal glucose tolerance (ABGLT).

Methods: Healthy adults (age 18–70 years) seen at Alexandra Hospital, Singapore, from July to December 2008 for health screening were enrolled in the study. Based on measurements of fasting glucose (FG) levels, participants were classified as impaired fasting glucose (IFG; FG 6.1–6.9 mmol/L) and type 2 diabetes mellitus (T2DM; FG ≥ 7.0 mmol/L). Of the 238 enrolled, all patients with T2DM (n = 24) and IFG (n = 27) were shortlisted for further study, and matched for age and gender by 60 random controls (CTLs; FG < 5.6 mmol/L). Metabolic profiling was performed using gas chromatography and mass spectrometry for these individuals. Metabolites were identified by comparing mass spectra and retention indices to customised reference mass

spectral libraries that used authentic standard compounds, under identical data acquisition parameters. Molecules with probability matching algorithm > 70% were considered for analysis.

Results: The mean age of participants was 42.8 ± 10.6 years, with a 4:1:1 ethnic distribution of Chinese: Malay: Indians. 71.2% of participants were men. Patients with ABGLT (IFG and T2DM) had higher body mass index (27.6 ± 5.1 kg/m^2 vs. 25.6 ± 4.9 kg/m^2, $p < 0.05$), systolic blood pressure (131 ± 17 mmHg vs. 120 ± 11 mmHg, $p < 0.001$), triglycerides (2.0 ± 1.5 mmol/L vs. 1.3 ± 0.8 mmol/L, $p < 0.05$) and low-density lipoprotein cholesterol (3.5 ± 1.2 mmol/L vs. 2.8 ± 0.4 mmol/L, $p < 0.001$) than CTLs. Significant increases in branch-chained amino acids (valine, leucine, isoleucine), and alanine, proline, phenylalanine, and uric acid were present in ABGLT.

Conclusion: Most amino acids that were raised in ABGLT patients were essential amino acids, most probably from dietary sources. This suggests that dysfunction in amino acid catabolism may play important roles in insulin resistance (IR) and the pathogenesis of diabetes mellitus. Understanding the mechanisms underlying the accumulation of these amino acids may provide important insights into IR, with a potential for therapeutic options for diabetes prevention and care.

Basic Science Category: B14

Urinary proteomics associated with progressive diabetic nephropathy secondary to type 2 diabetes mellitus

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Introduction: Diabetic nephropathy (DN) is a leading cause of end-stage renal disease (ESRD) in Singapore. The rate of progression of DN is highly variable. As risk factors predictive of DN progression are incompletely understood, there is a need to search for biomarker(s) associated with the progression of the disease. This ongoing study was designed to examine the baseline urinary polypeptide pattern associated with DN progression over two years in men using two-dimensional differential in-gel electrophoresis (2D-DiGE) proteomic analysis.

Methods: Patients were classified and grouped as progressive DN (n = 5; δ-creatinine ≥ 50%) vs. stable DN (n = 5; δ-creatinine ≤ 10%) over two years. Protein precipitation by ethanol was carried out on 6 ml urine. To improve spot resolution and labelling efficiency, a 2D clean-up kit was used to remove interfering substances, such as salt. Protein concentration was determined using a 2D Quant kit. A total 75 ug protein from each group was labelled with CyDye and separated by pH and then by molecular weight using gel electrophoresis. Urinary proteome was analysed using the DeCyder software. Protein identification is yet to be performed by matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry (MALDI/TOF).

Results: The gels yielded a global spot count of 410, out of which 194 spots matched between the gels. There were 34 spots that passed stringent Student's *t*-test, showing a nominally significant p-value of ≤ 0.05. The spots were further screened to eliminate false positive signals from abundant proteins and dust particles, and 14 spots were selected as proteins of interest; five spots were downregulated and nine spots were upregulated in patients with progressive DN. Peptide identification using MALDI/TOF is planned for these spots.

Conclusion: The peptides associated with DN progression, when eventually identified, may serve as urinary markers that are useful for the clinical prediction of individuals at high risk for ESRD.

Basic Science Category: B15

Differential gene expression of inflammatory cytokines and receptors between human visceral and subcutaneous adipose tissue

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Introduction: Obesity is characterised by enlarged adipocytes that release more inflammatory cytokines and are more insulin resistant. This results in a heightened state of inflammation in obese patients. Inflammatory markers were found to be highly secreted by visceral adipose tissue (AT), suggesting that visceral AT contributes significantly to the pathophysiology of metabolic syndrome. However, the exact mechanism by which visceral adipocytes cause dysmetabolism is poorly understood. Our preliminary observations based on SuperArray revealed possible differential gene expression between visceral and subcutaneous adipocytes. We sought to validate this observation using Lonza Human StellARray™ qPCR Array. As the normalisation procedure in the latter array is based on global gene expression patterns, no presuppositions were made regarding the constancy of expression of a particular normaliser. This is purported to provide better discriminative efficiency in deciphering differentially expressed candidate genes. We hypothesised that inflammatory cytokines and the expression of receptor genes differ between visceral and subcutaneous adipocytes.

Methods: Preadipocytes were isolated from paired human visceral and subcutaneous AT and cultured *in vitro*. Total RNA was extracted and reverse transcribed to cDNA with random primers. Real-time polymerase chain reaction (PCR) using Lonza Human StellARray™ qPCR were performed on three pairs of AT (n = 3). A p-value less than 0.05 was considered statistically significant and fold change was calculated using the Global Pattern Recognition™ software.

Results: Our data revealed differential expression of inflammatory genes between visceral and subcutaneous adipocytes. Chemokine receptor-2 (CCR2) was downregulated (–31.1 fold, $p < 0.02$) and chemokine receptor 5 (CCR5) was upregulated (38.3 fold, $p < 0.04$) in visceral adipocytes. The panel of differentially expressed genes on SuperArray was different from that obtained via the StellARray platform probably due to erroneous assumptions that the level of expression of selected housekeeping normalisers is invariant.

Conclusion: Inflammatory secretome differs between depot-specific adipocytes. These adipocyte-derived chemokines may attract macrophage infiltration, resulting in subsequent paracrine crosstalk between macrophage and visceral adipocytes, thereby accentuating its proinflammatory disposition.

Basic Science Category: B16

Effect of rosiglitazone on subcutaneous versus visceral adipocytes on miRNA profiling

Toy W C[1], Cheng K S A[2], Tan J J[2], Lau P X D[1], Tan S H C[1], Wong D S M[1], Tavintharan S[1,3], Sum C F[3], Lim S C[1,3]

[1] Clinical Research Unit, [2] Department of Surgery, [3] Department of Medicine, Khoo Teck Puat Hospital, Singapore

Introduction: Visceral adiposity is associated with increased risks for metabolic disease. It has been widely suggested that subcutaneous and visceral fat exhibit differential metabolic function. MicroRNAs (miRNAs) are potential regulatory molecules affecting the stability and translation of mRNA in different fat depots. miRNA microarrays (paired visceral and subcutaneous preadipocytes) were performed on two obese individuals (body mass index > 30 kg/m^2) to establish the global miRNA profile in visceral and subcutaneous adipocytes. The effects of rosiglitazone, an agonist of

PPAR-γ (peroxisome proliferator-activated receptor-γ) with specific adipogenic action, was also tested on visceral and subcutaneous adipocytes. We hypothesised that miRNA expression differs systematically between visceral and subcutaneous adipoctyes.

Methods: Preadipocytes were isolated from visceral and subcutaneous adipose tissue and cultured *in vitro*. The cells, grown in serum-free Dulbecco's modified Eagle's medium and supplemented with high glucose (24.98 mmol/L), were treated with 1 μmol/L rosiglitazone maleate for 48 hours. Control cells were cultured in the same culture medium without rosiglitazone. Total RNA, including miRNA, was extracted using the miRNeasy mini kit. Agilent miRNA microarray (8 × 15 K) was performed with biological duplicates. Data were analysed using GeneSpring and the molecular pathways were assessed using the Pathway Studio software.

Results: The miRNA profile reported three upregulated miR- (miR-126, miR-145 and miR-503) and three downregulated miR- (miR-196b, miR-10b and miR-503) in both controls and rosiglitazone-treated visceral and subcutaneous adipocytes. Interestingly, an increase in miR-21 expression (2.45 fold, $p < 0.05$) was also observed in the visceral adipocytes with rosiglitazone challenge. The predicted targets regulated by miR-21 include adipocytokine signaling, T-cell activation, NK cell activation, NTRK (neurotrophic tyrosine kinase) signaling and mast cell activation.

Conclusion: Global miRNA profiles differ between visceral and subcutaneous adipocytes with and without PPAR-γ agonist challenge. miR-21 might be an important factor mediating genomic post-translational regulation of preadipocytes, and thereby determining its differentiation-plasticity toward white or brown adipocytes.

Basic Science Category: B17

Effects of adiponectin expression in 3T3-L1 cells treated with Apo-A1

Jauhar N[1], Woon K[2], Pek L S[2], Lim S C[2], Sum C F[2], Tavintharan S[2]

[1] Department of Medicine, [2] Clinical Research Unit, Khoo Teck Puat Hospital, Singapore

Introduction: HDL cholesterol (HDL-C) is an independent predictor of cardiovascular disease. Adiponectin is an adipocytokine, with antiatherogenic and insulin-sensitising properties, involved in the pathophysiology of metabolic syndrome. In an earlier study investigating the association of low HDL-C and cardiovascular risk factors among women healthcare workers, we found that low HDL-C levels were associated with increased cardiovascular risk factors, including lower adiponectin levels (9.1 μg/ml vs. 4.9 μg/ml), when compared with desirable HDL-C. It is not known if this association between HDL-C and adiponectin is causal. We hypothesised that increasing HDL-concentrations would directly increase adiponectin secretion in adipocytes.

Methods: Adipocytes were used to study the effects of apolipoprotein-A1 (Apo-A1), the major apolipoprotein in HDL-C, treatment on adiponectin expression. 3T3-L1 preadipocytes were cultured in 6-well plates until confluence in Dulbecco's modified Eagle's medium (DMEM) containing 10% foetal bovine serum and induced to differentiation. Cells were exposed to induction media for three days and transferred to DMEM containing insulin for an additional three days. Cells were serum-starved for 24 hours prior to treatment with different concentrations of Apo-A1. Adiponectin was measured by enzyme-linked immunosorbent assay in cell lysate.

Results: Successful maturation of preadipocytes was observed in six days, with accumulation of fat globules in mature adipocytes. Treatment with Apo-A1 was not associated with any increase in cell death and no change in total protein content was noted in the lysate. Apo-A1 at 100 μg/ml, compared to control media, was associated with a 23% increase in adiponectin levels.

Conclusion: In this preliminary study using an *in vitro* model, increasing the levels of Apo-A1 in the medium was found to increase adiponectin levels. This suggests that the association between the reduced adiponectin levels noticed in women with low HDL-C in our earlier study was indeed causal, and this may have possible therapeutic implications. Further *in vitro* studies are planned on the effects of Apo-A1 expression in hepatocytes, with increasing adiponectin concentrations, which will contribute further to our understanding of the interrelationships between these antiatherogenic agents.

Acknowledgements

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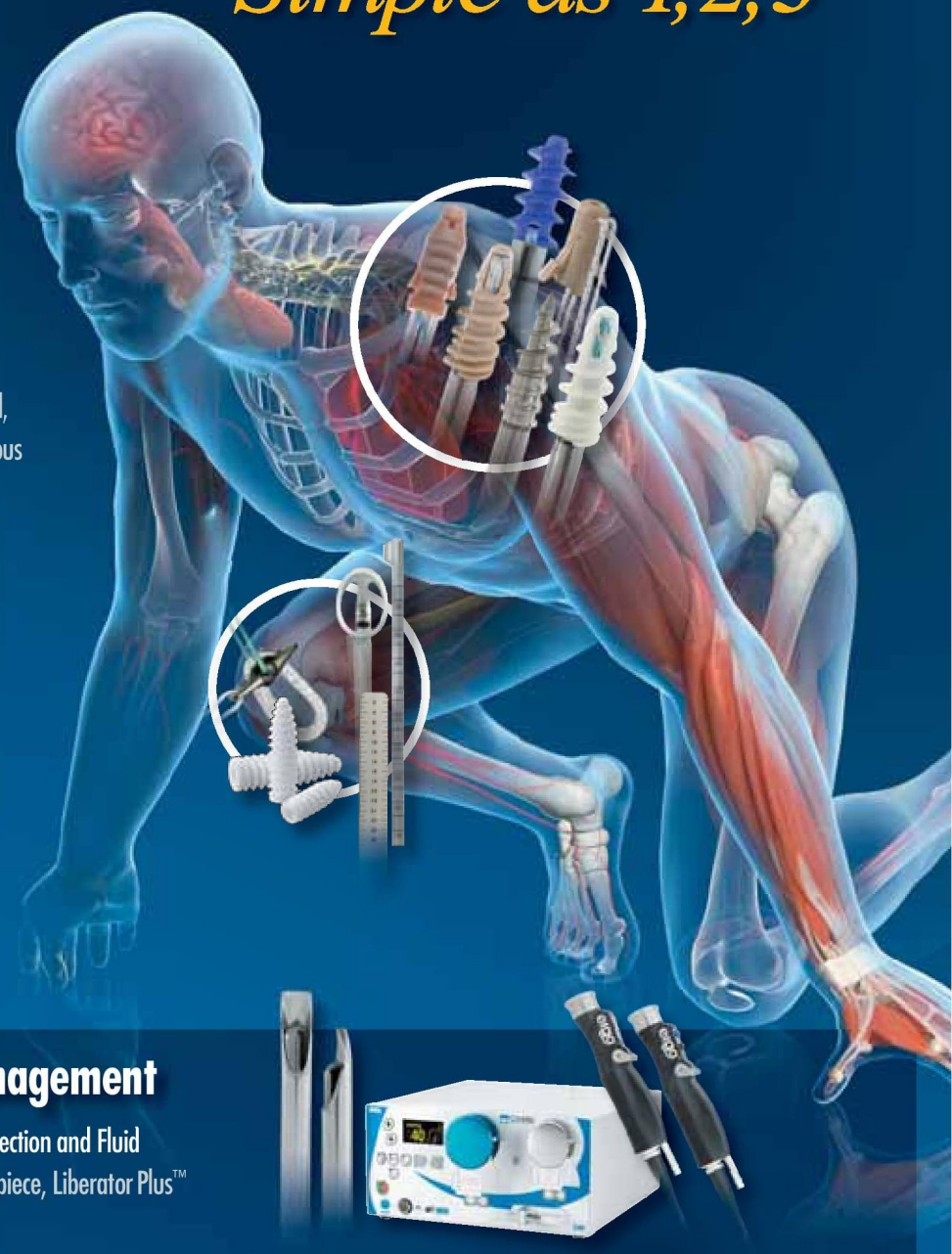

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Welcome Message by the Organising Chairman, Alexandra Health Research Forum 2011 – New Frontiers

It gives me great pleasure in welcoming everyone to the first Alexandra Health Research Forum at Khoo Teck Puat Hospital. The theme "New Frontiers" not only emphasises the new challenges that we face as a brand new hospital in Singapore, but also the need to break old boundaries and redefine new ones in the quest for excellent patient care.

This Research Forum aims to provide a platform for discussion among healthcare workers on how patient care can be enhanced through research and innovation, and in doing so, facilitate transdisciplinary cooperation. At this Forum, we are extremely privileged and excited to have participation from the Genome Institute of Singapore, Nanyang Technological University, Yishun Polyclinic and Jurong General Hospital who will be presenting some of their work. There are in total 87 abstracts to be presented in oral or poster format.

The event will also be graced by a clinician respected by the community, Dr Lim Wee Kiak, our Guest of Honour, and two leading researchers of Singapore: Professor Lee Eng Hin, Executive Director of Biomedical Research Council, A*STAR and Professor Edison Liu, Executive Director of Genome Institute of Singapore, who will be giving plenary lectures.

The organising committee hopes that this Forum will bring about fruitful sharing and discussions for future cooperations, leading to new frontiers in medical science. Lastly, I would like to thank the organising committee for their hard work in making this a memorable event and also our Chairman, Medical Board, A/Prof Pang Weng Sun and Chief Executive Officer, Mr Liak Teng Lit for their unconditional support.

Dr Tan Kok Yang
Organising Chairman
Alexandra Health Research Forum 2011 – New Frontiers

Message from the Guest of Honour

In current times, with an ageing population, coupled with an exponential surge in medical technology, knowledge and discovery in diagnostic and therapeutic options and devices, healthcare systems worldwide face challenging times, and Singapore too is not spared. As has been in the past, we continue to need to deliver healthcare in most timely, appropriate and cost-efficient ways. Only through constant innovation and redefinition of current boundaries can advancements into new frontiers in medicine be made.

It is with this understanding that I am very excited about the research works of our latest hospital in Singapore. In addition to continuing with its aims of being not just a garden in a hospital but also a hospital in a garden, Khoo Teck Puat Hospital aims to deliver seamless and exciting models of healthcare through research innovation.

I look forward to the academic contributions and presentations by the staff of this hospital in their quest to be Singapore's premier hassle-free hospital.

Dr Lim Wee Kiak, PBM
Member of Parliament, Sembawang GRC
Vice-Chairman, Sembawang Town Council

Message from the Chief Executive Officer, Alexandra Health

Most of us are in healthcare because we find meaning in our work – to cure some time, to heal often and to comfort always. We would like to think that we are doing our best and achieving the best outcomes for our patients. But are we?

The truth is, we do not know unless we check.

When we look at outcomes across institutions and among individuals, we often see a bell-shaped distribution. The best is often many times better and safer than the average. As a professional, everyone of us would like to be among the best in our profession. Our patients expect us to be too. The hard truth is that most of us are probably delivering average care. Our complication rates may be three times or more than those of our best colleagues. If we want to provide safer and better care, we need to know where we are now before we can even start to improve.

Mark Twain said over a hundred years ago: *"It ain't what you don't know that gets you into trouble. It's what you know for sure that just ain't so."*

In this era of explosive growth in scientific knowledge, we have to be humble enough to acknowledge that we do not know many things. But with mobile phones, the Internet, Google and Wikipedia, we can find out soon enough.

We need to go about our work with the confidence that 'what we know for sure' is good for our patients. Otherwise, we would all be nervous wrecks and unable to function, even as human beings. Fortunately, most of the time, 'what we know for sure' has been right and has served us and our patients well.

But when 'what we know for sure' turns out to be wrong, we hurt our patients and waste their money, and sometimes, we kill them.

Unfortunately, it is also difficult for us to unlearn 'what we know for sure'. The greater the effort we make to learn something, the harder it is for us to question it. Our colleagues around us too reinforce our perspectives. The professional bodies that we belong to mandate that we conform to the norm. We therefore hang onto 'what we know for sure', long after evidence clearly points the other way.

We need to be inquisitive. Search the literature, attend conferences, look worldwide to seek out the people who are achieving the best results and study what they do. We need to examine what we are doing, and measure our outcomes and benchmark against the very best. We need to experiment, learn and apply what we learn.

Research is pivotal to keep us on track, ensuring that we are indeed doing our best and achieving the best outcomes for our patients. We need to make sure that what we know for sure is indeed so.

Mr Liak Teng Lit
Chief Executive Officer, Alexandra Health

Message from the Chairman, Medical Board, Khoo Teck Puat Hospital

It has been almost a year since Khoo Teck Puat Hospital opened its clinics in March 2010 and the wards and emergency services in June 2010. Within weeks, the wards were overflowing and we had to manage the flow of emergency ambulances. We are more settled now and the hospital was officially opened on 15 November 2010.

I am encouraged that despite the busy workload, our Clinical Research Committee is able to organise this Alexandra Health Research Forum, the first to be held in Khoo Teck Puat Hospital.

I recall that our first Research Forum was held in Alexandra Hospital in 2008. It was a modest one-day forum with several departments chipping in with poster presentations in the rehabilitation medicine gym. We repeated this in 2009 and had medical students participating as well.

We have made much progress since. While clinical service has been a major thrust of the hospital—the biggest wheel in the tricycle—there is a need to develop the two smaller wheels: education and research, without which there would be no breakthroughs or improvements in patient care.

As we settle into the northern community, we need to grow our expertise in research and build clinicians with enquiring minds, eager to find new answers to questions, new and old. We need to create a stimulating and supportive environment. This will be a constant challenge in the presence of a heavy clinical and teaching workload, but we must strive to make it possible.

My congratulations and thanks to the Organising Committee for making this Forum possible, to all who have contributed to the papers and posters, and to all of you for supporting and attending this forum. Have a fruitful time.

Clinical A/Prof Pang Weng Sun
Chairman, Medical Board, Khoo Teck Puat Hospital

Message from the Director, Clinical Research Unit, Khoo Teck Puat Hospital

The theme chosen for this year's Research Forum – New Frontiers – is a very appropriate one. Given the breathtaking pace of advances in science in recent decades, there is no better time for health professionals to exploit these advances for the purpose of setting new frontiers in healthcare. We now understand the pathobiology of diseases better, have better tools in diagnosing diseases and have rapidly expanding choices of preventive and interventional strategies.

However, setting new frontiers will not happen without directed effort. Leaving things to take its natural course of action is incompatible with this goal. To begin, it requires one to adopt a new mindset and thinking paradigm. Our colleagues in information technology call it a T-shaped expertise. I would like to phrase it as ***'embracing breadth and depth'*** – an extremely demanding but exciting challenge for all of us in this time of history. We are enabled but also challenged by the daily voluminous output of information. Therefore, there is a need to read widely. This, however, is not enough. We need to be able to 'connect the dots' in the midst of staring at a starry sky to see the constellation, i.e. to derive meaning and messages from the mass (mess) of information and data. To acquire this skill, one will need considerable training and thinking. Therefore, continual learning (i.e. maintaining 'teachability') is paramount.

We need to strive toward looking beyond boundaries. It is intuitive to call for avoidance of over-specialisation. It is less intuitive to call for avoidance of over-generalisation.

To set new frontiers, we need to embrace breadth and depth, because the stake is high (our patients' well-being) and the reward is great (a fulfilled life well lived in history).

May I congratulate the organising committee and secretariat for an outstanding Forum. May I also sincerely thank our guests, collaborators, sponsors and attendees, for without you, the Forum would not be a meaningful and successful one.

A/Prof Lim Su Chi
Director, Clinical Research Unit, Khoo Teck Puat Hospital

ALEXANDRA HEALTH RESEARCH FORUM 2011 - NEW FRONTIERS		
Day 1 : 18th February 2011		
Time	**Programme**	**Speaker**
0730 – 0800	Registration	
0800 – 0810	All to be seated	
0810 – 0820	Arrival of Guest of Honour - Dr Lim Wee Kiak, Member of Parliament, Sembawang GRC	
0820 – 0825	Welcome Address by the Organising Chairman	Dr Tan Kok Yang
0825 – 0840	Address by Guest of Honour	
0840 – 0855	Opening Address by the Chairman of Medical Board	A/Prof Pang Weng Sun
0855 – 0925	**Plenary Lecture 1** *"A Road Less Travelled: Chronicles of an Orthopaedic Clinician Researcher"*	Prof Lee Eng Hin
0925 – 1010	Research Oral Presentations – Doctors' Category I	
1010 – 1030	Tea Break	
1030 – 1140	Research Oral Presentations – Doctors' Category II	
1140 – 1315	Lunch Break	
1200 – 1300	Manuscript Writing Workshop	
1315 – 1455	Research Oral Presentations – Basic Science Category	
1455 – 1515	Tea Break (Launch of Clinical Research Unit website)	
1515 – 1645	**Combined Genome Institute of Singapore (GIS) – Alexandra Health Symposium**	
1515 – 1535	*"Comprehensive Paired-End-Tag Mapping Reveals Characteristic Patterns of Structural Variations with Mechanistic Implications in Epithelial Cancer Genomes"*	A/Prof Ruan Yijun, GIS
1535 – 1555	*"Genetic Dissection of Disease Susceptibility: GWAS and Beyond"*	A/Prof Liu Jianjun, GIS
1555 – 1615	*"A Genomic Understanding of Infectious Diseases, from Host and Pathogen Genomes to Transcriptomes"*	A/Prof Martin Hibberd, GIS
1615 – 1635	*"Genomic Medicine: A Clinician's Perspective"*	A/Prof Lim Su Chi, KTPH
1635 – 1645	*Panel Discussion*	
Day 2 : 19th February 2011		
0730 – 0830	Manuscript Writing Workshop	
0835 – 0840	All to be seated	
0845 – 0915	**Plenary Lecture 2** *"Personalised Medicine through Genomics"*	Prof Edison Liu
0915 – 1015	**Engineering Innovations & Medicine Symposium**	
0915 – 0935	*"Tissue Engineering – Using Engineered Materials to Grow Tissues"*	A/P Ng Kee Woei, NTU
0935 – 0955	*"Designer Particles – A Platform for Revolutionising Drug Delivery"*	A/P Loo Say Chye Joachim, NTU
0955 – 1015	*"Healthcare Innovation through Design Thinking"*	Dr Eugene Shum, KTPH
1015 – 1030	Tea Break	
1030 – 1210	Research Oral Presentations - Nursing and Allied Health Category	
1210 – 1220	Closing Speech by CEO, Alexandra Health	Mr Liak Teng Lit
1220 – 1255	Closing Ceremony and Prize Presentation	
1400 – 1600	GP Forum	

Professor Lee Eng Hin
Executive Director, Biomedical Research Council (BMRC), A*STAR
Emeritus Consultant, Department of Orthopaedic Surgery, National University Health System

*As the Executive Director of BMRC, A*STAR, Prof Lee's predominant role today is in research administration. Over the years, as Head of Department of Orthopaedic Surgery in NUS/NUH, and subsequently as Dean of Medicine and Director of Division of Graduate Medical Studies, he has played a crucial role in undergraduate medical education, postgraduate medical training as well as continuing medical education for the medical community. He joined NUS after finishing his orthopaedic training in Toronto, Canada, and has established himself as a leading paediatricorthopaedic surgeon, a respected teacher and mentor and a clinician researcher. His research on stem cells and musculoskeletal tissue engineering has won him many international and national awards. He has published over 150 peer-reviewed articles in clinical and basic science journals, delivered over 250 conference papers and written many book chapters. He has co-edited a book with Prof Ariff Bongso entitled "Stem Cells: from Bench to Bedside" which has been very well received internationally and is now in its second edition.*

A ROAD LESS TRAVELLED: CHRONICLES OF AN ORTHOPAEDIC CLINICIAN RESEARCHER

The research landscape has changed dramatically in the last 25 years. When I returned from my training in Canada in 1983, the research environment was still very nascent. Funding for research was limited and the clinical work load was immense. Protected time for research was unheard of. Research was mainly in the form of retrospective clinical reviews. However, with the support of NUS a small research infrastructure developed within the Orthopaedic Department. At that time, research funding by the National Medical Research Council was helpful but insufficient. The quantum leap in impactful research and publications came after A*STAR was set up and more sizeable competitive research funds were made available by the Biomedical Research Council. Today, there is also significant funding available from the National Research Foundation.

An academic orthopaedic surgeon has to juggle teaching and research with clinical practice which tends to take up a large proportion of his time. To be a credible clinician researcher, it is essential that physicians and surgeons stay relevant clinically. It is through patient contact that the right questions are asked which may lead to meaningful solutions for improvement of health outcomes. The clinician also plays a key role in helping to translate discoveries by basic scientists from the bench to the bedside. In this presentation, I will share my experience with you using relevant examples of my own basic, translational and clinical research on the musculoskeletal system.

The sustained commitment to biomedical research has led to an increase in the overall research budget for the biomedical sector by about 15% for the next five years. There is increased support to grow the number of clinician scientists and there is a call for more meaningful collaborations between scientists and clinicians to enhance translational and clinical research that will lead to better health outcomes and economic impact.

Professor Edison T Liu
Executive Director, Genome Institute of Singapore (Biomedical Sciences Institutes)
Professor of Medicine, National University of Singapore
President, Human Genome Organization (HUGO)
Chairman, Health Sciences Authority

*Prof Edison T Liu is the Executive Director, Genome Institute of Singapore, (A*STAR) and Professor of Medicine, National University of Singapore. He received his degrees at Stanford University. Prof Liu's research focus is on the functional genomics of human cancers, particularly breast cancer. He has authored over 260 scientific papers, reviews and books, and is the recipient of the following awards: Leukemia Society Scholar (1991–96); the Brinker International Award (1996); the Rosenthal Award from the American Association for Cancer Research (2000); the President's Public Service Medal (2003) and a Doctor of Medicine Sciences honoris causa, Queen's University, Belfast (2007). He was elected as a Foreign Associate Member of the European Molecular Biology Organization (EMBO) in 2008. Currently, Prof Liu is serving his second term as President of Human Genome Organization (HUGO). Prof Liu is also Chairman of Health Sciences Authority, a health regulatory and blood banking agency in Singapore.*

PERSONALISED MEDICINE THROUGH GENOMICS

Genomic medicine involves the provision of medical care that uses the power of genomic knowledge and technologies to resolve complex problems. The fundamental difference between this and older strategies in medicine research is the comprehensiveness and the precision of the analyses afforded by new genomic technologies, such as in sequencing, cloning, and genotyping. The new challenge will be the assembly and management of this high volume of data with dimensional complexity. Genomic medicine therefore means computational and systems medicine as well. Systems biology, as a discipline, seeks to explain biological phenomenon through the net interactions of all cellular and biochemical components within a cell or organism. Operationally, systems biology requires the digitalisation of biological output, the computational power to analyse comprehensive and massive datasets, and the capacity to integrate heterogeneous data into a usable knowledge format.

We will describe how genomic approaches are changing our understanding of cancer, as a model system. Our work, at Genome Institute of Singapore, in transcriptional profiling has led to transcription factor binding site dynamics and human variations in those binding sites. We employ a strategy of using genomic data to reconstruct systems maps of critical regulatory networks. This integrative approach permits modelling of complex interactions and allows us to quickly uncover complex mechanisms of drug action. Coupled with the dramatic expansion of disease gene discovery in population studies, we now find that rather than a few genes, hundreds of genes may be involved in the genesis of a single complex disease.

Combined Genome Institute of Singapore (GIS) – Alexandra Health Symposium

Associate Professor Ruan Yijun
Associate Director, Genomics Technology, Genome Institute of Singapore (GIS)
Senior Group Leader, Genomics Technology, GIS

A/Prof Ruan Yijun is currently the Senior Group Leader and Associate Director of Genomics Technology at GIS. His primary interest is to elucidate the structures and dynamics of all functional DNA elements in complex genomes through transcriptome characterisations and genome interrogation. To facilitate such understanding, A/Prof Ruan's lab has developed pair-end-tag (PET) based high-throughput and high-precision DNA sequencing and mapping methodologies. These sequencing-based measurements are used to address complex biological questions such as how cancer cells progress and how stem cells maintain their unique properties. Another major interest of A/Prof Ruan is to discover previously uncharacterised microbial genes and genomes that are relevant to human health. To this end, his lab has established a metagenome analysis capability that includes a filtration system for isolating uncultured microbes, shotgun and PET sequencing of metagenomes to uncover viral and bacterial genome sequences from a variety of environment settings and cavities of the human body.

COMPREHENSIVE PAIRED-END-TAG MAPPING REVEALS CHARACTERISTIC PATTERNS OF STRUCTURAL VARIATIONS WITH MECHANISTIC IMPLICATIONS IN EPITHELIAL CANCER GENOMES

Somatic genome rearrangements are thought to play important roles in cancer development. However, our ability for thorough characterisation of cancer genome structural variations is still limited. We optimised the paired-end-tag (PET) sequencing approach for analysing large genomic DNA fragments to study human genome structural variations, and have applied this approach to comprehensively characterise the structural variations of 15 cancer genomes and 2 non-cancer genomes as normal controls. Our analyses revealed that most inversions, deletions, and insertions are germ-line structural variations, whereas tandem duplications, unpaired inversions, inter-chromosomal translocations, and complex rearrangements are over represented among somatic rearrangements in cancer genomes. Large tandem duplications are probably among the initial rearrangements that trigger genome instability for extensive amplification in cancer genomes.

Associate Professor Liu Jianjun
Associate Director, Human Genetics, Genome Institute of Singapore (GIS)
Senior Group Leader, Human Genetics, GIS

A/Prof Liu obtained his PhD in genetics at Duke University and did his postdoctoral training in genetics of psychiatric disorders at Columbia University. A/Prof Liu joined GIS in 2002 and is currently leading its Human Genetics Programme. A/Prof Liu's main research interest is to understand the genetic basis of human diseases. Currently, the main focus of his lab is to identify genetic risk factors for human diseases by using large-scale genetic association analysis. More recently, the research effort has been expanded to include the identification of rare mutations by using next-generation sequencing technologies. In addition, his lab is also working on functional studies using various molecular techniques and animal models to understand the molecular mechanism underneath identified disease risk factors.

Combined Genome Institute of Singapore (GIS) – Alexandra Health Symposium

GENETIC DISSECTION OF DISEASE SUSCEPTIBILITY: GWAS AND BEYOND

Rapid development of large-scale genotyping technology and greatly expanded understanding of the genetic variation pattern of human genome has lead to a surge of genome-wide association study (GWAS) efforts around the world, which have discovered thousands of genetic variants that can influence the development of human diseases. However, for most of the diseases, only a small proportion of genetic risk or heritability of disease can be explained by these identified genetic variants, and there has been limited progress in revealing the 'biology' underlying these identified disease susceptibility genes through functional investigations. This has caused many to question whether GWAS has been 'over-sold' in terms of promises. Furthermore, the emergence of next-generation sequencing has also raised the question of whether current genotyping-based GWAS will soon be replaced by sequencing-based human genetic study, such as exome sequencing analysis. In this presentation, I will first introduce our efforts of GWAS in the Chinese population and some recent developments beyond the initial GWAS. I will then discuss the current concerns over GWAS as well as its future.

Associate Professor Martin Hibberd
Associate Director, Infectious Diseases, Genome Institute of Singapore (GIS)
Senior Group Leader, Infectious Diseases, GIS
Associate Professor, Epidemiology and Public Health, National University of Singapore

A/Prof Martin Hibberd is the Senior Group Leader and Associate Director of Infectious Diseases at GIS, and has adjunct positions at the National University of Singapore and Imperial College (London, UK). A/Prof Hibberd graduated with Honours from Brunel University in 1985 (West London, UK) and received his Doctorate on the immune-genetics of the human T-cell antigen receptor from King's College, London. A/Prof Hibberd has a broad scientific background spanning both microbial and human determinants of infectious and inflammatory diseases. His previous appointments include WHO-funded Senior Microbiologist at UK's central Public Health Laboratories, and Lecturer and Senior Lecturer in Paediatric Infectious Diseases at Imperial College School of Medicine, a top-ranking British university, for seven years prior to his current appointment. A/Prof Hibberd's current research interests cover both pathogen and host aspects of infectious disease, understanding how microbial agents cause the observed disease (including pathogen identification and sequence characterisation) and why specific individuals are susceptible to the disease (using host genetics on a genomic scale). Approaching infectious disease from these two directions also allows specific host pathogen responses to be investigated (utilising RNA arrays or sequencing). This work aims to identify key host responses to specific pathogens that could be targeted by new therapies.

A GENOMIC UNDERSTANDING OF INFECTIOUS DISEASES, FROM HOST AND PATHOGEN GENOMES TO TRANSCRIPTOMES

Human infections can result in a wide variety of clinical outcomes, with severe disease usually being a rare occurrence. For example, in areas with endemic dengue disease, such as Vietnam, seroprevalence studies have shown that infection occurrs in over 88% of children by the age of 15 and yet hospitalised disease occurs in less than 0.1%. The cause of this variation in clinical outcome is unclear. Using whole-genome unbiased approaches, we have investigated this problem from the pathogen, host and host response perspectives to look for synergistic effects that might explain and predict outcome.

In dengue, this has lead to the identification of the interferon pathway as a key player, and interferon response molecules as potential biomarkers for outcome. In an initial study of 200 patients, a clinical algorithm using just one biomarker together with clinical signs, showed 87.5% sensitivity and 84.7% specificity for clinically severe disease three days before hospitalisation (at 42 hours of undifferentiated fever). This work aims to build up a molecular understanding of the host-pathogen interaction that may also point the way to novel therapeutic interventions.

Combined Genome Institute of Singapore (GIS) – Alexandra Health Symposium

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A/Prof Lim Su Chi is a Senior Consultant general physician cum endocrinologist at KTPH. His other responsibilities and appointments include: Deputy Director of Diabetes Centre and Clinical Director of Clinical Research Unit at KTPH. He is also an Adjunct Associate Professor at the Department of Epidemiology and Public Health, Yong Loo Lin School of Medicine, National University of Singapore. A/Prof Lim sits on the Ministry of Health's Clinical Management Guidelines Development Committee for Diabetes Mellitus. His present research interests include in vivo endothelial function in diabetes mellitus, genetics of diabetic nephropathy and adipocytes biology in bariatric surgical interventions.

GENOMIC MEDICINE: A CLINICIAN'S PERSPECTIVE

Genomic medicine refers to using genetic information for the diagnosis, prevention and treatment of disorders. Several powerful enabling tools have empowered the spectacular development of genomic medicine. Just to name a few: network information technology, super-computing resources, creative biostatistical approaches and revolutionary molecular genetics platforms, such as microarray and next-generation sequencing.

The dazzling success of Genome Wide Association Study (GWAS) in shedding light on the pathogenetic basis of complex diseases have stretched our minds that 'impossible is nothing'. Better understanding of the pathophysiology of diseases promises to usher in better diagnostic, preventive and therapeutic measures. However, the horizon charted by GWAS has also revealed our deficiency in understanding the functional significance of these genetic variants associated with disease. The journey to unravel the biology of these variants has only just begun.

The ability of genetic information to predict complex disease susceptibility is a little frustrating. This is largely due to the underlying intricate genetic architecture of such diseases and perhaps the near-limitless combination and permutation of gene-gene and gene-environment interactions. Our ability to identify rare variants with moderate-to-large effect size may improve our predictive power. However, it is obvious that more needs to be done to realise our dream of complex disease susceptibility prediction.

Pharmacogenomics is probably one of the most promising fields whereby genetic information may guide therapeutic options. One good recent example is the emerging data that genetic variations in cytochrome P450 enzymes (CYP2C19) and efflux pump P-glycoportein (ABCB1) may affect therapeutic responses to platelet inhibition by certain thienopyridine during acute ischaemic events. Such individuals may do better on alternative antiplatelet agents.

Ethical and regulatory framework needs to keep pace with the above developments, so that we will not lose our souls in the midst of technical advances.

Engineering Innovations & Medicine Symposium

Assistant Professor Ng Kee Woei
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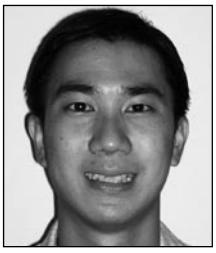
*A/P Ng Kee Woei was one of the first recipients of the A*STAR Graduate Scholarship. A mechanical engineer by training, he completed his PhD at Yong Loo Lin School of Medicine, National University of Singapore, in 2005. A/P Ng underwent postdoctoral training at Institute of Molecular and Cell Biology and at Institute of Medical Biology, A*STAR. He has worked on a number of projects on tissue engineering of skin, bone and cartilage. More recently, he has extended his research to fundamental understanding of stem cell biology and cell-material interactions. He is currently Assistant Professor at the School of Materials Science and Engineering, Nanyang Technological University.*

TISSUE ENGINEERING: USING ENGINEERED MATERIALS TO GROW TISSUES

The acute shortage of human tissues and organs for transplantation led to the birth of tissue engineering, a field that was officially conceptualised at a National Science Foundation workshop in 1988. In essence, tissue engineers strive to grow functional tissues and organs in a laboratory setup. In the last two decades, encouraging results have been obtained for several tissues including skin, cartilage, bone, nerve, muscle, bladder and liver. Some successes have resulted in commercially available products today but widespread clinical use of tissue engineered products is still unlikely in the near future. A few examples of tissue engineering projects will be discussed in this talk, demonstrating how engineered materials can potentially be used to provide clinicians with transplantable tissues. The limitations and possible pitfalls of current technologies will also be discussed.



Assistant Professor Loo Say Chye Joachim
Assistant Professor, School of Materials Science and Engineering, Nanyang Technological University
Secretary, Materials Research Society of Singapore

*A/P Joachim Loo graduated with a Bachelors degree in Applied Science (Materials Engineering) and received his PhD (recipient of the A*STAR Graduate Scholarship) from Nanyang Technological University (NTU). He did his postdoctoral fellowship in Mayo Clinic (MN, USA) before joining NTU as a faculty staff in 2006. His research interests include particulate drug delivery systems, drug-eluting balloons (DEB) and nanotoxicology. He has published more than 40 papers and has filed 6 patents. A/P Loo is currently a Principal Investigator, as well as a collaborator, for several local and international research grants amounting to more than S$10M. He is currently an Assistant Professor at the School of Materials Science and Engineering, NTU. He is also currently serving as Secretary of Materials Research Society of Singapore (MRS-S).*

"DESIGNER" PARTICLES: A PLATFORM FOR REVOLUTIONISING DRUG DELIVERY

Particulate systems, in the form of micro- or nano-sized particles, have tremendous potential to achieve controlled release and targeted delivery of drugs. However, single-layered polymeric particles have several inherent limitations, including initial burst release of drugs, a lack of time-delayed or pulsatile release of drugs and the inability to achieve constant drug release. Multi-layered particles have shown huge potential in overcoming these disadvantages. Herein, we show how to exploit the use of a simple, reliable and economical one-step solvent evaporation technique to fabricate drug-loaded multilayered biodegradable microparticles, with selective drug localisation in different layers. This fabrication process can therefore be used to tailor microparticle designs, allowing such "designer" particulate drug delivery systems to function across a wide range of applications.

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Engineering Innovations & Medicine Symposium

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Adjunct Practice Faculty, School of Information Systems, Singapore Management University
Vice-Chairman, Chapter of Public Health and Occupational Physicians, Academy of Medicine

Dr Eugene Shum is Director of Medical Affairs & Innovation at KTPH. He is responsible for the development and management of clinical services and medical manpower at KTPH. Dr Shum also oversees the Innovation Unit at KTPH, which aims to transform the way healthcare is experienced and delivered. Dr Shum is Associate Programme Director of National Preventive Medicine Residency Programme at KTPH and Adjunct Assistant Professor in the Department of Epidemiology and Public Health, Yong Loo Lin School of Medicine, National University of Singapore (NUS). He is also Adjunct Practice Faculty, School of Information Systems, Singapore Management University. Dr Shum is Vice-Chairman of the Chapter of Public Health and Occupational Physicians, Academy of Medicine, Singapore. Dr Shum was awarded the MBBS by NUS, and Masters in Public Health by Johns Hopkins Bloomberg School of Public Health.

HEALTHCARE INNOVATION THROUGH DESIGN THINKING

The ageing of the population and the rising prevalence of chronic diseases will lead to increasing demand for healthcare services. The growth of healthcare infrastructure and medical manpower to meet this demand is not sustainable due to limited resources. There is a need to transform the delivery of healthcare.

Healthcare organisations, such as Mayo Clinic and Kaiser Permanente, have applied design thinking to transform the delivery of healthcare. Using design as a strategy, they have observed and studied the needs of users, and carried out many iterative prototypes before reaching the final solutions.

This presentation will explore the use of design thinking in healthcare. We will describe the set-up of the Innovation Unit at Alexandra Health and how it has facilitated innovation in the organisation. We will also share our experience in setting up the Dream Room in Ward 82 in Khoo Teck Puat Hospital. The Dream Room is the first of its kind in Singapore and allows a patient to control his environment from his bed.

Doctors' Category: D01

A collaborative geriatric surgery team ensures consistent successful outcomes in elderly colorectal surgery patients

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Introduction: We hypothesised that a dedicated collaborative transdisciplinary geriatric surgery team (GST) would improve care and outcomes in elderly colorectal surgery patients.

Methods: Patients over 75 years old who were undergoing major colorectal surgery were included. The GST employed a transdisciplinary collaborative model of care. There were frequent quality reviews and a patient-centred culture was ensured. Prospective data from the GST were compared to similar patients not managed by them.

Results: 29 patients managed by the GST were compared to 52 patients who underwent standard treatment. The median age in the GST group was higher, but there was no difference in ASA (American Society of Anesthesiologists) scores and predicted POSSUM (Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity) morbidity scores. The GST achieved lower rates for mortality and major complications. 84.6% of patients managed by the GST returned to preoperative functional status by six weeks. The GST attained a trend of successive desired outcomes, which is evident from the downward sloping CuSum (Cumulative Summation) curve. This was in contrast to patients not managed by the GST.

Conclusion: The GST, through its transdisciplinary collaborative care practices, was able to achieve sustained superior outcomes in elderly colorectal surgery patients when compared with the patient group provided standard treatment.

Doctors' Category: D02

How would the new diagnostic criteria for gestational diabetes mellitus affect us?

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Introduction: The International Association of Diabetes and Pregnancy Study Groups (IADPSG) recently recommended a revised diagnostic criteria for gestational diabetes mellitus (GDM). According to the new criteria, the recommended plasma glucose levels for fasting, one hour and two hours post 75 g oral glucose tolerance tests (OGTT) have become ≥ 5.1 mmol/L, 10.0 mmol/L and 8.5 mmol/L, respectively. This study aimed to investigate the implications of the new diagnostic criteria for GDM.

Methods: Demographic data and 75 g OGTT results were retrospectively collected from patients who visited the high-risk pregnancy clinic at Singapore General Hospital, Singapore, in 1999. Women with two-hour post 75 g OGTT plasma glucose values ≥ 7.8 mmol/L were diagnosed as GDM in this group.

Results: The mean age of the study population (n = 481) was 32 ± 5 years, with a racial distribution of 53.2% Chinese, 34.1% Malays, 10.0% Indians and 2.7% others. Prevalence of GDM by the old and new criteria differed minimally at 56.5% and 55.3%, respectively, with a similar distribution by age and ethnicity. However, the degree of agreement between the two diagnostic criteria (κ = 0.60) was moderate, with approximately one in five patients being reclassified – about 20% of women with GDM according to the old criteria would become normal under the new criteria; similarly, about 20% of women who were earlier adjudjed normal according to the old criteria would now be reclassified as GDM under the new criteria ($p < 0.001$).

Conclusion: In an Asian population at high risk for GDM, the revised IADPSG diagnostic criteria for GDM would reclassify approximately 20% of pregnant women into different diagnostic categories.

Doctors' Category: D03

Accuracy of ProSeal™ laryngeal mask airway intracuff pressure estimation by the finger palpation technique

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Introduction: The incidence of pharyngolaryngeal adverse events after general anaesthesia with laryngeal mask airways (LMAs) can be more than 40%. These adverse outcomes can be reduced by 70% if manometry is used to limit LMA intracuff pressure (< 60 cmH_2O). Routine monitoring of intracuff pressure using manometry has not been widely adopted as the standard of care amongst anaesthesiologists, with many still estimating LMA intracuff pressures by finger palpation of the valve pilot balloon. In this study, we determine the accuracy of finger palpation technique in different anaesthesia personnel against actual readings obtained from a handheld manometer.

Methods: 80 patients undergoing general anaesthesia with LMA were prospectively recruited. After induction with propofol and fentanyl, LMA ProSeal™ was inserted and the cuff inflated with a standard volume of air as per manufacturer's recommendation. The LMA intracuff pressure of every patient was then independently estimated and recorded by finger palpation of the pilot balloon by two anaesthesiologists (one senior and one junior) and one anaesthetic nurse assistant. The actual intracuff pressure was then obtained using a manometer and adjusted to 60 cmH_2O. Estimated vs. actual intracuff pressures were correlated using the Pearson's test. A p-value of less than 0.05 was considered significant.

Results: A scatter plot correlation was plotted for the pressure readings recorded by the anaesthesia nurse assistant, junior anaesthesiologist and senior anaesthesiologist. The strength of association, that is, R values were 0.21 (weak), 0.35 (moderate) and 0.78 (strong), respectively, for the anaesthesia nurse assistant, junior anaesthesiologist and senior anaesthesiologist, while the mean difference between the actual and estimated intracuff pressures was 15.6 ± 25.4, 12.8 ± 24.4 and 2.5 ± 16.2, respectively, for these personnel. Subgroup analysis showed that anaesthesiologists with more than three years experience were more accurate than those with less than three years experience. The mean difference between the actual and estimated intracuff pressures for senior and junior anaesthesiologists was 3.7 ± 17.4 and 19.1 ± 26.9 ($p < 0.001$). In all groups, the palpation technique underestimated the actual intracuff pressure by a mean pressure of 10.3 cmH_2O. Accuracy of the palpation technique correlated poorly when actual intracuff pressures were more than 80 cmH_2O.

Conclusion: Senior anaesthesiologists are more accurate at estimating LMA ProSeal™ intracuff pressures than nurses and junior anaesthesiologists. Medical personnel tend to underestimate intracuff pressures, especially when the pressures are more than 80 cmH_2O, putting patients at risk of postoperative pharyngolaryngeal adverse events. Manometry should be recommended as a standard of care for use with LMAs.

Doctors' Category: D04

Safety, efficacy and postoperative pharyngolaryngeal adverse events of laryngeal mask airway Supreme™ at different intracuff pressures: a randomised controlled trial

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Introduction: Higher oropharyngeal leak pressure (OLP) is a marker of the efficacy and safety of laryngeal mask airways (LMAs), as it indicates airway protection and feasibility for positive pressure ventilation under general anaesthesia. The new disposable polyvinylchloride single-cuffed LMA Supreme™ (LMA-S) has lower OLP compared to the silicone-based

double-cuffed ProSeal™. Increased LMA intracuff pressure may improve the glottic seal, but may also result in more postoperative pharyngolaryngeal adverse events. This study was designed to compare OLP of LMA-S at varying intracuff pressures.

Methods: Approval for the study was obtained from the hospital ethics committee. 104 patients consented to the study and were randomly allocated to three LMA-S intracuff pressure groups of 40 cmH_2O, 60 cmH_2O and 80 cmH_2O. The method for general anaesthesia was standardised with propofol-fentanyl induction and desflurane in air-oxygen for maintenance. Experienced anaesthesiologists performed all LMA-S insertions. Intracuff pressures were calibrated at 40 cmH_2O, 60 cmH_2O and 80 cmH_2O according to the patient's group allocation. The primary outcome was OLP. Secondary outcomes were postoperative pharyngolaryngeal adverse events, and patient and anaesthesiologists satisfaction scores. OLP was compared between the groups using Bonferroni and Scheffe tests. A p-value less than 0.05 was considered significant.

Results: 104 patients were analysed for the primary outcome according to the intention-to-treat. Baseline demographic data for all groups were comparable. The mean OLP in the 80 cmH_2O group (25.9 ± 5.8 cmH_2O) was significantly higher when compared to that in the 40 cmH_2O (18.0 ± 4.8 cmH_2O) and 60 cmH_2O (20.5 ± 5.9 cmH_2O) groups ($p < 0.001$). The incidence of postoperative pharyngolaryngeal adverse events ($p = 0.52$), patient satisfaction scores ($p = 0.16$) and anaesthesiologist satisfaction scores ($p = 0.80$) were comparable between the three groups. No complications of aspiration or nerve injuries were encountered.

Conclusion: For LMA-S, a higher intracuff pressure of 80 cmH_2O gave higher OLP than lower intracuff pressures of 40 cmH_2O or 60 cmH_2O without resulting in more postoperative pharyngolaryngeal adverse events or nerve injuries. As the LMA-S design for cuff and material is different from that of LMA ProSeal™, we recommend an intracuff pressure of 80 cmH_2O when using LMA-S in order to achieve a higher OLP and a superior glottis seal.

Doctors' Category: D05

Risk factors associated with arterial stiffness in type 2 diabetes mellitus

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Introduction: Emerging evidence indicates that arterial stiffness may be an intermediate step in linking type 2 diabetes mellitus (T2DM) to cardiovascular disease (CVD). There is limited data on arterial stiffness in Asian patients with T2DM. We hypothesise that arterial stiffness may be predicted by metabolic parameters associated with the development of CVD.

Methods: 211 patients with T2DM from a hospital-based diabetes clinic consented to enrolment in the study. Anthropometric parameters, and fasting venous blood and urine samples were obtained. Central aortic systolic pressure (CASP), measured using a BPro™ device, was used to estimate arterial stiffness. Factors significantly associated with CASP in bivariate correlation analysis ($p < 0.05$) were analysed using linear regression.

Results: The group consisted of 72% Chinese, 16% Malay and 10% Indians. Majority of the population were men (65%). Study parameters included age (60 ± 11 years), body mass index (27.1 ± 4.5 kg/m^2), systolic blood pressure (137 ± 19 mmHg), diastolic blood pressure (77 ± 10 mmHg), glycated haemoglobin (8.2 ± 1.5%), high-density lipoprotein cholesterol (HDL-C; 1.2 ± 0.3 mmol/L), low-density lipoprotein cholesterol (2.6 ± 0.8 mmol/L) and triglyceride (1.9 ± 1.7 mmol/L), median CASP (124 mmHg, 5th–95th percentile 98–159), estimated glomerular filtration rate (eGFR; 76 ml/minute/1.73 m^2, range 12–142 ml/minute/1.73 m^2), and urine albumin-creatinine ratio (UACR; 46 μg/mg, range 0–3,831 μg/mg). Univariate analysis suggested age, UACR, eGFR and HDL-C were significantly correlated with CASP ($p < 0.05$). Multivariate analyses indicated that these four factors collectively accounted for approximately 97% variation in CASP ($p < 0.001$).

Conclusion: Arterial stiffness is almost exclusively defined by increasing age, HDL-C levels, UACR and diminishing eGFR. Results of the present study may shed light on the pathogenic mechanisms underlying variation in CASP among patients with T2DM.

Doctors' Category: D06

Effect of the treatment of hyperthyroidism on body composition and its correlation with ghrelin levels

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Introduction: Disturbances in thyroid function are associated with changes in body composition, energy expenditure and food intake, with weight loss being a key feature of hyperthyroidism. Ghrelin, an orexigenic hormone, is associated with food intake and energy balance. This study aims to observe the relationship between the treatment of hyperthyroidism, changes in body composition and its correlation with ghrelin levels.

Methods: Patients with Graves' hyperthyroidism were enrolled in the study (n = 10). The mean age of patients was 42 (range 21–75) years. Study parameters included free thyroxine (fT4), thyroid stimulating hormone (TSH) and total triiodothyronine (T3) levels as well as body weight, fat mass (FM), fat free mass (FFM) and ghrelin levels which were measured before and after treatment.

Results: The mean value observed for fT4 was 48.3 (range 29.7–100; normal range 11.8–24.6) pmol/L and T3 was 5.21 (range 2.90–9.78; normal range 1.60–2.60) nmol/L. TSH ranged from <0.005–0.013 (normal range 0.270–4.20) mIU/L. Mean treatment duration to euthyroidism was 118 days. Nine patients gained weight, with a mean weight gain of 3.3 (range 0.9–9.1) kg. Mean change in FM was 1.87 ± 1.73 kg and FFM was 1.43 ± 1.98 kg. Linear regression analysis showed a positive correlation between the level of T3 and weight gain ($p = 0.031$). Ghrelin levels increased during the course of treatment, with a mean ghrelin level of 17.17 (range 11.01–27.57) pg/ml at hyperthyroidism and 35.47 (range 13.31–95.16) pg/ml at euthyroidism; the mean change in ghrelin levels was 18.3 ± 26.31 pg/ml. This rise in ghrelin levels post-treatment reached near significance ($p = 0.051$) and was significantly associated with pre-treatment ($p = 0.003$) and post-treatment ($p = 0.007$) FM. No correlation was found between ghrelin levels, weight change and FFM.

Conclusion: In hyperthyroidism, ghrelin levels increased upon achieving euthyroidism. This rise in ghrelin was associated with an increase in FM. Results also suggest that baseline T3 may be a useful predictor of weight gain.

Doctors' Category: D07

Effect of fasting during the month of Ramadan on body composition and glycaemic control in Muslims with type 2 diabetes mellitus

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Introduction: Millions of diabetic Muslims worldwide fast during the month of Ramadan. However, little is known about the metabolic impact of Ramadan on individuals with type 2 diabetes mellitus (T2DM). With a hypothesis that fasting would bring about favourable changes in glycaemic control and body composition, the study aimed to investigate the effects of fasting on body weight, composition and glycaemic control in Muslims with T2DM.

Methods: Ten T2DM patients from a secondary-care diabetes centre were recruited for the study. The mean age of patients was 54 (range 44–72) years. Parameters measured before and after the fasting month of Ramadan were glycated haemoglobin (HbA1c) levels, body mass index (BMI), waist-hip-ratio (WHR) and body composition, which included skeletal muscle mass (SMM), body fat mass (BFM) and percentage body fat (PBF). Self-monitoring of blood glucose

was mandated for three consecutive days of fasting. Body composition was measured using the multifrequency bioimpedence method. These patients were treated according to the Ramadan-management guidelines recommended by the American Diabetes Association.

Results: Mild hypoglycaemia, self-aborted by food intake, was seen in three patients. Two of these patients required medication adjustment. Two patients did not complete the full 30 days of fasting. Changes in the measured parameters were significant for HbA1c (pre-Ramadan 9.01 ± 2.41%, post-Ramadan 7.86 ± 1.58%; p = 0.011), BFM (pre-Ramadan 31.7 ± 12.8 kg, post-Ramadan 29.1 ± 11.9 kg; p = 0.011) and PBF (pre-Ramadan 38.2 ± 11.4%, post-Ramadan 35.8 ± 11.0%; p = 0.026), but not significant for body weight (pre-Ramadan 81.0 ± 11.8 kg, post-Ramadan 79.5 ± 11.4 kg; p > 0.05), BMI (pre-Ramadan 31.7 ± 6.4 kg/m^2, post-Ramadan 31.2 ± 6.2 kg/m^2; p = 0.067), WHR (pre-Ramadan 0.99 ± 0.08, post-Ramadan 0.99 ± 0.08; p > 0.05) and SMM (pre-Ramadan 26.6 ± 4.8 kg, post-Ramadan 27.2 ± 4.9 kg; p > 0.05).

Conclusion: Fasting during Ramadan brings about improvement in glycaemia, body weight and composition with a seemingly low risk of hypoglycaemia. Determinants for these improvements, if identified, may be helpful in guiding future T2DM management. Future larger studies with more detailed metabolic assessment may uncover factors useful in guiding T2DM interventions in this group of patients.

Doctors' Category: D08

Is minimally invasive video-assisted thyroidectomy feasible in Graves' disease?

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Introduction: Although the safety and advantages of minimally invasive video-assisted thyroidectomy (MIVAT) are well documented in nodular thyroid disease, its use in Graves' disease remains controversial. We compared the outcomes of patients undergoing MIVAT with those undergoing conventional thyroidectomy for Graves' disease.

Methods: Of the 497 patients with Graves' disease referred for surgery between 1999 and 2009, 157 (31.6%) patients underwent the MIVAT procedure (VA-group). The control group consisted of the remaining 340 patients who underwent a conventional thyroidectomy (CT-group). MIVAT was proposed if the thyroid volume was ≤ 30 ml. Data was gathered through a prospectively maintained surgical database.

Results: A majority of patients in both groups underwent total thyroidectomy (VA-group 98%, CT-group 96.5%). Three conversions to open surgery (1.9%) occurred in the VA-group. Hospital stay was significantly shorter in the VA-group (2.1 ± 0.4 days) compared to the CT-group (2.4 ± 1.4 days, p = 0.008). The mean operative time was shorter for the VA-group (84 ± 29 minutes, range 15–240 minutes) compared to the CT-group (94 ± 43 minutes, range 20–360 minutes) although not statistically significant (p = 0.05). A comparison of the incidence of postoperative transient hypocalcaemia (VA-group 14 [8.9%], CT-group 23 [6.8%]), transient recurrent laryngeal nerve palsy (VA-group 2 [1.3%], CT-group 11 [3.2%]) and postoperative haematoma (VA-group 5 [3.2%], CT-group 8 [2.3%]) between the two groups showed no statistical significance.

Conclusion: MIVAT was feasible for the patients with Graves' disease who were selected for this study. MIVAT can be performed safely for such patients, with results being comparable to those of open surgery.

Doctors' Category: D09

Multivariate analysis of poor outcome predictors of perianal fistula surgery

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Introduction: We hypothesised that expertise of the operating surgeon and complexity of the pathology may have an impact on patient outcomes following perianal fistula surgery in a general surgery department setting.

Methods: A retrospective review of all patients who underwent surgery for anal fistula from January 1, 2006 to December 31, 2009 was performed. Patient demographics, fistula pathology, surgical management, surgeons involved and outcomes of the first surgery were recorded. Outcome measure was defined as cases subjected to repeat unplanned definitive reoperation. A multivariate regression model was used to evaluate the effects of operating surgeons and complexity of the fistula as independent predictors of surgical outcome.

Results: Of 228 patients analysed, seven (3.1%) patients needed unplanned reoperation within 30 days of the surgery and 30 (13.2%) patients required unplanned definitive operation subsequently. The first surgeries were performed by registrars (47.6%), medical officers (27.6%), consultants (17.5%) and associate consultants (7.5%). Compared with surgeries done by surgeons of the rank registrar and above, patients first operated by a surgical medical officer were at a higher risk of requiring subsequent definitive unplanned operations (OR 4.00, 95% CI 1.81–8.83). On multivariate analyses, independent predictors for patients requiring unplanned definitive surgery were initial operation by a junior staff (OR 3.47, 95% CI 1.46–8.25), complex fistula (OR 3.33, 95% CI 1.21–9.16) and presentation as abscess rather than fistula (OR 8.84, 95% CI 2.52–31.01). Factors such as surgery performed by colorectal surgeons, age, gender and diabetes mellitus were not associated with unplanned reoperation.

Conclusion: Study findings clearly show that perianal fistula surgery by junior surgeons has a significant impact on patient outcome, with an associated higher risk of reoperation. It is suggested that surgeries done by junior surgeons be supervised by more experienced surgeons, especially for patients with more complex fistulae.

Doctors' Category: D10

Predictors for extracorporeal shockwave lithotripsy outcome

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Introduction: Extracorporeal shockwave lithotripsy (ESWL) is a well-established treatment for renal and ureteric calculi. Although several studies abroad have evaluated predictors for ESWL outcome, their conclusions remain conflicting. This study aimed to determine the predictors of ESWL outcome from local patient data using a multivariate analysis approach.

Methods: We reviewed our database for patients who underwent ESWL within an 18-month period. Patient variables and stone variables that were potential predictors of ESWL outcome were analysed. These variables were correlated to outcome at two weeks using the chi-square and Pearson correlation tests. After preliminary univariate analyses, all variables with a significant effect on ESWL outcome were further analysed to determine independent predictors using simultaneous regression analyses. As the presence of hydronephrosis has been commonly associated with either neutral or negative effects on ESWL outcome in previous studies, a hierarchical regression analysis was performed to determine if the effect of hydronephrosis on outcome was moderated by stone location, while controlling for stone size and number. Patients with lower pole renal stones were excluded to minimise any confounding effects from anatomical factors.

Results: Results from preliminary analyses showed stone location, size, number and presence of hydronephrosis as significant predictors of ESWL outcome. Simultaneous regression analyses showed larger stone size ($p = 0.009$) and the presence of

multiple stones (p = 0.012) to adversely affect ESWL outcome; the presence of hydronephrosis positively affected outcome (p = 0.046). Patients with ureteric stones had better outcomes than those with renal stones (p = 0.09). Hydronephrosis was found to have no significant effect on ESWL outcome for ureteric stones, but maintained a positive effect for renal stones (p = 0.046).

Conclusion: This study showed that stone size and number are independent predictors for ESWL outcome at two weeks. ESWL for ureteric stones may have a marginally better outcome than renal stones. Hydronephrosis has no effect on ESWL outcome for ureteric stones, but may improve outcome for renal stones.

Doctors' Category: D11

Transanal radical endoscopic resection of the rectum on swine model: surviving model

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Introduction: A novel technique of transanal endoscopic radical resection of the rectum (TRRR) was reported in 2009 by this research group. In this present study, we hypothesised that this procedure is not only technically feasible but also safe, and can be performed with survival of the animal model.

Methods: This procedure was performed on two swines as a surviving model. The project was approved by Innoheart Institutional Animal Care and Use Committee (IACUC). After radical resection of the rectum and primary anastomosis, the two swines were monitored in an animal holding area for a period of one week, following which the anastomoses were inspected.

Results: Both swines had good postoperative outcomes and intact anastomoses at one week after the procedure. Both could eat and had bowel action within three days of surgery. The postoperative period was captured in a multimedia video presentation.

Conclusion: We conclude that TRRR is not only technically feasible but also safe for swine. The procedure can be performed with good postoperative outcomes for the animal model.

Doctors' Category: D12

Use of complementary and alternative medicine in head and neck cancer patients in Singapore

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Introduction: A cross-sectional survey was conducted to determine the use and prevalence of complementary and alternative medicine (CAM) by a cohort of patients with head and neck cancer in Singapore.

Methods: 55 consecutive patients with head and neck cancer attending the Otorhinolaryngology Head and Neck Surgery Clinic at Alexandra Hospital, Singapore, between May 2008 and November 2009 were surveyed using a questionnaire via telephone interview.

Results: The prevalence of CAM use was 49.1%. The most commonly used CAMs were traditional Chinese medicine (66.7%), vitamins (14.8%) and cod liver oil (11.1%). Patients used CAM mostly for physical health and well-being (48.1%) or to provide symptomatic relief for the cancer or its treatment (29.6%). 55.6% of patients failed to inform their primary physician of their CAM usage. 63% of patients perceived their CAM therapies to be effective. Information about CAM was obtained most commonly from friends (40.7%), family (33.3%) and CAM practitioners (14.8%).

Conclusion: The high prevalence of CAM usage among patients with head and neck cancer emphasises the need for otolaryngologists to educate themselves on CAM and its interactions. Physicians should routinely ask patients about their use of CAM in order to facilitate communication and provide appropriate advice regarding the use of such therapies.

Doctors' Category: D13

Pitfalls in the management of traumatic haemothoraces and tension pneumothoraces

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Thoracostomy tube insertion is a common procedure performed for patients with chest trauma. However, it is not without its dangers. Minor complications include subcutaneous emphysema, haematoma and pain at the insertion site. Major complications include vascular and visceral injuries, infection, re-expansion pulmonary oedema and malpositioning. We report a case of traumatic bilateral occult haemopneumothoraces from blunt injury in a middle-aged man. Soon after insertion of bilateral thoracostomy tubes and tracheal intubation, the patient developed haemodynamic instability and respiratory distress. The clinical impression was that of a unilateral tension pneumothorax. Diagnosis based on frontal chest radiographs was difficult. Repositioning of the thoracostomy tube lead to the ventilatory and haemodynamic stabilisation of the patient. Computed tomography showed a malpositioned thoracostomy tube with a large left-sided tension pneumothorax with mediastinal shift. This report highlights the fact that classical signs that are commonly used for a clinical diagnosis of tension pneumothoraces can often be absent. Diagnosis based on supine anteroposterior chest radiographs can also be difficult, especially in the context of concurrent injuries, such as rib fractures, haemothoraces and pulmonary contusions. Although tube thoracostomies are accepted as life-saving management for tension pneumothoraces, up to 30% of these may be malpositioned. Tension pneumothorax must be suspected even with a tube thoracostomy *in situ* in the face of sudden clinical deterioration. This highlights the need for vigilance and rapid action by physicians involved in the care of trauma patients.

Doctors' Category: D14

Lateral lymph node dissection in the management of lower rectal cancer

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Introduction: The aims of this study were to elucidate the oncological and functional outcomes of total mesorectal excision (TME) in combination with lateral lymph node dissection (LLND; TME + LLND) for the management of low rectal cancers as given in the literature and to compare these outcomes to those achieved using the more standard approach of TME combined with adjuvant radiotherapy (RT; TME + RT).

Methods: A review of the literature was performed. Outcome measures selected were five-year local recurrence, overall survival and disease free survival, urinary dysfunction, sexual dysfunction and bowel dysfunction rates.

Results: The overall five-year survival rates for TME + LLND and TME + RT were reported to be 30.8%–83.2% and 43.0%–79.5%, respectively. The oncological outcomes for TME + LLND were comparable with those of TME + RT. Functional outcomes varied; some studies showed no significant difference between mortality following the two treatment modalities; others reflected a difference of over 27%–76% for patients having urinary and sexual dysfunction following TME + LLND. Superior results were seen in nerve-sparing lymph dissection. However, the quality of literature in this area is far from ideal. With poor standardisation of definitions and criteria, it is nearly impossible to compare the assorted treatment modalities across these studies.

Conclusion: There is an urgent need for well-organised studies comparing the modalities of TME + LLND against TME + RT for the management of low rectal cancers, with an emphasis on standardised classification of tumours and definition of outcomes.

Doctors' Category: D15

Outcome studies on geriatric surgery patients are missing the mark

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Introduction: With a rapidly ageing population, surgeries on geriatric patients have become more prevalent. Although the traditional outcome measures of morbidity and mortality remain important for such surgeries, an additional dimension of functional outcome after surgery should be included for elderly patients. This study reviewed the literature for data on postoperative functional outcomes in elderly patients following major abdominal surgery.

Methods: A review of the literature was performed for all studies with outcome reports of patients over 70 years of age who underwent major abdominal surgery. A prospectively collected database of patients over 75 years old who underwent colorectal resection at Alexandra Health, Singapore, was also performed.

Results: Our review found a paucity of studies that reported the functional outcomes of patients who had undergone major surgery. 13 out of 16 studies did not include functional outcome data. Only 35.8% of elderly patients had documentation of measurable functional outcome data.

Conclusion: Although functional outcomes are far more important as outcome measures for elderly surgical patients than mortality and morbidity, inadequate attention appears to have been given to these in the literature. There is an urgent need to redefine suitable outcome measures for elderly patients undergoing surgery, so that all efforts can be directed toward ensuring their optimal well-being after surgery.

Doctors' Category: D16

Choroidal neovascularisation following laser *in situ* keratomileusis for high myopia: a case-series

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Introduction: The study reports three patients who developed unilateral choroidal neovascularisation (CNV) following laser *in situ* keratomileusis (LASIK) for high myopia.

Methods: Data was retrospectively reviewed for these patients.

Results: Two women and one man (mean age 34 ± 2.8 years) underwent LASIK for high myopia in both eyes. The mean spherical equivalent was –9.92 (range –6.75 to –18.00) D. The mean time interval between LASIK and the appearance of symptoms was 9.3 ± 8.5 weeks. One patient developed a recurrent juxtafoveal CNV, one developed a new subfoveal CNV and one developed a new juxtafoveal CNV. The mean best-corrected visual acuity (BCVA) at the time of CNV presentation was 0.44 (range 0.10–0.70) logMAR. All patients were treated with a combination of intravitreal ranibizumab and photodynamic therapy with verteporfin. Following treatment, the mean BCVA improved to 0.17 logMAR, with complete resolution of CNV in two patients.

Conclusion: CNV is a rare but potentially blinding complication following LASIK. Short-term good visual outcome can be achieved with timely intervention using current treatment modalities.

Doctors' Category: D17

Spatial profile of macular pigment in Singaporean Chinese

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Introduction: This study aimed to measure the spatial profile of macular pigment (MP) in Singaporean Chinese and to examine its relationship with serum levels of lutein (L) and zeaxanthin (Z).

Methods: 80 patients were recruited for the study. Data collected included demographic data, lifestyle information, anthropometric measurements, spatial profile of MP using a macular densitometer, and blood sample for serum analysis of L and Z.

Results: The mean age of the study population was 44.7 ± 12.0 (range 21–68) years. There were 56 women (70%) and 24 men (30%) in the group. The mean MP at 0.25°, 0.50°, 1.0° and 1.75° of retinal eccentricity was 0.63 ± 0.19, 0.53 ± 0.19, 0.35 ± 0.16 and 0.17 ± 0.11, respectively. MP levels were lower in patients aged ≥ 40 years (MP 0.52) than in younger patients (MP 0.56), but the difference was not statistically significant. 71% of patients within the lowest tertile of MP (< 0.25) were aged ≥ 40 years. The difference in the mean MPs of women (MP women, 0.504) and men (MP men, 0.605) was statistically significant (p = 0.04). MP and serum levels of L (serum L 0.14; p = 0.20) and Z (serum Z 0.25; p = 0.02) were positively correlated, but the only relation that reached statistical significance was that between MP and Z.

Conclusion: Study results suggest that old age and female gender, the two known risk factors for age-related macular degeneration (AMD), are associated with a relative lack of MP. Furthermore, a positive relationship between MP and serum levels of L and Z suggests that dietary modification and/or nutritional supplementation may augment MP in people at risk for developing AMD. Future studies with larger sample sizes are warranted to confirm these findings.

Doctors' Category: D18

Preoperative dexamethasone for postoperative analgesia and recovery after laparoscopic cholecystectomy: a qualitative systematic review

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Introduction: Laparoscopic cholecystectomies are increasingly common as the procedure is the gold standard surgical treatment for cholelithiasis. Postoperative pain, fatigue, nausea and vomiting may delay recovery and hospital discharge. Opioid analgesics have conventionally been used despite evidence of their manifold adverse effects. Dexamethasone is a long-acting, anti-inflammatory glucocorticoid with antinocioceptive and antiemetic action. It has been recognised to be useful for the prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy. We postulate that preoperative dexamethasone may also be used as an adjunct to ameliorate pain, decrease analgesic consumption and hasten postoperative recovery in laparoscopic cholecystectomy patients.

Methods: A systematic online literature search was performed for the keywords laparoscopic cholecystectomy, gallbladder, pain, analgesia and dexamethasone on PubMed, MEDLINE and Google Scholar. Additional studies were identified by manually searching references from published articles. Only randomised clinical trials involving human studies in the English language were shortlisted for review. A qualitative analysis of the 16 trials was carried out based on systematic review questions.

Results: Of the 16 trials included in our review, five of 13 trials showed a reduction in pain scores, while six of 13 trials showed a reduction in analgesic consumption. Five of seven trials, where pain was the primary outcome, had positive findings for dexamethasone as an analgesic adjunct. Negative results were mainly found in trials where pain outcomes were secondary measures. Five of seven trials showed faster postoperative recovery, with a shorter length of hospital stay, less fatigue and better quality of recovery scores. A dose of dexamethasone of ≥ 8 mg was associated with positive outcomes. Dexamethasone was also associated with more favourable patient satisfaction scores. There were no reported adverse effects from a single dose administration.

Conclusion: Patients treated with preoperative dexamethasone showed a trend toward less pain, analgesic-sparing effect and faster recovery in the postoperative period without the risk of adverse effects. Dexamethasone may be recommended as an analgesic and antiemetic in laparoscopic cholecystectomy patients.

Doctors' Category: D19

In-plane short-axis approach to femoral catheter insertion works well for postoperative pain management for total knee replacement

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Introduction: Use of continuous femoral nerve catheters and perineural local anaesthetic infusions for postoperative pain management in patients undergoing total knee replacement (TKR) has been shown to achieve significant reduction in pain scores, need for rescue analgesics, better patient satisfaction and early rehabilitation. Traditionally, catheters have been inserted along the long axis of the nerve to facilitate catheter migration along the nerve. This has necessitated the use of an out-of-plane (OOP) approach for ultrasonography. We hypothesised that in-plane (IP) techniques may be safer as the needle and its trajectory remain visible along the whole length during insertion.

Methods: The acute pain services provided on catheter insertion to 37 patients who underwent TKR surgery at Khoo Teck Puat Hospital, Singapore, were reviewed. The technique of catheter insertion, pain scores at rest and on movement on postoperative Days 1, 2 and 3, patient satisfaction scores and any complications observed in these patients were noted.

Results: The IP technique was used for catheter insertion in 22 patients while the OOP technique was used for 15 patients. 48% of the catheters were tunnelled. Pain scores on postoperative Days 1, 2 and 3 were comparable. More patients had pain scores greater than 6 in the OOP group (0.00% vs. 6.67%), but the difference was not significant. On postoperative Day 2, 63.6% of patients in the IP group had no pain at rest vs. 33.0% in the OOP group. Overall, patient satisfaction scores for the IP or OOP groups were similar. In the OOP group, three of 15 catheters (20%) slipped out before their time, but no such instances were seen in the IP group.

Conclusion: Femoral catheter insertion, via either the IP or OOP technique, is a good analgesic option for patients undergoing TKR. The benefit of being able to view the needle shaft in its entirety while using the IP short-axis view for femoral catheter insertion and its attendant advantages make the IP technique safer when compared to the traditional OOP short-axis view for catheter insertion.

Doctors' Category: D20

Novel uses for the new laryngeal mask airway Classic Excel™

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Laryngeal mask airways (LMAs) have been used in the clinical practice of anaesthesia since the prototype was invented by Dr Archie Brain in 1981. It has gained worldwide recognition and popularity among anaesthesiologists and is used routinely as an airway management device in more than 50% of routine general anaesthetics. A new LMA Classic Excel™ was introduced in 2009, which has improved features including an epiglottic elevating bar and a removable airway connector that facilitates intubation via the LMA. We report a novel diagnostic surgical use for the new LMA Classic Excel™. A 61-year-old woman, with a long-standing history of Graves' disease, presented with an enlarged 4 cm × 5 cm thyroid mass and a histological diagnosis of papillary carcinoma. Computed tomography of the neck showed a heterogeneous thyroid mass with multiple cystic areas and focal calcification. Clinically, there were no compressive symptoms associated with the thyroid carcinoma. Fibreoptic brochoscopy was requested prior to surgery by the otolaryngology surgeons to assess for tracheal invasion. The patient was induced with inhaled sevoflurane, intravenous propofol and remifentanil. The LMA Classic Excel™ was inserted and hand ventilation was assessed to be adequate. The patient was allowed to breath spontaneously on the supraglottic airway device. Bronchoscopic assessment of the trachea was performed through a 15-mm fibreoptic bronchoscope swivel connector while the patient was maintained under general anaesthesia. The patient was subsequently paralysed and intubated via the LMA Classic Excel™. Surgery proceeded uneventfully. En bloc dissection and removal of the thyroid gland with overlying strap muscles, and excision of the tumour adherent on the first tracheal cartilage was performed. The patient was extubated successfully at the end of the operation. Newer modifications of the original LMA, such as LMA Fastrach™, have been used to aid diagnostic and therapeutic laryngeal surgical procedures. Novel uses for the LMA Classic Excel™ may include facilitating various diagnostic procedures, such as bronchoscopic tracheal assessment of malignant thyroid tumours.

Doctors' Category: D21

Clarithromycin-induced depression during *Helicobacter pylori* eradication therapy

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With the discovery of *Helicobacter (H.) pylori* as the main causative agent of peptic ulcer disease, the use of triple therapy has become its mainstay eradication treatment in recent years. Clarithromycin has been reported to cause psychiatric complications in patients on triple therapy and patients receiving this treatment must be monitored. This report describes a 56-year-old man who developed depression, insomnia and suicidal intent after consuming clarithromycin for *H. pylori* eradication. Literature searches were conducted on PubMed and MEDLINE for articles published from 1990 through October 2010 using the search terms peptic ulcer, *Helicobacter pylori*, clarithromycin, psychiatric and triple therapy. Relevant articles were retrieved and referenced in this report. Patients on triple therapy with no past psychiatric history who present with new onset psychiatric symptoms should prompt the surgeon to investigate for drug-related causes. Surgeons must be cognisant of the possible psychiatric problems that may arise from the use of clarithromycin with triple therapy.

Doctors' Category: D23

Ocular manifestations of spitting cobras: a report of two patients

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Spitting cobras have a strangely modified venom apparatus that enables them to spit venom across a distance of metres into the eyes of their predators or enemies. The resulting venom ophthalmia can have a host of clinical presentations. Most literature reports are about incidents seen in the rural milieu. We hereby report two patients who were victims to the spitting cobra in urban Singapore. A retrospective study of the two patients was carried out. Two men were exposed to the spitting cobra while at work. Both patients had conjunctival injection and corneal involvement in the form of punctuate epithelial erosions. One patient had chemosis of pre-existing pterygium as well as anterior uveitis. Irrigation of the eyes with tap water was done as first aid for both the patients by coworkers. Both the patients were treated with topical antibiotics and lubricants and had a good visual outcome after a week of treatment without any permanent sequelae. Early treatment of the venom ophthalmia can minimise complications and result in a good clinical outcome.

Doctors' Category: D24

Knowledge and attitudes of Singaporean women toward breast cancer

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Introduction: Breast cancer is the most common cancer among women in Singapore, with three being diagnosed everyday and as many dying every four days. Participation in the screening programme is, however, subject to patient knowledge and attitudes toward the disease, with many still harbouring misconceptions about its diagnosis and treatment. This study aimed to identify related false beliefs shared by symptomatic and asymptomatic women, so that clinicians are able to conduct more purpose-led consultations in addressing them. By correcting these misconceptions, it is hoped that more women will attend screening, thereby reducing morbidity and mortality.

Methods: A questionnaire study was conducted with 55 randomly selected respondents from Northern Singapore. Respondents were grouped by age into those above and below 40 years, as mammogram screening is recommended for women older than 40 years in Singapore.

Results: 10% of respondents thought all breast lumps were cancerous. 36% of respondents felt mammograms were painful, nearly half of who were aged < 40 years and had not yet taken a mammogram. This latter finding highlights the damaging preconceived notions that could be harboured in the target group even in the absence of first-hand experience. Those aged > 40 years were generally less informed and more pessimistic about the prognosis of breast cancer and its treatment. 51% of respondents aged > 40 years believed that a complete mastectomy was unavoidable in the course of treatment and 40% believed that breast cancer was incurable. This finding suggests that some women may view screening as a futile exercise that leaves one with a diagnosis and, at best, a quiescent disease.

Conclusion: Study results highlight the possibility of women harbouring misconceptions regarding breast cancer and its treatment. In view of the rising incidence of breast cancer among Singaporean women, this study calls attention to an urgent need for efforts aimed at correcting prevalent false beliefs and encouraging women to participate in the screening programme, enabling the medical fraternity to effectively address the disease.

Doctors' Category: D26

Providing acupuncture for patients with chronic knee pain at Yishun Polyclinic

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Introduction: Acupuncture, which is one of the best known complementary and alternative therapies, originated more than 3,000 years ago in China. It is part of the therapeutic methods used in traditional Chinese medicine (TCM), with its theories based on the doctrine of channels. In recent years, acupuncture has gained popularity and wide usage locally, especially in the management of acute and chronic pain. On October 13, 2008, Yishun Polyclinic started its acupuncture clinic, which offers acupuncture therapy as a complementary modality to patients with painful musculoskeletal conditions.

Methods: 23 patients with chronic knee pain for more than six months were referred to the acupuncture clinic by the polyclinic doctors with a diagnosis of osteoarthritis of the knees. All the patients were treated with eight sessions of acupuncture at intervals of 4–7 days, by the same acupuncturist who used similar acupuncture points.

Results: Using the Wong-Baker Faces Pain Rating Scale, 55% of the patients achieved a 50% improvement in the pain score at completion of all the sessions.

Conclusion: This unique complementary health model utilising both scientific medicine and acupuncture is set to be highly popular in the evolving model of integrative medicine. This is especially important in polyclinics, which provide both primary healthcare services and pain management.

Doctors' Category: D28

Incision and drainage versus saucerisation in the treatment of cutaneous abscesses: a randomised controlled trial

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Introduction: Cutaneous abscesses are mostly treated by saucerisation in Singapore, although they result in a large skin defect and have long healing times. Incision and drainage (ID) is considered inferior as an alternative because of the recurrent suppuration caused by the perceived premature closure of the drainage wound. However, historic data suggests that ID is equally effective in draining such abscesses. This randomised control study aimed to establish that ID is not inferior to saucerisation as a treatment option for cutaneous abscesses, but has instead the advantage of faster healing and better cosmesis.

Methods: Approval for the study was obtained from the institutional review board. 98 patients who required drainage of cutaneous abscesses at Alexandra Hospital, Singapore, between December 2007 to October 2009 were recruited for the study and randomised into two treatment arms, ID and saucerisation, after obtaining informed consent. Randomisation was carried out using a sealed envelope and assignment of treatment was carried out using a computer programme. The procedures were performed by on-duty surgical teams at Alexandra Hospital using predetermined protocols. The patients were followed up after operation and data was collected on wound closure and complications. The primary endpoint of the study was the time taken for complete healing of the surgical wound.

Results: 49 patients were recruited in each treatment group. Patient characteristics, such as age, gender distribution and presence of comorbidities, were comparable between the two groups. The mean healing time for the ID and saucerisation groups was 24.34 days and 45.84 days, respectively. One patient from each group required reoperation. Statistically, the ID group healed significantly faster without any increase in the abscess recurrence rates.

Conclusion: This study provides level 1 evidence that ID is a superior surgical option for treatment of abscesses when compared to saucerisation.

Doctors' Category: D29

Influence of injury characteristics and timing of primary surgical repair on visual outcome of open globe injury

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Introduction: This study was conducted to determine the influence of injury characteristics and timing of primary surgical repair on the visual outcome of open globe injury.

Methods: 75 consecutive patients with open globe injury that were repaired surgically over a period of one year were retrospectively analysed. Data collected included demographic details, nature of injury and the initial and final best-corrected visual acuities (BCVA). The BCVA was graded as > 20/40, 20/50 to 20/100, 19/100 to 5/200, 4/200 to light perception (PL), and no light perception (NPL). The zone of injury was defined as isolated to cornea including the corneoscleral limbus (zone I), limbus to a point 5 mm posterior to the sclera (zone II), and posterior to the anterior 5 mm of the sclera (zone III). All patients were classified as either positive or negative for relative afferent pupillary defect (RAPD) in the affected eye. In addition, the patients were categorised into three groups based on the time interval from injury to primary surgical intervention as group I (< 24 hours), group II (24–36 hours), and group III (> 36 hours). The groups were compared with each other with respect to the various parameters studied. The chi-square test was used for comparison of categorical data. A p-value of less than 0.05 was considered significant.

Results: On analyses, statistically significant associations were found between final visual outcome and the presenting BCVA ($p < 0.05$), zone of injury ($p < 0.05$) and presence of RAPD ($p < 0.001$). No significant difference in the postoperative BCVA was found between the early and late repair groups ($p > 0.05$).

Conclusion: The presenting BCVA, zone of injury and RAPD were associated with a better final visual outcome following surgical repair in patients with open globe injury. The timing of intervention did not significantly alter the visual outcome in these patients.

Doctors' Category: D31

Uncommon benign breast tumours

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Pseudoangiomatous stromal hyperplasia (PASH) is a benign tumour arising from myoepithelial cells of unknown aetiology and pathogenesis. Reports have suggested an association between PASH and the hormonal fluxes occurring during the perimenopausal period in women. PASH is usually managed by wide local excision (WLE), with a reported recurrence of 15%–22%. Adenosis tumour is not associated with increased risks of developing breast cancer. Similarly, fibrocystic changes without atypical epithelial components are not associated with any oncologic risks. However, studies have reported patients with adenosis tumour along with non-infiltrating carcinoma. Most breast tumours in adolescents are fibroadenomas, with juvenile fibroadenomas typically being 1–10 cm in size and occurring at age 10–18 years. Fibroadenomas less than 5 cm are managed conservatively due to the low malignant risk in this age group. In this report, we present four uncommon benign breast tumours that were diagnosed accurately on core biopsy. Case A was a 53-year-old postmenopausal Chinese woman who underwent WLE of a 2.3 cm solitary breast lump. Histology showed benign mesenchymal proliferation consistent with nodular PASH, with positive CD34 staining. Case B was a 56-year-old postmenopausal Malay woman who presented with a 8 cm left breast mass and a 7 cm left axillary mass over a five-month period. Ultrasonography of the breast and axilla showed well-circumscribed and homogeneous hypoechoic masses measuring 8 cm and 6 cm, respectively. The patient underwent mastectomy with excision of the axillary lump. Histology showed PASH with fibroadenomatoid features positive for CD34 and CD31. Case C was a 17-year-old Malay girl who presented with a 5 cm mass in the left breast. She underwent WLE and histology showed juvenile fibroadenoma. Case D was a 41-year-old premenopausal Chinese woman who underwent WLE of a 2 cm solitary breast lump. Histology showed adenosis tumour with fibrocystic changes.

Doctors' Category: D32

Correlation between the integrity of the plantar arch and the number of runoffs and amputation rates in patients with peripheral vascular disease

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Introduction: This study aimed to determine the effect of the integrity of the plantar arch and the number of runoffs in legs on amputation rates in patients with peripheral vascular disease (PVD). We hypothesised that a good plantar arch or higher number of runoffs may be associated with a lower amputation rate.

Methods: This was a retrospective study of all patients who underwent angiographic study of the lower limb from June 1, 2008 to January 22, 2010.

Results: The study group (n = 90) had 48 men and 42 women. 19 patients had bilateral disease while 71 patients had unilateral disease. 156 angiograms were performed. Indications included PVD (89.9%), acute limb thrombosis (9.2%) and Raynaud's disease (0.9%). Average age was 68 (range 36–97) years. Common comorbidities included hypertension (76.7%), diabetes mellitus (87.8%) and hyperlipidaemia (65.6%). The plantar arch was good in 15 patients, moderate in 28 patients and poor in 60 patients. Among patients with a good plantar arch, 11 patients did not need any amputation, two required ray amputations (RA) and two needed below-knee amputations (BKA). Among patients with moderate arches, 18 patients did not need an amputation, five underwent RA, one had transmetatarsal amputation (TM) and four underwent BKA. In those with poor arches, 43 patients did not need an amputation, eight had RA, four needed TM, four underwent BKAs and one needed an above-knee amputation (AKA) [$p > 0.05$]. There were no runoffs in four patients, one runoff in 56 patients, two runoffs in 31 patients and three runoffs in 18 patients. In patients with three runoffs, 14 needed no surgery, two underwent RA, one had TM and one needed BKA. In those with two runoffs, 21 patients needed no amputation, six had RA, one required TM and three needed BKAs. Among patients with one runoff, 39 patients did not need surgery, seven had RA, four needed TM, five underwent BKAs and one had AKA ($p > 0.05$).

Conclusion: Study results suggest that the integrity of the plantar arch and the number of runoffs do not influence the level or rate of amputation in patients with PVD.

Doctors' Category: D33

Use of radioisotope and blue dye for sentinel lymph node identification: a single surgeon's results

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Introduction: The blue dye method and radioisotope technique are used to reduce routine axillary clearance (AC) during sentinel lymph node (SLN) identification. Our aim was to determine whether the blue dye alone could satisfactorily achieve SLN identification when compared with the radioisotope technique or dual studies.

Methods: This was a single-surgeon prospective study of 74 consecutive patients from July 1, 2006 to October 30, 2009. SLN was detected preoperatively by injecting 2 MBq radioisotope into the subareolar region and performing an axillary scan. Intraoperatively, 2 ml methylene blue was injected into the subareolar region with a five-minute massage. Dye staining was scored as negative when there was no uptake (0), and positively stained for light uptake (1+), moderate uptake (2+) and strong uptake (3+). A gamma probe radioisotope counter was used to pick up radioactivity in the periareolar region and background. This was then used to locate SLN in the axilla to settle the place of incision over an area of maximal count. The SLN with the highest count was taken as the first SLN using a ten-second count. The other SLNs were required to be 10% of the highest node or blue stain positive.

Results: 138 SLNs were identified in total. 73 SLNs were identified in 53 (71.6%) patients using the dye technique while radioisotope helped identify 122 SLNs in 71 (95.9%) patients. The two methods had a 100% combined identification rate. Mean time taken for SLN biopsy was 31.61 minutes. The average number of SLNs harvested was 1.85. 21 patients had positive SLN on immunohistochemistry; 19 (90.4%) were detected by the dye and 21 (100%) by the radioisotope. 19 patients went on to have AC while two did not. Seven patients had positive SLN and AC. 14 patients had positive SLN but negative AC. Three (4.1%) patients underwent mastectomy and 95.9% of patients underwent wide local excision.

Conclusion: Study results indicate that the blue dye method is less effective than the radioisotope technique for SLN identification. Although radioisotopes can be used alone, best results are achieved following dual localisation.

Doctors' Category: D34

Metaplastic breast carcinoma: a case report

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Metaplastic breast carcinoma (MBC) is a rare form of breast cancer, occurring in less than 1% of patients. MBC is heterogeneous and characterised by epithelial or mesenchymal cells with adenocarcinoma. Although Wargotz et al originally divided MBC into five histological subtypes, more subtypes have since been identified. Clinically, it presents with larger tumour size and few lymph node metastases, with frequent systemic metastases to the lungs. A high proportion of these tumours are triple-negative. A large tumour size and triple-negative status have implications for both treatment and prognosis, as such patients do not benefit from hormone or targeted therapy and chemotherapy is often needed. Preoperative histology of MBC could, however, allow for a mastectomy without axillary nodal clearance (ANC). MBC displays more aggressive behaviour than typical breast cancer, with almost all tumours showing recurrence in the first five years. Long-term follow up is necessary for this tumour regardless of hormone receptor status. We report a 54-year-old woman who presented with a painless left breast lump noticed three weeks ago. Menstrual and family histories were unremarkable. Medical history revealed a benign mass in the left breast that was excised 23 years ago. On clinical examination, a 5 cm × 5 cm central breast lesion was found with skin tethering and nipple retraction. No palpable axillary lymph nodes were found. Ultrasonography and mammogram showed a lobulated partially defined non-homogeneous hypoechoic mass measuring 52 mm × 50 mm × 32 mm with irregular cystic foci (BIRADS 4). Core biopsy showed grade invasive ductal carcinoma with negative estrogen receptor, progesterone receptor and HER-2 status. Liver ultrasonography and bone scintiscan were unremarkable. The patient underwent a left simple mastectomy with ANC. A retroareolar tumour measuring 4.5 cm was also observed. Histology showed a 60 mm × 41 mm × 37 mm matrix-producing poorly differentiated carcinoma with chondroid mesenchymal differentiation (Grade 3) but no lymphovascular invasion. Hormone receptor status was triple-negative. Axillary lymph nodes were negative.

Doctors' Category: D35

Does home cycloplegia for children help in turnaround times in busy ophthalmic practice?

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Introduction: Cycloplegic refraction is carried out in children to paralyse the ciliary muscles in order to eliminate accommodation, which can otherwise mask hyperopia. Patients currently undergoing such refraction need to wait for the cycloplegic eye drops to work after they have been instilled when they are in the eye clinic. This study aimed to determine whether home cyclopegia could help reduce waiting time for patients undergoing such refraction.

Methods: Patients requiring cycloplegia on arrival at Jurong Medical Centre, Singapore, from August to September 2010 were identified by looking through the appointment schedule. These patients were randomly assigned into two groups; the home cycloplegia group and the cycloplegia on arrival group. Waiting times before patients saw the eye doctor were recorded and compared.

Results: 14 patients underwent home cycloplegia and 20 underwent cycloplegia on arrival. The two groups were comparable for age ($p = 0.102$). The home cycloplegia group showed an improvement in waiting time ($p < 0.001$) and a reduction in the total number of eye drops instilled ($p < 0.05$).

Conclusion: Home cycloplegia showed an improved waiting time for patients requiring cycloplegic refraction and their parents. This will also help improve patient and parent satisfaction at the clinic.

Doctors' Category: D36

Laparoscopic fingeroscopic appendicectomy aids dissection in complicated acute appendicitis

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Introduction: Laparoscopic fingeroscopic appendicectomy was described in 1999 by Katkhouda to reduce conversion rates to open surgery for patients requiring complicated appendicectomy. We describe our experience with this procedure with a video segment.

Methods: When a difficult appendicectomy is anticipated on initial evaluation by laparoscopy, an additional 10 mm port is placed in the right iliac fossa (RIF) just below or caudal to the appendix instead of at the suprapubic port. The index finger replaces the RIF port and is then used to gently dissect the appendix from adhesions similar to the open method. This gives tactile feedback that is lost in the standard laparoscopic approach.

Results: Four patients with appendiceal phlegmon underwent appendicectomy; three procedures were successfully completed laparoscopically and one required conversion to open surgery following perforation in the pelvis by the fingertip during finger dissection.

Conclusion: Fingerscopy has several benefits. It does not require any additional instruments, as all instruments are available in the standard laparoscopic set, there is no learning curve for surgeons as it borrows on techniques from the open method, and it reduces conversion to open surgery even for patients with complicated appendicitis.

Doctors' Category: D37

A multimodality approach for the treatment of Dialysis-access Steal Syndrome with preservation of vascular access

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Introduction: Dialysis-access Steal Syndrome (DASS) is a devastating complication of vascular access surgery that results in ischaemia of the limb. Although simple ligation of the fistula is the simplest method of treating Steal Syndrome, the problem of dialysis access persists in this approach. Moreover, DASS could recur during the subsequent dialysis access procedure. We report the outcome of a multimodality approach that treats renal failure patients with DASS but preserves the vascular access at the same time.

Methods: A retrospective review was conducted of all patients with DASS who were treated at a tertiary institution over one year by the same surgeon. Upper limb arterial duplex was performed immediately for all DASS patients with no immediate risk of limb loss. Arteriogram was performed if the duplex study suggested suspicion of radial or ulnar artery disease. Angioplasty was performed in the same session if a treatable lesion was identified. For patients with arteriovenous fistula and large size outflow vein, banding or refashioning of the anastomoses was the first line of treatment. Proximal brachial artery to distal vessel bypass with or without interval ligation was performed for those with failed first-line treatment. Intraoperative duplex was used to help assessment of the fistula and native arterial flow condition. Data collected included patient demographics, type of procedure, outcome in terms of resolution of ischaemia and preservation of vascular access and complications, if any.

Results: Seven of 76 (9.2%) patients with vascular access operations developed DASS. Majority were women (male-to-female ratio 2:5). Median age of the group was 62 years. All patients had upper arm arteriovenous fistulae or grafts that required brachial artery inflow (three brachiocephalic, three brachiobasilic and one brachioaxillary). Nine procedures were performed in total for the seven DASS patients, including one angioplasty of the radial artery, three bandings, two refashioning of fistula anastomosis, two bypasses without interval ligation and one distal revascularisation interval ligation. Two of three patients who underwent banding needed further procedures (one refashioning and one bypass) to alleviate their ischaemic symptoms. One patient died in the early postoperative period due to acute myocardial infarction and one patient had wound infection. None of the DASS patients had tissue loss or persistent deformity or disability of the hand and finger after treatment. Dialysis access was successfully preserved in all patients.

Conclusion: A multimodality approach to DASS can achieve the aim of ischaemia correction while preserving the vascular access at the same time.

Doctors' Category: D38

Acute kidney injury secondary to focal renal cortical necrosis

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Renal cortical necrosis is an unusual presentation in adults, with involved mechanisms being vascular spasm, microvascular injury, or intravascular coagulation. However, there is also a possibility for thromboembolic phenomena, as in the patient reported here. We report a 27-year-old previously healthy Indian man, who presented with non-oliguric acute kidney injury and a one-week history of acute gastroenteritis. The patient was a smoker, and appeared dehydrated clinically

although no hypotension was documented. Serum creatinine and blood urea levels were 1,544 umol/L and 43 mmol/L, respectively. Metabolic acidosis, microscopic haematuria and proteinuria of 0.5 g/dl were noted. There was no evidence of haemolysis. Although ultrasonography of the kidney was unremarkable, a renal biopsy was performed in view of persistent elevated urea and creatinine levels despite rehydration. Histology revealed focal cortical necrosis and acute tubular injury without features of thrombotic microangiopathy. The patient's serum creatinine gradually improved to 374 umol/L. Ultrasonography of the renal artery was unsuccessful. However, the patient returned three weeks later with acute left lower limb ischaemia, and underwent embolectomy for femoral artery thrombi. A thrombophilia screen was negative except for raised homocysteine levels (49.3 umol/L), which was of uncertain significance. Transthoracic echocardiogram revealed left ventricular thrombus. The patient was started on anticoagulant therapy. The serum creatinine at discharge was 249 umol/L. It is possible that the history of diarrhoea in this patient might have precipitated a hypercoagulable state. The presence of left ventricular thrombus could also have contributed to thromboembolic events in the kidneys and lower limb. Epidemiological studies have suggested that mild hyperhomocysteinemia is associated with thrombotic risk in the absence of renal disease. Further studies are needed to confirm this association, as homocysteine levels are known to be elevated in renal failure.

Doctors' Category: D39

Early experience of laparoscopy-assisted distal gastrectomy for gastric cancer in Singapore: a case control study and cost analysis

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Introduction: This study investigated the short-term outcomes of the initial experience with laparoscopy-assisted distal gastrectomy (LADG) for early gastric cancer and compared the economic cost of LADG with open surgery.

Methods: Clinical and pathological data were prospectively collected for patients who underwent LADG with nodal dissection for stage I or II gastric cancer. 21 patients treated between 2005 and 2009 were included in the LADG group. Patients who underwent conventional open distal gastrectomy (CODG) during the same period were matched to the LADG group for demographics and clinical and pathological variables. Perioperative data, short-term postoperative outcomes, patient satisfaction and economic cost were compared between the LADG and CODG groups.

Results: LADG was associated with longer operation time (295 ± 83 vs. 241 ± 62 minutes, p = 0.001), reduced blood loss (239 ± 125 ml vs. 335 ± 143 ml, p = 0.008), less postoperative pain (pain score on postoperative Day [POD] 1: 2 vs. 3, p = 0.001; score on POD 2: 1 vs. 2, p = 0.003), less requirement for analgesics (morphine: 52 ± 47 mg vs. 62 ± 14 mg, p < 0.001), faster recovery of bowel function (5 [range 4–8] days vs. 6 [range 4–10] days, p = 0.001), early ambulation (4 [range 3–7] days vs. 7 [range 4–11] days, p ≤ 0.001) and shorter hospital stay (7 [range 5–103] days vs. 9 [range 5–66] days, p = 0.011) when compared to CODG. Complication rates were similar between the two groups. The number of resected lymph nodes was comparable (24 ± 10.40 vs. 25 ± 15.16, p = 0.364). LADG achieved a higher degree of patient satisfaction. Total hospitalisation bills were similar for both groups (US$8,946 ± US$30,127 vs. US$9,256 ± US$11,112, p = 0.653).

Conclusion: LADG with lymph node dissection is a safe treatment option for early gastric cancer. Recovery is faster in patients undergoing LADG although the technique is comparable to open resection for radicality. In addition, LADG ensures increased patient satisfaction, without inviting an appreciable increase in the costs incurred.

Nursing and Allied Health Category: NA01

Assessment for frailty is useful for predicting morbidity in elderly patients undergoing colorectal cancer resection whose comorbidities are already optimised

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Introduction: Elderly patients undergoing major colorectal surgery have a relatively higher morbidity rate. This happens even when the comorbidities have been adequately optimised. We hypothesised that frailty is useful in predicting adverse outcomes in optimised elective elderly patients undergoing colorectal surgery.

Methods: A prospective study was conducted at two centres, Singapore and Japan. All patients over 75 years undergoing colorectal resection were assessed for the presence of frailty based on assessment of weight loss, physical exhaustion, physical activity level, grip strength and walking speed. All assessments were performed by a nurse clinician in Singapore. Frailty was classified as positive when three of five criteria were satisfied. All patients had already had their comorbidities optimised for surgery. Outcome measures were major postoperative complications. The study was approved by ethics committees in both Singapore and Japan.

Results: 75 patients were studied from February 2008 to April 2010. Mean age was 81.5 (range 75–96) years. Mean comorbidity index was 3.2 (range 0–11). 19 (24.4%) patients were ASA 3 and above. Chi-square analysis revealed that the odds ratio of major postoperative complications was 7.05 (95% CI 2.288–21.721) when the patient satisfied the criteria for frailty. Albumin < 35, ASA > 3, comorbidity index > 5 and POSSUM scores were not predictive of major postoperative complications.

Conclusion: Preliminary findings show that the assessment of frailty by a trained nurse is a potent adjunctive tool for predicting postoperative morbidity. Frailty can be used to identify elderly patients needing further optimisation prior to major surgery.

Nursing and Allied Health Category: NA02

A dedicated nurse clinician has a positive impact on elderly colorectal surgery patients

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Introduction: We hypothesised that a dedicated nurse clinician (NC) plays an important role in improving the outcomes of elderly patients undergoing colorectal surgery.

Methods: We studied the nursing care of 81 patients aged over 75 years who underwent major colorectal resections from January 2007 to July 2010. A review of the prospectively collected database was performed. Nursing failures identified included inaccurate documentation, delayed recognition of deterioration, non-compliance of orders and improper discharge planning. Statistical analyses were performed using chi-square and *t*-tests. Cumulative Summation (CuSum) methodology was used to plot sequential performance of nursing care, with the minimum standard set at 70% success. Sequential performance of the Geriatric Surgery Service (GSS), Khoo Teck Puat Hospital, Singapore, which introduced a NC to their management protocol, was compared to the performance of standard service.

Results: 22 patients managed perioperatively by a NC were compared to 59 patients who were managed without one. There were no significant differences in the mean age, ASA scores, comorbidity index and POSSUM model predicted morbidity and mortality rates in both groups. Patients not managed perioperatively by a NC had five times the

risk of major complications (OR 5.34, 95% CI 1.43–20.02). Overall nursing failures were lower in the NC group at 13.3% compared to 33.9% in the group without NC, although the difference was not statistically significant (p = 0.07). CuSum curve indicated that sequentially consistent good nursing care was rendered to the patients after inclusion of a NC, which was in contrast to patients managed without a NC.

Conclusion: Results support the premise that a dedicated NC has a positive impact on the nursing standard and outcome of elderly patients undergoing colorectal surgery.

Nursing and Allied Health Category: NA03

Peripheral intravenous catheter-related complications from routine replacement versus clinically indicated replacement: a systematic review

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Introduction: Communicable Diseases Centre (CDC), Singapore, and Ministry of Health (MOH), Singapore, guidelines advocate the routine replacement of peripheral intravenous catheters (PICs) every 72 hours. However, both guidelines have not been reviewed since 2002. This systematic review aimed to evaluate the relationship between PIC indwell time and the incidence of catheter-related complications, as well as to investigate the efficacy of routine replacement vs. clinically indicated replacement of PICs for preventing complications in adult patients in an acute inpatient local setting.

Methods: An exhaustive literature search was conducted on 15 databases including hospital databases, the Internet, MOH Clinical Practice Guidelines, and Local Hospital Standard of Practice from 1998 to February 2009 using keywords, such as nursing, systematic review, adult patients, peripheral intravenous catheter, intravenous cannula, duration, indwell time, catheter/cannula-related, infection, complications, obstruction, phlebitis, infiltration and extravasations. The review included randomised controlled trials (RCTs) and cohort studies related to PIC indwell time and complications in an adult inpatient setting. Five reviewers assessed the data found to satisfy predetermined criteria. Outcome measures considered were phlebitis, catheter-related infections, catheter-related complications, obstruction of the catheter, infiltration and extravasations. Studies were analysed utilising the Scottish Intercollegiate Guidelines Network (SIGN 50) methodological appraisal checklist. The CDC and MOH practice guidelines were evaluated using the Appraisal of Guidelines for Research & Evaluation (AGREE) Instrument assessment tool.

Results: Eight studies were selected for review, of which two were RCTs and six were cohort studies. All articles suggested that clinically indicated replacement of PICs reduce the incidence of phlebitis and severity of complications when compared to routine replacement as per MOH guidelines.

Conclusion: An assessment of available evidence did not reveal any conclusive evidence supporting a relationship between PIC indwell time and the incidence of catheter-related complications. Study results highlight the need for a reexamination of current guidelines in view of recent evidence challenging the need for routine replacement of PICs in an inpatient setting.

Nursing and Allied Health Category: NA04

Predictors of progression of moderately advanced diabetic nephropathy secondary to type 2 diabetes mellitus

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Introduction: Diabetic nephropathy (DN) secondary to type 2 diabetes mellitus (T2DM) is a leading cause of end-stage renal disease. The natural history of DN is heterogenous. KDOQI (Kidney Disease Outcomes Quality Initiative) recommends the control of certain factors for retardation of DN progression. We examined these factors in patients attending the DN clinic at Khoo Teck Puat Hospital, Singapore, to determine whether they correlated with the likelihood of worsening renal function.

Methods: Among 257 DN patients attending the clinic over a two-year follow-up period, 70 patients were identified as progressors, with serum creatinine levels elevated ≥ 50%, and 89 patients were identified as non-progressors, with serum creatinine levels either improving or increasing by < 10%. Univariate (Student's *t*-test) and multivariate (binary logistic regression) analyses were performed. Area under the receiver-operator-curve (ROC; C statistics) was used to explore the parameter test for discriminating progressors from non-progressors.

Results: At baseline, progressors and non-progressors showed similar distribution for gender (men 55% vs. women 53%, p = 0.71), age (59 ± 11 years vs. 59 ± 11 years, p = 0.89), duration of diabetes mellitus (14 ± 8 years vs. 12 ± 8 years, p = 0.27), HbA1c (8.4 ± 2.2% vs. 8.0 ± 2.0%, p = 0.34) and serum creatinine (166 ± 84 uM vs. 156 ± 88 uM, p = 0.48). However, baseline systolic blood pressure (SBP; 159 ± 23 mmHg vs. 144 ± 20 mmHg, p < 0.01), diastolic blood pressure (DBP; 83 ± 13 mmHg vs. 79 ± 11 mmHg, p = 0.027) and urinary albumin-creatinine ratio (ACR; 2,562 ± 1,864 mg/g vs. 858 ± 1,022 mg/g, p < 0.01) were significantly higher among progressors. Multivariate analysis revealed baseline SBP, DBP and urinary ACR as strong independent predictors of DN progression (p < 0.01). SBP had the best discriminative performance (C statistics 0.823, 95% CI 0.73–0.91; p < 0.01). SBP of approximately 146 mm Hg had ~80% sensitivity and specificity for identifying progressors.

Conclusion: Among the DN patients studied, clinical measurements, such as SBP, DBP and ACR, were strong and independent predictors of worsening renal function. These findings may be helpful in identifying individuals who require intensive renal retardation interventions.

Nursing and Allied Health Category: NA05

Inpatient diabetes training for nurses: using interactive sharing, case-scenario experiential learning and ground-practice observations to strengthen learning effectiveness

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Introduction: An inpatient diabetes training programme was recently initiated for nurses, with an emphasis and design that focuses on interactive sharing and experiential learning and highlights on-the-ground incidents. The objective was to encourage participation, enhance understanding and create awareness of current diabetes-related ward issues. This study aimed to assess the effectiveness of this training. A set of diabetes care assessment questionnaires was

instituted for use both before and after the training was conducted.

Methods: Two rounds of inpatient diabetes training were conducted for nurses in 2009. Training included ice-breaking sessions, a quick run-through of important must-know information, real scenario-based case discussions, hands-on sessions on hypoglycaemia treatment and insulin administration, sharing on specific ground situations and misses as well as difficulties faced on the ground. A set of 20 questions was administered immediately before and after the training. The paired *t*-test was used to compare pre- and post-training test scores.

Results: A total of 27 registered nurses and one principal assistant nurse from the inpatient wards of Alexandra Hospital, Singapore, participated in the training. Participants were from the medical, surgery, orthopaedic or geriatric wards, and had experience nursing patients with diabetes mellitus and its related comorbidities. The mean length of experience post registration was 9.75 years. The post-training assessment revealed an improvement in the mean correct answers given from 61.42% (pre-test) to 90.36% (post-test), with significant improvement ($p < 0.05$) on 17 paired questions; four were hypoglycaemia related, five were insulin related and eight were diabetes related.

Conclusion: Interactive group learning, experiential scenario sharing and realisation of current issues helps create better understanding and improves knowledge retention among nurses. Individual vigilant observation and care can contribute toward better care of patients with diabetes mellitus.

Nursing and Allied Health Category: NA06

Risk of raised serum creatinine and potassium levels in patients treated with ACEIs or ARBs among type 2 diabetes mellitus patients with albuminuria and/or hypertension

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Introduction: Angiotensin converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) are recommended as antihypertensive treatment for patients with diabetes mellitus and albuminuria. Hyperkalaemia and serum creatinine elevation are two common concerns. In our centre, for patients with Stage 1–3 chronic kidney disease (CKD), ACEIs or ARBs are titrated by diabetes nurse educators (DNEs) based on an algorithm that recommends lowering the dose or discontinuing these medications should serum creatinine level rise by more than 20% or when serum potassium rises above 5.2 mmol/L. This study evaluated the risk for raised serum creatinine and potassium among Stage 1–3 CKD diabetes patients with albuminuria and/or hypertension who were treated with ACEIs/ARBs.

Methods: Patients with diabetes mellitus who were prescribed ACEIs or ARBs for treatment of hypertension or albuminuria were assessed at baseline and within four weeks of initiation or uptitration for serum potassium, creatinine, estimated glomerular filtration rate (eGFR), and other clinical variables.

Results: 112 patients with type 2 diabetes mellitus (Stage 1 CKD 43.75%, Stage 2 CKD 36.60%, Stage 3 CKD 19.64%) who were treated with ACEIs/ARBs were included in the analysis. Mean age (55.9 years), HbA1c (8.1%), systolic blood pressure (137.7 mmHg) and diastolic blood pressure (73.6 mmHg) were noted. 36.6% patients were normoalbuminuric; 38.4% patients had microalbuminuria while 25% had macroalbuminuria. Only 4.46% patients (n = 5; Stage 1 CKD 1, Stage 2 CKD 4) had creatinine elevation of more than 20% after exposure/dose escalation of ACEI/ARBs. Similarly, only 3.57% patients had serum potassium more than 5.2 mmol/L (n = 4; Stage 1 CKD 2, Stage 2 CKD 2).

Conclusion: Study results indicated an approximate 4.5% risk of significant elevation of creatinine and 3.6% risk of elevation of potassium to be associated with the use of ACEIs/ARBs in diabetes patients with Stage 1–3 CKD. If confirmed by a larger study, the need for reevaluation of serum creatinine and potassium within four weeks of ACEI/ARB initiation/uptitration in early-stage CKD could be reviewed.

Nursing and Allied Health Category: NA08

Registered nurses' perceived competence in asthma care: a survey

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Introduction: Patient education improves outcomes in asthma. Besides the asthma nurse educator, ward registered nurses (RNs) must be prepared and confident to discuss asthma management with their patients under any setting. Locally, no study has evaluated the competence of nurses in asthma care. This study aimed to determine the perception of competence among RNs in asthma care.

Methods: A 26-question survey was developed, piloted and sent to all RNs across the wards. The questionnaire covered areas on asthma definition, causes/triggers, diagnosis, classification, control, management, use of inhaler techniques and patient education. All RNs were asked to answer questions based on honest self evaluation of competence in the subject matter as 'yes, I know', 'no, I don't know', or 'not sure'.

Results: 297 (82%) RNs responded to the survey. The proportion of 'yes' answers was 66%, 'no' was 8%, and 'not sure' was 26%. Chi-square analysis showed no association between RNs' perception of competence and designation or gender. An analysis of departmental affiliation showed a statistically significant association only for questions 23 and 24 ($p < 0.05$), where a significant number of nurses reported as 'not sure' what asthma exacerbation was and 'no' to confident enough to provide asthma education to patient/family/caregiver. RNs who had previous asthma training perceived more competence in asthma care across most questionnaires (chi-square, $p < 0.05$).

Conclusion: RNs perceived suboptimal competence in asthma care. Nurses who had previously received asthma training apparently felt more competent than those who were without such training. Survey results highlight the urgent need for in-house asthma training to ensure that every RN is confident of providing basic asthma education in the course of duty.

Nursing and Allied Health Category: NA09

Antidepressant treatment and psychosocial intervention improves depression, diabetes mellitus control and quality of life in diabetic patients

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Introduction: Patients with diabetes mellitus are at higher risk of developing depression than non-diabetics. However, the need to provide and evaluate appropriate intervention for depression or distress in these patients is under-recognised. This longitudinal study assesses the efficacy of antidepressant and psychosocial interventions in improving depression, HbA1c and quality of life in these patients.

Methods: 211 outpatients were screened using the Center for Epidemiologic Studies Depression Scale (CES-D), Problem Areas in Diabetes (PAID) and World Health Organization Quality of Life-Brief (WHOQOL-BREF). 39 (18.5%) patients screened had scores of CES-D ≥ 16 or PAID ≥ 40, reflecting high levels of depressive symptoms or diabetes-related distress, while 20 (9.5%) patients had both. Patients with CES-D ≥ 16 and diagnosed with depression were treated with antidepressants and received counselling, while the rest received counselling only. Within six months to one year, 23 patients completed the same instruments. Change in HbA1c was also recorded.

Results: Patients reported a significant decline in CES-D (t[22] = 6.68, p < 0.01) and PAID (t[22] = 4.07, p = 0.001). 70.6% of patients with initial CES-D ≥ 16 fell below the cutoff values, while 78.6% of patients with PAID ≥ 40 reported scores below the cutoff. There was significant increase in quality of life in the physical (t[22] = 5.18, p < 0.01) and psychological domains (t[22] = 2.59, p = 0.017), but not in the social and environmental domains. There was no significant change in HbA1c, but 60.9% of patients had lower HbA1c readings compared with baseline.

Conclusion: Antidepressant and psychosocial interventions were able to reduce depression and diabetes-related distress and improve quality of life in patients with diabetes mellitus. More than half of the patients showed improved diabetes control, although the mean improvement in HbA1c for the group was not significant. This could be due to the small sample size of the present study, limited range of values for HbA1c and the effect of patients who did not show improvement. However, study results demonstrate the importance of screening for depression and providing appropriate intervention.

Nursing and Allied Health Category: NA10

Patient medication list: improving patient's understanding and adherence to medication regime

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Introduction: Inadequate understanding of medication, their indications and adverse effects often leads to poor adherence among patients, resulting in negative patient health outcomes. This study aimed to determine the impact of a personalised patient medication list (PML) on patients' understanding of their medication and identify the patients who were more likely to benefit from the PML in a hospital setting.

Methods: Patients on three or more chronic medications were prospectively studied over four months. A drug database with names, corresponding images, pronunciation, common indications, side effects and patient advice was created along with a standard template. Upon recruitment, this template was personalised with the patient's medication and corresponding information from the drug database to generate the PML. Baseline understanding of medication was assessed at recruitment and follow-up appointment via direct interviews. Pearson's correlation and paired sample t-test were used for statistical analyses.

Results: 93 patients were recruited of which 41 completed the study. Overall understanding of medication (p = 0.000), administration (p = 0.005) and awareness of indication(s) (p = 0.015) were areas which showed statistically significant improvement after the provision of PML. Patients on more medications had poorer understanding, especially with regard to indication(s) (p = 0.001). Stratified analysis showed that patients on 5–8 medications (n = 24) had the most knowledge improvement, particularly in overall understanding (p = 0.002), knowledge of adverse effects (p = 0.015), indication(s) (p = 0.033) and administration (p = 0.047). More than 60% of patients strongly agreed that PML was useful in improving their understanding and in managing their medication regime and that they would like to continue receiving it.

Conclusion: PML significantly improves patients' overall understanding of medication, their administration and knowledge of their indication(s) in a hospital setting. Patients on 5–8 medications benefited most from provision of a PML.

Nursing and Allied Health Category: NA12

Gerontological care in nursing education programmes

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Introduction: While in recent years the average age of patients has increased, nurses do not always have the knowledge, competencies or attitudes necessary to care for older people. The complexities of caring for elderly patients are also not recognised. This report is of a study conducted to identify the coverage of gerontological care in diploma and degree nursing programmes.

Methods: A descriptive cross-sectional survey of three nursing education programmes in Singapore was conducted. The three institutions included in the study were Nanyang Polytechnic and Ngee Ann Polytechnic, which provide a three-year diploma in nursing, and National University of Singapore, which provides a three-year nursing degree programme.

Results: While there was great variability among nursing education programmes in terms of gerontology courses, clinical placements and number of experts, it was encouraging that most programmes had integrated gerontology content into non-gerontology courses, all programmes offered gerontology clinical placements, and many nursing educators and clinicians were considered to be experts in gerontology. Lack of interest in care for older people in general, lack of gerontology-related competencies within curricula, and a negative image of gerontological care were reported as the most frequently-encountered barriers to incorporating gerontological care aspects into curricula.

Conclusion: Gerontology content in basic nursing curricula should be increased in view of the rising trend in the average age of patients needing nursing care. A minimum standard curriculum and specific competencies for care of older people should be formulated for all diploma and degree nursing education programmes. Strengthening educators' expertise and investing in role models, such as clinicians in gerontology care, remain important priorities for the nursing profession.

Nursing and Allied Health Category: NA13

Registered nurses' knowledge of nursing documentation in geriatric wards

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Introduction: Registered nurses' (RNs) knowledge of nursing documentation is important, as its purpose is to communicate health information, facilitate quality assurance and research and demonstrate the nurses' accountability. This study investigated RNs' knowledge of the documentation used in two geriatric wards in Khoo Teck Puat Hospital, Singapore.

Methods: A cross-sectional retrospective study was conducted on a sample of 40 RNs in two geriatric wards using a modified version of Edelstein's questionnaire. Participants completed a questionnaire in which they identified factors that influence their knowledge and understanding of documentation.

Results: Participants reported that they have considerable knowledge of nursing documentation. They also indicated that they were most knowledgeable about policies on documentation and writing discharge instructions. However, their knowledge of nursing assessments ranked fifth and they were least knowledgeable about reading reports for each shift.

Conclusion: The modified Edelstein's questionnaire provided a valid and reliable instrument for measuring RNs' knowledge of nursing documentation. A factor analysis of the 16 items in the Knowledge scale showed excellent reliability. RNs in the two geriatric wards have high levels of knowledge about documentation. Specific recommendations relate to the implementation of comprehensive documentation education programmes that reflect the needs of organisations and the level of RNs' skills and knowledge concerning documentation.

Nursing and Allied Health Category: NA14

The use of glucometrics to evaluate quality of inpatient glycaemic control

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Introduction: While outpatient glycaemic control is easily assessed by the HbA1c test, no equivalent examination exists for inpatients. Glucometrics is a mathematical analytical process that permits objective comparisons of inpatient glycaemic control among hospitals and patient care units. It utilises time-averaged glucose readings from which the patient-day glucose (average glucose for each patient's hospital day) is used, as it is the most reasonable metric that allows for fair patient-to-patient comparison. The aim of this study was to show that glucometrics could be used as a tool to evaluate the quality of inpatient glycaemic control in a general medical ward.

Methods: Capillary blood glucose readings from a general medical ward over a two-month period were collected using the hospital Cobas-IT system. The readings were converted into patient-day average values using the glucometrics software developed at Yale University. The readings were benchmarked against the best patient care unit in the Yale-New Haven Hospital, which achieved a 65% patient-day mean of between 3.9 to 8.3 mmol/L.

Results: A total of 6,245 samples were collected over the study period with 324 patient-days. The median patient-day glucose was 7.3 mmol/L. 60.5% of patient-days had glucose readings within our defined target range of 3.9 to 8.3 mmol/L. 3.4% of patient-days had hypoglycaemia of < 3.9 mmol/L and 6.8% had severe hyperglycaemia of > 16.6 mmol/L. The median duration of glucose monitoring was 1.3 days.

Conclusion: We achieved 60.5% patient-days with glucose readings within the target range, which is lower than the Yale-New Haven figure of 65%. This study demonstrates that glucometrics can be used to compare inpatient diabetes management across institutions. It can also be used to help institutions benchmark their services against centres of excellence and act as a means for improvement.

Nursing and Allied Health Category: NA15

Nurses' perception of the benefits of patient education II

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Introduction: Patient education (PE) is a core responsibility of nurses. Nursing shortage and resource constraints have increased the challenges faced by nurses in coping with patient/family expectations as well as organisational needs to discharge patients quicker and sicker to optimise bed utilisation. Therefore, it has become crucial that nurses actively participate in PE to help patient/family make decisions for self-directed care. This study assessed nurses' perception of the importance of PE. Results were also compared against a similar 2004 study with an aim to promote, encourage and empower nurses to practice PE by exploring ways to overcome barriers.

Methods: A cross-sectional survey was conducted across the nursing workforce in Alexandra Hospital, Singapore. Questions were drawn from literature reviews. A convenience sample of 500 nurses from various disciplines participated in the study.

Results: The response rate was 93.6%. All participants rated PE as important vs. 93.6% in the 2004 survey, 97.4% agreed that health education was helpful to patients. 97.6% of respondents agreed that PE was a part of nursing. 83.2% participants were prepared to provide PE vs. 69% in the 2004 survey. 91.9% respondents felt that protected time would

encourage participation in PE vs. 80.5% in the 2004 survey. Barriers to PE were lack of communication skills (26%), knowledge (24.1%), teaching tools (16.2%), training (15.9%), insufficient time (17.8%) and distractions from other work. Patient factors that hindered effective education were language barrier (17.7%), emotional barriers (42.6%), low education level (14.1%), beliefs (13.9%) and pain (11.7%).

Conclusion: Participation in PE improved from 42.5% in year 2004 to 56.8% in the current study. More nurses viewed PE as important and expressed willingness to actively participate in PE if protected time and training were provided. However, significant barriers to effective PE still continue to exist and there is a need for concerted efforts to address these issues.

Nursing and Allied Health Category: NA16

Knowledge of asthma care among registered nurses: a survey study

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Introduction: Patient education improves the outcomes in asthma. Medical professionals, including ward registered nurses (RNs) require sound knowledge of asthma care in order to discuss asthma management with patients under any setting. To date, no local study has evaluated the knowledge level of asthma among ward nurses. This study was designed to determine the level of asthma knowledge of ward RNs.

Methods: A cross-sectional survey study was conducted among ward RNs using a purpose-designed and pilot-tested questionnaire. A total of 21 multiple-choice questions were developed based on patient education packages, such as definition, causes/triggers, diagnosis cum classification and control, treatment of asthma, inhaler techniques and patient education.

Results: 295 out of 361 RNs (82%) responded to the survey questionnaire. Many RNs were unable to participate in the survey due to busy work schedules. The responses included 63% correct answers, 25% incorrect answers, and 12% 'not sure' responses. The mean score among the RNs was 63.81 ± 13.9. When benchmarked against the hospital competency-based programme passing score of ≥ 80, only 37 (12.5%) RNs achieved the target while 258 (76.5%) failed to meet the target.

Conclusion: Study results point at insufficient knowledge of asthma care among RNs and highlight the need for asthma training. Nursing training institutions should consider incorporating additional asthma education modules, including inhaler techniques, into nursing skill curricula to bridge the gap between knowledge and service needs.

Nursing and Allied Health Category: NA17

Prevalence study of methicillin-resistant *Staphylococcus aureus* in Alexandra Hospital

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Introduction: Asymptomatic methicillin-resistant *Staphylococcus aureus* (MRSA) carriers are often not recognised. In 2003, a Society for Healthcare Epidemiology Association (SHEA) taskforce advocated a strategy of using active surveillance cultures to identify MRSA carriers. However, universal MRSA screening remains controversial. At Alexandra Hospital, Singapore, only patients classified as high risk for MRSA are screened on admission. This study aimed to investigate the prevalence of MRSA and assess the need for universal MRSA screening according to risk stratification.

Methods: Surveillance screening for MRSA was conducted on all adult inpatients on admission. MRSA surveillance swabs were taken from nasal, axilla, groins and wound, if present. Patients were stratified into high risk, moderate risk and low risk groups according to disease processes, history of

hospitalisation and nursing home stay. Prevalence of MRSA was tabulated according to the different risk groups.

Results: 377 patients were admitted to the hospital from April 27, 2010 to May 4, 2010. Prevalence of MRSA on admission was 10.3%. MRSA prevalence was 22% in the high risk group (n = 127), 5.5% in the moderate risk group, and 2.9% in the low risk group. Although the high risk group had the highest prevalence of MRSA, it represented only 34% of all inpatients, as 66% of patients admitted to the hospital belonged to either the moderate or low risk groups, which accounted for 28% of all MRSA on admission.

Conclusion: Screening of only the high risk group patients for MRSA would imply that 28% of patients with MRSA woud go undetected on admission. This would lead to poor MRSA control in the hospital due to ineffective contact precautions. Study findings support the need for universal MRSA screening on patient admission to enable successful control of MRSA transmission among hospitalised patients.

Nursing and Allied Health Category: NA18

Surveillance of *Enterobacteriaceae* producing extended spectrum β-lactmase in Alexandra Hospital from January 2009 to June 2010

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Introduction: The Alexandra Hospital Antibiogram 2008 and the Network for Antimicrobial Resistance Surveillance Singapore (NARSS) data revealed a high prevalence of extended spectrum β-lactmases (ESBLs) in Alexandra Hospital, Singapore. The infection prevention and control team at Alexandra Hospital investigated the factors associated with ESBL in order to put in place interventions that could arrest the trend as well as the disturbing sequelae associated with infections.

Methods: An 18-month prospective study was carried out on specimens sent for laboratory investigations in the hospital. Results of these examinations and patient biodata were collected and analysed. The criteria for community- and nosocomial-acquired infections were based on definitions from Centers for Disease Control and Prevention, United States.

Results: Urine (53.3%) accounted for majority of the specimens (223/418). Most urine samples (50.6%) were taken via urinary catheters (113/223). 11.4% urine specimens were from patients admitted from nursing homes. *Escherichia coli* (47.1%) and *Klebsiella* spp. (31.6%) accounted for 78.7% of ESBL-producing enterobacteria (329/418).

Conclusion: Findings suggest the need to focus on factors associated with the infection of ESBL-producing enterobacteria, such as care management of urinary catheter.

Nursing and Allied Health Category: NA19

Relatives accompanying PACS 2 and above patients in emergency department treatment areas: a literature review

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Introduction: Emergency departments (EDs) in Singapore, other than for paediatric patients, keep relatives of patients who are triaged as Patient Category Scale (PACS) 2 and above away from the designated treatment areas. Such access control raises anxiety levels, leading to complaints from these individuals, and also affects patients' psychological well-being. This study evaluates existing evidence supporting or opposing the concept of relatives accompanying patients in ED treatment areas.

Methods: Literature searches were conducted using EBSCOHost, MEDLINE, PsycINFO and CINAHL databases for the search terms relatives and emergency department, and family and emergency department. Searches were limited to studies reported in the English language. No predetermined year of publication was set. Related evidence was extracted and synthesised. Reports related to paediatric patients and relatives witnessing resuscitation or invasive procedures in the ED were excluded from the study.

Results: Most reports agree that family crisis and their needs must be considered while attending to patients in the ED. Several studies have suggested inventory lists to measure and manage the anxiety of relatives. Nevertheless, most studies also acknowledge the reluctance of medical staff to having relatives in the ED treatment areas. The leading worry of medical personnel in the ED was the possible misinterpretation of clinical situations by relatives and needless legal implications thereafter. There is inadequate evidence to draw any conclusive deduction, as most studies were carried out in the critical care setting and were cardiopulmonary resuscitation-related and did not involve acute treatment in the ED. The relevance of the present findings might consequently be applicable in a parallel manner at best.

Conclusion: Allaying the anxiety of relatives and patients is the cornerstone for customer service satisfaction initiatives in the ED. Further controlled prospective studies are warranted in the ED setting in Singapore to gather further evidence supporting or opposing the concept of relatives accompanying patients in treatment areas.

Nursing and Allied Health Category: NA20

Wetness Alert Diaper for assisting with timely diaper replacement among patients with dementia

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Introduction: Urinary incontinence is highly prevalent and diaper use is common among patients with dementia. Timely diaper replacement is necessary to avoid complications secondary to prolonged lying in soiled diapers for such patients. Current scheduled diaper change is labour intensive, inefficient and cannot guarantee immediate detection of diaper wetness, which is an important step toward timely diaper replacement. The Wetness Alert Diaper (WAD) system was developed to enable timely detection of diaper wetness and prompts for assistance through appropriate reminders for a diaper change once the diaper is soiled. The goal of this study was to explore the real needs, practical usability issues and their influence on functioning, and efficacy of WAD under institutional care settings.

Methods: A clinical trial with WAD was conducted on 6 patients with dementia at a local nursing home to test the effectiveness of the system in an institutional setting.

Results: Preliminary analysis of the data collected indicated 75% sensitivity and 96% specificity when using WAD for detecting soiled diapers.

Conclusion: Trial outcomes demonstrate promising results for the automated and timely detection of diaper wetness using WAD. Study findings are being used to effect improvements in WAD. With proper usage and functioning of the system, timely diaper replacement will become a reality with WAD. As the sample size of this study was small, a bigger clinical trial on 12 patients with dementia is planned.

Nursing and Allied Health Category: NA21

MRSA registry at Alexandra Hospital to identify risk for methicillin-resistant *Staphylococcus aureus*

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Introduction: The methicillin-resistant *Staphylococcus aureus* (MRSA) burdens are increasing in Singapore according to the Network for Antimicrobial Resistance Surveillance (Singapore). Alexandra Hospital, Singapore, reported high MRSA rates between January and June 2009, which suggests significant implications for patient outcomes and the hospital's infection control programme. This study was designed to identify patients at high risk for the pathogenic development of MRSA colonisation or infection.

Methods: A prospective study was conducted on MRSA positive screening results of patients admitted from April 2009. Biological data from over 200 patients were collated and studied in detail, with information including age, gender, site of specimen collection, preexisting risk factors such as premorbid conditions, wound type, and whether patients were admitted from their homes or nursing homes. MRSA colonisation was defined as MRSA positive within 48 hours of hospital admission (CA-MRSA). MRSA infection was defined as MRSA positive after 48 hours of hospital admission with signs and symptoms of infection. Multivariate analyses were performed.

Results: 65.6% of patients were men. A majority of the patients were aged above 65 years. 65% of patients had community-acquired MRSA (CA-MRSA), with a majority having one or more risk factors in the preceding 12 months. Wounds comprised 33% of specimens processed.

Conclusion: The increasing MRSA burden in Singapore calls for concerted efforts toward controlling and preventing the spread of infection in hospital patients. Decolonisation of carriers and careful use of antibiotics is the key to preventing, reducing and resisting antibiotic resistance. Therefore, stringent control over the use of antibiotics must be implemented. Wound care excellence should be developed, as it is critical to give patients the best treatment and care to ensure both a hassle-free hospital stay and rapid recovery.

Nursing and Allied Health Category: NA22

Hook-composite flexion and finger-wrist extension for the rehabilitation of flexor tendon repaired at zone 2: a case study

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The rehabilitation and repair of ruptured flexor tendons in the hand has been the subject of extensive research generating volumes of literature. This study presents the debut rehabilitation of zone 2 flexor tendon repair using the hook-composite flexion and full finger-wrist extension (HCFE) exercise regime to achieve maximal tendon excursion and differential gliding. HCFE differs from traditional rehabilitation techniques as it allows simultaneous full finger-wrist extension at postoperative Day 2. We report a man who sustained a left ring finger zone 2 flexor digitorium profundus and flexor digitorium superficialis tendon lacerations, and middle phalanx comminuted fracture. Both tendons were repaired, and the fracture treated conservatively. Following surgery, the patient was informed that he was unlikely to flex his distal interphalangeal joint (DIPJ), and to expect a 300–400 proximal interphalangeal joint (PIPJ) flexion contracture. To achieve maximal tendon excursion and reduce PIPJ flexion contracture, the HCFE exercise regime was used. The patient was instructed to exercise 6 × 10 repetitions daily. The traditional dorsal extension block splint was used in between exercises to prevent tendon rupture. Although instructed to exercise more often, the patient was able to only do 3 × 10 repetitions daily due to pain. The range of motion of the left ring finger at week three was 0°–75° for metacarpophalangeal joint (MCPJ), 0°–85° for PIPJ and 15°–15° for DIPJ. At week 5, the range of motion was 0°–80° for MCPJ, 0°–85° for PIPJ and 0°–0° for DIPJ. There

was no change in the range of motion at week 8 for MCPJ and DIPJ. However, the range of motion for PIPJ improved to 0°–95°. The patient achieved full PIPJ extension in spite of only exercising three times daily, and despite the possibility of PIPJ flexion contracture due to a failure to achieve full extension in the postoperative period; such flexion contracture would compromise any subsequent attempts at salvage by secondary tendon surgery. The key to preventing contracture of the repaired flexor tendons is to allow them a greater finger and wrist range of extension and maximal proximal tendon excursion. This simultaneous extension was achieved in the HCFE exercise regime. Furthermore, the synergistic pattern of the exercise regime, which allows for increased finger flexion with low flexion tension, is also an excellent alternative for achieving safe maximal tendon gliding without rupturing the repaired tendon.

Nursing and Allied Health Category: NA23

Factors influencing emergency department patient turnaround time

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Introduction: This study aimed to identify the impact of various factors on emergency department turnaround time (ED TAT) for acuity scale 3 (P3) patients who are ambulant with mild-to-moderate conditions that require acute treatment.

Methods: Patient data over four consecutive weeks were analysed from the administrative databases of Khoo Teck Puat Hospital, Singapore. ED TAT was calculated as the interval between patient registration time and case end time. A multivariate linear regression model was constructed with the presence of various ED subprocesses, such as admission, laboratory test, medication, point-of-care test, procedure, radiology investigation and referral, as dependent variables. The regression coefficients demonstrated the actual impact of each of these subprocesses on TAT after adjusting for patient arrival time, that is non-peak and various peak hours identified from historical arrival patterns.

Results: Based on a total of 4,438 ED visits, all subprocesses significantly affected ED TAT ($p < 0.001$). The presence of admission, medication, laboratory test, radiology investigation, referral, point-of-care test and procedure resulted in a TAT increase of 46.7, 45.5, 43.7, 22.7, 19.0, 13.7, 13.0 minutes, respectively. Different patient arrival times also had a statistically significant influence on TAT. Arrival during morning peak (10 am to 12 pm) timings, afternoon peak (12–1 pm and 3–4 pm) timings and night peak (8–10 pm) timings increased TAT by 7.4, 9.6 and 20.0 minutes, respectively, when compared with non-peak hours.

Conclusion: The presence of admission, medication and laboratory test resulted in greatest increases to ED TAT, which may be substantially shortened by more targeted efforts to streamline these subprocesses. Additional resources may also be deployed during night peak hours to reduce TAT.

Nursing and Allied Health Category: NA24

MONICA: toward a continuous non-intrusive monitoring system for the care of patients in hospitals

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Introduction: Current practices for monitoring patient health status and well-being in hospitals is tedious, time consuming and intrusive, as it typically involves manual periodic checks by medical professionals or requires the patients to wear specialised probes that cause at least some level of discomfort. Furthermore, such monitoring is infrequent and may miss the onset of crisis events. The aim of this study was to develop a non-intrusive intelligent monitoring system that can continuously monitor the health status of patients, including their vital signs, and evaluate events of interest that threaten their well-being in hospitals.

Methods: The proposed system uses Fiber Bragg Grating sensors that are placed beneath the bed to obtain an indicative spatial-temporal signature of signals for patient monitoring. It is non-intrusive as patients only need to lie on the bed. It allows continuous monitoring of patient's vital signs, such as respiratory and heart rate, in addition to monitoring for posture and movement from pressure points to prevent bedsore and bed occupancy. Wavelet transform-based processing techniques are used to separate the vital sign signals from other movement-related signals. In an emergency, such as weakening of the patient's vital signs, caregivers can be informed promptly through an alert system for immediate attention.

Results: Initial trials suggest that the system is stable and robust for continuous non-intrusive monitoring. The results are promising as it shows near 100% accuracy for respiratory monitoring, with a maximum estimated error of ± 2 breaths per minute. However, challenges remain for heart rate monitoring as the results obtained were not comparable to those achieved in the laboratory, where the maximum error was ± 3 beats per minute for heart rate.

Conclusion: The system is an innovative means of providing continuous monitoring of patients in an unobtrusive manner. It obviates the need for intrusive probes and minimises labour-intensive manual procedures.

Nursing and Allied Health Category: NA25

Depression and distress in patients with diabetes mellitus

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Introduction: Research has shown that patients with diabetes mellitus are twice as likely to develop depression as compared to the general population. Comorbid depression was also found to be associated with poor glycaemic control and quality of life. There is no known study on the effect of depression or diabetes-related distress on disease control and patient well-being among diabetic patients in Singapore. We hypothesised that patients with depressive symptoms or diabetes-related distress are more likely to have higher HbA1c and lower quality of life.

Methods: 445 outpatients attending full diabetes assessment were interviewed using the Center for Epidemiologic Studies Depression Scale (CES-D), Problem Areas in Diabetes (PAID), and World Health Organization Quality of Life Brief (WHOQOL-BREF). Their HbA1c readings were also recorded. Patients with CES-D ≥ 16 or PAID ≥ 40 were considered to have met the criteria for presence of depressive symptoms or diabetes-related distress.

Results: 62 (13.9%) patients were found to have depressive symptoms or diabetes-related distress. 33 (7.4%) patients had both depressive symptoms and diabetes-related distress. Compared with non-depressed and non-distressed diabetic controls, patients with depressive symptoms or diabetes-related distress had significantly higher HbA1c ($F[1,443] = 11.1$, $p = 0.001$), lower general quality of life ($F[1,436] = 55.6$, $p < 0.001$) and lower scores on all four domains (physical, psychological, social and environmental) of the WHOQOL-BREF.

Conclusion: This study shows that depressive symptoms or diabetes-related distress in diabetic patients affects their diabetes management and well-being. In addition to physical and laboratory assessment of diabetic patients, screening for psychological symptoms, such as depression, distress or coping difficulties, should be carried out as part of a holistic assessment.

Nursing and Allied Health Category: NA26

Improving the efficacy of nutritional supplementation in elderly patients

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Introduction: Protein-energy malnutrition delays wound healing, extends length of stay, and increases complications and readmission rates. Identification of patients at risk of malnutrition, together with early interventions, may prevent further deterioration in the nutritional status of elderly patients. The main objectives of this study were to investigate the efficacy of delivering nutritional supplements to malnourished elderly patients using a 'nutrition as medication' programme for improving consumption rates, and to ascertain the acceptance of this intervention and compliance with the programme among nursing staff.

Methods: 40 malnourished geriatric patients (10 male and 30 female) were recruited for the study. Data collected included age (82.4 ± 9.1 years), height (1.55 ± 0.08 m), weight (35.5 ± 5.9 kg), body mass index (14.8 ± 2.3 kg), and baseline albumin (32.6 ± 5.0 g/L). The patients were randomly divided into two groups, with Group 1 receiving mid-meal supplements (n = 20) and Group 2 receiving 60 ml of a 2 kcal/ml supplement given four times daily at medication rounds (n = 20). Outcome measures included comparison of supplements and changes in he consumption of hospital food. The patients' length of stay was also monitored. Nursing staff (n = 20) were surveyed using a short qualitative questionnaire midway through the study to assess their acceptance of the 'nutrition as medication' programme.

Results: Patient compliance with the programme was excellent compared with current practices. The consumption rate of 80% in the intervention group was significantly different from that of 53% in the control group (p = 0.002, 2-tailed *t*-test). The survey showed that none of the nurses found it difficult to dispense the 2 kcal/ml supplement. 75% of nurses felt that it was an effective means of supplementing patients, while the remaining 25% felt that it was the same as before.

Conclusion: The 'nutrition as medication' programme is an acceptable and effective means of delivering nutritional supplements to malnourished elderly patients, thereby attenuating deterioration in their nutritional status.

Nursing and Allied Health Category: NA27

Use of blister packs to improve medication adherence: a pilot study

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Introduction: Study aims included determining the impact of blister packs on medication adherence and associated objective outcome measurements in patients on chronic medications for diabetes mellitus (DM), hypertension (HT) and/or hyperlipidaemia (HL).

Methods: Patients deemed as non-adhering by physicians were recruited from outpatient clinics at baseline visit. Inpatients who did not obtain a full score using the medication transfers were likewise also recruited. Medications were packed into blister packs on the second outpatient visit or upon discharge. Adherence was assessed by pill count method. Systolic blood pressure (SBP), HbA1c and low-density lipoprotein cholesterol (LDL-C) were objective outcome measures employed. Measurements were obtained upon recruitment and during subsequent follow ups. Feedback on the blister pack was also collected via satisfaction surveys.

Results: 29 patients were recruited of which 14 completed the study. All patients had HT, with eight patients having DM and HL. Mean patient age was 65.4 ± 13.4 years. Outpatients (n = 2) showed an increase in compliance from 72.5% to 75.5% and from 77.5% to 111.7% at the second and third visits, respectively. Inpatients (n = 12) showed high adherence (97.8 ± 19.9%) at follow-up. Five (62.5%) patients had objective decreases in LDL-C (up to 2.6 mM, p = 0.86) and HbA1c (up to 0.9%, p = 0.31) over a mean duration of 53.8 ± 33.7 days and 55.9 ± 29.3 days, respectively. Five (41.7%)

patients had decrease in SBP (up to 19 mmHg, p = 0.27) over a mean duration of 46.9 ± 30.8 days. All patients reported that blister packs simplified their medication regime; 92.8% patients felt that blister packs improved adherence to medications. Most patients (78.6%) were keen to continue with this service.

Conclusion: Blister packs improved medication adherence in patients with DM, HT and/or HL, thus resulting in a potential decrease in HbA1c, SBP and LDL-C levels. As its use was well received among the study group, it is possible that it could prove helpful in optimising adherence and health outcomes in patients with chronic diseases.

Nursing and Allied Health Category: NA28

Pharmacoeconomic analysis of nursing home medication reviews by pharmacists

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Introduction: Elderly patients in nursing homes (NHs) are known to be on polypharmacy. Medication reviews by pharmacists have been shown to improve rational prescribing and effect cost savings for the NHs. This study analyses the interim results of direct cost savings from interventions made by pharmacists in four NHs from January 2008 to December 2010, while reporting on data from January 2008 to December 2008 only.

Methods: A retrospective evaluation of all NH reviews in 2008 was performed. Medication interventions were identified from the drug evaluation forms, which contained information on medication issues, recommendations from pharmacists and actions taken by doctors. Direct cost-saving interventions accepted by doctors were identified. Such interventions included overdose, over frequency, over duration and therapeutic duplication; drug use without indication, drug substitutions and better drug selection also lead to cost reduction. Direct cost savings from following such medication interventions were calculated based on a one-year projection.

Results: 235 direct cost-saving medication interventions were identified from 780 residents in the four NHs in 2008. Total cost savings for the four NHs amounted to S$27,380.94 per year. Top four direct cost-saving medication interventions were drug use without indication (61%; savings $16,005.82 per year), over frequency (29%; savings $7,736.34 per year), overdose (5%; savings $1,290.19 per year), and better drug selection leading to cost reduction (5%; savings $1,421.08 per year).

Conclusion: Interim analysis of this ongoing study showed that interventions suggested by pharmacists in the four NHs during 2008 resulted in direct medication cost savings amounting to S$27,380.94. Drug use without indication was the most common direct cost-saving medication intervention (61%; savings $16,005.82 per year). Further analysis of the data available when the study ends in December 2010 will help provide a clearer picture.

Nursing and Allied Health Category: NA29

Preventing falls in the elderly after discharge through follow-up home visits

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Introduction: Home visits (HVs) aim to promote and enhance independence and safety at home whereas phone calls (PCs) made two weeks after discharge ensure that instructions are being followed. However, such reports are based on the client's feedback alone. Reports in the literature indicate that frequent follow-up HV and PC can reduce falls in the elderly by nearly 80%. No studies have evaluated the effectiveness of HV by occupational therapists (OTs) in reducing falls in discharged elderly patients in Singapore. This study was designed to assess the effectiveness of an HV programme

being conducted by OTs. The programme included three HVs and three PCs by an OT, and addressed the physical, emotional and psychological needs of elderly people after a fall.

Methods: 65 participants were recruited based on the inclusion and exclusion criteria selected. An initial HV was made after discharge, which was followed up with PC at two weeks. At the 3rd and 6th month, follow-up HVs were conducted, and the programme was concluded with a PC at the 9th month. The Barthel Index (BI), Frenchay & Lawton Activities Index (FAI), Modified Fall Efficacy Scale (MFES), Falls Calendar and SF-12 were the outcome measures employed.

Results: 78.2% of the participants had improvement in their Basic Activity of Daily Living (ADL) with their BI score within the range of 0.2–8.0, and 76.1% of them experienced improvement in their Instrumental ADLs through their FAI. 78.2% had improvement in their MFES, showing a reduction in their fear of falling. 84.3% of the participants did not experience recurrent falls and 92.2% did not have any hospital readmission due to falls after the follow-up HV. Improvements in the average score of the emotional and physical components of SF-12 were also observed.

Conclusion: Follow-up HVs significantly prevent further falls and functional decline in elderly people. It also enhances their psychological, social and physical well-being.

Nursing and Allied Health Category: NA30

Nail resection with phenolisation is the treatment of choice for onychocryptosis

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Introduction: Onychocryptosis is a common presentation in podiatry clinic secondary to poor nail-trimming techniques or abnormal nail anatomy. These often lead to pain and risk of infections where conservative treatment requires frequent follow-up, which may not always relieve symptoms. Surgical treatment for such patients can offer a more permanent solution. We hypothesised that nail resection with phenolisation reduces recurrence of ingrown toenail-related problems in podiatry patients. A clinical audit was conducted for nail resection with phenolisation performed by podiatrists in the outpatient clinic.

Methods: A retrospective analysis of data collected from February 2009 to October 2010 was performed for all nail resections conducted by podiatrists at Alexandra Hospital (AH), Singapore, and Khoo Teck Puat Hospital (KTPH), Singapore. Data related to postsurgical infection and recurrence were reviewed. 80% phenol was used in all resections.

Results: Nail resections were performed for 46 (90.2%) toes in AH and five toes in KTPH. The mean age of patients was 32.3 ± 16.8 (range 17–87) years. 13 patients were women (25.5%). Six (11.8%) patients had type 2 diabetes mellitus and two had rheumatoid arthritis. Ten (19.6%) toes had previous total nail avulsions (TNA) and six had partial nail avulsions (PNAs) without phenolisation in the same affected toe. Four (7.8%) toes were infected prior to surgery. Six (11.8%) toes had acute ingrown toenails while 55 toes had chronic growth for over six months. 26 (51.0%) toes had unilateral PNAs, 22 (43.1%) had bilateral PNAs and three had TNAs. After surgery, four (7.8%) toes had infection and two (3.9%) toes had nail regrowth; mild pain was seen for three (5.9%) toes. Mean healing time was 2.43 ± 1.15 (range 1.0–6.0) weeks.

Conclusion: Nail resection with phenolisation is an easy, yet effective treatment for onychocryptosis. The low post-surgery infection and recurrence rates associated with the procedure are encouraging evidence for offering such options to patients with nail-related problems.

Nursing and Allied Health Category: NA31

A clinical framework for music therapy in palliative care: analysis of the Alexandra Hospital experience

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Introduction: Music therapy has been clinically accessible to patients receiving palliative care at an acute hospital since January 2008. A retrospective analysis was conducted for music therapy over one year (March 2009 to March 2010) to review the demographics, trends and efficacy of the modality. Data was based on the statistics and case notes collected by the author.

Methods: 177 patients (men 100, women 77) were referred to and assessed for music therapy by an overseas-trained board-certified clinician; 28 patients refused the offer. 188 sessions were conducted for the patients who accepted the therapy (n = 124) during which 65% patients engaged in the session passively, 13% patients actively played instruments or sang and engaged in entertainment experiences or song-writing, and 21% patients did both. Parameters tracked included pain, breathlessness, coping, sleep, relaxation, validation of feelings, and support of family, leisure and faith. Tools employed were the Visual Analogue Scale (VAS), DoloPlus-2 Scale, Body Colouring Tool, and patient or family self-reports.

Results: Of the 89 (72%) patients who experienced relaxation, 47 verbalised their relaxing music experience and 16 fell asleep. All 24 (19%) patients who were in acute pain experienced relief after music entertainment, and two patients refused pain medication following the session as they felt able to manage without it. 29 (23%) patients stated it as an effective coping strategy while 23 (19%) framed a positive statement about their hospitalisation. 33 patients and 21 families received psychosocial support. 12 family members were able to utilise music experiences to engage with the patients. 36 (29%) patients achieved deep relaxation toward sleep outcomes through music while 19 (15%) reported increased ease of breathing. 44 (35%) patients were not in acute distress and utilised music therapy services for leisure.

Conclusion: Music therapy interventions were useful in reducing acute symptoms of pain and breathlessness, and supported the coping strategies of patients and their families, with increased perceptions of relaxation or comfort as valuable outcomes. Future research will be focused toward the efficacy of various music interventions.

Basic Science Category: B01

Association of pigment epithelium-derived factor and insulin resistance

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Introduction: Pigment epithelium derived-factor (PEDF) is known as a multifunctional protein secreted by adipocytes that has antiangiogenic and neurotrophic functions. Recent studies in rodents suggest a relationship between PEDF and insulin resistance. The evidence of PEDF influencing insulin resistance in humans is scarce. We hypothesised that circulating PEDF levels are significantly different between healthy controls (CTL) and those with abnormal glucose tolerance (ABGLT).

Methods: 238 healthy adults (age 18–70 years), with no past history of type 2 diabetes mellitus (T2DM), who presented to Alexandra Hospital, Singapore, for health screening from July 2008 to July 2009 were enrolled. Based on their fasting glucose (FG) levels, these individuals were classified as T2DM (FG 7.0 mmol/L or greater), impaired fasting glucose (IFG; FG 6.1–6.9 mmol/L) or CTL (FG < 5.6 mmol/L). All participants with T2DM and IFG were shortlisted for further study along with 31 CTLs matched for age and gender. Demographic and anthropometric data and fasting lipids were measured. Serum PEDF was determined using enzyme-linked immunosorbent assay. Insulin and highly sensitive C-reactive protein (hs-CRP) were measured according to standard laboratory techniques. HOMA-IR was calculated from fasting glucose and insulin levels, as a marker of insulin resistance.

Results: Compared to CTLs, participants with ABGLT had higher PEDF levels (11.90 ± 2.889 μg/ml vs. 13.60 ± 3.079 μg/ml, $p < 0.05$), HOMA-IR (2.66 ± 2.38 vs. 8.21 ± 10.99, $p < 0.05$), waist circumference (86.57 ± 11.50 cm vs. 95.34 ± 15.10 cm, $p = 0.05$) and triglyceride levels (1.35 ± 0.59 mmol/L vs. 1.99 ± 1.54 mmol/L, $p < 0.05$). PEDF was positively associated with body mass index ($r = 0.270$, $p = 0.05$), diastolic blood pressure ($r = 0.340$, $p < 0.05$), waist circumference ($r = 0.384$, $p < 0.05$) and hs-CRP ($r = 0.292$, $p < 0.05$), but negatively associated with high-density lipoprotein ($r = –0.405$, $p < 0.05$). Women had significantly lower PEDF compared to men (12.1 ± 3.28 μg/ml vs. 13.51 ± 2.79 μg/ml, $p < 0.05$).

Conclusion: In this cross-sectional study, PEDF was found to be significantly increased in ABGLT. Further prospective and *in vitro* studies are warranted to better understand the mechanisms of association between PEDF and insulin resistance.

Basic Science Category: B02

Serum haemopexin and haptoglobin are differentially expressed in individuals with type 2 diabetes mellitus and impaired fasting glucose

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Introduction: Type 2 diabetes mellitus (T2DM) accounts for about 80% of all diabetes. Current understanding of the development of impaired fasting glucose (IFG) and T2DM is incomplete. We hypothesised that serum proteins in T2DM, IFG and healthy individuals are differentially expressed and may serve as potential early biomarkers, thus improving our understanding of the pathogenesis of glucose tolerance deterioration and producing potential therapeutic targets.

Methods: Previously healthy men (age 21–70 years) seen at Alexandra Hospital, Singapore, for health screening from July 2008 to March 2010 were recruited for the study. Individuals were categorised based on fasting glucose (FG) levels as T2DM (FG ≥ 7.0 mmol/L), IFG (FG 6.1–6.9 mmol/L), and control (CTL; FG < 5.6 mmol/L). Anthropometric data and fasting lipids were measured. Serum from T2DM and IFG individuals and CTLs were compared. CTLs were individuals

with normal blood pressure (BP) and desirable lipid profile, and were matched for age and body mass index (BMI). Albumins and immunoglobulins were depleted and protein analysis was performed by two-dimensional differential in-gel electrophoresis (2D-DiGE). Protein spots that showed significant differences were picked and digested in-gel. Mass spectrometry and database searching allowed spot identification.

Results: 181 men were enrolled in the study of whom 11.6% and 8.3% participants had T2DM and IFG, respectively. Seven men with T2DM, seven with IFG and six CTLs were selected. Mean age (48.50 ± 7.30 years), BMI (25.16 ± 3.89 kg/m^2) and FG (CTL 4.35 ± 0.49 mmol/L, IFG 6.33 ± 0.10 mmol/L, T2DM 10.83 ± 4.55 mmol/L) were significantly different ($p < 0.05$). BP, cholesterol and triglyceride levels were not significantly different. Ten protein spots were upregulated while 11 were downregulated in participants with T2DM and IFG compared to CTLs. Haemopexin was found to be significantly upregulated by 1.3 fold while haptoglobin was upregulated by 2.8 fold in individuals with IFG and T2DM ($p < 0.05$).

Conclusion: Results suggest that serum proteins are differentially expressed in individuals with T2DM and IFG compared to healthy CTLs. Haptoglobin binds to haemoglobin while haemopexin binds to haeme, and thereby prevent haemoglobin-induced oxidative tissue damage. Whether these proteins are causal or associated with abnormal blood glucose is unknown and remains to be elucidated.

Basic Science Category: B03

Blood microRNA profiles in women with impaired fasting glucose

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Introduction: Prediabetes is a state of abnormal glucose homeostasis that is characterised by the presence of impaired fasting glucose (IFG) and impaired glucose tolerance. These individuals are at risk for type 2 diabetes mellitus. Molecular understanding of the onset and progression of IFG remains incomplete. MicroRNAs (miRNAs) are a class of small non-coding RNAs functioning as translational modifiers, typically as repressors. Blood miRNA levels vary with disease states, and so represent an attractive class of potential biomarkers. We hypothesised that blood miRNAs in IFG were different from those in healthy controls (CTL), mainly at the pathways controlling glucose homeostasis.

Methods: Healthy adult women (age 21–70 years), seen at Alexandra Hospital, Singapore, for health screening from July 2008 to March 2009 were recruited for the study. Anthropometric data, fasting glucose (FG) and lipids were measured. Individuals were categorised based on FG levels as IFG (FG 6.1–6.9 mmol/L) or CTL (FG < 5.6 mmol/L). RNAs (including miRNAs) were isolated using the RiboPure-Blood kit. 1 μg of RNA was ^{3}H-labelled and hybridised on miRNA microarray. Data was quantified using the median fluorescence intensity of four spots for each miRNA and normalised using global LOWESS (locally weighted scatterplot smoothing). A 1.5-fold increase, 0.3-fold decrease, or p-value less than 0.05 was considered significant up/downregulation.

Results: 60 healthy women, not on any medications, were enrolled in the study; 16 women had IFG. Pooled RNA from nine randomly selected women with IFG was compared with nine CTLs, matched for body mass index, blood pressure and lipids. Mean FG was statistically different between CTLs (4.67 ± 0.78 mmol/L) and participants with IFG (6.47 ± 0.10 mmol/L) ($p < 0.05$). An upregulation of 114 miRNAs and a downregulation of 219 miRNAs was observed in women with IFG when compared to CTLs, with 39 miRNAs having ≥ 50% upregulation and 49 miRNAs showing ≥ 30% downregulation ($p < 0.05$). miR-519d which potentially targets PPAR-α (peroxisome proliferator-activated receptor α) expression was increased 115-fold in individuals with IFG. PPAR-α mediates the balance between fatty acid metabolism and glucose homeostasis.

Conclusion: Identification of differentially expressed miRNAs may provide new insights into the pathophysiology of abnormal glucose homeostasis. Future studies, including studies on the effects of a modified expression of miR-519d on PPAR-α expression, are planned.

Basic Science Category: B04

Validation of adipocytokine zinc alpha-2 glycoprotein as novel urinary biomarker for normoalbuminuria diabetic nephropathy using western blot analysis

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Introduction: A substantial proportion (up to 55%) of individuals with diabetic nephropathy (DN) has normal urinary albumin. These patients, at risk for progressive renal impairment and cardiovascular disease, cannot be identified using standard screening for urine albumin. Zinc alpha-2 glycoprotein (ZAG) was identified in previous experiments by this research group as a potential biomarker using two-dimensional differential in-gel electrophoresis (2D-DiGE). Using the results from previous 2D-DiGE protein profiling, this study aimed to validate the urinary biomarker ZAG in an independent cohort of patients with classical DN and non-albuminuric DN using western blot analysis.

Methods: Group 1 patients had classical DN (urinary albumin-creatinine ratio [ACR] > 1,000 mg/g, estimated glomerular filtration rate [eGFR] < 60 ml/minute/1.73 m^2) and group 2 patients had non-albuminuric DN (ACR < 30 mg/g, eGFR < 60 ml/minute/1.73 m^2). Urine proteins (10 μg/sample) were separated on 12.5% sodiumdodecyl sulphate–polyacrylamide gels at 90 V for 2.5 hours. Resolved proteins were blotted onto Hybond nitrocellulose membrane at 100 V for one hour. The membrane was rinsed with 0.05% phosphate buffered saline–Tween and blocked with 10% non-fat milk for two hours at room temperature. Membranes were probed overnight at 4°C with primary antibody (rabbit anti-human ZAG polyclonal, 1:2,000). The membranes were then incubated with a secondary antibody (horseradish peroxidase-labeled donkey anti-rabbit IgG) at room temperature for one hour. Detection was done using an enhanced chemilumiscence plus reaction kit. Band intensities were scanned using a Typhoon Trio scanner with appropriate lasers and filters and a photomultiplier tube voltage set between 500 and 600. Urinary creatinine was used to normalise ZAG protein expression.

Results: Using western blot analysis, the ZAG protein was confirmed and quantified to be upregulated 3-fold in men and 2.6-fold in women for the non-albuminuric vs. albuminuric cohorts. This finding is consistent with our earlier 2D-DiGE results suggesting that ZAG protein could be a robust biomarker for screening of non-albuminuric DN.

Conclusion: ZAG may be a novel target urinary biomarker for the screening of non-albuminuric DN.

Basic Science Category: B05

Association of MYH9 gene with diabetic nephropathy secondary to type 2 diabetes mellitus among Singapore Chinese

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Introduction: Diabetic nephropathy (DN) is a leading cause of end-stage renal disease (ESRD). Epidemiological evidence suggests that DN is strongly influenced by genetic determinants. Recent studies reported a novel candidate gene (non-muscle myosin heavy chain-9 [MYH9], and in particular, its E1 haplotype) that confers increased risk for focal segmental glomerulosclerosis and ESRD in non-diabetic individuals. Given the notion that aetiologically diverse renal injury,

such as hypertension, diabetes and autoimmunity, share a final common pathogenic pathway, the E1 haplotype of MYH9 may also be associated with DN. We hypothesised that the E1 haplotype of MYH9 was associated with DN among Singaporean Chinese adults.

Methods: A case-control study was carried out (n = 960). Patients were defined as individuals with spot urinary albumin-creatinine ratio (ACR) ≥ 1,000 μg/mg and/or serum creatinine > 113 μmol/L whereas controls were defined as those with ACR ≤ 30 μg/mg and serum creatinine < 113 μmol/L. Based on the Haploview database for Hans-Chinese-Beijing, 13 single nucleotide polymorphisms (SNPs) were selected to tag for the E1 haplotype region. Genotyping experiments were performed using the Illumina BeadXpress platform. Binary logistic regression and maximal likelihood ratio was used to estimate effect size and statistical significance.

Results: Patients and controls were comparable in distribution of gender, age, duration of diabetes and HBA1c levels. Single locus analysis revealed that an intronic SNP-rs735853G > C (MAF = 0.117, OR for G allele 1.465, 95% CI 1.105–1.941, p = 0.001) conferred increased susceptibility to DN, which was significant even after Bonferroni correction for multiple testings (0.05/13 = 0.0038). A 5' haplotype formed by the above SNP-rs735853 and rs735854 (D' 1.0, frequency 0.117) showed similar association with DN suggesting that the causal variant may reside within this gene region.

Conclusion: Our results suggest that the E1 haplotype of MYH9 gene conferred increased susceptibility to DN in Singaporean Chinese participants. Replicating these preliminary results in a larger cohort may further clarify the role of MYH9 in DN.

Basic Science Category: B06

Differential gene expression of angiogenic factors between human visceral and subcutaneous adipose tissue

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Introduction: Obesity is a medical condition characterised by enlarged adipocytes. The expansion of adipose tissue (AT) is linked functionally to active angiogenesis. It is believed that adipogenesis is associated with local microhypoxia in expanding AT, which induces angiogenesis to provide the needed oxygen. However, little is known about the differences in proangiogenic potential between subcutaneous and visceral adipocytes. Our preliminary observations based on SuperArray revealed possible differential gene expression between visceral and subcutaneous adipocytes. We sought to validate this observation using Lonza Human StellARray™ qPCR Array. As the normalisation procedure in the latter array is based on global gene expression patterns, no presuppositions were made regarding the constancy of expression of a particular normaliser. This is purported to provide better discriminative efficiency in deciphering differentially expressed candidate genes. We hypothesised that the gene expression of angiogenic factors differs between subcutaneous and visceral adipocytes.

Methods: Preadipocytes were isolated from paired human visceral and subcutaneous AT (n = 3) and cultured *in vitro*. Total RNA was extracted and reverse transcribed to cDNA with random primers. Real-time polymerase chain reaction (PCR) using Lonza Human StellARray™ qPCR was performed on three pairs of AT. A p-value less than 0.05 was considered statistically significant and fold change was calculated using the Global Pattern Recognition™ software.

Results: Our data revealed differential expression of angiogenic factors in visceral and subcutaneous adipocytes. Genes found to be upregulated in visceral adipocytes were pleiotrophin (18.6-fold, p < 0.01) and leptin (143.4-fold, p < 0.05). Genes that were downregulated in visceral adipocytes were HOXD3 (–108.6-fold, p < 0.02) and aminopeptidase N (–3.4-fold, p < 0.03). The panel of differentially expressed genes on SuperArray was different from that obtained via the StellARray platform probably due to erroneous assumptions that the level of expression of selected housekeeping normalisers is invariant.

Conclusion: Angiogenic potential differs between depot-specific adipocytes. This may contribute to site-dependent differential adipogenesis that is associated with visceral adiposity.

Basic Science Category: B07

Asian study of clopidogrel pharmacogenomics (ASCLOP)

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Introduction: The bioactivation of clopidogrel is highly influenced by genetic variations that require further characterisation. This study aimed to investigate the prevalence of such variations in our local population and the manner in which they correlate with platelet reactivity.

Methods: 53 patients on a stable dose of clopidogrel were recruited for genotyping. P2Y12 reaction units (PRU) were measured using a VerifyNow® meter. Patients with PRU > 235 were regarded as poor responders.

Results: Variations in CYP2C19*2 (49%) and CYP3A5*3 (37.3%) were most prevalent; 2C19*17 heterozygotic variations occurred in 11.8% of patients. There were less than 20% variations with CYP2C9*2, *3, CYP2C19*3 and CYP3A5*6. The poor responder CYP2C19*2 variations were seen more often in Malay patients (66.7%) than Chinese (42.3%) or Indians (45.5%). Similarly, more Malays (58.3%) displayed the CYP3A5*3 poor metaboliser homozygote variants than Chinese (33.3%) and Indian (35%) patients. The average PRU (avPRU) was 220 (range 54–432). 24 (45.3%) patients had PRU > 235 (poor responders). The avPRUs displayed by wild 2C19*2 status (51% patients) was 214 against 221 in heterozygotes variants (43% patients) and 258 in homozygotic variants (6% patients) (p = 0.686). The avPRUs of patients with preserved 3A5*3 function (63%) was 218 compared to 224 in patients with loss of function (37%) [p = 0.804]. Amongst 3A5*3 poor responder homozygote variants with wild 2C19*2 and *17 status, statistically more patients were non-responders (6 vs. 2, p = 0.019; Fischer's exact test), and this observation was clinically significant (avPRU 247 vs. 174, p = 0.051). Among 3A5*3 poor responders, patients on concurrent 3A4 inhibiting drugs had higher avPRU than those not on concurrent 3A4 inhibitors (275 vs. 194, p = 0.079).

Conclusion: Previous studies have shown significant relationships between 2C19*2 variations and poor response and/or increased adverse outcomes. Our findings suggest that 3A5*3 variations are more significant in the local population than 2C19*2 variations, with the latter being more common in Caucasians. Important trends were observed with patients who were 3A5*3 poor responders receiving concurrent 3A4 inhibitors, which is the most common drug interaction. We propose that a larger study be conducted to confirm the significance of these findings in the local population.

Basic Science Category: B08

Effects of α and β poly (vinylidene fluoride) phase conformations on cell attachment and proliferation

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Introduction: Membranes of poly (vinylidene fluoride) [PVDF] have good potential for use in biomedical applications due to their stability and biocompatibility. More interestingly, PVDF possesses variable piezoelectric properties depending on the polymorph conformations present. Although many reports have described PVDF as suitable biomaterial, few have considered the specific effects that different polymorph conformations exert on cellular behaviour. We hypothesised that different polymorphs, specifically α- and β-phase PVDF, would exert direct but different influences on cell attachment and proliferation.

Methods: PVDF films were fabricated using N, N dimethylformamide and hexamethylphosphoramide by solvent casting. Samples were characterised by differential scanning calorimetry, Fourier transform infrared spectroscopy and X-ray diffraction.

Results: Films containing 85% α-phase PVDF and predominant β-phase PVDF were produced and used to evaluate *in vitro* attachment and proliferation of L929 cells. Cell metabolic activity on both PVDF conformations increased by about 3-fold over the one-week culture period, with higher cell metabolic activity observed on α-phase dominant PVDF on Day 5 of culture compared to β-phase dominant PVDF. Cells grown on α-phase dominant PVDF were spindle shaped and well spread, expressing spotted paxillin in focal adhesion points mainly localised to perinuclear regions of the cells; a high proportion of cells on β-phase dominant PVDF were round and less spread, expressing relatively fewer paxillin spots.

Conclusion: Our results suggested that α- and β-phase PVDF conformations can evoke different cellular behaviour. Such variations can potentially be useful for different biomedical applications.

Basic Science Category: B09

Designing multilayered polymeric microparticles for drug delivery

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Introduction: Particulate systems have tremendous potential to achieve controlled release of drugs. However, single-layered polymeric microparticles have several inherent limitations, including initial burst release of drugs, a lack of time-delayed or pulsatile release of drugs and the inability to achieve constant drug release. Multilayered particles have the potential to overcome these disadvantages. Herein, we show how triple-layered microparticles comprising poly (D,L-lactide-co-glycolide, 50:50) [PLGA], poly (L-lactide) [PLLA] and poly (ethylene-co-vinyl acetate, 40 wt% vinyl acetate) [EVA] can be fabricated through a simple, economical, and versatile one-step solvent evaporation technique.

Methods: Multilayered microparticles were prepared by using an emulsion solvent evaporation method. The three polymers and a model drug, ibuprofen, were first dissolved in dichloromethane (DCM). The resultant polymer solution was subsequently added to a poly (vinyl alcohol) aqueous solution and emulsified using an overhead stirrer at room temperature (25°C). The evaporation of DCM results in the phase separation of PLLA, PLGA and EVA, yielding triple-layered microparticles. Finally, the microparticles were centrifuged, rinsed, lyophilised and stored in a desiccator. Processing parameters, such as the starting polymer solution concentration, stirring speed, oil-to-water ratio and polymer mass ratio, were carefully manipulated to form the multilayered structure. Particle morphologies, layer configurations and drug distribution were determined using scanning electron microscopy and Raman mapping.

Results: The particles exhibited a triple-layered PLGA (shell)/PLLA (middle layer)/EVA (core) morphology. A higher stirring speed resulted in smaller triple-layered particle sizes. Layer thickness and the layer inversion of these microparticles were altered by changing the polymer mass ratios — a higher mass polymer forms the outer layer. Strong affinity between hydrophobic long ethylene chains of EVA and hydrophobic ibuprofen drove the drug to be localised in the EVA core.

Conclusion: Triple-layered microparticles composed of PLGA, PLLA, and EVA with controllable layer thicknesses, configurations and localisation of drug were fabricated using a one-step solvent evaporation method.

Basic Science Category: B10

Bone-targeting drug delivery systems

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Introduction: Osteomyelitis is one of the most serious orthopaedic complications, especially following open fracture treatments and during post surgery follow-up of orthopaedic implants. The objective of this study was to develop a particulate system that both delivers the drug to the diseased site through surface modification and also promotes cell adhesion and bone regeneration, thus accelerating the healing process. Coating polymer particles with a calcium phosphate (CaP) layer provides them with similar properties to bone, thus increasing the bioactivity of these particles. Similarly, bisphosphonate (BP) tags have been used as bone targeting ligands to facilitate drug delivery to infection sites in the bone. BPs are a group of compounds that have a strong affinity to bone due to the strong bonding between Ca^{2+} from bone mineral and O^{-} from the phosphonate group in these compounds.

Methods: Poly (lactic-co-glycolic acid) [PLGA] particles were prepared by emulsion solvent evaporation method using the anionic surfactant poly (ethylene-alt-maleic anhydride). The CaP layer was deposited by a simple coprecipitation method and surface functionalisation of BP to the particles was achieved via conventional silane chemistry. Amine-terminated silane was first functionalised onto the surface to introduce amine groups and subsequently carbodiimide chemistry was employed to covalently attach an aliphatic chain containing the BP moiety.

Results: The presence of CaP coating was confirmed by electron microscopy, Fourier transform infrared spectroscopy (FTIR) and energy-dispersive X-ray spectroscopy (EDX). FTIR and EDX analyses showed the presence of both PLGA and CaP layer. For the functionalisation of silane, X-ray photoelectron spectroscopy survey analysis confirmed the presence of silane grafting and amide bonding.

Conclusion: Novel ceramic-polymer hybrid systems with bone ligand on the surface were synthesised in this study for bone targeting applications. In the long term, the delivery system of choice could be further explored for treating other bone-related diseases, such as osteosarcoma and osteoporosis.

Basic Science Category: B11

ncRNAs as novel theranostics in diseased contexts

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Introduction: RNA interference (RNAi) is triggered by double-stranded RNA (dsRNA) that results in the degradation of homologous mRNA or in the inhibition of mRNA translation. The selective recognition of regulatory DNA sequences is widely accepted as a basis for differential gene regulation in stem cells. Most transcription factor binding sites are, however, short, degenerate and have a strong affinity for homologous proteins, even ones with antagonistic effects, begging the question *'What is regulated in gene regulation?'*.

Methods: Genome-wide transcription factor binding site studies show that key regulators co-occupy many binding sites. Thus, the prediction of gene activities based on such data is poor. Our studies with embryonic stem cells, deficient for *Dicer (dcr–1–)* and targeted with either *dcr–1* or *dcr–2* from *Drosophila melanogaster*, give insight into the pathways that underlie the si- and miRNA networks in both wildtype and diseased contexts.

Results: Many of the non-coding transcripts show a differential expression in differentiation and disease and transcriptional interference plays an important role when transcripts compete for transcription. Typical ncRNAs appear to be spliced, polyadenylated, and exported just like regular mRNA and processed from longer precursors. Our experiments with *Dicer* give functional insights into the RNA mediated gene silencing pathways and provide novel cellular models for studying the individual effects of ncRNAs, for assay/drug development and biomarker identification.

Conclusion: At the interface of therapy and diagnostics (theranostics), interest has grown in combining both paradigms into clinically effective formulations. Our ncRNA profiling allows for the identification of specific signatures associated with diagnosis, prognosis and response to treatment of human diseases and, in particular, tumours. Our cellular models, which can be used for drug screening and biomarker identification, are a first step to bringing ncRNAs into the clinic.

Basic Science Category: B12

Influence of crystalline polyethylene glycol on paclitaxel drug release and mechanical properties of poly (lactic-co-glycolide) 53:47/polyethylene glycol formulated thin films

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Thin films of poly (lactic-co-glycolic acid) [PLGA] incorporating paclitaxel have typically had slow release rates of paclitaxel in the order of 1 μg/day.cm^2. For implementation in medical devices, a range of zero-order release rates, that is 1–15 μg/day.cm^2, is desirable for different tissues and pathologies. Polyethylene glycol (PEG) of 8 k and 35 k molecular weight was incorporated at 15%, 25%, and 50% weight ratios in PLGA containing 10% w/w paclitaxel. The mechanical properties were assessed for potential use in medical implants and the rates of release of paclitaxel were quantified in percent release and the more clinically useful μg/day.cm^2. Paclitaxel quantification was correlated to the release of PEG from PLGA to further understand its role in paclitaxel/PLGA release modulation. PEG release was found to correlate with paclitaxel release and the level of crystallinity of the PEG in the PLGA film, as measured by Raman spectra. This supports the concept of using a phase separating, partitioning compound to increase the release rates of hydrophobic drugs such as paclitaxel from PLGA films, where paclitaxel is normally homogenously distributed or dissolved. Two formulations could be promising for medical device thin films, when optimised for tensile strength, elongation, and drug release. Both slow and fast drug release were well controlled; an average of 3.8 μg/day.cm^2 using 15% 35 k PEG for > 30 days was achieved for slow rates of paclitaxel release, while a high 12 μg/day.cm^2 rate of drug release was maintained using 25% 8 k PEG for up to 12 days.

Basic Science Category: B13

Abnormalities in protein metabolism are associated with impaired fasting glucose and diabetes mellitus in previously healthy adults

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Introduction: Metabolic profiling of small molecules from body fluids gives a snapshot of physiological processes. We hypothesised that there exists in blood, apart from the well-known differences in glucose and fatty acids, differences in metabolic profiles between healthy controls (CTL) and those with abnormal glucose tolerance (ABGLT).

Methods: Healthy adults (age 18–70 years) seen at Alexandra Hospital, Singapore, from July to December 2008 for health screening were enrolled in the study. Based on measurements of fasting glucose (FG) levels, participants were classified as impaired fasting glucose (IFG; FG 6.1–6.9 mmol/L) and type 2 diabetes mellitus (T2DM; FG ≥ 7.0 mmol/L). Of the 238 enrolled, all patients with T2DM (n = 24) and IFG (n = 27) were shortlisted for further study, and matched for age and gender by 60 random controls (CTLs; FG < 5.6 mmol/L). Metabolic profiling was performed using gas chromatography and mass spectrometry for these individuals. Metabolites were identified by comparing mass spectra and retention indices to customised reference mass

spectral libraries that used authentic standard compounds, under identical data acquisition parameters. Molecules with probability matching algorithm > 70% were considered for analysis.

Results: The mean age of participants was 42.8 ± 10.6 years, with a 4:1:1 ethnic distribution of Chinese: Malay: Indians. 71.2% of participants were men. Patients with ABGLT (IFG and T2DM) had higher body mass index (27.6 ± 5.1 kg/m^2 vs. 25.6 ± 4.9 kg/m^2, $p < 0.05$), systolic blood pressure (131 ± 17 mmHg vs. 120 ± 11 mmHg, $p < 0.001$), triglycerides (2.0 ± 1.5 mmol/L vs. 1.3 ± 0.8 mmol/L, $p < 0.05$) and low-density lipoprotein cholesterol (3.5 ± 1.2 mmol/L vs. 2.8 ± 0.4 mmol/L, $p < 0.001$) than CTLs. Significant increases in branch-chained amino acids (valine, leucine, isoleucine), and alanine, proline, phenylalanine, and uric acid were present in ABGLT.

Conclusion: Most amino acids that were raised in ABGLT patients were essential amino acids, most probably from dietary sources. This suggests that dysfunction in amino acid catabolism may play important roles in insulin resistance (IR) and the pathogenesis of diabetes mellitus. Understanding the mechanisms underlying the accumulation of these amino acids may provide important insights into IR, with a potential for therapeutic options for diabetes prevention and care.

Basic Science Category: B14

Urinary proteomics associated with progressive diabetic nephropathy secondary to type 2 diabetes mellitus

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Introduction: Diabetic nephropathy (DN) is a leading cause of end-stage renal disease (ESRD) in Singapore. The rate of progression of DN is highly variable. As risk factors predictive of DN progression are incompletely understood, there is a need to search for biomarker(s) associated with the progression of the disease. This ongoing study was designed to examine the baseline urinary polypeptide pattern associated with DN progression over two years in men using two-dimensional differential in-gel electrophoresis (2D-DiGE) proteomic analysis.

Methods: Patients were classified and grouped as progressive DN (n = 5; δ-creatinine ≥ 50%) vs. stable DN (n = 5; δ-creatinine ≤ 10%) over two years. Protein precipitation by ethanol was carried out on 6 ml urine. To improve spot resolution and labelling efficiency, a 2D clean-up kit was used to remove interfering substances, such as salt. Protein concentration was determined using a 2D Quant kit. A total 75 ug protein from each group was labelled with CyDye and separated by pH and then by molecular weight using gel electrophoresis. Urinary proteome was analysed using the DeCyder software. Protein identification is yet to be performed by matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry (MALDI/TOF).

Results: The gels yielded a global spot count of 410, out of which 194 spots matched between the gels. There were 34 spots that passed stringent Student's *t*-test, showing a nominally significant p-value of ≤ 0.05. The spots were further screened to eliminate false positive signals from abundant proteins and dust particles, and 14 spots were selected as proteins of interest; five spots were downregulated and nine spots were upregulated in patients with progressive DN. Peptide identification using MALDI/TOF is planned for these spots.

Conclusion: The peptides associated with DN progression, when eventually identified, may serve as urinary markers that are useful for the clinical prediction of individuals at high risk for ESRD.

Basic Science Category: B15

Differential gene expression of inflammatory cytokines and receptors between human visceral and subcutaneous adipose tissue

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Introduction: Obesity is characterised by enlarged adipocytes that release more inflammatory cytokines and are more insulin resistant. This results in a heightened state of inflammation in obese patients. Inflammatory markers were found to be highly secreted by visceral adipose tissue (AT), suggesting that visceral AT contributes significantly to the pathophysiology of metabolic syndrome. However, the exact mechanism by which visceral adipocytes cause dysmetabolism is poorly understood. Our preliminary observations based on SuperArray revealed possible differential gene expression between visceral and subcutaneous adipocytes. We sought to validate this observation using Lonza Human StellARray™ qPCR Array. As the normalisation procedure in the latter array is based on global gene expression patterns, no presuppositions were made regarding the constancy of expression of a particular normaliser. This is purported to provide better discriminative efficiency in deciphering differentially expressed candidate genes. We hypothesised that inflammatory cytokines and the expression of receptor genes differ between visceral and subcutaneous adipocytes.

Methods: Preadipocytes were isolated from paired human visceral and subcutaneous AT and cultured *in vitro*. Total RNA was extracted and reverse transcribed to cDNA with random primers. Real-time polymerase chain reaction (PCR) using Lonza Human StellARray™ qPCR were performed on three pairs of AT (n = 3). A p-value less than 0.05 was considered statistically significant and fold change was calculated using the Global Pattern Recognition™ software.

Results: Our data revealed differential expression of inflammatory genes between visceral and subcutaneous adipocytes. Chemokine receptor-2 (CCR2) was downregulated (–31.1 fold, $p < 0.02$) and chemokine receptor 5 (CCR5) was upregulated (38.3 fold, $p < 0.04$) in visceral adipocytes. The panel of differentially expressed genes on SuperArray was different from that obtained via the StellARray platform probably due to erroneous assumptions that the level of expression of selected housekeeping normalisers is invariant.

Conclusion: Inflammatory secretome differs between depot-specific adipocytes. These adipocyte-derived chemokines may attract macrophage infiltration, resulting in subsequent paracrine crosstalk between macrophage and visceral adipocytes, thereby accentuating its proinflammatory disposition.

Basic Science Category: B16

Effect of rosiglitazone on subcutaneous versus visceral adipocytes on miRNA profiling

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Introduction: Visceral adiposity is associated with increased risks for metabolic disease. It has been widely suggested that subcutaneous and visceral fat exhibit differential metabolic function. MicroRNAs (miRNAs) are potential regulatory molecules affecting the stability and translation of mRNA in different fat depots. miRNA microarrays (paired visceral and subcutaneous preadipocytes) were performed on two obese individuals (body mass index > 30 kg/m^2) to establish the global miRNA profile in visceral and subcutaneous adipocytes. The effects of rosiglitazone, an agonist of

PPAR-γ (peroxisome proliferator-activated receptor-γ) with specific adipogenic action, was also tested on visceral and subcutaneous adipocytes. We hypothesised that miRNA expression differs systematically between visceral and subcutaneous adipoctyes.

Methods: Preadipocytes were isolated from visceral and subcutaneous adipose tissue and cultured *in vitro*. The cells, grown in serum-free Dulbecco's modified Eagle's medium and supplemented with high glucose (24.98 mmol/L), were treated with 1 μmol/L rosiglitazone maleate for 48 hours. Control cells were cultured in the same culture medium without rosiglitazone. Total RNA, including miRNA, was extracted using the miRNeasy mini kit. Agilent miRNA microarray (8 × 15 K) was performed with biological duplicates. Data were analysed using GeneSpring and the molecular pathways were assessed using the Pathway Studio software.

Results: The miRNA profile reported three upregulated miR- (miR-126, miR-145 and miR-503) and three downregulated miR- (miR-196b, miR-10b and miR-503) in both controls and rosiglitazone-treated visceral and subcutaneous adipocytes. Interestingly, an increase in miR-21 expression (2.45 fold, $p < 0.05$) was also observed in the visceral adipocytes with rosiglitazone challenge. The predicted targets regulated by miR-21 include adipocytokine signaling, T-cell activation, NK cell activation, NTRK (neurotrophic tyrosine kinase) signaling and mast cell activation.

Conclusion: Global miRNA profiles differ between visceral and subcutaneous adipocytes with and without PPAR-γ agonist challenge. miR-21 might be an important factor mediating genomic post-translational regulation of preadipocytes, and thereby determining its differentiation-plasticity toward white or brown adipocytes.

Basic Science Category: B17

Effects of adiponectin expression in 3T3-L1 cells treated with Apo-A1

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Introduction: HDL cholesterol (HDL-C) is an independent predictor of cardiovascular disease. Adiponectin is an adipocytokine, with antiatherogenic and insulin-sensitising properties, involved in the pathophysiology of metabolic syndrome. In an earlier study investigating the association of low HDL-C and cardiovascular risk factors among women healthcare workers, we found that low HDL-C levels were associated with increased cardiovascular risk factors, including lower adiponectin levels (9.1 μg/ml vs. 4.9 μg/ml), when compared with desirable HDL-C. It is not known if this association between HDL-C and adiponectin is causal. We hypothesised that increasing HDL-concentrations would directly increase adiponectin secretion in adipocytes.

Methods: Adipocytes were used to study the effects of apolipoprotein-A1 (Apo-A1), the major apolipoprotein in HDL-C, treatment on adiponectin expression. 3T3-L1 preadipocytes were cultured in 6-well plates until confluence in Dulbecco's modified Eagle's medium (DMEM) containing 10% foetal bovine serum and induced to differentiation. Cells were exposed to induction media for three days and transferred to DMEM containing insulin for an additional three days. Cells were serum-starved for 24 hours prior to treatment with different concentrations of Apo-A1. Adiponectin was measured by enzyme-linked immunosorbent assay in cell lysate.

Results: Successful maturation of preadipocytes was observed in six days, with accumulation of fat globules in mature adipocytes. Treatment with Apo-A1 was not associated with any increase in cell death and no change in total protein content was noted in the lysate. Apo-A1 at 100 μg/ml, compared to control media, was associated with a 23% increase in adiponectin levels.

Conclusion: In this preliminary study using an *in vitro* model, increasing the levels of Apo-A1 in the medium was found to increase adiponectin levels. This suggests that the association between the reduced adiponectin levels noticed in women with low HDL-C in our earlier study was indeed causal, and this may have possible therapeutic implications. Further *in vitro* studies are planned on the effects of Apo-A1 expression in hepatocytes, with increasing adiponectin concentrations, which will contribute further to our understanding of the interrelationships between these antiatherogenic agents.

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