



Abstract Book



**22<sup>nd</sup> Health Sciences Centre Poster Conference; 7-9 March 2017**

**22<sup>nd</sup> HSC POSTER CONFERENCE 2017**

**Under the Patronage of the President of Kuwait University**



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**21<sup>st</sup> HSC Poster Conference 2016  
Organizing Committee**

- Prof. Rajaa Al-Attiyah, *Vice Dean Research & Postgraduate Studies, FOM*
- Prof. Khalid Khan, Anatomy, Chairman, FOM
- Dr. Farook Thameem, Biochemistry, FOM
- Dr. Abdullah Al-Taiar, Community Medicine, FOM
- Dr. Muath Al-Anbaei, Medicine, FOM
- Dr. Tariq Al-Fahad, Medicine, FOM
- Dr. Hanady Amoudy, Microbiology, FOM
- Dr. Mona Al-Ahmad, Microbiology, FOM
- Dr. Shorouk Dannoon, Nuclear Medicine, FOM
- Dr. Abdul Rahman Al-Serri, Obse & Gyne, FOM
- Dr. Abeer El Abdallah, Pathology, FOM
- Dr. Wafaa Al Qabandi, Pediatrics, FOM
- Dr. Shaima Karam, Pharmacology, FOM
- Dr Abdelslam Mouihate, Physiology, FOM
- Dr. Ahmed Al Kandari, Surgery, FOM
- Dr. Ahmed El-Hashim, Faculty of Pharmacy
- Dr. Andreas Henkel, Physiology, FOM
- Dr. Arjuna Ellepola, Bioclinical Sciences, Dentistry
- Dr. Suad M Al-Fadhli, FAHS
- Mr. Dheya Abu Hassan, Finance Chairman
- Ms. Amna Safar, TSA

**Special Acknowledgements**

- Prof. Adel K Ayad, *Dean, Faculty of Medicine*
- Mrs. Teena Sadan, *Technical Staff, CRC, Faculty of Medicine*



**Inaugural Ceremony: Tuesday March 7, 2017**

**Venue: HSC Auditorium, Health Sciences  
Centre, Jabriya**

*Moderator: Dr. Shaima Karam*

<b>8.00 AM</b>	<b><i>Registration</i></b>
<b>9:00 AM</b>	<b><i>National Anthem, Recitation of Holy Quran</i></b>
<b>9:10 AM</b>	<b><i>Welcome Address: Professor Rajaa Al-Attiyah</i></b> <i>Vice-Dean for Research &amp; Postgraduate Studies, Faculty of Medicine</i>
<b>9:15 AM</b>	<b><i>Introduction of Keynote Speaker: Professor Khalid M. Khan</i></b> <i>Chairman of Organizing Committee</i>
<b>9:20 AM</b>	<b><i>Keynote Lecture: “Vascular stiffness and systolic hypertension”</i></b> <i>Professor Pierre Moreau, B. Pharm., PhD</i>
<b>10:15 AM</b>	<b><i>Opening of Poster Conference</i></b> <i>Vice President for Research, Assistant Vice President for Research, HSC Deans and Vice-Deans, All Participants</i>
<b>10:20 AM</b>	<b><i>Poster Viewing: Faculty of Medicine Lobby</i></b>
<b>Closing Ceremony: Thursday, March 9, 2017</b>	
<b>12:00 PM</b>	<b><i>Welcome Address: Dr. Shorouk Dannoon</i></b>
<b>12:05 PM</b>	<b><i>Announcement of Awards by Chief Judge</i></b> <i>Presentation of Awards to the Winners by Keynote Speaker and Dean, FOM</i>
<b>12:30 PM</b>	<b><i>Vote of Thanks: Dr. Shorouk Dannoon</i></b>

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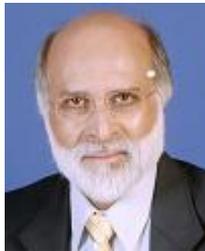
Photograph of Organizing Committee

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*Prof. Rajaa Al-Attayah, Vice Dean for Research & Postgraduate Studies, FOM*

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*Prof. Khalid Khan, Anatomy,  
Chairman, FOM*



*Dr. Farook Thameem,  
Biochemistry, FOM*

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*Dr. Abdullah Al-Taiar, Community  
Medicine, FOM*



*Dr. Muath Al-Anbaei, Medicine, FOM*

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*Dr. Tariq Al-Fahad, Medicine, FOM*



*Dr. Mona Al-Ahmad, Microbiology,  
FOM*

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*Dr. Hanady Amoudy,  
Director of CRC; Microbiology, FOM*



*Dr. Shorouk Dannoon, Nuclear  
Medicine, FOM*



*Dr. Abeer El Abdallah, Pathology,  
FOM*



*Dr. Abdul Rahman Al-Serri, Obse &  
Gyne, FOM*



*Dr. Wafaa Al Qabandi, Pediatrics,  
FOM*



*Dr. Shaima Karam, Pharmacology,  
FOM*



*Dr. Abdelslam Mouihate, Physiology,  
FOM*



*Dr. Ahmed Al Kandari, Surgery,  
FOM*



*Dr. Ahmed El-Hashim, Faculty of  
Pharmacy*



*Dr. Andreas Henkel, Physiology, FOM*



*Dr. Arjuna Ellepola, Bioclinical  
Sciences, Dentistry*



Dr. Suad M Al-Fadhli, FAHS



*Mr. Dheya HA Al-Hasan  
Dept. of Finance, FOM*



## **Message from the Vice-Dean for Research and Post-Graduate Studies, Faculty of Medicine**

The first Poster Conference was introduced in April 1996 in the Faculty of Medicine. We have since then held this conference annually with great success with staff and students of all the faculties of Health Sciences Centre participating and presenting their research. Strong research is a prerequisite for academic excellence, and this concept was clearly understood when the First Poster Day was held 21 years ago, in April 1996, in the Faculty of Medicine. The founders of Poster Day started this event with a premise that scientific progress depends on investigation, critical analysis and exchange of ideas. The Poster Day started with an aim of stimulating communication between scientists in various health-related specialties and has grown progressively to involve diverse scientific fields in all the faculties of the Health Sciences Center (HSC).

In continuing the tradition of inviting internationally recognized Scientists whose work has great impact upon the Health Sciences, this year we would like to welcome Prof. Pierre Moreau, Dean, Faculty of Pharmacy, Kuwait University, who will give the keynote speech on “Vascular Stiffness and Systolic Hypertension”. This year we have 208 poster abstracts and I have no doubt that the 22<sup>nd</sup> HSC Poster Conference will be a great success. I would like to thank Kuwait Foundation for the Advancement of Sciences (KFAS) for their sponsorship and support for this scientific event. I thank Kuwait University for the continuing support and sponsorship of the Poster Conference and Prof. Pierre Moreau for accepting our invitation as a keynote speaker in this year Poster Conference. I would like also to express my appreciation to the Vice-President Health Sciences Centre, Deans of different Faculties of HSC for their encouragement and support and to all HSC technical and support staff who assisted in the organization and implementation of this meeting. I am especially very grateful to the Chairman and the members of the Organizing Committee for their commitment and efforts to make this a very successful event.

Prof. Raja'a Al-Attayah  
Vice-Dean for Research & Postgraduate Studies  
Faculty of Medicine



**Message from the Chairman,  
22<sup>nd</sup> HSC Poster Conference Organizing Committee**



It is my great pleasure to welcome you all to the 22<sup>nd</sup> Annual Health Sciences Centre Poster Conference, a very popular and beneficial HSC tradition. The conference is enthusiastically supported by all faculties within the Health Sciences Centre and other faculties of Kuwait University. Submission of abstracts from other institutions in Kuwait further indicates its importance among the local research community. As in the past years, submission of abstracts from other countries adds an international flavor and also indicates its true vitality. This year, despite the deadline of submission of abstracts being earlier, there were 222 submissions. Unfortunately, there were few rejections, therefore, the number of posters are 208; 179 research-based and 29 case reports. These presentations cover a wide range of biomedical topics. This is, in fact, a proper place for basic and clinical sciences to come together. The conference serves as a pivotal point around which the faculties of the HSC rotate about. It is an important venue for our undergraduate and graduate students to present their work and we hope that this year's event will result in even more exciting research and open new doors for future years.

Organizing any event, small or big, is not possible without involvement of several dedicated individuals. At the outset I would like to thank Professor Raja'a Al-Attiyah, Vice Dean for Research and Postgraduate Studies, for entrusting me with the responsibility to chair the Organizing Committee. I sincerely thank the members of the organizing committee for the superb work that they have put in. I also thank all the judges for the very difficult task of selecting the best posters for awards in various categories. On behalf of the organizing committee I offer our thanks to Kuwait Foundation for Advancement of Science for financial support and to Kuwait University for supporting the event in spirit. But my biggest debt is to the Centre for Research Support and Conferences under the leadership of its Director, Dr. Hanady Amoudy. Ms. Teena Sadan and her colleagues have worked tirelessly, efficiently and



enthusiastically to make this event not only possible but a big success as well. The dedication of staff of the Centre for Research Support and Conferences made it truly pleasurable experience for the Organizing Committee. Lastly, thanks to everyone for coming and joining in. It is the enthusiasm of the participants that makes this conference the success that it is.

Every poster conference is different from the previous year's conference in terms of the science presented. However, this year's conference is different from all the previous conferences, at least, on two counts. This conference is being held 10 months after the 21<sup>st</sup> conference, thus this is the second conference in one Fiscal Year. This means that we had a budget of KD 0.000. Secondly, the keynote speaker for this conference is from among us. If I can use a cliché, I can get away by stating that the keynote speaker "needs no introduction". But I will not go that route. Ladies and gentlemen, this year's keynote speaker is the Dean of the Faculty of Pharmacy, Professor Pierre Moreau. Professor Moreau obtained PhD in 1993 in Biochemical Pharmacodynamics from Faculty of Pharmacy, University of Montréal, Canada. After two postdoctoral trainings, one in Bern, Switzerland and the other in Montreal, young Pierre Moreau joined the Faculty of Pharmacy at his alma mater. In a short span of 10 years he not only attained full professorship, but he assumed the administrative position of Acting Dean in 2006 and in 2007 he became the Dean. The Faculty of Pharmacy at Kuwait University was lucky to make him come here in August, 2014. He has an enviable funding record; his total research funding prior to joining us is staggering \$ 5,348,000. He has mentored close to 100 graduate and postgraduate students. He has close to 100 publications and is a much sought-after guest speaker. He a widely-travelled scientist and he has delivered over 60 lectures in Canada, USA and several European countries.

Professor Khalid M. Khan

Chairman, 22<sup>nd</sup> HSC Poster Conference Organizing Committee



**Keynote Speaker**

**Prof. Pierre Moreau, B.Pharm., Ph.D.**  
*Professor and Dean, Faculty of Pharmacy  
Health Sciences Center, Kuwait University*

Pierre Moreau has obtained a Baccalaureate of Pharmacy from Université de Montréal in 1988. He then trained in cardiovascular pharmacology at Université de Montréal (PhD) and Bern University Hospital in Switzerland (post-doc). In 1997, he was appointed Assistant Professor at the Faculty of Pharmacy of Université de Montréal, where he initiated his independent research career. During this period, he was awarded several young investigator prizes in the field of hypertension research. He was promoted to the rank of Associate Professor in 2002 and Professor in 2007. He has published more than 85 peer-reviewed articles in the best cardiovascular journals on the topic of vascular remodeling and vascular aging, with continuous funding from the Canadian Institutes for Health Research.

Awarded several teaching awards, he joined the development team for an entry-level PharmD in 2003, and developed a keen interest for pharmacy education. In 2006, he served as Acting Dean and was nominated Dean in early 2007. Under his leadership, the Faculty of Pharmacy at Université de Montréal implemented the PharmD, developed a baccalaureate in pharmaceutical sciences (2009) and a training program for foreign pharmacists (2011). In August 2014, he joined the Faculty of Pharmacy at Kuwait University, as the third Dean of this young Faculty established in 1996, with the intention of bringing pharmacy education to North American standards, developing pharmaceutical research and fostering fruitful collaborations with local stakeholders.



## Keynote Abstract

### Vascular stiffness and systolic hypertension

**What are chemokines?** The term “chemokines” stands for chemotactic cytokines and has been coined >20 years ago. This large family of cytokines are composed of >45 individual members of structurally related proteins that bind to either a single or multiple cell surface receptors expressed on immune cells. Since their discovery, chemokine research has rapidly progressed into a major field in immunology.

**What do chemokines do?** The primary function of chemokines is the control of immune cell traffic throughout the body under conditions of immune homeostasis as well as infections and inflammatory diseases. Accordingly, chemokines are grouped into two classes: "homeostatic" chemokines and "inflammatory" chemokines. Early research has focused on inflammatory chemokines, i.e. those that are produced at sites of inflammatory diseases. Since inflammatory diseases are caused by continuous recruitment of immune cells, all major pharmaceutical companies worldwide have invested in new drugs that target inflammatory chemokines and their receptors.

**What is the role of chemokines in health?** This area of research deals with homeostatic chemokines, i.e. those that control immune cell traffic under steady-state (non-inflammatory) conditions, and is less well understood. However, it is becoming increasingly clear that the health of body-lining tissues, such as skin, lung and intestinal tract, fully depends on a complex immune surveillance system composed of different types of local immune cells. The control of tissue localization of these immune surveillance cells by homeostatic chemokines is the topic of this lecture. We conclude that the proper functioning of our peripheral tissues is critically dependent on immune surveillance cells that keep our tissues healthy over a very long period of time. The key for understanding why we can reach old age (80 years or more) lies with research focusing on immune processes controlling tissue integrity and health.



**Best Poster Award Winners: 21<sup>st</sup> HSC Poster Conference 2016**

**PhD, MSc, Undergraduate, Graduate Resident Original Research and Case Report**

**Award Winners Poster Conference 2016**

**Undergraduate: Poster No. 14**

**Monoamine Oxidase-B inhibitor Protects Degenerating Spinal Neurons, Enhances Nerve Regeneration and Functional Recovery in Sciatic Nerve Crush Injury Model.**

**\*Al-Shimali HM, Kayali NM, Al Salem A, Renno WM, Rao MS, Khan KM**

<sup>1</sup>5th Year Medical Student, Faculty of Medicine Kuwait University; <sup>2</sup>3rd Year Medical Student, Faculty of Medicine Kuwait University; <sup>3</sup> Department of Anatomy Faculty of Medicine Kuwait University, Kuwait

**Undergraduate: Poster # 15**

**Thymoquinone enhances neurogenesis, learning and memory in young adult rats born to diabetic rats**

**\*Kayali NM<sup>1</sup>, Al-Kandari AH<sup>1</sup>, Smitha S<sup>2</sup>, Rao MS<sup>2</sup>**

<sup>1</sup>3rd Year Medical Student, Faculty of Medicine Kuwait University, Kuwait; <sup>2</sup>Department of Anatomy Faculty of Medicine Kuwait University, Kuwait.

**Undergraduate: Poster # 140**

**Cloning and expression of three major antigenic proteins of pathogenic Mycobacterium tuberculosis in non-pathogenic Mycobacterium smegmatis and Escherichia coli**

**\*Haider A<sup>1</sup>, Alazmi E<sup>1</sup>, Alazmi M<sup>1</sup>, Safar H<sup>2</sup>, Amoudy H<sup>2</sup>**

<sup>1</sup>Medical students, Faculty of Medicine, Kuwait University; <sup>2</sup>Department of Microbiology, Faculty of Medicine, Kuwait

**MSc: Poster # 71**

**Discovery of two novel deletions in the CELSR1 gene and CRYAA gene in a Kuwaiti multigenerational family diagnosed with autosomal dominant bilateral congenital cataract**

**\*Al-Barjes TA<sup>1</sup>, Sidky A<sup>2</sup>, Al-Fadhli S<sup>1</sup>**

<sup>1</sup> Department of MLS, Kuwait University, Faculty of Allied Health; <sup>2</sup> Al-Bahar Eye Centre, Ministry of Health, Kuwait.

**MSc: Poster # 12**

**(-)-Epigallocatechin-3-gallate (EGCG) enhances learning and memory and adult neurogenesis in streptozotocin induced diabetic rats**

**\*Al-Mohri SFA<sup>1</sup>, Renno WM<sup>2</sup>, Rao MS<sup>2</sup>**



<sup>1</sup>MSc student, Department of Anatomy, Faculty of Medicine, Kuwait University, Kuwait; <sup>2</sup>Department of Anatomy Faculty of Medicine Kuwait University, Kuwait

**PhD: Poster # 182**

**Expression and role of miRNA in thyroid cancer**

\*Jahanbani I<sup>1</sup>, AlAbdullah A<sup>1</sup>, Hamdawi H<sup>1</sup>, Ali R<sup>1</sup>, Allbrahim N<sup>2</sup>, Mojiminiyi SO<sup>1</sup>

<sup>1</sup>Department of Pathology, Kuwait University; <sup>2</sup>Farwaniya Hospital, Kuwait

**Distinguished Graduate Research for Resident Doctors: Poster # 130**

**Performance of CarbR GeneXpert® assay against culture and PCR for the detection of carbapenemase-producing Enterobacteriaceae (CPE) in rectal swabs**

\*Al Merdasi N<sup>1</sup>, Jamal W<sup>1,2</sup>, Rotimi VO<sup>1,2</sup>

<sup>1</sup>Department of Microbiology, Mubarak AL Kabeer Hospital; <sup>2</sup>Department of Microbiology, Faculty of Medicine, Kuwait University

**Young Researcher for Basic Sciences: Poster # 74**

**Association of the I allele of the common ACE I/D polymorphism with type 2 diabetes mellitus among Kuwaiti cardiovascular disease patients**

\*Al-Serri A<sup>1</sup>, Ismael FG<sup>2</sup>, Al-Bustan SA<sup>2</sup>, Al-Rashdan I<sup>3</sup>

<sup>1</sup>Human Genetics Unit, Department of Pathology, Faculty of Medicine, Kuwait University; <sup>2</sup>Department of Biological Sciences, Faculty of Science, Kuwait University; <sup>3</sup>Department of Medicine, Faculty of Medicine, Kuwait University

**Young Researcher for Clinical Sciences: Poster # 190**

**Does vitamin D deficiency increase the risk of fractures in children?**

\*Ayyad SH<sup>1</sup>, Fahmy ML<sup>1</sup>, Emad M<sup>1</sup>, Almutair A<sup>1</sup>

<sup>1</sup>Department of Orthopaedic Surgery, Al-Razi Hospital, Kuwait

**Award for Case Reports: Poster # 256**

**Recurrent meningitis and brain abscess due to infected fibrin glue sealant following functional endoscopic sinus surgery**

Al-Kaji AW<sup>1</sup>, Dhar R<sup>1</sup>, \*Alfouzan W<sup>1,2</sup>

<sup>1</sup>Microbiology Unit, Department of Laboratories, Farwaniya Hospital;

<sup>2</sup>Department of Microbiology, Faculty of Medicine, Kuwait University, Kuwait



## Past Poster day Keynote Speakers and Lectures

**2016**

Chemokines: Key players in immune surveillance and aging Prof. Bernhard Moser; Chair (Infection & Immunity), Institute of Infection and Immunity, Cardiff University, Heath Park, Cardiff, UK

**2015**

The Future Healthcare: Personalized Medicine for Cancer Patients; Prof. Ramzi M. Mohammad, Ph.D., Director, GI-Cancer Research, Karmanos Cancer Institute, Michigan, Department of Immunology and Microbiology, Barbara Ann Karmanos Cancer Institute, Wayne State University, MI

**2014**

Image-guided surgery – from bench to bedside; Professor Samuel Achilefu; Professor of Radiology, Mallinckrodt Institute of Radiology, Washington University School of Medicine

**2013**

Stem Cells: Building and Rebuilding the Nervous System; Professor Freda Miller; Senior Scientist, Research Institute, Developmental & Stem Cell Biology, University of Toronto

**2012**

Cardiovascular health in the 21st century; Professor Barry McGrath, Professor of Vascular Medicine & Medicine, Southern Clinical School, Monash University, Australia

**2011**

Cardiovascular Outcome Trials in Diabetes.; Prof. Rury Holman, Director of the University of Oxford Diabetes Trials Unit, University of Oxford, Canada

**2010**

New mycobacterial vaccine candidates: from lab to clinical trials. Prof. Abu Salim Mustafa, PhD, FRC Path. Department of Microbiology, Faculty of Medicine, Kuwait University

**2009**

Evidence-Based Medicine and Knowledge Translation Research for Better Health Care.; Prof. Brian Haynes, Professor of Clinical Epidemiology and Medicine, Chief of the Health Information Research Unit at McMaster University, Hamilton Ontario, Canada



**2008**

What Ails The World? How Do We Respond?  
Prof. Abdallah S Daar, D.Phil (Oxon), FRSC, FRCP (Lon), FRCS (Eng), FRCS (Ed), FRCS (C), Director of Ethics and Policy, McLaughlin Centre for Molecular Medicine, Professor of Public Health Sciences and Professor of Surgery, Senior scientist and Co-director, Program on Life Sciences, Ethics and Policy, McLaughlin Rotman Centre for Global Health, University of Toronto, Ontario, Canada

**2007**

From Molecular Imaging to Molecular Medicine.  
Prof. Henry N. Wagner, Jr. MD, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, USA

**2006**

Stem cell research.; Prof. Sir Martin Evans FRS, DSc (Nobel Laureate), Director of the School of Biosciences and Professor of Mammalian Genetics at Cardiff University, UK.

**2005**

How Corticosteroids Work in inflammatory Diseases: New Molecular Insights.; Prof. Peter Barnes is of Thoracic Medicine at the National Heart and Lung Institute, Head of Respiratory Medicine at Imperial College and Honorary Consultant Physician at Royal Brompton Hospital, London, UK.

**2004**

The Nitric Oxide/Cyclic GMP Pathway: Targets for Drug Development Prof. Ferid Murad, Nobel Prize recipient, Chairman, Department of Integrative Biology and Pharmacology, Director, Institute of Molecular Medicine, University of Texas Medical School, Houston, Texas, USA

**2003**

The Post-Genomic Era: Global Impact on Medicine and Health Care Delivery Prof. Seyed E. Hasnain, Director, Centre for DNA Fingerprinting & Diagnostics (CDFD) Hyderabad, India

**2002**

Genetics and World Health: Fact or Fantasy Prof.(Sir) David J Weatherall, Emeritus Professor, Weatherall Institute of Molecular Medicine, University of Oxford, UK



**2001**

Genomic View of Human History Prof. Mary-Claire King, American cancer Society Research Professor, Department of Medicine and Genetics, University of Washington, Seattle, Washington, USA

**2000**

Molecular Mechanisms and Biomedical Implications of Apoptotic Cell Death Dr. Sten Orrenius, Professor and Chairman, Division of Toxicology, Institute of Environmental Medicine, Karolinska Institute, Stockholm, Sweden

**1999**

Nutrition, Immunity and Infection: Basic Considerations and Public Health Significance Dr. Ranjit Kumar Chandra, Professor & Director, Allergy, Asthma and Immunology Centre, Gurgaon, India

**1998**

Futurology in Biomedical Research: From Crystallography to Crystal Gazing Prof. Jasbir S. Bajaj, All India Institute of Medical Sciences, New Delhi, India

**1997**

The Impact of Research on the Development of an Academician Dr. Elia Ayoub, Distinguished Professor of Pediatrics, Department of Pediatrics, Pediatric Immunology and Infectious Diseases, College of Medicine, University of Florida USA.



## ***Original Research Abstracts List: By Subject Area***

### **Allied Health**

**1**

Al-Sayegh N, Al-Obaidi S, Al-Qurba T, Al-Enezi K, Dean E: Health of the Health Sciences Community of Kuwait University

**2**

\*Bouzubar FF, Aljadi SH, Alotaibi NM, Irrgang JJ: Cross-cultural Adaptation and Validation of the Arabic Version of the Knee Outcome Survey-Activities for Daily Living Scale (KOS-ADLS)

### **Anatomy**

**3**

Al-Awadhi A, Rahman A, Khan KM: Effects of Lead on Vitamin D Metabolism in Rats

**4**

\*Al-Bahouh NA, Rao MS: Effects of prenatal diabetes on postnatal hippocampal neurogenesis, learning and memory

**5**

\*Al-Harbi A, Rahman A, Khan KM: Developmental vitamin D deficiency impairs spatial learning but has no effect on memory

**6**

Alsaqobi A\*, Joy J, Najem A, Abd-El-Basset EM: Effect of Interferon-Gamma on the Survival of Cortical Neurons

**7**

\*Khan KM, Rahman A: Exposure to low level of lead effects the expression of metallothionein-3 in the brain of young rats

**8**

\*Shaikh S, Smitha S, Rao MS: Neuroprotective role of thymoquinone in vivo-early effects

**9**

\*Upton HJ, Rao MS: Neuroprotection by thymoquinone in intracerebro-ventricular kainic acid model of temporal lobe epilepsy- Role of neurotrophic factors

### **Behavioral Sciences**

**10**

Al-Ramadan R, Salem A, Al-Brahim A, Jarah T, Al-Sabah R, Al\_Majran A: Violent Video Games and Aggression among Male High School Students in Kuwait



## **Biochemistry**

**11**

\*Al-Mutairi R, Thomas M, Benov L: Photodynamic treatment does not induce antimicrobial resistance

**12**

\*Esmail A, Al-Najem A, Al-Maghrebi M, Renno WM, Patillath S, George P: Regulation of the Matrix Metalloproteinase System in Testicular Ischemia Reperfusion Injury: Involvement of the Notch 2/Jagged 1/ Hes-1 Pathway

**13**

\*Madhu D, Khadir A, Kavalakatt S, Tiss A: Protective effects of GLP-1 analogues against cellular stress in glucose up-taking tissues under lipotoxic conditions

**14**

\*Mazumder K, Nahid S, Rahman Z, Islam, Dey S, Kerr PG: Biochemical and Histopathological evident of Cardio- and hepato-protective potential of Syzgium cumini (L.) Skeels seeds methanolic extract.

**15**

Moghnieh S, Craik J, Benov L: Mechanisms of yeast photoinactivation

**16**

Salwa Issa Al-Refaee: Thyroid hormones and dialysis

## **Cell and Molecular biology**

**17**

Irina AlKhairi, Mohamed G Qaddoumi, Preethi Cherian, Muath Alanbaei, Jehad Abubaker, Mohamed Abu-Farha: Higher level of ANGPTL8/betatrophin and ANGPTL4 in people with Hypertension.

**18**

\*Preethi T Cherian, Irina AlKhairi, Mohamed Abu-Farha, Jehad Abubaker: Proteomics analysis of betatrophin and its variants and their role in Insulin resistance and lipid metabolism

## **Community Medicine**

**19**

\*Abbas N, Fayrouz S, Al Mutairi A, Al Obadili K, Badr H: Extent and factors associated with bulimic thoughts among high school girls in Kuwait

**20**

\*Al-Anzi S, Hanna L, Al-Mutairi N, Al-Hajji R, Al-Shami A, Al-Safi H, Al-Mutawa N: Motivation and Job Satisfaction among Nurses in Public Hospitals of Kuwait



**21**

AlBeloushi A, AlKhudhair A, AlZaid D, AlEnezi D, AlShamali M, Badr H: Body Image Satisfaction and Weight Losing Behaviors Among University Students in Kuwait

**22**

\*Shemia Hussein F Hussein, Almajran Abdullah, Albatineh Ahmed N: Association of health literacy with glycemic control and Its correlates among patients with type II diabetes in Kuwait: a cross-sectional study

**23**

\*Al-Hilal MA, Al-Qaoud NA, Al-Taiar AA: Assessment of food and catering services at six public hospitals in Kuwait (Work in Progress)

**24**

\*Alkhader Hamad, Emran Basel, AL-Sulaimi Maryam, AL-Abdulhadi Dalal, Alobaidly Khalid, Al-Deai Aisha, Albatineh Ahmed N: Prevalence and gender difference in cognition and mental health among multiple sclerosis patients in Kuwait: a cross sectional study

**25**

\*AlNasrallah N, Ziyab AH: Prevalence of self-reported food allergy and its association with allergic diseases among university students in Kuwait: a cross-sectional study

**26**

Al-Sharaf D\*, Al-Enezi G, Al-Awadhi H, Al-Otaibi M, Al-Towaijri N, Khaleefa S, Akhtar S: Smoking prevalence, attempt(s) to quit and factors associated with failure to quit smoking among public employees in Kuwait

**27**

Al-Taiar A: Developing and validating physical activity questionnaire for adolescents and young adults in Kuwait.

**28**

\*Al-Taiar A, Al-Sumaie M: Kuwait Nutritional Surveillance System (KNSS): Indicators for infant and young child feeding practices

**29**

\*Al-Terkait H, Hamood H, Al-Ruwaieh S, Al-Duwaikhi A, Ali M, Al-Refae B, Ziyab AH: Knowledge, attitude, and practices towards mental health among Kuwait University students: a cross-sectional study

**30**

\*Eliwa J, Alashqar A, Abdulghaffar M, Alhaj A, Mohammad F: Breast Cancer and Mammography Screening: Knowledge, Attitudes, and Practices among Females Attending Primary Healthcare Centers in Kuwait



31

\*El-Muzaini H, Akhtar S, Alroughani R: Tobacco smoking and multiple sclerosis risk in Kuwait: A population-based matched case-control study

32

\*Faisal AM, Aljunid SM: Determinants of effectiveness of Assisted Reproductive Technology (ART) in a private hospital in Kingdom of Saudi Arabia.

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**Allied Health**

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**Health of the Health Sciences Community of Kuwait University**

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**Introduction:**

Does being a healthcare professional mean that we are healthy? In reality, are all healthcare professionals leading a healthy lifestyle as they themselves promote the same to their patients? Our study provides an awareness of having a healthy lifestyle and also evaluate the health status of all the Health Science Center (HSC) campus of Kuwait University.

**Methods:**

This study includes data from the third year of collection to evaluate the health indicators of students, and staff of the HSC of Kuwait University. This includes a health assessment questionnaire and objective measures such as heart rate, blood pressure, waist-to-hip ratio, and random blood glucose testing

**Results:**

This study included 955 subjects (270 staff, 685 students). Results showed that the staff and students had overweight/obesity percentile of 78% and 74%;  $p < 0.001$ , moderate/high stress levels of 84.8% and 91.1%, respectively. About 28.9% of staff and 10.8% of students discovered high blood pressure. The percentiles of staff and students reported having slept an average of eight hours per night were 22.8% and 26.7%, those being moderately physically active 2.5 hours of activity/week were 59.3%, 53.1% and those eating fast-food more than once per week were 97.8% and 94.0% respectively.

**Conclusions:**

Our findings revealed the continued unexpected poor status of our Health Sciences Center community. This can be a potential danger to the general community as many patients look up to their healthcare providers. In general, the sampled population indicated their knowledge of healthy lifestyle behaviors. However, time, attainable exercise facilities, and the discipline to pursue these healthy lifestyle behaviors have been a challenge to many. Hence, methods to encourage or create a healthy lifestyle behaviors in this community need to be identified.  
Kuwait University OVPR NP02/14

*Key Words: Health in Kuwait; Health care providers; Obesity and diabetes;*



## Cross-cultural Adaptation and Validation of the Arabic Version of the Knee Outcome Survey-Activities for Daily Living Scale (KOS-ADLS)

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### Introduction:

The Activities of Daily Living Scale of the Knee Outcome Survey (KOS-ADLS) is a knee-The Activities of Daily Living Scale of the Knee Outcome Survey (KOS-ADLS) is a knee-specific, patient-reported scale that has been shown to be reliable, valid, and responsive to specific, patient-reported scale that has been shown to be reliable, valid, and responsive to change. The purpose of this study was to cross-culturally adapt the original English KOS-change. The purpose of this study was to cross-culturally adapt the original English KOS-ADLS into Arabic and to validate the Arabic version. ADLS into Arabic and to validate the Arabic version.

### Methods:

In accordance with standard procedure, the original version of the KOS-ADLS was cross-In accordance with standard procedure, the original version of the KOS-ADLS was cross-culturally adapted into Arabic. The Arabic version of the KOS-ADLS was subjected to cultural adapted into Arabic. The Arabic version of the KOS-ADLS was subjected to further psychometric evaluation with 106 individuals with knee disorders. Each further psychometric evaluation with 106 individuals with knee disorders. Each participants completed the KOS-ADLS-Arabic three times: at baseline, 2-4 days later to participants completed the KOS-ADLS-Arabic three times: at baseline, 2-4 days later to evaluate test-retest reliability, and 4 weeks later to evaluate responsiveness. Arabic Short Form Health Survey (SF-36), numeric pain rating scale (NPRS), Get Up and Go (GUG) test Form Health Survey (SF-36), numeric pain rating scale (NPRS), Get Up and Go (GUG) test and ascending/descending stairs (ASC/DES<sub>stairs</sub>) tests were used to and ascending/descending stairs (ASC/DES<sub>stairs</sub>) tests were used to evaluate the validity of the KOS-ADLS-Arabic. evaluate the validity of the KOS-ADLS-Arabic.

### Results:

The cross-cultural adaptation procedure revealed no major problems with content or the cross-cultural adaptation procedure revealed no major problems with content or language. Cronbach's alpha of KOS-ADLS-Arabic was 0.97. Test-retest reliability was language. Cronbach's alpha of KOS-ADLS-Arabic was 0.97. Test-retest reliability was excellent with an ICC=0.97. The standard error of measurement was 3.14 and the minimal excellent with an ICC=0.97. The standard error of measurement was 3.14 and the minimal detectable change at 95% was 8.70. The KOS-ADLS-Arabic showed significant detectable change at 95% was 8.70. The KOS-ADLS-Arabic showed significant correlations with the SF-36-Arabic and NPRS( $r=0.28$  to  $0.63$ ,  $p < 0.001$ ), and with the GUG correlations with the SF-36-Arabic and NPRS( $r=0.28$  to  $0.63$ ,  $p < 0.001$ ), and with the GUG test and ASC/DES<sub>stairs</sub> tests ( $r=-0.47$  to  $-0.60$ ,  $p < 0.01$ ). KOS-ADLS-Arabic test and ASC/DES<sub>stairs</sub> tests ( $r=-0.47$  to  $-0.60$ ,  $p < 0.01$ ). KOS-ADLS-Arabic was able to detect changes over time (effect size=1.12, standard response mean=1.09, and was able to detect changes over time (effect size=1.12, standard response mean=1.09, and minimum clinically important difference=14 points). minimum clinically important difference=14 points).

### Conclusions:

The KOS-ADLS-Arabic is a reliable, valid and responsive measure for assessing knee- The KOS-ADLS-Arabic is a reliable, valid and responsive measure for assessing knee-related symptoms and functional limitations. related symptoms and functional limitations. (Research Grant No. [NP03/14]; Key Words: Knee; Outcome measure; KOS-ADLS;



**Anatomy**

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## **Effects of Lead on Vitamin D Metabolism in Rats**

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### **Introduction:**

High blood lead (Pb) levels and vitamin D (VD) deficiency both affect cognitive function. Blood Pb level is negatively associated with serum VD level. We therefore, investigated the effect of Pb exposure on the expression of 25-hydroxylase (25-OHase), 1 $\alpha$ -hydroxylase (1 $\alpha$ -OHase) and VD receptor (VDR) in rats.

### **Methods:**

Newborn Wistar rat pups were exposed to 0.2% Pb-acetate via their dams' drinking water from post-natal day (PND) 1 to 21 and directly in drinking water until PND30. Control rats were given tap water. Expression of the 25-OHase and 1 $\alpha$ -OHase, and VDR in liver, kidney and whole brain were analyzed by western blot (WB) and immunohistochemistry (IHC). Serum vitamin D3 (VD3) was measured by LC-MS/MS.

### **Results:**

Pb exposure did not significantly affect body, brain, liver and kidney weights. Serum VD3 level was significantly decreased in Pb-exposed rats at PND21 and PND30 ( $p < 0.05$ ). WB analysis revealed that the brain 1 $\alpha$ -OHase was insignificantly increased (by 10%) in Pb-exposed rats compared to controls at PND21, whereas at PND30 it was not affected by Pb exposure. The kidney 1 $\alpha$ -OHase was significantly decreased ( $p = 0.004$ ) by Pb exposure at PND21 but was not affected at PND30. The effect of Pb on liver 25-OHase was age-dependent; it significantly decreased at PND21 ( $p = 0.04$ ) but significantly increased at PND30 ( $p=0.02$ ). The expression of VDR in the brain was significantly increased by Pb exposure at both PND21 and PND30. IHC analysis confirmed cytoplasmic presence of VD metabolizing enzymes in the tissues tested, whereas nuclear expression of VDR in brain was observed.

### **Conclusions:**

Early postnatal Pb exposure of rats results in low serum VD levels, and causes significant increase in VDR expression in the brain. The effect of Pb on VD metabolizing enzymes is tissue specific and depends on the developmental stage of the rat pups. Further research is needed to elucidate the biochemical mechanism(s) of these effects and their physiological relev  
Supported by KU Grant # YW01/14

*Key Words: Vitamin D metabolizing enzymes; Vitamin D Receptor; Lead exposure;*



**Anatomy**

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## **Effects of prenatal diabetes on postnatal hippocampal neurogenesis, learning and memory**

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### **Introduction:**

Diabetes mellitus is a chronic metabolic endocrine disorder, characterized by abnormally high glucose levels in blood. Studies have shown that gestational diabetes produces a number of complications including a significant decrease in hippocampal neurogenesis, reduction in the pyramidal cell density in the sub regions of the hippocampus. Present experiment was aimed to study the effects of prenatal streptozotocin (STZ) induced diabetes on postnatal rat learning and memory, hippocampal cell proliferation, neurogenesis, levels of brain derived neurotropic factor (BDNF) and vascular endothelial growth factor (VEGF)

### **Methods:**

Pregnant rats were injected with STZ (60mg/kg) on gestational day10. Pups born to the STZ-injected mother were divided into two age groups [40 days (STZ-40) and 60 days (STZ-60)] Pups born to the normal control mother were also divided into two age groups [40days (NC-40) and 60days (NC-60)]. Learning and memory was tested in these rats on 31st-37th (NC-40, STZ-40) and 51st, 57th (NC-60, STZ-60) postnatal day. Rats in all groups were sacrificed after learning and memory test, brain was dissected and processed for immunostaining, western blot and ELIZA analysis.

### **Results:**

Results showed that both STZ-40 and STZ-60 had significantly poor memory retention, decreased cell proliferation, and decreased neurogenesis, less number of doublecortin positive neurons in the crest, supra-pyramidal blade and infra-pyramidal blade regions of dentate gyrus compared to NC-40 and NC-60 groups. Further BDNF and VEGF were found to be significantly decreased in hippocampal tissue in STZ-40 and STZ-60 groups compared to control groups.

### **Conclusions:**

We conclude from these results that gestational diabetes leads to an adverse effects on off-springs. (This study was supported and founded by Kuwait university research grant No.YM 01/15)

*Key Words: Hippocampus; Diabetes; Neurogenesis;*



**Anatomy**

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## **Developmental vitamin D deficiency impairs spatial learning but has no effect on memory**

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### **Introduction:**

Recent evidence suggests that Vitamin D deficiency (VDD) affects cognitive functions in adults but the effect of developmental vitamin D deficiency (DVDD) on brain development and cognitive functions has not been well-established. This study was conducted to explore the functional and structural effects of DVDD in rat pups.

### **Methods:**

The effects of DVDD on spatial learning and memory in Wistar rats at postnatal day 24 (PND24; weaning) and PND45 were analyzed by Morris water maze (MWM) test. Rat pups were divided into four groups: C (control), dG (deficient during gestation), dL (deficient during lactation), dGL (deficient during gestation and lactation). We also measured cortical thickness after MWM test at PND63 at the level of hippocampus, and counted synapses in the hippocampus at PND32 and PND63.

### **Results:**

Repeated measure ANOVA revealed that at PND24 and PND45 the dGL group learned significantly slower compared to all other groups ( $P < 0.05$ ). At PND45, also the dL learned significantly slower than the control groups ( $P < 0.05$ ). Probe test was performed after 2 days of learning sessions for Short term memory (STM) and after 10 days for long term memory (LTM). Neither STM nor LTM were affected by DVDD at both PND24 and PND45. The number of synapses at PND32 and PND63 were significantly lower in the DVDD groups than C group ( $P < 0.001$ ). All groups with DVDD showed significant reduction in cortical thickness compared to control group ( $P < 0.05$ ). No significant differences were observed among the different DVDD groups.

### **Conclusions:**

Early postnatal DVDD impairs learning, but once learning has occurred there is no significant effect on memory. Prenatal or pre-weaning VDD alone does not affect learning. Long-term effects of the DVDD-induced structural changes in the brain needs further investigation. Supported by KU Grant #YW02/15

*Key Words: Developmental Vitamin D deficiency; Learning; Brain Development;*



**Anatomy**

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## **Effect of Interferon-Gamma on the Survival of Cortical Neurons**

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### **Introduction:**

Inflammation in the brain occurs as a consequence of trauma and is associated with production of cytokines, which directly influence neuronal and glial function. Among the effects of inflammatory cytokines is regulation of neurotrophic factors. The interactions of cytokines and neurotrophic factors in the brain have important consequences for neuronal survival and function. Although the pro-inflammatory cytokine interferon-  $\gamma$  (IFN-  $\gamma$ ) is thought to be a major mediator of neuroinflammation, its role in case of brain injury remains ill-defined. The objective of this study is to examine the effect of IFN-  $\gamma$  on the cortical neuron survival in stab wound injury.

### **Methods:**

BALB/c mice were subjected to stab wound brain injury. The animals were subdivided into two groups: A and B. Group A received IP injection of IFN-  $\gamma$  (10  $\mu$ g), whereas, group B received IP injections of PBS. Animals were killed 1, 3 and 7 days after injection. Immunostaining of frozen brain sections for glial fibrillary acidic protein (GFAP) specific for astrocytes, Iba-1 (specific for microglia), Fluorochrome-B and cresyl violet (specific for degenerating neurons) were used. Western blotting was done from the tissues isolated from the injured sites.

### **Results:**

There was a gradual increase in the number of both astrocytes and microglia with a significant increase in group A. The number of degenerating neurons significantly decreased in group A. In addition, it was found that IFN-  $\gamma$  stimulated the expression of

### **Conclusions:**

IFN-  $\gamma$  induces astrogliosis and promotes the survival of cortical neurons in stab wound brain injury.

*Key Words: Astrocytes, neurons; microglia; interferon gamma;*



**Anatomy**

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## **Exposure to low level of lead effects the expression of metallothionein-3 in the brain of young rats**

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### **Introduction:**

Lead (Pb), a neurotoxicant, impairs learning and memory. Metallothioneins (MTs), metal binding proteins, protect cells from heavy metal toxicity. The brain-specific MT-3 has a role in the etiology of neurodegeneration. In this study we investigated the effect of low level of Pb exposure on the expression of MT-3 in the brain of young rats.

### **Methods:**

Wistar rat pups (n=10/group) were exposed to 0.2% Pb-acetate via their dams' drinking water from PND 1 to 21 and directly via drinking water from weaning until PND 30. The control group (n=10) was given tap water. Expression of MT-3 was measured by Western blot (WB) and by immunohistochemistry in various regions of the brain.

### **Results:**

WB analysis of the whole brain lysate from PND21 rats showed two distinct bands; one at ~30kD and one at ~10kD. In PND30 rats, only the 30kD band was seen. Quantitation of these bands revealed that Pb exposure significantly increased MT-3 expression in both age groups (p=0.0001 & 0.04). From the hippocampal lysate, only the 30kD band was observed and its quantitation revealed that in both groups the expression of MT-3 was significantly decreased after Pb exposure (p=0.02 & 0.0068). Number of immunoreactive (IR) neurons in a standardized area of different brain regions were counted and compared between control and Pb-exposed rats. At PND21, more IR neurons were observed in the cortex and in the CA1, CA2 and CA3 regions of the hippocampus in the Pb-exposed rats compared to control. No effect was seen in the dentate gyrus and the thalamus. At PND30, MT-3 IR neurons were increased only in the cortex of Pb-exposed rats compared to control, whereas in the thalamus and the CA2 and CA3 regions of the hippocampus fewer MT-3 IR neurons were observed in the Pb-exposed rats compared to control. CA1 and dentate gyrus were largely unaffected.

### **Conclusions:**

These results suggest that the effect of Pb on MT-3 expression is dependent on the developmental stage of the rats and is brain-region specific.

Funding: RW01/14

*Key Words: Lead toxicity; Metallothionein-3; Brain;*



**Anatomy**

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## **Neuroprotective role of thymoquinone in vivo-early effects**

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### **Introduction:**

Thymoquinone (TQ), an active constituent of *Nigella sativa* seeds, possesses anti-inflammatory and neuroprotective properties. TQ is reported to enhance the neuroprotection in different CNS diseases and animal models of neurodegeneration. Objective of the present experiment was to study the neuroprotective role of TQ, in kainic acid model of temporal lobe epilepsy (KA-TLE) at an early stage.

### **Methods:**

Four months old male Wistar rats were divided into three groups: (i) normal control (NC, n=12), (ii) lesion only (LO, n=12) and (iii) lesion + thymoquinone (L+TQ, n=12). Rats in the NC group remained undisturbed. Rats in the LO group received kainic acid lesion bilaterally in the hippocampus (0.5µg/ventricle). Rats in the L+TQ group were lesioned as in LO group and were treated with TQ (10mg/kg) orally, three hours before lesion and daily thereafter for 12hrs, 24hrs, 48hrs 72hrs and 4days post lesion period. A day after last treatment, all rats were anesthetized and perfused with 4% paraformaldehyde. Brains were dissected and processed for cresyl violet, fluorojade-B staining, BrdU, BrdU-DCX, Iba1 and GFAP immunostaining.

### **Results:**

Cresyl violet and fluorojade-B staining showed a typical lesion and significantly ( $p < 0.01-0.001$ ) more neurodegeneration in the dentate hilus in LO group at 12hrs, 24hrs, 48hrs 72hrs and 4days post lesion period compared to L+TQ group. BrdU, BrdU-DCX double labeling showed significantly ( $p < 0.001$ ) more proliferating cells and increased neurogenesis in the dentate gyrus in L+TQ groups compared to LO groups at all-time points studied. GFAP and Iba1 immunostaining showed significantly more number of astrocytes and microglial cells in the dentate hilus in L+TQ groups compared to LO group

### **Conclusions:**

Results of the experiment strongly suggest that TQ provides neuroprotection in KA-TLE at early stage. TQ enhances gliosis in the hippocampus and provides support to neurons and enhance neurogenesis in the dentate gyrus.

*Key Words: Thymoquinone; Neuroprotection; Epilepsy;*



**Anatomy**

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## **Neuroprotection by thymoquinone in intracerebro-ventricular kainic acid model of temporal lobe epilepsy- Role of neurotrophic**

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### **Introduction:**

Temporal lobe epilepsy (TLE) is the most common type of epilepsy among other types of epilepsies. Recent studies and our earlier studies have indicated the neuroprotective role of thymoquinone (TQ), the active component of nigella sativa oil in intracerebro-ventricular kainic acid (ICV-KA) model of temporal lobe epilepsy. Although TQ, to be effective in restraining ICV-KA induced epileptic changes in the hippocampus, its mechanisms of actions have not previously been studied. Present study was aimed to investigate the mechanisms of actions of (TQ) in neuroprotection in intra-cerebro-ventricular kainic acid (ICV-KA) model of temporal lobe epilepsy in young rats.

### **Methods:**

Male Wistar rats (4 months old) were divided into groups: Normal control (NC, n=12), lesion only (LO, n=12), and lesion + thymoquinone (L+TQ, n=12). Rats in the control group remained undisturbed. Rats in the lesion only group received a kainic acid lesion bilaterally in the hippocampus (0.5µg/ventricle). Rats in the lesion + Thymoquinone group were treated with TQ (10mg/kg) intraperitoneally, 3 hours before lesion and daily thereafter for four days. On 5th post-lesion day rats in all groups were anesthetized and perfused with 4% paraformaldehyde, and processed for cresyl violet and Fluoro-jade-B staining and NeuN, OX-42 and GFAP immunostaining. Fresh hippocampal tissues were processed for Western blot analysis of (GFAP), BDNF and VEGF.

### **Results:**

Results of the study showed significantly decreased neurodegeneration in the KA+TQ treated rats compared to LO group. Astrocyte number and GFAP content and microglial cells were significantly increased in TQ treated group ( $p<0.01$ ) compared to NC and LO groups. Further, TQ treatment also increased the levels of BDNF and VEGF in the hippocampus ( $p<0.01$ ) in TQ treated group.

### **Conclusions:**

We conclude that TQ protects the neurons by increasing the astrogliosis and increasing the release of neurotrophic factors. (Supported by College of Graduate studies, KU)

*Key Words: Hippocampus; EPILEPSY; BDNF;*



## **Violent Video Games and Aggression among Male High School Students in Kuwait**

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### **Introduction:**

The literature is inconclusive about the link between violent video games and aggression among young people. Some studies implicate the violent content itself while other studies have found the process of playing a violent video game (e.g., frustration, competitiveness) as more plausible explanation for aggression. The current study sought to assess the relationship between violent video games and aggression among 10th grade male students in Kuwait, explore socio-demographic variables related to video games and aggression, and to investigate factors related to the use of violent video games.

### **Methods:**

Cross-sectional study conducted on a randomly selected sample (N = 589; tenth grade male students from all six governorates of Kuwait). This study employed a questionnaire composed of socio-demographic questions, video gaming characteristics, and the Buss & Perry aggression questionnaire.

### **Results:**

Most of the participants were Kuwaiti with a mean age of 15.21 and a standard deviation of 0.84. Before controlling for variables (such as age and parent's education level), the number of hours of playing violent video games, whether during school days or weekends showed no statistically significant association with aggression scores. After controlling for such variables, it appears that longer playing hours during weekdays (2-5 hours) is associated with lower aggressive behavior. Having a lower GPA and playing video games that contain elements of fighting or online gameplay are each associated with aggression. Additionally, higher mother's education is associated with more monitoring and supervision of the adolescent.

### **Conclusions:**

Longitudinal studies are needed to explain cause and effect, as well as whether frustration and competitiveness influence aggressive behavior. However, playing violent video games could decrease aggression possibly through, for example, sublimation or sense of achievement. Also higher mother's education is associated with more supervision of the child.

*Key Words: Violent; videogames; aggression ;*



## **Photodynamic treatment does not induce antimicrobial resistance**

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### **Introduction:**

Recently WHO declared antibiotic resistance as one of the biggest threats to global health. This poses a demand for the development of alternative antimicrobial treatments to which bacteria do not develop resistance. Photodynamic inactivation (PDI) of bacteria, viruses, and fungi is a promising new antimicrobial approach. So far, it is questionable if microbes can develop resistance against PDI. The aim of this work was to answer this question using *E. coli* as a Gram-negative repetitive with Zn(II) meso-tetrakis(N-hexylpyridinium -2-yl)porphyrin as a photosensitizer.

### **Methods:**

The strains of *E. coli* were GC4468 (antibiotic sensitive) and QC1799 (antibiotic resistant). Sublethal PDI treatment was performed for ten consecutive cycles. After each cycle, cell viability was assessed by MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide ] assay while the ability to proliferate was tested using plating and enumerating colonies.

### **Results:**

PDI killed approximately 90% of the cells in both non-treated and sublethally-treated populations. The survival rate remained the same even after ten cycles of PDI exposure. Resistance to antibiotics did not protect the cells against PDI.

### **Conclusions:**

In contrast to antibiotics, surviving bacterial fractions were not capable of developing resistance against PDI. Antibiotic-resistant and antibiotic-susceptible bacteria are equally sensitive to PDI, which makes photoinactivation an attractive option for fighting antibiotic resistance. Funding: Kuwait University Grant MB02/12

*Key Words: photodynamic therapy; antimicrobial resistance; photosensitizer ;*



## **Regulation of the Matrix Metalloproteinase System in Testicular Ischemia Reperfusion Injury: Involvement of the Notch 2/Jagged 1/Hes-1 Pathway**

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### **Introduction:**

The aim of the study is to examine the role of Matrix metalloproteinases (MMPs) and their inhibitors (TIMP) during testicular ischemia reperfusion injury (tIRI), the involvement of the Notch pathway, and their modulation by the antioxidant, Genistein.

### **Methods:**

Three groups of male Sprague–Dawley rats were used: sham, tIRI, and genistein-treated (10mg/Kg). ELISA assay, colorimetric assay, and H&E staining were used to evaluate the protein expression of MMPs and TIMPs, activation of the Notch 2/Jagged 1/hes-1 signaling pathway, apoptosis induction, as well as damage to spermatogenesis.

### **Results:**

Testicular IRI induced severe tubular damage, a significant increase in MMP-2 and MMP-9 expression and decreased expression TIMP-1 and TIMP-2. Rats subjected to tIRI had low total antioxidant capacity of the testis, decreased superoxide dismutase activity, and increased oxidative DNA damage. Enhanced activities of caspase 8, caspase 3 and PARP were also observed during tIRI. Genistein reversed the tIRI-induced suppression of the Notch 2/Jagged 1/hes-1 pathway.

### **Conclusions:**

Genistein was able to salvage the testicular structure and function through restoring the MMP-TIMP anti-proteolytic balance, suppressing spermatogenic damage, alleviating oxidative stress and apoptosis. The Notch pathway was partly involved in inhibiting the tIRI-induced testicular impairment

*Key Words: Testicular ischemia reperfusion injury; Matrix metalloproteinase system;*



## Protective effects of GLP-1 analogues against cellular stress in glucose up-taking tissues under lipotoxic conditions

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### Introduction:

Increase in glucagon-like peptide-1 (GLP-1) activity has recently emerged as a useful therapeutic tool for the treatment of type 2 diabetes (T2D) by enhancing the glycemic control and also helping in maintaining or even decreasing body weight of most patients. The action of GLP-1 and its mimetics on pancreatic  $\beta$ -cells as well as on nervous and digestive systems are relatively well established. The effect of this peptide and its analogues in other tissues including adipose, muscles and liver, however, are still poorly defined. We therefore investigated the potential beneficial effects of GLP-1 mimetics on those peripheral tissues using established cell lines.

### Methods:

Using cell lines from liver (HEPG2), muscle (L6) and adipose tissue (3T3-L1), we analysed the effect of GLP-1 mimetic (Exendin-4) on MAPKs in the presence of stressing amounts of palmitic acid (PA). Differential protein expression pattern was investigated using LC-MS/MS Orbitrap system and label-free quantification with a focus on the MAPKs. Results were validated using Western blotting, RT-PCR approaches. Cell viability assay was also performed.

### Results:

In all used cell lines, Under lipotoxic conditions (400uM PA) a set of proteins related to lipid homeostasis were also modulated by GLP-1 analogues. We showed that JNK and ERK MAP-Kinases were among the proteins that were highly modulated by GLP-1 analogues both at the expression and phosphorylation levels which was validated by proteomic profiling, and mRNA and protein expression levels. Furthermore, cell viability assays have shown that exendin-4 alleviated the palmitate induced cell death.

### Conclusions:

Our results suggest that GLP-1 mimetics alleviate the lipotoxicity-related cellular stress in peripheral cells and thus restoring their normal homeostatis  
KFAS,RC-14015001

*Key Words: GLP-1 analogues; ER stress; MAPKs;*



## **Biochemical and Histopathological evident of Cardio- and hepato-protective potential of *Syzigium cumini* (L.) Skeels seeds methanolic extract.**

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### **Introduction:**

Objective: To evaluate the effect of *Syzigiumcumini* (L.) Skeelsseeds methanolic extract (MESC) on major organs during diabetes by using animal model through biochemical and histopathological study.

### **Methods:**

100 and 200 mg/kg body weight of MESC doses were administered to alloxan-induced diabetic rats daily with fasting blood glucose levels being measured by glucometry at one-day intervals for the duration of the 2-week study. Biochemical assays to evaluate any changes in the functions of heart, liver, pancreas and kidney were carried out. Histopathological changes in diabetic rat organs (pancreas, liver, heart, kidney and spleen) were also observed after the 14 days of treatment with the extract.

### **Results:**

Oral administration of MESC (100 and 200 mg/kg body weight), and glycazide as a positive control (25 mg/kg), showed beneficial effects on lowering blood glucose levels ( $P < 0.001$ ) as well as improved heart and liver functions and hyperlipidemia due to diabetes. At 200 mg/kg, MESC reversed cardiac and liver damage caused by alloxan.

### **Conclusions:**

Beside the antihyperglycemic activity of MESC, the extract demonstrates potential to stop cardiac and hepatic complications

*Key Words: Syzigium cumini seeds; albino rats; biochemical analysis;*



## **Mechanisms of yeast photoinactivation**

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### **Introduction:**

The relatively small number of available antifungal medications, and emerging problems of resistance, pose a demand for development of new methods for fighting fungal infections. Photodynamic therapy (PDT) is a novel antimicrobial approach that avoids resistance. In PDT, a photosensitizer (PS) and molecular oxygen combine to produce reactive species that damage the target cell. Development of new, more efficient, PSs requires knowledge of targets whose photodamage is essential for efficient antifungal activity. The aim of this study was to investigate potential targets and mechanisms of photo-induced fungal cell

### **Methods:**

Zn (II) N-alkylpyridylporphyrins (ZnPs) were used as PSs, and photodamage was studied on *Saccharomyces cerevisiae* as a model fungal system. Cells were incubated with different concentrations of PSs for 90 minutes and illuminated for 60 min. Potential metabolic and structural targets were investigated by flow cytometry and assessment of enzymatic activity. Experiments were repeated at least 3 times with 3 replicates. Results were expressed as means  $\pm$  S.E.

### **Results:**

Upon illumination, ZnPs suppressed yeast metabolism and inflicted life-incompatible membrane damage. Among the sensitive cellular targets were the metabolic enzymes isocitrate dehydrogenase and lactate dehydrogenase. Illumination of membrane-associated ZnPs compromised plasma membrane integrity and caused leakage of metabolites and macromolecules.

### **Conclusions:**

Photo-dependent inactivation of yeasts involves damage to essential metabolic enzymes and the plasma membrane. As a consequence, fungi lose their ability to generate ATP and lyse due to loss of plasma membrane barrier function. Amphiphilic character is an important feature of PSs with high antifungal activity.

YM 03/13 from Kuwait University

*Key Words: photoinactivation; antifungal; photosensitizer;*



## Thyroid hormones and dialysis

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### Introduction:

Dialyzed patients have increased incidence of primary hypothyroidism and subclinical hypothyroidism. At the same time, renal failure affects circulating thyroid hormones in multiple ways, including low concentration, altered peripheral metabolism, disturbed binding to carrier proteins, possible reduction in tissue content, and increased iodine store in thyroid glands. Meanwhile, hypothyroidism is an under-appreciated in renal-impaired patients since classical clinical signs and symptoms may be absent, even in severe hypothyroidism. We investigated the benefit of ordering dialysis tests received by our renal function test

### Methods:

We studied retrospectively, the results of patients attending jabber al-Ahamd armed forces hospital for dialysis during the period 2015-2016. We compared the results of free T4 (FT4), thyroid stimulating hormone (TSH) ferritin and parathyroid hormone (PTH) using SPSS statistical package. Receiver operating curves (ROC) constructed for these parameters in reference to renal failure.

### Results:

700 dialyzed patients were involved showed significant difference between males and females for ferritin ( $p = 0.00$ ), FT4 ( $p = 0.05$ ), & PTH ( $p = 0.018$ ) concentrations but not TSH ( $p = 0.3$ ); Mann-Whitney test. FT4 correlated significantly with PTH ( $p < 0.05$ ; Spearman's correlation). Ferritin didn't show correlation with any parameter ( $p > 0.05$ ) so excluded from further analysis. ROC curves showed TSH having highest area 0.744 ( $p = 0.04$ ) 90% sensitivity and 85% specificity.

### Conclusions:

TSH can be considered as a marker of renal impairment & therefore preservation of renal function in dialyzed patients could be approached by thyroid hormone replacement. Further studies needed.

*Key Words: thyroid; dialysis; ROC;*



*Cell and Molecular biology*

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## **Higher level of ANGPTL8/betatrophin and ANGPTL4 in people with Hypertension.**

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### **Introduction:**

Objective: To compare the plasma and adipose tissue level of ANGPTL3, 4 and 8 in age and BMI matched subjects with or without hypertension.

### **Methods:**

A total of 119 subjects were enrolled in this study, 50 non-hypertension and 69 with hypertension. Plasma level of ANGPTL 3, 4 and 8 were measured by ELISA. Real time PCR was used to measure their level in adipose tissue.

### **Results:**

In this study, we showed that ANGPTL 4 and 8 were higher in subjects with hypertension. ANGPTL4 level in subjects with hypertension was  $202.49 \pm 17.44$  ng/mL compared to subjects without hypertension  $160.64 \pm 10.36$  ng/mL, (p-Value=0.04). ANGPTL8 level in subjects with hypertension was  $2310.96 \pm 194.88$  pg/mL vs  $1583.35 \pm 138.27$  pg/mL in subjects without hypertension (p-Value=0.001). ANGPTL3 level was not significantly different between the two populations. Dividing the subjects according to their diabetes status showed a similar trend for both ANGPTL4 and 8 where T2D subjects with hypertension had higher levels of ANGPTL4 and 8. ANGPTL4 and 8 showed a similar expression profile in adipose tissues.

### **Conclusions:**

our data show that ANGPTL 4 and 8 are increased in subjects diagnosed with hypertension in both plasma and adipose tissue. ANGPTL3 was not significantly different between both groups. ANGPTL4 and 8 increased level in hypertension highlights their potential involvement in this disease and their potential role as biomarkers for hypertension and even their therapeutic value given their role in regulating lipid metabolism.

KFAS RA-2014-021

*Key Words: betatrophin/ANGPTL8; ANGPTL4; hypertension;*



## **Proteomics analysis of betatrophin and its variants and their role in Insulin resistance and lipid metabolism**

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### **Introduction:**

Diabetes is a global health problem that is caused by impaired insulin production from pancreatic  $\beta$ -cells. Betatrophin has been recently shown to induce beta-cell proliferation and to regulate triglyceride (TG) and fatty acid metabolism. We performed a cross-sectional study on 283 nondiabetic Arabs to examine the betatrophin levels. On the same sample set, using Sanger sequencing method two sequence variants were identified in betatrophin gene (Rs.892066 and Rs.2278426). The heterozygote form of the Rs.2278426 SNP showed higher level of fasting blood glucose (FBG) than the homozygote form in Kuwaitis. Objective: Our current objective is to understand the effect of the mutation on the role of betatrophin in glucose and lipid metabolism. Also to identify new target proteins that might be involved in its function and in lipid regulation.

### **Methods:**

Flag Tagged Betatrophin and its variants were cloned and transfected into HepG2 cells. Their expression was tested using FLAG antibody by western blot. Protein profiling was done using LC/MS.

### **Results:**

Overexpression of betatrophin in HepG2 cells resulted in changes in a number of expressed proteins. A selected number of differentially expressed proteins were identified by LC/MS such as SEC24 family members that are involved in lipid metabolism.

### **Conclusions:**

Proteomics data sheds more light into the possible role of betatrophin in regulating cholesterol synthesis through its regulation of SEC24 family members. KFASTAC-14013003.

*Key Words: betatrophin; lipid and glucose; Type 2 diabetes;*



## **Extent and factors associated with bulimic thoughts among high school girls in Kuwait**

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### **Introduction:**

Bulimia Nervosa (BN) is an eating disorder characterized by compulsive overeating usually followed by self-induced vomiting. Our study aimed to assess the extent of BN thoughts its association with body mass index, depression and other contributing factors among 12th grade school girls in Kuwait.

### **Methods:**

In this cross-sectional study, a two-stage cluster sample was employed to collect data from 1606 female students. The self-administered questionnaire covered students' socio-demographics, self-reported weight and height, Bulimic Automatic Thoughts Test questionnaire to screen for bulimic thoughts, environmental factors that might be associated with bulimic thoughts, and Kutcher Adolescent Depression Scale to screen for depression. Spearman's correlation and binary logistic regression were used for analysis.

### **Results:**

The extent of BN thoughts more than the median score among female adolescents was 46.9%. There was significant positive correlations between BN thoughts and obesity and depression. The multivariate analysis revealed that relatively older adolescents, poor academic performance, studying Arts major, environmental factors (parental, peers, media and exposure to bullying because of obesity), obesity, and depression were significantly

### **Conclusions:**

Psycho-socio-demographic factors and overweight/obesity were significant correlates to the presence of BN thoughts among adolescent girls. These findings may aid the health planners and policy makers in both Ministries of Education and Health in Kuwait to activate the role of school health programs to promote adopting healthy lifestyle amid students. Moreover, the imperative role of school psychological workers to help students to adopt healthy methods in coping with stressors can't be neglected.

*Key Words: Bulimia Nervosa; Depression; Adolescents;*



*Community Medicine*

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## **Motivation and Job Satisfaction among Nurses in Public Hospitals of Kuwait**

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### **Introduction:**

Introduction: Attempts are constantly being made to improve global healthcare systems. An important prerequisite of such initiatives is a well-motivated and satisfied workforce. Thus, an understanding of what motivates and satisfies nurses in their jobs and work environment is crucial and mandatory in order to accomplish a positive attitude towards their work. This study aimed to evaluate the level of job satisfaction and motivation and identify factors associated with motivation and job satisfaction among nurses in the public hospitals of Kuwait.

### **Methods:**

This was a cross-sectional study conducted in the five public hospitals of Kuwait, where 417 randomly selected nurses from Medical, Surgical, and Emergency specialties were included. Response rate was 75.8%. The nurses were given a self-administered questionnaire with 59 questions and three sections, which are sociodemographic factors, motivation, and job satisfaction.

### **Results:**

The mean age of respondents was 34.1 years. The majority of the study population was composed of female (71%) and Indian (62.0%) nurses. The prevalence of motivation and job satisfaction was 53.9% and 56.1%, respectively. The feel of being respected by doctors or not was the major factor affecting both motivation (adjusted odds ratio of 2.5;  $p=0.002$ ) and job satisfaction (adjusted odds ratio of 8.4;  $p<0.001$ ), after adjusting for confounding variables.

### **Conclusions:**

In general, no significant difference in the levels of job satisfaction and motivation between the five public hospitals was found. A number of work-related and sociodemographic factors were found to be significantly associated with motivation and job satisfaction.

*Key Words: Motivation; Job Satisfaction; Nurses ;*



## **Body Image Satisfaction and Weight Losing Behaviors Among University Students in Kuwait**

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### **Introduction:**

Body image satisfaction is an important issue among adolescents and young adults. This study aimed to assess body image perception, to examine its association with self-esteem, and weight losing behaviors, and to determine the factors associated with body image dissatisfaction amid university students in Kuwait.

### **Methods:**

A cross-sectional study was conducted among a convenience sample of 1022 students. A self-administered anonymous questionnaire was used to collect socio-demographic data in addition to modified version of the Body Shape Questionnaire, and Rosenberg self-esteem scale. Data were also collected on environmental factors influencing body image perception, a set of weight losing methods and self-reported weight and height.

### **Results:**

About 65% of students reported body image dissatisfaction. The study found an indirect association between body image dissatisfaction and self-esteem ( $p < 0.001$ ), and direct association with weight losing behaviors ( $p < 0.001$ ). The multinomial logistic regression analysis revealed that high income, increased BMI, bullying victims due to body image, media and friends' pressure, and strong beliefs about advantages of being thin were significant correlates to body image dissatisfaction.

### **Conclusions:**

Body image dissatisfaction was prevalently high among university students in Kuwait. Biological and psycho-social factors significantly contributed to body image dissatisfaction. Low self-esteem and weight losing behaviors were concomitant with body image dissatisfaction. These findings are important to policy makers and health planners to aid in preventing these modifiable risk factors through implementing youth campaigns aiming to promote healthy lifestyles to keep normal body weight and healthy methods of losing weight. Counseling services ought to be available in all universities in Kuwait to help students to overcome environmental pressures associated with body image dissatisfaction to prevent the risk of evolving low self-esteem.

*Key Words: body image,; self-esteem,; Adolescents;*



## Association of health literacy with glycemic control and Its correlates among patients with type II diabetes in Kuwait: a cross- sectional study

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### Introduction:

Health literacy (HL) is a combination of information and numeracy skills and how to apply them in order to improve health outcomes. Limited HL is common among elderly people and patients with chronic diseases such as diabetes. Patients with limited HL tend to have more hospitalization rates, less medication adherence and poor disease management. A cross-sectional study was conducted to estimate the prevalence of HL in patients with type II diabetes, investigate the association between HL levels and glycemic control and assess the effect of several factors on HL.

### Methods:

A sample of 359 eligible patients with type II diabetes identified from Public Primary Health Care Clinics across the six governorates of Kuwait. HL was assessed using the Short form Test of Functional Health Literacy in Adults questionnaire (STOFHLA). The most recent Glycated hemoglobin (HbA1c) was taken from patients records.

### Results:

Participants were mainly female (51.5%), married (79.9%), employed (58.8%), had high school or diploma (39%), Kuwaiti (50.7%), had monthly income less than 500 KD (35%), treated with oral hypoglycemic drugs alone (58.5%), had poor glycemic control (78%), obese (51.4%) and live in Farwaniya (29.5%). The Median (IQR) of HbA1c was 8.1% (2.9). Overall, 45.5% of the participants had inadequate HL, 19% had marginal HL and 35% had adequate HL. There was significant association between HL and HbA1c levels ( $p < 0.007$ ) after adjustment for Age, gender, marital status, nationality, governorates, education level, employment status, monthly income, years living with diabetes, treatment regimen and BMI using multiple linear regression.

### Conclusions:

HL scores in patients with type II diabetes is low. HL level you will have. HL is significantly associated with HbA1c levels. Effective interventions should be implemented among patients with inadequate HL to improve their diabetes outcomes.

*Key Words: Health literacy, Glycemic control; Type II Diabetes, HbA1c; STOFHLA,*



## **Assessment of food and catering services at six public hospitals in Kuwait (Work in Progress)**

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### **Introduction:**

**Background:** Hospital foodservices are essential in patient recovery and wellbeing. Quality of this service has an impact on patient satisfaction with overall hospital experience. Understanding of the dimensions of the foodservice satisfaction is an important element in understanding patient expectations and promoting patient's health. Identification of contributing variables to foodservice dissatisfaction assist in making further modifications in meeting patient expectations with regard to foodservice offered at the hospital

Objectives: To evaluate food and catering services offered to patients at six public hospitals in Kuwait

### **Methods:**

A cross-sectional study was conducted using a 26-item questionnaire by interview by a trained dietitian or specialist staff from foodservices department. The questionnaire was pilot tested on 26 patients that were excluded from this study. Patients were included if admitted for at least two days in Adan, Amiri, Mubarak Al-Kabeer, Farwaniya, Rehabilitation and Maternity hospitals, and were on normal diet and have physical ability to communicate with the researcher. Chi-Square or Fisher's exact test were used as appropriate to test for the difference in proportion of satisfaction between different hospitals

### **Results:**

A total of 491 patient participated in this study. Approximately half of the participants were Kuwaitis. Of the study participants, 44.4% and 38.7% rated hospital food as either very good or good, respectively. This was lower among Kuwait compared to non-Kuwaiti (P=0.001). The majority of the patients were satisfied with the amount and appearance of food served at the three meals. The difference in satisfaction between different hospitals could be explained by nationality of patients

### **Conclusions:**

Majority of admitted patients were satisfied with the food and catering service in the six public hospitals. Further qualitative studies should be conducted to investigate the higher level of dissatisfaction among Kuwaiti patients

*Key Words: foodservice; patient satisfaction; nutrition;*



## **Prevalence and gender difference in cognition and mental health among multiple sclerosis patients in Kuwait: a cross sectional study**

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Kuwait University

### **Introduction:**

Multiple sclerosis (MS) is a chronic neurological disease which is considered the most common autoimmune disorder of the central nervous system. It has a dramatic impact on a person's emotional and mental well-being. The main objectives of this research are (1) estimate the prevalence of cognition and mental health impairment among MS patients in Kuwait (2) test their association with socio-economic/demographic factors.

### **Methods:**

Data were collected from 224 MS patients. As part of MS quality of life inventory (MSQOLI), mental health inventory (MHI) was used to estimate the score for mental health, while perceived deficit questionnaire (PDQ) was used to estimate the score for cognition.

### **Results:**

The prevalence of cognition and mental health impairment was 23.3% and 14.1%, respectively. When stratified by gender, there was significant difference in mental health impairment. When stratified by nationality, there was significant difference between Kuwaiti and Non-Kuwaiti Arabs in cognition. People with income less than 500 Kuwaiti Dinars had median cognition score worse than all others.

### **Conclusions:**

Future interventions should be directed toward women, low income people, and non-Kuwaiti-Arabs. Allowing non-Kuwaiti-Arabs and low-income patients' free access to MS medical care may substantially reduce cognition and mental health impairment among MS patients in Kuwait.

*Key Words: Multiple Sclerosis, Cognition; Mental Health, Prevalence; Quality of Life*



## Prevalence of self-reported food allergy and its association with allergic diseases among university students in Kuwait: a cross-

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### Introduction:

Food allergy (FA), defined as an adverse immunologic response to a dietary protein, is a challenging public health problem. Epidemiologic evidence suggests that the prevalence of FA is increasing; however, empirical knowledge on the burden of FA is lacking in Kuwait. Hence, this study sought to estimate, for the first time, the prevalence of self-reported FA and assess its association with allergic diseases among university students in Kuwait.

### Methods:

A cross-sectional study was conducted among Kuwait University students (n = 1,154). Participants self-completed a questionnaire on symptoms and history of clinical diagnosis of FA and allergic diseases, including asthma, rhinitis, and eczema. Associations between FA and personal history of allergic diseases were evaluated using log-binomial regression. Prevalence ratios (PR) and their associated 95% confidence intervals (CI) were estimated.

### Results:

The current study enrolled 1,154 students out of the 1,561 students who were approached (response proportion: 73.9%). Of the total study sample, 892 (77.3%) were female and 262 (22.7%) were male participants. Prevalence of self-reported FA was estimated to be 16.6% (95% CI: 14.3-18.9) in the total study population. Self-reported FA was more common among female (18.8%) than male (8.9%) study participants (p-value < 0.001). The most common food allergies reported were to eggplant (2.7%), seafood (2.5%), eggs (2.4%), and milk/dairy-products (1.4%). Self-reported FA was associated with increased prevalence of asthma (PR = 2.50, 95% CI: 1.77-3.53), rhinitis (PR = 2.01, 95% CI: 1.55-2.59), and eczema (PR = 2.66, 95% CI: 1.76-4.01).

### Conclusions:

This study demonstrated, for the first time, that FA affects a considerable proportion (16.6%) of university students in Kuwait. The estimated prevalence of self-reported FA in this study is comparable to estimates from westernized countries. FA was associated with higher prevalence of asthma, rhinitis, and eczema.

Research Grant No. [ZM01/15]

*Key Words: Food allergy; Epidemiology; Prevalence;*



## Smoking prevalence, attempt(s) to quit and factors associated with failure to quit smoking among public employees in Kuwait

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### Introduction:

Globally, smoking is considered as the number one behavioral cause of death. This study aimed to assess prevalence of smoking, attempt(s) to quit and failure to quit smoking and factors associated with failure to quit smoking among public sector employees in Kuwait.

### Methods:

A cross-sectional study was conducted during October 2016. A structured and self-administered questionnaire was used to collect data from public sector employees in Kuwait. The questionnaire composed of questions on socio-demographics and smoking-related variables. Prevalence of smoking in sampled employees, attempt(s) to quit and failure to quit smoking among smokers in the sample was computed. Multivariable logistic regression analysis was carried out to identify the factors associated with failure to quit smoking.

### Results:

The prevalence of current and past smoking (ex-smokers) was 23.7% (188/793), and 5.2% (41/793) respectively. Of smokers (current and ex-smokers), 83.8% (192/229) attempted to quit smoking. Of smokers who tried to quit, 77.1% (148/192) failed to quit smoking. Compared to the participants who were more than 50 years of age, the participants were significantly more likely to fail to quit smoking if they were in the age band of 21-30 years (adjusted OR = 12.0; 94% CI: 2.9 – 49.9) or 31-40 years (adjusted OR = 4.9; 94% CI: 1.2 – 20.5). Furthermore, smokers were more likely to fail in their attempts to quit smoking if they reportedly have been smoking 11-20 cigarettes per day compared to those who reported their daily consumption of 5 or less cigarettes (adjusted OR = 4.9; 95% CI: 1.1 – 22.2).

### Conclusions:

The prevalence of current and past smoking (ex-smokers) was 23.7%, and 5.2% respectively. Of ever smokers, 83.8% attempted to quit and 77.1% failed to quit smoking. Targeted intervention may help quit-smoking efforts to succeed in this population and similar populations elsewhere.

*Key Words: Smoking prevalence; Failure-to-quit smoking; Factors;*



## Developing and validating physical activity questionnaire for adolescents and young adults in Kuwait.

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### Introduction:

**Background:** Developing and validating a reliable tool to measure Physical activity (PA) for adolescents is essential to identify groups with low PA, to monitor the trends in PA and evaluate the impact of interventions that aim to improve PA.

**Objectives:**

This study aimed to develop and validate a questionnaire that measures PA among adolescents and young adults in Kuwait using accelerometers.

### Methods:

Two questionnaires have been simultaneously validated on 62 participants selected from five schools. The first questionnaire was PA questionnaire for youth which we translated and adapted using standard protocol. The second questionnaire was developed de novo after extensive literature review. Both questionnaires were validated against ActiGraph® GT3X accelerometers which were fitted on each participants for 7 days. The Actigraph files were analyzed using ActiLife® 6.13.3 software and Spearman's (rho) correlation coefficient was used to estimate the relative validity of the two questionnaires.

### Results:

Of 62 participants, 34 were male and the mean (SD) age was 16.2 (0.96) years. The time spent on PA measured by the developed questionnaire, was significantly linked to the measured PA using accelerometers, including MET rate and total steps count, ( $\rho=0.73$ ; 95%CI: 0.33- 0.91; p-value=0.003) and ( $\rho=0.92$ ; 95%CI: 0.76- 0.97; p-value<0.001), respectively. Similarly, score of PA measured by the translated questionnaire showed significantly correlation with measured PA using accelerometers, ( $\rho=0.69$ ; 95%CI: 0.25- 0.89; p-value=0.006) and ( $\rho=0.83$ ; 95%CI: 0.54- 0.94; p-value<0.001), for MET rate and total steps count, respectively.

### Conclusions:

Both questionnaires seem to be a valid measure of PA among adolescents and young adults in Kuwait. A study with larger sample size among high school students and middle school students is warranted before these two questionnaires are used routinely to measure PA among adolescents in Kuwait

*Key Words: Adolescents; validity; accelerometer;*



## Kuwait Nutritional Surveillance System (KNSS): Indicators for infant and young child feeding practices

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### Introduction:

Kuwait Nutritional Surveillance System (KNSS) collects data from Kuwaiti children on various aspects of nutrition. We summarized the results of the KNSS related to the indicators for assessing infant and young child feeding practices as outlined by WHO.

### Methods:

Children  $\leq 2$  years were selected from health centres during vaccination from all governorates of Kuwait. Data were collected by face-to-face interviews on infant feeding practices. Weight of children was measured using digital scale to the nearest 100 gm; while length was measured to the nearest 0.1 cm using length board. Data collectors were trained to conduct the interview and measurements in a standardized manner.

### Results:

Data were collected on 1723 children of whom 876(50.8%) were males. Approximately, 83% of mothers, reported they had received an advice to breastfeed their child in the hospital with no significant difference between public and private hospitals ( $p=0.08$ ). Overall, 31.54% initiated breastfeeding within the first hour of delivery or cesarean section. This was higher in public hospital compared to private hospitals (36.88% vs.30.27%,  $p=0.04$ ). Of children  $\leq 2$  years, 89.26% were ever breastfed with no difference by the gender of child or the place of delivery. This was lower in Jahra and Mubarak Al-Kabeer Governorates compared to other governorates ( $p<0.001$ ). Current breastfeeding was 35.6% and 26.2% among children  $\leq 3$  months and children  $\leq 6$  months, respectively. Exclusive breastfeeding was rare; 7.3% among children  $\leq 3$  months and 4.3% among children  $\leq 6$  months. Finally, the minimum dietary diversity indicator was 39.80% with no significant difference between different governorates ( $p=0.003$ ).

### Conclusions:

Efforts should be made to improve breastfeeding practices among Kuwaiti mothers. The majority of deliveries by Kuwaiti mothers occur in private hospitals, therefore, private sectors should be involved in the strategies that aim to increase breastfeeding among Kuwaiti mothers.

*Key Words: Surveillance; Kuwait; infant ;*



## **Knowledge, attitude, and practices towards mental health among Kuwait University students: a cross-sectional study**

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### **Introduction:**

Globally, mental illnesses are considered one of the leading public health challenges. In Kuwait, there is limited information regarding mental health among the general population. Thus, this study aimed to assess the knowledge, attitudes, and practices towards mental illnesses among Kuwait University (KU) students. It also sought to investigate barriers to seeking professional help for mental illnesses.

### **Methods:**

This cross-sectional study enrolled 1,392 students attending KU. Data were collected using a self-administered questionnaire. Two knowledge scores, assessing condition-based and general knowledge, were calculated based on a previously developed scaling system. Chi-square tests were used to determine differences in proportions.

### **Results:**

Based on the knowledge scoring system, 41.8% and 46.2% of the participants had 'good knowledge' regarding mental health conditions and general mental health, respectively. Knowing a family member or a close friend with a mental illness was associated with more positive attitudes towards the mentally ill. Furthermore, females (53.7%) were more likely than males (43.1%) to believe that the public needs to be protected from people with mental illnesses. Our study demonstrated that the most perceived barriers to seeking help for mental illnesses were 'stigma' and 'trust and confidentiality issues'. Talking to family or friends was shown to be the most preferred help-seeking option for mental conditions (42.2%) followed by religious practices (21.1%) and seeing a psychologist or a psychiatrist (11.7%).

### **Conclusions:**

Our findings indicate that knowledge and attitudes towards mental illnesses were influenced by gender and knowing someone with a mental illness. Stigma was the most perceived barrier to seeking professional help, whereas talking to family or friends was the preferred help seeking option. Actions should be taken to improve the public's understanding towards mental health.

*Key Words: Mental Health; Barriers; Knowledge;*



## **Breast Cancer and Mammography Screening: Knowledge, Attitudes, and Practices among Females Attending Primary Healthcare**

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### **Introduction:**

Breast cancer is the most frequent cancer of women. This study aims to assess the level of knowledge, attitudes, and practices of women regarding breast cancer and mammography screening.

### **Methods:**

A cross-sectional survey was conducted on 1178 females attending Kuwait's primary healthcare centers. A self-administered questionnaire was used. A knowledge score was devised based on 44 items regarding risk factors, signs and symptoms of breast cancer and mammography screening. A logistic regression model was used to identify the determinants of low knowledge level.

### **Results:**

The median knowledge score was 27 out of 44 (61.4%) with a range from 2 to 41. Respondents misrecognized few items as risk factors (e.g. tight bra), signs and symptoms. Moreover, respondents wrongly reported that evil spirits can lead to breast cancer, and that women affected with it have to remove both breasts. Knowledge score and attitude score towards mammography were significantly correlated (Spearman-rank correlation,  $rs=0.222$ ,  $p<0.001$ ). Additionally, 85.5% of participants believed that health authorities should mandate mammography for women aged 40 years and above regularly. Logistic regression analysis showed that age (adjusted odds ratio,  $OR=2.6$ ,  $p=0.011$ ), number of children ( $OR=3.9$ ,  $p=0.006$ ), educational level ( $OR=1.8$ ,  $p=0.003$ ) and history of benign breast lump ( $OR=1.8$ ,  $p=0.027$ ) were independently and significantly associated with low knowledge level.

### **Conclusions:**

A large proportion of females attending Kuwait's primary healthcare centers experience a relatively low knowledge level about breast cancer and mammography screening. Hence, providing education programs can be valuable for promoting females' awareness about breast cancer, improving their attitudes towards mammography screening and its practice. Health authorities may consider mandating mammography for women aged 40 years and above regularly.

*Key Words: breast cancer, screening, mammography,; cross-sectional. survey,;*



## Tobacco smoking and multiple sclerosis risk in Kuwait: A population-based matched case-control study

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### Introduction:

Genetic and environmental factors seem to have an etiologic role in multiple sclerosis (MS). Elsewhere, both active smoking and exposure to environmental tobacco smoke have been implicated in MS risk. However, studies published in past few years from Kuwait were unable to demonstrate an association between tobacco smoking and MS. Therefore, this population-based matched case-control study examined the association between exposure to tobacco smoke (active and passive) and MS risk in Kuwait.

### Methods:

Confirmed 110 MS cases and age ( $\pm 5$  years), gender and nationality matched population controls (1:1) were enrolled. A structured questionnaire was used to collect the data in face-face interview both from cases and controls. Conditional logistic regression was used to analyze the data.

### Results:

Both among cases and controls, majority were Kuwaiti (82.7%), and female (76.4%). The mean (SD) age (years) of cases and controls was 34.8 (10.3) and 34.9 (10.6) respectively. Multivariate model showed that cases compared to controls were significantly more likely to have a family history of MS (Adjusted matched OR = 4.6; 95% CI: 2.0 – 10.6;  $p < 0.001$ ) or less likely to have been vaccinated against influenza A and B viruses before MS diagnosis (Adjusted matched OR = 0.3; 95% CI: 0.2 - 0.7;  $p = 0.005$ ). Both active tobacco smoking and exposure to environmental tobacco smoke were not significantly related to MS status in this study.

### Conclusions:

This study was unable to demonstrate a significant relationship between tobacco smoking (both active and exposure to environmental tobacco smoke) and MS risk. However, family history of MS had significantly direct, whereas, vaccination against influenza A and B viruses had inverse associations with MS. Future studies are indicated to verify or otherwise refute the observed results.

*Key Words: multiple sclerosis; smoking; matched case-control study;*



## **Determinants of effectiveness of Assisted Reproductive Technology (ART) in a private hospital in Kingdom of Saudi Arabia.**

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### **Introduction:**

Around four decades has passed since the first successful birth after In-Vitro Fertilization (IVF) procedure in 1978. Since then, IVF and other techniques that are included under the umbrella of assisted reproductive technology (ART) have been implemented in clinics around the world to help infertile couples fulfill their desire to have children. ART services was started in the Kingdom of Saudi Arabia (KSA) in 1986. Presently there are around ART centers performing around 20,000 ART cycles annually in the Kingdom. The objective of this study is to explore the effectiveness of ART cycle among various subgroups of women in one of the most active private hospital in KSA.

### **Methods:**

All patients that received ART services from the hospital over a three-year period from January 2014 to December 2016 were included in the study. Altogether 3,000 ART cycles were analysed in this study. Data were extracted from electronic medical records as well as well hard-copy records maintained by the IVF unit. The outcome measure for this study was the number of successful pregnancies per started cycle.

### **Results:**

The overall successful pregnancy rate was 35%. Successful pregnancy rates declined with age; the highest was 37.8% for female below 36 years, 32.3 % of those between 36-40 years, and 12.9% of 41-45 years age group. No pregnancy was achieved among women age above 45 years. Indications for ART are important factors that influenced the outcome. The pregnancy rates for cases of polycystic ovary, endometriosis and female age above 40 were 51.3%, 11% and 9%, respectively. Using fresh semen improved the outcome of ART as compared to frozen sample (35.2% vs 24.3 %).

### **Conclusions:**

There are multiple factors that determine outcome of ART services including female age, underlying cause of infertility and use of fresh or frozen semen sample for the fertilization of oocyte. Infertile couples seeking ART should be counseled of their likelihood of pregnancies in relation to these important prognostic factors.

*Key Words: Assisted Reproductive Technology; Effectiveness; Determinants;*



## **Implementation of hospital accreditation for quality assurance in Kuwait: roles and functions of Quality and Accreditation Directorate of Ministry of Health.**

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### **Introduction:**

Quality assurance (QA) is an essential element in management of health organisation. Health care managers are responsible in undertaking planned and systematic approach in monitoring, assessing and improving quality of health services that encompass three elements: clinical governance, risk management and client satisfaction. A study was carried out to assess the roles of Directorate of Quality and Accreditation of Ministry of Health in carrying out accreditation of hospitals in Kuwait

### **Methods:**

In-depth interviews were carried out with senior officers of the Directorate to understand its roles and functions. Annual reports were reviewed to obtain additional information.

### **Results:**

The Directorate is headed by a Director, who is responsible to the Assistant Undersecretary of Health. There are six major departments in the Directorate: Five are technical departments and one administrative Department. The Directorate has a strong mandate from MOH to carry out the accreditation of public hospitals in the country and has developed strategic alliance with an international accreditation body. The main focus of the hospital accreditation is on clinical governance and risk management. The Directorate has good information technology system to support its function and the staffs receive regular training to update their skills. The major challenges facing the Directorate include inadequate number of skilled-staff, high turnover of physicians due to lack of promotion, highly centralised decision-making and lack of communications with the hospitals.

### **Conclusions:**

The Directorate is currently carrying out the hospital accreditation activities successfully. However, in the future the Directorate may have to evolve into a more independent organisation and manage the human resource issues effectively.

*Key Words: Accreditation; Quality Assurance; Public Hospitals;*



## **Roles of government health centre in providing preventive and promotive health services in Kuwait: An explorative study of Adan Special Health Centre.**

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### **Introduction:**

Preventive and promotive health service is one of the most important services provided by the government of Kuwait to its population due to increasing prevalence of chronic non-communicable disease. A case study was carried out to understand the roles of a Special Health Centre in Adan region in providing preventive and promotive services at primary care level. The strengths, weaknesses as well as challenges faced by the Centre were explored in the study.

### **Methods:**

Qualitative methodology using in-depth interviews and participant observations were carried out after the approval from the management of the Centre. Additional information was obtained through the review of administrative reports and internal documents of the Centre.

### **Results:**

Adan Special Health Centre provides primary, secondary and tertiary preventive services to around 90,000 people living in AlQusoor and Adan areas. Primary prevention services are provided through an extensive and well-planned vaccination programme following the guidelines of Ministry of Health. The Centre provides 24-hours service covering preventive and curative services for acute and chronic diseases. The main secondary level preventive services are screening services for breast, bowel and cervical cancers. The major challenges facing the Centre include inadequate number of technically qualified medical staff, absence of regular professional development for support staff especially the nurses, lack of information technology system to manage the medical records, excess in the number clerical staff and lack of regular staff turn-over leading to low level of productivity.

### **Conclusions:**

Adan Special Health Centre plays significant role in providing preventive and promotive services to the target population at the grass-root level. Management of the centre has to take active steps to rectify the human resource issues in order for the Centre to function optimally in the future.

*Key Words: Preventive Sevices; Promotive Services; Health Centre;*



## **Challenges in managing morbidity and mortality data in Kuwait: An organisational analysis on the roles and functions of Department of Vital and Health Statistics of Ministry of Health.**

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### **Introduction:**

Mortality and morbidity data provides valuable source of information on health status of the population and is often use to support effective decision making by health policy makers. A study was undertaken to analyse the roles and functions of Department of Health and Vital Statistics of Ministry of Health (MOH) in managing health information system of Kuwait.

### **Methods:**

In-depth interviews were carried out with senior officers of the Department to analyse its roles and functions. Annual reports were reviewed to obtain additional information.

### **Results:**

Department of Health and Vital Statistics is one of the technical departments under the National Centre for Health Information. The main function of the Department is to plan, supervise, collect and analyse the morbidity and mortality data from public and private health facilities. Data is coded using ICD-10 classification system of the World Health Organisation. The Department is given the task to train MOH employees on health information and prepare the annual and quarterly statistical reports. The Department is also responsible to monitor the validity and quality of the data collected from the various sources. Among the major challenges facing the Department include lack of communication with health facilities, use of out-dated data collection forms, inadequate trained personnel especially clinical coders and epidemiologists and high turnover of clinical staff. The software currently being used to manage the data need to be updated in-order to take into account changes in ICD-10 codes structure.

### **Conclusions:**

Despite all the challenges, the Department has made significant contribution in managing data for health and vital statistics of Kuwait. However, in the future the Department may need to be re-organised in order to attract and retain trained personnel for the provision of effective and efficient services.

*Key Words: Morbidity; Mortality; ICD-10;*



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## **Smartphone App As an Aid in Emergency Management of Avulsed**

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### **Introduction:**

The initial response by bystanders to an avulsed tooth is a significant factor that can affect its survival and long-term outcome. This study was to assess the knowledge of emergency management of tooth avulsion in a group of schoolteachers and to compare the effects of three different educational interventions.

### **Methods:**

Baseline knowledge was assessed using a questionnaire developed for this study. The same questionnaire was used to test changes in the knowledge level following each educational intervention. A convenience sample of elementary and intermediate school teachers (n = 87) participated in this study. Teachers were divided into three groups: Group 1 (Lecture only) was given a 30-min lecture on the emergency management of tooth avulsion. Their knowledge was assessed immediately after the lecture. Group 2 (Lecture and App), the same lecture was given, but participants also had access to a smartphone App, Dental Trauma App (Dental Trauma AB, Linköping, Sweden), when assessed on their knowledge after the lecture. Group 3 (App), this group was only given the smartphone App to explore and had access to that when being assessed.

### **Results:**

All three interventions increased the knowledge of tooth avulsion management. A marked increase in the knowledge, regardless of the type of intervention, was observed in the following areas: handling the tooth on the ground (16–96.8%); holding the tooth while being cleansed (19.1–62.5%); and on the best storage medium (10.1–59.3%). Participants using the App only had a significantly higher mean score than participants receiving the lecture only (group 3; P = 0.019) and participants subjected to both Lecture and App (group 3) (p = .000)

### **Conclusions:**

The Dental Trauma App alone is an effective means of providing accessible knowledge to guide laypeople in managing tooth avulsion, and it can be superior to a lecture-based delivery of information.

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*Key Words: Dental trauma; Tooth avulsion; Smart Phone App;*



**Dentistry**

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## **Parental perceptions of dental visiting habits among disabled and normal children in Kuwait**

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### **Introduction:**

The objective of this study was to describe the dental visiting habits for disabled and normal children in Kuwait from their parents' perspectives.

### **Methods:**

A total of 308 parents of children with a physical or developmental disability and 112 parents of normal children completed the questionnaire regarding the dental visits of their children.

### **Results:**

Majority of the parents of disabled children (84%) did not have adequate information regarding regular dental visits. Less than a quarter of parents of disabled children expressed that they had received information about the importance of dental visits. Disabled children had more dental visits (46%) during the last 12 months compared to normal children (40%) ( $p = 0.003$ ). Fewer disabled children (12%) had visited a dentist for first dental check-up, when they were younger than three years of age compared to normal children (17%). Nearly half (47%) of Down syndrome children and over one-third (37%) of physically disabled had their first dental visit, when they were 6 years of age or above compared to 28% of normal children ( $p < 0.01$ ). About one-fourth (21%) of disabled children and more than one-third (37%) of normal children had never visited a dentist ( $p = 0.003$ ). Normal children (29%) had more often dental check-ups than Down syndrome children (21%) and physically disabled (16%). About 27% of Down syndrome children; 35% of physically disabled and 38% of normal children visited dental clinic for restorations. Nearly two-thirds of the parents of disabled children (69%) and of normal children (64%) stated that the dentist should check the teeth of their children regularly.

### **Conclusions:**

Regular dental visits should be encouraged for comprehensive coverage of the national oral health program for the disabled in Kuwait.

*Key Words: Dental visits; Disabled children; Normal children;*



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## **Characterization of the Time Dependence of Chemical Analysis of Biodentine (Dental Cement) Following Preparation Using FTIR**

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### **Introduction:**

Biodentine (Septodont, Saint Maur des Faussés, France) is a new inorganic class of calcium silicate-based cement. Its being mainly used for endodontic applications.

### **Methods:**

Samples of the Biodentine were prepared according to the manufacturer's instructions. The Fourier Transformation Infra-Red (FTIR) Instrument (Tensor 27, Bruker, Germany) was used to measure the molecular vibration spectra of the various components of the material. Samples were analyzed with attenuated total reflectance technique (ATR). After the **Background** scanned and subtracted, a smear of biodentine was placed directly on the ATR crystal. A wavelength between 600 cm<sup>-1</sup> and 4000 cm<sup>-1</sup> was selected. Afterward, 20 scans were generated for each sample and then the spectra were generated automatically.

### **Results:**

The FTIR spectrum of Biodentine is based on different time intervals. Biodentine spectrum immediately after mixing shows a peak at 3370cm<sup>-1</sup>, which is a characteristic of O-H groups. Also, the spectrum showed calcium carbonate characteristic groups in the absorption peaks at 1438, 905, 873 and 712cm<sup>-1</sup> in the C-O group. After one hour of mixing, the Biodentine sample spectrum also showed O-H groups at 3405 cm<sup>-1</sup>. Shortly after setting reaction commenced a new peak was observed at 2330 cm<sup>-1</sup> corresponding to the presence of C-H bond. One day after mixing, multiple peaks were as shown in figure <sup>3</sup> formed. The band at 817cm<sup>-1</sup> corresponds to Si-O group. The band at 1139 cm<sup>-1</sup> is assigned to SO<sub>4</sub>, while that at 1457 cm<sup>-1</sup> is characteristic of Zr-O-C group. After one week of mixing, carbonate bond at 711. 872, and 1400 cm<sup>-1</sup> was present. These bands correspond to different compounds being formed by the chemical reactions occurring in the Biodentine during setting.

### **Conclusions:**

FTIR can be effectively used to identify the chemical reactions in dental cement in different time intervals that will help in better understanding of dental materials and its clinical applications.

*Key Words: Biodentine; FTIR; Calcium Silicate Cement;*



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## **Orthodontic Educational Background Affects General Dental Practitioners' Interceptive Knowledge and Referral Decisions**

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### **Introduction:**

Timely access to an orthodontist for patients with early treatment need is dependent on the knowledge of the general dental practitioner. This study assessed the level of orthodontic knowledge, referral preference and communication with orthodontists ratings among general dental practitioners (GPs) in Kuwait's Ministry of Health (MOH) clinics. It also investigated different factors that may be related to orthodontic knowledge and referral preferences.

### **Methods:**

Information was collected using a questionnaire containing 36 questions to assess the participants educational **Background**, referral preferences and orthodontic knowledge with particular focus on issues related to posterior crossbites and early treatment. A knowledge score was calculated for each participant using a standardized algorithm and used as an outcome measure for testing associations with different factors.

### **Results:**

Ninety-one GPs answered the survey. Communication between GPs and orthodontists at the MOH was rated as poor or very poor by 77% of GPs. Only 4% of GPs used a standardized system or index for screening and referral. The country where dental education was received, orthodontic instruction program length, requirement to treat orthodontic cases in school, and whether or not the GP has passed standardized dental examinations were factors significantly associated with the knowledge score ( $p < 0.026, 0.005, 0.004$ , respectively).

### **Conclusions:**

There is a need to establish better communication and orthodontic referral training programs for GPs in Kuwait. The dental-school educational **Background** of GPs is significantly associated with their orthodontic knowledge and referral choices.

*Key Words: General Dental Practitioner; Orthodontic Knowledge; Referral;*



Dentistry

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## **In vitro antifungal drug susceptibility of *Candida* species isolated from Kuwait University Dental Clinic**

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### **Introduction:**

The oral cavity is considered a favorable place for the growth of *Candida* species. Antifungal treatment of oral candidiasis is widely recommended. The most commonly recommended topical antifungals (nystatin and amphotericin B) have been in the market since last sixty years. There are only a few recent data available on the susceptibility of different oral *Candida* species to these antifungals, especially related to the isolates taken from the patients attending Kuwait University Dental Clinic (KUDR). In this study, an attempt was made to determine the in vitro susceptibility profile of recent clinical isolates of oral *Candida* spp. to the most commonly recommended topical antifungals like nystatin and amphotericin B.

### **Methods:**

Oral samples were collected from the 109 patients attending KUDR. The samples were spread on the Sabouraud's Dextrose Agar plates for the growth of *Candida*. Species identification was done through Gram staining, CHROMagar technique and VITEK 2 system. Antifungal drug susceptibility was assessed using a broth microdilution method following the NCCLS Standards.

### **Results:**

Of the 109 samples, 60 (55%) showed *Candida* species in culture medium. The majority of species isolated were *C. albicans* (n= 34), and *C. dubliniensis* (n= 13). Few species were *C. glabrata* (n= 6), *C. tropicalis* (n= 3), *C. kefyr* (n= 1), *C. krusei* (n= 1), *C. lusitanae* (n= 1), and *C. parapsilosis* (n= 1). The MIC<sub>90</sub> was defined as the lowest concentration of test compound that resulted in 90% inhibition of visible fungal growth. The MIC<sub>90</sub> values of amphotericin-B ranged from 0.12 to 1.95 µg/ml, whereas MICs values of nystatin ranged from 0.5 to 4 µg/ml, respectively.

### **Conclusions:**

To conclude this work reveals that the commonly used antifungal drugs like amphotericin B and nystatin were found to be an effective anticandidal agents. Results obtained in MIC assay demonstrated that increase in concentration of test compounds leads to significant killing activity.

Funding: DR04/14

*Key Words: Clinical isolates; Candida species; Anticandidal test;*



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## Nano-mechanical properties of a porcelain-based feldspathic ceramic: Mark II

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### Introduction:

The aim of this study was to quantify the nano-mechanical properties and composition of the different phases in a machinable dental ceramic (Mark II, Vita Zahnfabrik Germany), which has been in successful clinical use for more than 25 years, yet, with minimal investigation of basic nano-structure and nano-mechanical properties.

### Methods:

An atomic force microscopy (AFM)-based nanoindenter system (Ti -700 Ubi, Hysitron, Inc. USA) was used to determine the force-displacement response of the various phases present. A Berkovich indenter with 4000  $\mu\text{N}$  load was used to create an array (10 x 10) as well as indent specific localized phases on a polished surface, to determine the reduced modulus and hardness. A crystallographic analysis was conducted using X-ray diffractometer (D8 Advance, Bruker, Germany) to determine the different phases. SEM imaging and elemental analysis (EDS) were also conducted for the different phases.

### Results:

Modulus and hardness results revealed the presence of three distinct phases, a glass phase and two crystalline phases with higher average elastic modulus and hardness values for the crystalline phases collectively (Er:  $72.69 \pm 5.37$  GPa, H:  $9.17 \pm 0.76$  GPa) than the glass phase (Er:  $64.72 \pm 2.51$  GPa, H:  $6.93 \pm 0.19$  GPa). X-Ray Diffraction (XRD) results revealed the presence of 'albite' of triclinic structure, 'tridymite' of a hexagonal structure, 'sanidine' of a monoclinic structure, 'nepheline' of hexagonal structure and 'orthoclase', of a monoclinic structure. EDS revealed (Si, O, Al, Na and K) in both glass and crystalline phases. The crystalline phases had K and Na in varying contents with one preferentially being higher than the other.

### Conclusions:

The difference in hardness and modulus values of the phases relative to enamel, may impact the abrasive nature of this material versus the opposing occlusion.

*Key Words: Nano-mechanical; feldspars; Mark II;*



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## **Antifungal effect of epigallocatechin gallate and magnolol on growth and ultrastructure of oral *Candida* species**

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### **Introduction:**

*C. albicans* is a normal commensal organism, which may cause oral candidosis in immunocompromised patients. There are several different antifungals for the treatment of oral candidosis. It is well known that most of these drugs could produce adverse side effects. At present well-known toxicity of amphotericin B and fluconazole requires discontinuation of their therapy. Therefore, the objective of the study was to determine the antifungal potency of less toxic plant molecules like epigallocatechin gallate and magnolol.

### **Methods:**

The present work investigates the antifungal potential of epigallocatechin gallate and magnolol against 4 standard and 60 oral *Candida* isolates. The oral *Candida* isolates were obtained from Kuwait University Dental Clinic. The MIC for each isolate was determined through broth microdilution assay. Cell damage was confirmed through Confocal Scanning Laser Microscopy. Effect on ultrastructure of the cell was examined through Scanning Electron Microscopy, and Transmission Electron Microscopy.

### **Results:**

MIC of epigallocatechin gallate and magnolol on *Candida* species ranged from 1.95-62.5 and 7.81-62.5 µg/ml, respectively. Confocal microscopy results confirmed that propidium iodide penetrates in test compound treated cells. SEM results showed damage to the cell wall and plasma membrane which is sharply defined by the deformity in cells and the outflow of the intracellular material. TEM results showed several changes including rupturing of cell wall and plasma membrane, disintegration of the cell wall, and oozing out of intracellular content, and swelling of cell wall.

### **Conclusions:**

To conclude, the plant-derived molecules used are found to be effective anticandidal agents against different *Candida* isolates. The molecules eventually lead to damage of membrane and cell wall as visible in confocal, SEM and TEM results. These results taken together make them eligible for further development as antifungals.

Funding: Kuwait University, Project No: DR04/14

*Key Words:* *Candida*; *Epigallocatechin gallate*; *Magnolol*;



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## **Parental perceptions of access to dental care among disabled schoolchildren in Kuwait**

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### **Introduction:**

The objective of this study was to identify barriers to dental care for disabled children in Kuwait from their parents' perspectives.

### **Methods:**

A total of 308 parents of children with a physical disability (n=211), Down syndrome (n=97) and 112 parents of normal children, participated in the study. Information was collected by structured anonymous questionnaires.

### **Results:**

Only 10% of the Down syndrome children perceived no barriers to seek dental care compared to 26% of the physically disabled and 32% of the normal children (p=0.008). Difficulty to get an appointment was the most common perceived barrier to dental care by the parents of Down syndrome and normal children (37%). Parents of disabled children considered difficulty in cooperation as a more important barrier to treatment (35%) than parents of normal children (20%). Distance and transport were more common barriers among Down syndrome (15%) than among physically disabled and normal children (5-7%). Cost was the least perceived barrier in all groups (3-5%). Majority of Down syndrome (72%) and physically disabled (59%) received curative dental care compared to 47% of normal children (p=0.016). A bigger proportion of disabled children (42%) visited the dentist due to tooth ache than the normal ones (25%) (p<0.01). Less than a quarter of Down syndrome (21%) and physically disabled (16%) had dental check-ups. Higher proportion of the parents of normal children (82%) regarded the present dental services as excellent/good compared to half (52%) of the parents of disabled children.

### **Conclusions:**

Parents perceived difficulty to get an appointment and lack of cooperation as the major barriers to dental care for their disabled children. Curative treatment need and tooth ache were the main reasons for dental visits among disabled children. Regular dental check-ups and preventive oral health care should be encouraged for comprehensive coverage of the national oral health program for the disabled children in Kuwait.

*Key Words: Access to dental care; Disabled; Schoolchildren;*



*Ethics*

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## **Kuwait Hospital Accreditation: Perception of Self-Assessment Team members in a National Hospital**

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### **Introduction:**

'Healthcare governance at its best facilitates effective and efficient quality care to all stakeholder at all times'. The Ministry of Health in Kuwait has introduced the National Accreditation Program since 2008. The aim of this study is to explore the impact of accreditation on quality of care as perceived by the members of self-assessment team members (SATMs) of a national hospital.

### **Methods:**

A cross-sectional survey utilized a self-reporting questionnaire with 7 scales adapted from Shortell and Pomey. It was distributed to all members of 11 accreditation SATMs. The scales focused on leadership, strategic planning, human resources utilization, quality management, quality of results, patient satisfaction, and accreditation impact. In addition questions on sociodemographic, professional experience and accreditation experience were added. Mean scores were computed based on the number of items in the scale rated on a five-point Likert scale with higher scores reflect positive impact. Data analyzed using SPSS

### **Results:**

The response rate was 45% (53 participants). The highest mean score was for accreditation impact 4.0 (SD  $\pm$  0.8). The lowest mean score was for human resources utilization 3.2 (SD  $\pm$  0.9) and was the only significantly different scale between Kuwaiti (3.1) versus non-Kuwaiti doctors (3.6), p value 0.044. Rewards and recognition of staff for improving quality had the lowest individual item score mean 2.4 (SD,  $\pm$  1.3) while perceiving that the 'hospital's participation in accreditation enables it to be more responsive when changes are to be implemented' had the highest item score (mean 4.2,  $\pm$  1.0).

### **Conclusions:**

Members of SATMs at a national hospital that recently went through the second cycle of accreditation perceived accreditation as a good tool for improving quality of care. There is a need however for further assessment of the human resources utilization, rewards and recognition of staff.

*Key Words: Accreditation; Quality; Kuwait;*



**Genetics**

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**Gender-dependent association of the common FTO gene polymorphism with obesity in Kuwait: A public health concern?**

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**Introduction:**

The fat mass and obesity-associated (FTO) gene is commonly associated with risk of obesity and inconsistently with type 2 diabetes (T2D). Recent studies have shown that the effect of the common variant rs9939609 of the FTO gene on obesity is both population and gender-specific. Our aim therefore, is to investigate the effect of this variant on Body Mass Index (BMI) and the risk of T2D in one of the most obese populations - Kuwait.

**Methods:**

FTO's rs9939609 genotypic data was available in 1034 unrelated subjects. The association between the polymorphism was tested using logistic regression and general linear model (GLM) adjusted for both age and gender assuming a dominant genetic model was performed using SNPassoc package from R statistics.

**Results:**

We found the A allele (47%) to be associated with increased (high) BMI in females only (B=2.23 (95% CI 0.395 – 4.06; p=0.017). However, no association was observed with risk of T2D (OR=0.83; 95% CI 0.65 – 1.07; p=0.161). Our lack of association with T2D and BMI in males suggests population differences in the effect of FTO's rs9939609 suggesting the involvement of other variants.

**Conclusions:**

The lack of association in T2D is consistent with other studies and may suggest the involvement of other polymorphisms in the FTO, whereas, association of the A allele with increased BMI in females suggests gender differences in the mechanisms underlying the development of obesity but also may raise public health concerns of females' lifestyle in Kuwait.

*Key Words: Obesity; Genetics; Polymorphism;*



**Genetics**

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## Identifying the genetic cause of Primary ciliary dyskinesia in Kuwaiti population

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### Introduction:

Primary ciliary dyskinesia (PCD) is one of the congenital thoracic disorders caused by dysfunction of motile cilia resulting in insufficient mucociliary clearance of the lungs. Approximately 50% of all PCD patients have Kartagener syndrome, a triad of bronchiectasis, sinusitis and situs inversus totalis. The overall aim of this study is to identify causative mutated genes for PCD and CHD in the Kuwaiti population.

### Methods:

A cohort of multiple consanguineous PCD families was ascertained from Kuwaiti patients and genomic DNA from the family members was isolated using standard procedures. The DNA samples from all affected individuals were analyzed using whole Exome Sequencing technology and Sanger sequencing method. Transmission electron microscopy (TEM) and Immunofluorescent analyses (IF) for patient samples obtained by nasal brushings in Kuwait was performed in order to identify specific the structural abnormalities within ciliated cells. Here we present one family from our cohort that has mutation in RSPH9 gene as a model result for the cases understudy.

### Results:

Family DAPCD03 is a multiplex family with three affected individuals that has severe PCD symptoms with situs solitus. TEM shows the patients have mislocalization of the peripheral microtubule doublets (MDs) and central pairs (CP) which indicates the presence of mutation affects the stabilization of the MDs and CP. Exome sequencing followed by Sanger sequencing confirmed the previous analyses and shows that the two patients carry a homozygous loss-of-function mutation (c.800\_803delGAA) in exon 6 of RSPH9 gene which predicts p.K268del. Future confirmation to the results has been shown by IF and that also confirms the absence of RSPH9 protein in nasal ciliated epithelial cells.

### Conclusions:

Most patients have hereditary mutations which indicated by having more than one affected individual carry the same phenotype. This study helped the selected families to get confirmed diagnosis of PCD firstly by determining the defects in the cilia ultrastructure and then by mapping the disease mutations.

Funding: Kfas P114-13MG-01

*Key Words: Genetics; Primary ciliary dyskinesia; congenital thoracic anomalies ;*



**Genetics**

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## **Expression of the filaggrin gene in umbilical cord blood predicts eczema risk in infancy: a birth cohort study**

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### **Introduction:**

Filaggrin gene (FLG) expression, particularly in the skin, has been linked to the development of the skin barrier and is associated with eczema risk. However, knowledge as to whether FLG expression in umbilical cord blood (UCB) is associated with eczema development and prediction is lacking. This study sought to assess whether FLG expression in UCB associates with and predicts the development of eczema in infancy.

### **Methods:**

Infants enrolled in a birth cohort study (n = 94) were assessed for eczema at ages 3-, 6-, and 12-months. Five probes measuring FLG transcripts expression in UCB were available from genome-wide gene expression profiling. FLG genetic variants R501X, 2282del4, and S3247X were genotyped. Associations were assessed using Poisson regression with robust variance estimation. Area under the curve (AUC), describing the discriminatory/predictive performance of fitted models, was estimated from logistic

### **Results:**

Increased level of FLG expression measured by probe A\_24\_P51322 was associated with reduced risk of eczema during the first year of life (RR = 0.60, 95% CI: 0.38-0.95). In contrast, increased level of FLG antisense transcripts measured by probe A\_21\_P0014075 was associated with increased risk of eczema (RR = 2.02, 95% CI: 1.10-3.72). In prediction models including FLG expression, FLG genetic variants, and sex, discrimination between children who will and will not develop eczema at 3-months of age was high (AUC: 0.91, 95% CI: 0.84-0.98).

### **Conclusions:**

This study demonstrated, for the first time, that FLG expression in UCB is associated with eczema development in infancy. Moreover, our analysis provided prediction models that were capable of discriminating, to a great extent, between those who will and will not develop eczema in infancy. Therefore, early identification of infants at increased risk of developing eczema is possible and such high-risk newborns may benefit from early stratification and intervention. This investigation was supported by the National Institute of Allergy and Infectious Diseases under Award Number R01 AI091905-01

*Key Words: Eczema; Filaggrin; Prediction;*



**Hematology**

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## **RDW status in iron deficiency anemia and $\alpha$ thalassemia in Kuwaiti Population**

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**Introduction:**

Red blood cell distribution width (RDW) is a measure of the range of variation of red blood cell (RBC). The "width" in RDW is sometimes thought to be misleading since it in fact a measure of deviation of the volume of RBCs, and not directly the diameter [1]. Mathematically, the RDW is calculated with the following formula: RDW is equal of (Standard deviation of MCV divided by the mean of MCV)  $\times 100^2$ . Normal reference range of RDW in human RBC is 11.5-14.5%<sup>3</sup> but it is higher in Kuwaiti (KT) population [4]. RDW has been proposed to be a more sensitive indicator to establish the possible origin of microcytic hypochromic anemia. RDW can be considered an index of heterogeneity, the equivalent of anisocytosis observed in the peripheral blood smear [5].

**Aim:** Our aim is to evaluate the RDW for more sensitive differentiation between iron deficiency anemia (IDA) and alpha thalassemia minor ( $\alpha$ TM).

**Methods:**

The blood results of normal group of 500 female and 500 male. In IDA group 32 female and 49 male. While in the group of  $\alpha$ -TM 290 female and 127 male were collected from Amiri Hospital electronic data.

**Results:**

The RDW in the normal adult KT female (12.4-16) and in normal adult KT male (12.5-15). In IDA female was (15.6-22), and in IDA male (14.0-19). While  $\alpha$ TM female (14.0-19) and  $\alpha$ TM male was (13.4-17). Table 1 and Table 2

**Conclusions:**

According to the adult provisional Kuwaiti reference range study, the RDW % in normal Kuwaiti population is more than the RDW% in normal UK population. RDW in IDA is higher than in  $\alpha$ TM although both of them are higher than normal reference range. Mixed anemic origin could interfere with RDW %. In this study RDW did not give a clear differentiation between IDA and  $\alpha$ TM.

Funding: KFAS.

*Key Words: RDW ; Iron deficiency anemia; alpha thalassemia major;*



## Development of competency-based interprofessional education curriculum at the Health Sciences Centre of Kuwait University

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### Introduction:

Interprofessional education (IPE) of healthcare students can foster the development of collaborative working relationships among future healthcare providers. Faculties of Medicine, Allied Health Sciences, Dentistry and Pharmacy at Kuwait University established a working group to develop a competency-based IPE curriculum. The group initially explored the competencies needed for the development of this curriculum and used them to design the IPE courses.

### Methods:

Five focus groups interviews were conducted with practicing healthcare professionals to explore their views on the necessary competencies for the development of the IPE curriculum. The interviews were audio-recorded, transcribed verbatim and analysed using thematic analysis. The emerged competencies were refined by comparing them with the competencies of international IPE frameworks and elements of these competencies (sub-domains) were identified. An IPE curriculum consisting of three courses that will span three professional years of each program was then developed to allow the students attain

### Results:

Three main IPE competencies were identified. These included communication, roles and responsibilities, and teamwork skills and leadership. These competencies aligned with those of several international IPE curricula. The identified competencies were used to guide selection of interactive teaching/learning activities to be used in the IPE courses such as guided discovery, e-learning, small group learning, role playing and simulated rounds, as well as proper assessment methods.

### Conclusions:

A competency framework that is based on a local needs assessment and comparison with international IPE curricula formed the basis of the IPE curriculum. In turn, these competencies were used as a basis for the development of the IPE program and guided the selection of interactive learning activities and assessment methods that would foster students' acquisition of these competencies.

*Key Words: Competency-based curriculum ; Interprofessional education;*



## Live recombinant *Mycobacterium smegmatis* as an antigen delivery system for the induction of antigen-specific and protective cellular immune responses in mice.

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### Introduction:

The identification of major *Mycobacterium tuberculosis*-specific antigens has paved the way to study their role in inducing protective immunity against tuberculosis and identify the antigens that could be used to protect against other immunological diseases, e.g. asthma. However, the delivery of these antigens is an important issue. In the past, non-living adjuvants have been tried with limited success. In contrast, the living adjuvants may provide better alternative. The aim of this study was to test live *M. smegmatis*, a non-pathogenic mycobacterium, as a delivery system for a dominant *M. tuberculosis*-specific antigen Rv3619.

### Methods:

The gene encoding Rv3619 was amplified from the genome of *M. tuberculosis* and cloned in a plasmid vector pDE22. The recombinant plasmids were electroporated into *M. smegmatis* and the expression of rv3619 in recombinant (r)*M. smegmatis* was determined by reverse-transcriptase (RT-PCR). Mice were immunized and boosted with r*M. smegmatis* and sacrificed two weeks after the last injection. The splenocytes were stimulated *in vitro* with a mitogen and synthetic peptides covering the sequence of Rv3619. The culture supernatants were assayed for the protective Th1 cytokine IFN-gamma and the pathologic Th2 (IL-5) and Treg (IL-10) cytokines in ELISA. The responses were considered positive with E/C >2, where E and C are the concentration of cytokines in stimulated and control cultures, respectively.

### Results:

RT-PCR showed that the rv3619 was expressed in r*M. smegmatis*. The immunized mice showed positive responses to the peptide pool in Th1 assays but not in Th2 and Treg assays. Furthermore, all individual peptides of Rv3619 showed positive responses in Th1 assays.

### Conclusions:

*M. smegmatis* selectively induced broad-based Th1 responses to Rv3619. Hence, this delivery system could be useful for the induction of protective immune responses against intracellular pathogens and non-infectious diseases like asthma. Supported by the College of Graduate Studies and the Research Sector Projects YM06/15 and SRUL02/13.

*Key Words: Recombinant M. smegmatis; Rv3619; Cytokines;*



**Medicine**

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## **The Prevalence of Renal Impairment in Adult Sickle cell Disease**

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Amiri Hospital

### **Introduction:**

Sickle cell disease (SCD) is a genetic disorder causes elevations of blood viscosity which Sickle cell disease (SCD) is a genetic disorder causes elevations of blood viscosity which lead to vaso-occlusive crises and multiple systemic micro-infarctions. The lack of red blood lead to vaso-occlusive crises and multiple systemic micro-infarctions. The lack of red blood cell deformability enhances its stickiness and result in obstructive adhesions of the sickle cell deformability enhances its stickiness and result in obstructive adhesions of the sickle cells to each other and the vascular endothelium. SCD is a variant of genetic disorders. cells to each other and the vascular endothelium. SCD is a variant of genetic disorders. SCD may result in both renal functional disturbances and anatomical alterations. The renal SCD may result in both renal functional disturbances and anatomical alterations. The renal failure in SCD in Africa is 40% .failure in SCD in Africa is 40% .

**Aim:** Detection of the prevalence of chronic kidney disease( CKD ) in SCD to control the renal complications and its sequancies . Also to detect which type of SCD is more renal complications and its sequancies . Also to detect which type of SCD is more susceptible to CKD.

### **Methods:**

This retrospective study conducted from our data base at Amiri Hospital, from 2010 to This retrospective study conducted from our data base at Amiri Hospital, from 2010 to 2016. The SCD patirnts are 141 adult SCD patients, 75 female, and 66 male, aged from 24-2016. The SCD patirnts are 141 adult SCD patients, 75 female, and 66 male, aged from 24-78 years. The patients included are Sickle cell anemia (SCA) 57, sickle cell thalassemia 78 years. The patients included are Sickle cell anemia (SCA) 57, sickle cell thalassemia (HbSthal) 34 and the double heterozygous (DHT) 50 . The CKD estimation based on GFR, (HbSthal) 34 and the double heterozygous (DHT) 50 . The CKD estimation based on GFR, creatinine proteinuria, hematuria, age and sex . creatinine proteinuria, hematuria, age and sex .

### **Results:**

CKD found in 56 out of 141 SCD patients as follow: in SCA 27 patients, HbSthal 11 CKD found in 56 out of 141 SCD patients as follow: in SCA 27 patients, HbSthal 11 patients and in DHT 18 patients. The CKD stages found as follow: CKD1 in 18 patients , patients and in DHT 18 patients. The CKD stages found as follow: CKD1 in 18 patients , CKD2 in 20 patients , CKD3 in 10 patients, CKD4 in 5 patients , CKD5 in 3 CKD2 in 20 patients , CKD3 in 10 patients , CKD4 in 5 patients , CKD5 in 3)patients. The prevalence of CKD in SCD is 56/141( 39.7 % ).)patients. The prevalence of CKD in SCD is 56/141( 39.7 % ).

### **Conclusions:**

The prevalence of CKD in SCD in Kuwait is high almost same as in Africa ; it could be The prevalence of CKD in SCD in Kuwait is high almost same as in Africa; it could be explained by including in this study the very early laboratory results as hematuria and explained by including in this study the very early laboratory results as hematuria and proteinuria when the serum renal function is normal in the CKD1 . SCA showed more proteinuria when the serum renal function is normal in the CKD1 . SCA showed more incidence of nephropathy than other types of SCD. This study confirms the necessity of incidence of nephropathy than other types of SCD. This study confirms the necessity of close renal follows up in SCD patients. close renal follows up in SCD patients.

**Funding:** KFAS

**Key Words:** SCD; Renal; Complication;



## Fractional Excretion of Vitamin D Binding Protein as a Novel Marker of Vitamin D Status in Subjects with Type 2 Diabetes

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### Introduction:

Vitamin D deficiency (VDD) has shown to play significant roles in the pathogenesis of Type 2 Diabetes mellitus (T2DM). Vitamin D-binding protein (VDBP) is a significant determinant of biologically active levels of 25(OH) Vitamin D (25(OH)D). Studies have shown increased urine excretion of VDBP in diabetic nephropathy (DN) patients resulting from postulated mechanisms linked to renal tubular damage. In this study, we evaluate the utility of the Fractional Excretion of VDBP (FEVDBP) as a novel index of VDD and DN.

### Methods:

Levels of 25(OH)D, HbA1c, serum and urine concentrations of VDBP, creatinine were measured in 405 (129M, 276F) T2DM patients. Ratio of urine microalbumin to creatinine was determined to categorize subjects as normoalbuminuric (NAO, ratio <30mg/g); microalbuminuric (MIA, ratio 30-300mg/g) and macroalbuminuric (MAA, ratio >300 mg/g). FEVDBP was calculated as  $100 \times (\text{UrineVDBP} \times \text{SerumCreat}) / (\text{SerumVDBP} \times \text{UrineCreat})$ . Univariate and multivariate analyses were used to compare subjects grouped by Vitamin D status, glycemic control and degree of microalbuminuria.

### Results:

VDD (<50nmol/L; n = 237) or insufficiency (VI) (50-75 nmol/L; n=84) was prevalent. Mean FEVDBP in subjects with normal 25(OH)D, VI and VDD were 5.5, 5.4 and 8.5 respectively; mean FEVDBP in NAO, MIA and MAA were 3.7, 23.3 and 55.9 respectively. Significant positive correlations of FEVDBP were with age, glucose, HbA1c, urine microalbumin:creatinine ratio and negative correlation with serum albumin. Receiver operating Curve (ROC) analyses of the use of FEVDBP for detection of VDD, microalbuminuria and poor glycemic control showed that the areas under the ROC are 0.545, 0.822 and 0.732 respectively.

### Conclusions:

We conclude that increased FEVDBP contributes to the mechanisms of VDD in T2DM. The strong associations of FEVDBP with glycemic control and DN suggests that this index could play a wider role in the pathogenesis and/or detection of diabetic complications. Grant Support: KFAS-2011-1302-01

*Key Words: Vitamin D Binding Protein; Vitamin D; Type 2 Diabetes;*



**Medicine**

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## **Cognitive Impairment among Egyptian Older Adults on Hemodialysis**

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### **Introduction:**

Older patients are now the rule rather than the exception in hemodialysis (HD). Cognitive impairment (CI) is common among persons with end stage renal disease (ESRD) and is associated with poor outcomes. We aimed to assess the prevalence of CI among Egyptian older adults on HD and its associations with different patients' demographics and characteristics.

### **Methods:**

This study was conducted as a cross-sectional study and included 94 subjects (aged  $\geq 60$  years old). All patients were subjected to comprehensive geriatric assessment for estimation of cognitive function, laboratory investigations including: hemoglobin, serum creatinine, serum urea, serum potassium, serum sodium and serum albumin. Kt/V as a marker of dialysis adequacy was calculated.

### **Results:**

Twenty-six patients (27.8%) had normal cognitive function, 32 (34%) had mild CI, 21 (22.3%) had mild dementia, 8 (8.5%) had moderate dementia, and 7 (7.4%) had severe dementia. Older age, low education level, and longer duration of dialysis were found to have significant associations with CI (P value  $< 0.001$ ,  $0.002$ , and  $0.012$  respectively); while hemoglobin, serum albumin, serum creatinine, serum urea, serum potassium, and Kt/V showed no significant association with CI. Serum sodium showed significant lower values in patient with cognitive impairment than those with normal cognitive function (P  $< 0.001$ ), on the contrary of dry weight that showed lower values in patients with normal cognitive function than patients with cognitive dysfunction (P  $< 0.001$ ).

### **Conclusions:**

CI is prevalent in Egyptian older adults on HD (72.2%) with rising percentage and severity with increase in age, low education, lower level of serum sodium, longer duration of dialysis history and higher dry weight.

*Key Words: Cognitive impairment; Elderly; Hemodialysis;*



**Medicine**

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## **Baseline results from PROOF – a 5-year observational study of long-term disease outcome in axial spondyloarthritis — subanalysis from Kuwait**

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### **Introduction:**

Axial spondyloarthritis (axSpA) is a relatively new disease concept. It encompasses ankylosing spondylitis (AS) and non-radiographic axSpA (nr-axSpA) without advanced structural lesions in the spine and sacroiliac joints. The natural disease course of the full spectrum of axSpA, including structural damage progression over time, has not yet been studied in large patient groups.

### **Methods:**

PROOF is a large multi-country prospective, observational study evaluating disease burden and progression of axSpA over 5 years. Patients with axSpA, fulfilling the ASAS classification criteria (either AS or nr-axSpA), were eligible, if diagnosed  $\leq 12$  months prior to enrollment. Pelvic x-rays were collected at baseline and during yearly follow-up visits. Images were read by a local reader and validated by  $\leq 2$  blinded central readers. Subdiagnosis I is based on clinical judgment of the investigator before x-ray grading. Subdiagnosis II is based on combined local and central x-ray readings.

### **Results:**

Of the 2126 patients enrolled globally, 28 were from Kuwait. Overall, the mean age of patients was approximately 36 years and 63.3% were male. Of these, 16 patients (57.1%) were classified as having AS and 12 (42.9%) as having nr-axSpA, according to subdiagnosis I. As of June 2015, 18/28 patients (64.3%) had subdiagnoses based on local readings, and central readings were completed for 12/28 patients (42.9%). Of these 12, 11 retained their initial classification (AS or nr-axSpA) after the central reading, and 1 was reclassified to nr-axSpA. The mean time to see a rheumatologist from symptom onset was 6.4 years. Average time between first physician visit and referral to rheumatologist was 4.27 years.

### **Conclusions:**

PROOF provides insights from patients from 29 countries. This baseline analysis from the subset of patients from Kuwait reveals that the long duration from onset of symptoms to axSpA diagnosis appears to be due to the delay in patient referral to a rheumatologist.

Funding: AbbVie Biopharmaceutical

*Key Words: Axial SpA; Kuwait; Time to Referral ;*



**Medicine**

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### **The rate of occurrence of migraine in multiple sclerosis patients**

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**Introduction:**

Several reports indicated that prevalence of migraine in patients with MS ranges between 20% and 45% in the literature. A deregulation of the serotonergic system caused by demyelinating lesions has been linked to the headache exacerbation Periaqueductal gray matter (PAG), located in the midbrain, is thought to be a key area in the pathogenesis of migraine.

**Methods:**

This is a cross-sectional study to assess the rate of occurrence of migraine in MS patients and to compare the demographic, clinical and radiological characteristics of MS patients with and without migraine who were attending a specialized MS clinic. MS diagnosis was based on the revised 2010 McDonald criteria while migraine diagnosis based on International Classification of Headache Disorders, 3rd edition (ICHD-III- beta) criteria.

**Results:**

Among 137 MS patients screen at the MS clinic between 1st June 2016 up to 31st August 2016, the occurrence rate of migraine was 35%. Although statistically insignificant, women and patients with younger age at MS onset were more likely to have migraine compared to MS patients without migraine. MS patients with migraine had significant involvement of the periaqueductal gray matter (PAG) (77% vs. 16%;  $p < 0.0001$ ). There was no significant association between the number of relapse or expanded disability status scale (EDSS) scores and migraine.

**Conclusions:**

Migraine is a common comorbidity in MS patients especially in women and MS patients with young age at onset. Periaqueductal lesions on MRI brain were more prevalent in MS patients with migraine. Future studies are warranted to further assess the correlation of demyelination lesions and migraine in large cohorts.

*Key Words: Multiple sclerosis; Migraine; Periaqueductal;*



**Medicine**

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## **Metabolic control and the prevalence of chronic complications among adolescents with type 1 diabetes**

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### **Introduction:**

Despite the advances achieved in the management of type 1 diabetes worldwide, the evidence shows that the prevention of the diabetes complications is complex and challenging, particularly among adolescents. This study aims to determine the level of metabolic control and the prevalence of the diabetes complications among adolescents (<20 years) compared to older adults with type 1 diabetes.

### **Methods:**

The medical records of 91 adults with type 1 diabetes were reviewed as part of an audit conducted for patients who attended diabetes OPD clinics at Al-Sabah Hospital in 2011. The data abstracted included demographics, diabetes-related data, and cardiovascular risk

### **Results:**

The audit included 91 patients (46 males and 45 females). Overall mean age was 23.0+8.4 years, and 48.4% of the patients were younger than 20 years. Compared to older adults, adolescents had higher HbA1c (10.3+2.2 vs. 9.3+1.9%), lower systolic (113.1+8.0 vs. 119.2+13.1 mmHg) and diastolic BP (73.4+6.9 vs. 77.4+7.5 mmHg), lower BMI (23.1+4.9 vs. 27.0+6.1), and shorter diabetes duration (6.3+4.0 vs. 12.6+7.5 years). Among the 65 patients who were testing their blood glucose, the prevalence of self-monitoring blood glucose >3 times/d was 39.4% among younger adolescents compared to 62.5% among older type 1 diabetics (p= 0.062). Mean levels for LDL-C, HDL-C, and triglycerides were 2.83+0.88, 1.31+0.32, 1.19+0.77 mmol/l respectively with no statistical difference. Albuminuria and any retinopathy were present in 18.5% and 16.5% of the patients respectively. Retinopathy was significantly related to longer duration (>10 years), and notably less prevalent in adolescents compared to older type 1 diabetics (8.1% vs. 23.8%, p=0.06).

### **Conclusions:**

The findings of this audit confirms the value of identifying psychosocial factors and incorporating self-management behaviors in the management of adolescents with type 1 diabetes, to optimize metabolic control and prevent chronic complications.

*Key Words: Diabetes; Metabolic control; Complications;*



**Medicine**

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## **Elderly kidney transplant recipients: single center experience in the Middle East**

Al-Otaibi T, Gheith O, Elsayed A, Nampoory N, Nair P, Halim MA  
OTC

**Introduction:**

The number of elderly patients accepted in renal replacement programmes is increasing as the age per se does not constitute a contraindication to transplantation. The aim of this study was to investigate whether or not transplantation provides any survival benefit in this group of patients.

**Methods:**

This study is a retrospective case controlled study comparing elderly transplant recipients, group I (n= 201; age>60 years) to a matched group of young adult recipients II (n= 1031; age<60 years). Data were collected from 11/1993 till 5/2014. Data were compared to those obtained in patients (Group II) who were matched for HLA mismatches and time of follow up. Primary end points were graft loss and/or patient death, while secondary end points were cardiovascular events, malignancies or rejection.

**Results:**

201 patients with mean age 65.5(±4.4), ranged from 60 to 81 years old (64.9% males) were compared with 1031 patients with mean age 41.1±10.4, ranged from 19 to 59 (63.9% males) (p=0.82). We found no significant difference between the two groups regarding basal graft function represented by serum creatinine (p>0.05). However, graft function was significantly better in elderly group at 6 months, 1-year, 3-years of follow up (p<0.05), but later on the 2 groups were comparable at 5, 10 years follow up (p>0.05). Despite the significantly higher number of cadaveric transplants and more potent immunosuppression given in group II, we did not observe any significant difference between the 2 groups regarding patient or graft survival (p>0.05). This could be attributed to significantly higher number of patients with cardiovascular risks (hypertension, diabetes, cardiac ischemia), lower mean number of rejection episodes in addition to higher number of cases with malignancies in elderly group (p<0.05).

**Conclusions:**

By less potent immunosuppression, elderly age experienced lower rejection rates with comparable graft and patient survival despite higher cardio-vascular risk factors.

*Key Words: elderly; renal transplant; outcome;*



**Medicine**

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## **Outcome of bariatric surgery in obese renal transplant recipients: single center experience**

Al-Otaibi T, Gheith O, Nampoory MRN, Halim M, Mosaad A, Nair P.  
OTC

### **Introduction:**

Obesity has been associated with poor graft and patient survival after kidney transplantation, requiring functional increase of anti-rejection drugs. Weight loss surgery may be a good alternative in this clinical scenario. We aimed to assess the outcomes of bariatric procedures among renal transplants compared to conventional group of patients.

### **Methods:**

In this retrospective study, we analyzed the collected data of obese patients (BMI>38) after kidney transplantation who underwent bariatric procedures during the last 5 years (n=25cases) in comparison to control obese group without this type of surgery (n=41 cases). Roux-en-Y gastric bypass was the most common procedure.

### **Results:**

The two groups of patients were matched regarding their demographic data, type of donor, cases with IHD, type of induction and maintenance immunosuppression. Most of patients in bariatric group were females (60% vs. 84% males in other group, p=0.03). The basal and last follow up mean BMI values were (38.3±8.9 and 33.3±7.3) vs. (44.2±5.6 and 44.2±6.7) with mean weight loss percentage 15.4±5.1% vs. 0.4±0.2% in the control group (p<0.05). The 2 groups were matched regarding pre-transplant diabetics but the total number of diabetics in the control group was significantly higher (73.3% vs. 40%, p=0.042). The 2 groups were matched regarding cases with gall bladder stones, sleep apnea and hyperuricemia management. We observed no significant difference between the 2 groups regarding rejection episodes, graft and patient outcomes (p>0.05). There were no postoperative complications except strangulated hernia in one case; and postoperative DVT and pulmonary embolism in another.

### **Conclusions:**

Bariatric surgical techniques may be used safely and effectively-with some precautions- to control obesity among renal transplant recipients. Longer term and larger studies are needed to evaluate metabolic parameters and long term patient and graft outcome.

*Key Words: bariatric; renal transplant; outcome;*



Medicine

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## Patterns of Circulatory and Peripheral Blood Mononuclear Cytokines in Rheumatoid Arthritis

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### Introduction:

Objective: An imbalance in pro- and anti-inflammatory cytokines is suggested to result in the tissue damage seen in rheumatoid arthritis (RA). This study was aimed at investigating profiles cytokines in circulation and those produced by mitogen-stimulated peripheral blood mononuclear cells (PBMC) in RA patients and healthy controls, and to study possible correlations with disease activity.

### Methods:

26 female patients with RA and 28 age-matched healthy control subjects were inducted. Levels of plasma cytokines and PBMC-secreted cytokines were estimated; five pro-inflammatory cytokines (IFN- $\alpha$ , TNF- $\alpha$ , IL-6, IL-17, IL-12) and three anti-inflammatory cytokines (IL-4, IL-10, IL-13) were assayed in a multiplex ELISA system.

### Results:

Patients with RA had significantly higher plasma levels of TNF- $\alpha$ , IL-12 and IL-4 compared to healthy controls ( $p=0.019$ ,  $0.042$  and  $0.013$  respectively). On the other hand, mitogen-activated PBMC secreted significantly higher levels of the pro-inflammatory cytokines TNF- $\alpha$ , IFN- $\beta$ , IL-17 and IL-12 ( $p=0.044$ ,  $0.004$ ,  $0.002$  and  $0.046$  respectively) but lower levels of the anti-inflammatory cytokine IL-10 ( $p=0.025$ ) in RA compared to healthy subjects. Further, the ratios TNF- $\alpha$ /IL-10, IFN- $\beta$ /IL-10, IL-17/IL-10, IL-12/IL-10 and IFN- $\beta$ /IL-13 were statistically significantly higher in RA patients as compared to healthy controls ( $p=0.002$ ,  $0.0001$ ,  $0.0001$ ,  $0.001$  and  $0.014$ ). The range and expression of cytokines was higher in mitogen-activated PBMC than in the plasma in all the groups studied. Multivariate pattern analysis of 8 cytokines revealed a prediction accuracy of 69% in differentiating RA patients from healthy controls and of 73% in classifying patients as in remission or active RA.

### Conclusions:

Our data suggests that it would be worthwhile to explore ratios of pro- to anti-inflammatory cytokines produced by mitogen-stimulated PBMC in RA and the use of multivariate cytokine pattern and algorithms for better delineation of this condition. This study is supported by Kuwait Foundation of Advancement of Science (KFAS) project no. 2013-1302-02.

*Key Words: Rheumatoid arthritis; Cytokines; Circulatory levels;*



**Medicine**

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## **Simultaneous Kidney-Pancreas Transplantation: Kuwait single center experience**

Balaha M, Ghaith O, Al-oteibi T, Said T, Medhat Abdul, Nampoory N  
OTC

**Introduction:**

Pancreas-kidney transplantation (SKP) is the best therapeutic option for diabetic patients with end-stage renal failure.

Aim of the work:

We aimed to describe early Kuwait experience regarding simultaneous (SKP).

**Methods:**

Data of patients who underwent simultaneous kidney pancreas transplantation were collected including their demographic and clinico-laboratory parameters. All patients were suffering type 1 diabetes. We have paid attention to patient and graft outcome, rejection episodes and associated complication. Rejection of the pancreas was diagnosed by combined clinical and laboratory parameters while kidney rejection was confirmed by

**Results:**

From January 2012 to December 2014, 9 SKP transplants (3 women and 6 men) have been performed at Hamed Al-Essa Organ transplant center of Kuwait. The median age of recipients was 28 years, with a range of 25 to 36 years. One-year patient survival rate was 100% while the graft survival was 95% for the pancreas graft and 90% for the kidney graft. One pancreas was lost in the first two weeks due to a graft artery thrombosis. All patients showed normalization of their blood sugar within one week after transplantation and remain so even at the time of rejection (2 cases). The mean creatinine was 82  $\mu\text{mol/L}$  at 1 year and 126  $\mu\text{mol/L}$  at two years follow up. We reported biopsy proven rejection in 2 patients which were treated successfully according to our antirejection protocols (pulse steroid for T-cell mediated rejection; and plasma exchanges, IVIG and rituximab for antibody mediated rejection).

**Conclusions:**

A successful pancreas transplant program can be established in a single small-volume institute. A meticulous surgical technique and early anticoagulation therapy are required for further improvement in the outcomes.

*Key Words: kidney pancreas; transplant; experience ;*



**Medicine**

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**Calcineurin inhibitors elimination: which m-TOR to be chosen?**

Gheith O, Al-otaibi T, A Halim M, Nampoory N, Said T, Nair P  
OTC

**Introduction:**

The mammalian target of rapamycin inhibitor (mTORi) are used to achieve adequate immunosuppression while decreasing the dose and possible toxicity of primary agents, such as calcineurin inhibitors. The aim of our work was to compare which mTORi is better to convert from calcineurin inhibitors (CNI) based regimen among

**Methods:**

Twenty renal transplant recipients converted from CNI to evirolimus based immunosuppressive (group 1) were compared with another group of patients who were converted from CNI to sirolimus based regimen (group 2, n=77). All patients were followed up during the period between 2000 and 2015 in Hamed Al-Essa organ transplant center of Kuwait. All patients were adults and received lymphocyte-depleting agents as induction. We evaluated the patient and graft outcomes after 1 year of conversion. The primary endpoint was a composite endpoint of graft survival (non-death censored) and biopsy proven acute rejection at 1 year.

**Results:**

The two groups were comparable regarding demographic data, patient sex, original kidney disease and virology screen were not different in both groups. However, cadaveric donors and overweight patients (BMI>25) were significantly more prevalent among group 2 (p<0.05). Moreover, we observed that despite the higher number of acute rejections (pre and post-conversion) and higher cholesterol (post-conversion) in group 2 (p<0.05), graft and patient outcome were comparable in both groups after 1 year follow up (p>0.05).

**Conclusions:**

CNI minimization can be successfully contemplated with either sirolimus or evirolimus with equal and similar outcome.

*Key Words: immunosuppression; renal transplant; outcome;*



Medicine

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## **BK virus among renal transplant recipients: Kuwait single center experience.**

Gheith O, Al-Otaibi T, A-Halim M, Yagan J, Said T, Nampoory N  
OTC

### **Introduction:**

BK viremia and nephropathy are increasing problems in renal transplant recipients. The lack of safe and effective antiviral therapy made screening-based prevention a recommended strategy. Aim of the work: Our objective was to determine the prevalence of BK virus (BKV) infection among renal transplant recipients.

### **Methods:**

All renal transplant recipients followed up in Hamed Al-Essa Organ transplant center clinics between 2011 and 2015 (n = 1523) were screened. Blood quantitative real-time polymerase chain reaction (PCR) for the BKV was performed in all of the study patients. Patients who showed positive BKV PCR were evaluated by quantitative PCR for viral load. Renal biopsy was performed only in patients with deteriorating renal function associated with positive PCR.

### **Results:**

Among the 1523 kidney transplant recipients studied, 956 (62.8%) were males, 40% were non-kuwaiti; with mean age  $46.6 \pm 15.6$  years. During the screening period, we found that the prevalence of positive BK virus patients was fluctuating between 2 to 8.3% while those with significant viral load represented 6.1 to 34% of positive cases. Renal biopsy confirmed the diagnosis of BK nephropathy in 31 cases. Cases that were managed by reducing the immunosuppressive treatment showed more stabilization of their graft function compared to those who actively managed by leflonamide, ciprofloxacin, IVIG. Till the end of 2015, diagnosis of BKN was documented in 58 patients with 21 rejection episodes, 21 graft failure and 3 mortalities.

### **Conclusions:**

Our screening program suggested that BKV is not uncommon in our kidney transplant recipients. It could help minimize its detrimental impact on the patient and graft outcome.

*Key Words: BKN; renal transplant; outcome;*



**Medicine**

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## **Human leucocyte antigen DR mismatch in elderly renal transplant recipients**

Gheith O, Al-Otaibi T, Nair P, Said T, Halim MA, Abdelmonem M, Aboatteya H, Zakareia Elsayed, Ahmed Fathy, Yagan J, Rida S.

OTC

### **Introduction:**

Renal allograft failure in elderly has been associated with several factors like age, race, donor, ischemia time, primary renal disease, HLA mismatch, and transplantation year. Graft survival has improved over the years owing to changes in immunosuppression regimens. Aim of the work: To determine the impact of HLA-DR mismatching on rejection, graft survival, and sensitization in elderly renal transplants.

### **Methods:**

In this retrospective analysis, elderly renal transplants performed in Hamed Al-Essa organ transplant center of Kuwait (n=220), between 1994 and 2011 were examined for the effect of HLA-DR mismatches on graft and patient survival. DR zero mismatch (group1, n=34); one mismatch (group 2, n=135) and two mismatches (group3, n=51) comprised the three groups of our study. Pre-transplant complement-dependent cytotoxicity and flow cytometry cross matches were negative. Basic immunosuppression comprised Tacrolimus, MMF and steroids.

### **Results:**

The three groups were matched regarding mean recipient age ( $63\pm 10$ ,  $64.8\pm 4.8$ ,  $65.3\pm 3.1$  years respectively); patient and donor sex; donor age ( $35\pm 8.2$ ,  $34\pm 7.4$ ,  $30\pm 9.3$  years), original kidney disease, pre-transplant co-morbidities, viral profile, type of maintenance immunosuppression and basal graft function. Most of patients with two DR mismatches received cadaveric grafts and ATG induction; while patients with grafts from live donors received simulect induction ( $p < 0.05$ ). We found that patient survival at 1, 5, and 10 years was comparable in all groups. Post-transplant complications were comparable in all groups especially infections (bacterial and viral), hypertension, mean rejection episodes and NODAT. Moreover, we found no significant difference in the graft function as represented by serum creatinine at 1, 3, 5, and 10 years of follow up ( $p > 0.05$ ).

### **Conclusions:**

HLA-DR mismatch elderly renal transplantation-especially with cadaveric donors- is feasible with potent induction and maintenance immunosuppression.

*Key Words: HLA DR; renal transplant; outcome elderly;*



**Medicine**

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**Systemic lupus erythematosus among renal transplant recipients:  
single center experience.**

Gheith O, Al-Otaibi T, Prasad Nair, Said T, Halim M, Nampoory MRN  
OTC

**Introduction:**

Long term outcome of renal transplantation among systemic lupus erythematosus (SLE) patients remains a debated topic.

Aim of the study: We compared the long-term outcome of kidney transplantation in ESRD patients secondary to lupus nephritis with that in an age, sex, and donor matched control group of recipients.

**Methods:**

This study comprised 192 kidney transplant recipients who received their grafts between 1994 and 2011 at Hamed Al-Essa Organ transplant center of Kuwait. These patients were further subdivided into two groups according to original kidney disease (36 secondary to SLE) and (156 secondary to non-SLE causes). All patients' data were assessed with special emphasis on graft and patient survival as well as post-transplant medical complications.

**Results:**

The two groups were comparable regarding pre-transplant patient demographic features (age and sex of donors and recipients), moreover pre-transplant diabetes, anemia, hypertension, tuberculosis, bone disease, type of dialysis, type of immunosuppression and viral profile were also matched. The overall incidence of post-transplant complications was comparable among the two groups especially NODAT, BK nephropathy and coronary heart disease ( $p>0.05$ ). Lupus patients needed significantly more anti-hypertensives ( $p=0.003$ ), and had higher prevalence of CMV ( $p=0.001$ ). On the other hand, we observed higher prevalence of hyperlipidemia in the control group ( $p=0.015$ ). We observed that the mean number of rejection episodes were significantly higher among lupus patients compared to the control group ( $0.94\pm 1.1$  vs.  $0.42\pm 0.66$ ;  $p=0.011$ ). Kidney graft survival was worse among the lupus group compared to the control group ( $p<0.001$ ); however, patient survival was comparable in both groups at 1, 5, and 10 years ( $p<0.05$ ).

**Conclusions:**

SLE as a cause of ESRD in renal transplant recipients is associated with worse allograft survival possibly due to higher prevalence of CMV, hypertension and acute rejection

*Key Words: lupus; renal transplant; outcome;*



**Medicine**

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## **Induction immunosuppression for kidney transplant recipients: is anti-IL2 receptor monoclonal antibodies needed?**

Gheith OA, Halim M, Al-Otaibi T, Zakareia A, Fathy A, Rida S, Yagan J, Nair P  
OTC

### **Introduction:**

Induction with biological agents is widely used after kidney transplantation. No large randomized trial has examined the effect of IL2RA vs. no induction in patients receiving tacrolimus, mycophenolic acid and steroids. Recent data questioned the need for IL2RA in kidney transplantation either in low or high risk patients. Aim: To evaluate the impact of IL2 receptor blocker induction on renal transplant

### **Methods:**

In this retrospective case controlled study including 320 low risk kidney transplant recipients with interleukin 2 receptor blocker as induction group I (n= 215) compared to those who did not receive any induction group II (n= 105). Data were collected from 11/1993 till 5/2014. Primary end points were Graft loss and/or patient death, while secondary end point were Cerebro-cardiovascular events, malignancies or rejection.

### **Results:**

Patients in the 2 groups were comparable regarding demographic data and pre-transplant comorbidities as anemia, hypertension, ischemic heart disease, type of dialysis and pre-transplant diabetes ( $p>0.05$ ) but bone disease was significantly higher in induction group ( $p<0.05$ ). Glomerulonephritis as an original kidney disease and the live related female donor transplant were significantly higher among no induction group ( $p<0.05$ ). We found no significant difference in basal parameters of patients in both groups like body weight, hemoglobin, eGFR, mean number of rejection episodes or mean number of antihypertensive agents ( $p>0.05$ ). However, follow up eGFR was significantly better in the no-induction group at 3years, 5 years, and 10 years follow up ( $p<0.05$ ). Also the two groups were comparable regarding renal graft outcome ( $p=0.084$ ), however, patient survival was better in IL2 induction group but this did not rank to significance ( $p=0.05$ ).

### **Conclusions:**

Induction immunosuppression in standard risk patients may no longer be beneficial among renal transplant recipients. Prospective controlled studies are needed.

*Key Words: induction immunosuppression; renal transplant; outcome;*



**Medicine**

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## **Chronic active antibody mediated rejection (CAMR) in renal transplant recipients – Is intervention justified?**

Nair MP, Al-Otaibi T, Gheith O, Said T, Zakaria A, Yagan J, Rida S, Sami A, Yahya A, Moneim MA

OTC

### **Introduction:**

Chronic renal allograft injury and dysfunction is a multifactorial process in which immunological and non-immunological factors contribute. Recent data showing the association of circulating antiHLA antibodies and C4d deposits in peritubular capillaries (PTC) in chronically failing renal allografts indicate a pathogenic role of humoral mechanisms leading to CAMR in a subset of patients with chronic allograft dysfunction. Aim:- We aimed to present 58 patients with CAMR who received our management according to our protocol and follow the renal function prospectively for one year.

### **Methods:**

58 renal transplant recipients fulfilling the diagnostic criteria of CAMR (Banff 07) were recruited in this observational study and were given the following treatment- increase in basic immunosuppression, daily plasma exchange for 5 days, intravenous immunoglobulin 25 grams/day for 5 days and one dose of Rituximab 1gm IV (in 73% of cases and the rest received rituximab alone). These patients were followed up prospectively for a period of 1 year.

### **Results:**

Most of kidney transplant patients (60%) were males below 40-years old, with live donor (84.7%) and 50% thymoglobulin induction and 77.8% immediate graft function. The mean pretreatment serum creatinine and estimated GFR were  $230 \pm 70.9$   $\mu\text{mol/L}$  and 27 ml/min; respectively. One month post-treatment serum creatinine and estimated GFR means were  $147 \pm 82$   $\mu\text{mol/L}$  and 47 ml/min; respectively. After one year the mean serum creatinine and estimated GFR were  $277.6 \pm 129$   $\mu\text{mol/L}$  and 22 ml/min. Addition of rituximab to the treatment had no significant impact on the graft or patient outcome. After one year follow up, graft outcome was poor (68% graft failure) and one patient died and other one lost follow up.

### **Conclusions:**

Rituximab did not add significant impact on the management of cases with chronic active antibody mediated rejection.

*Key Words: chronic active antibody mediated rejection; renal transplant; outcome ;*



**Medicine**

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**Zero-HLA mismatches renal transplant recipients: Kuwait**

Nair MP, Gheith O, Al-Otaibi T, Halim MA, Moneim MA, Said T, Nampoory MRN.  
OTC, Sabah area

**Introduction:**

The higher the HLA match the better the renal graft outcome. Therefore the compatibility at all three HLA loci is desirable for optimal graft outcome. Aim: To assess the long-term outcome of HLA zero-mismatched renal transplant recipients in Kuwait.

**Methods:**

From 1993 to 2010, 1050 renal transplants were performed in Hamed Al-Essa Organ transplant center, including 40 (3.8%) kidney transplant recipients with zero-HLA mismatches with their initial transplants. There were 21 (52.5%) males, 19 (47.5%) females with their mean age  $28.8 \pm 7.1$  years (range 7-53 yrs). The primary renal disease was chronic glomerulonephritis (GN) in 17 (42.5%), chronic tubule-interstitial nephritis in 12 (30%), diabetes mellitus in 2 (5%) and idiopathic in 9 (22.5%). All recipients had negative lymphocytotoxicity cross match prior to transplantation. Without induction, they were maintained on triple immunosuppressive protocol based on steroid, anti-proliferative agent and calcineurin inhibitor (cyclosporine or tacrolimus).

**Results:**

Mean follow up period was  $8.76 \pm 2.1$  years and the mean serum creatinine on last follow-up was 112  $\mu\text{mol/L}$ . Graft survival was 100%, 97.2%, 93.9% and 84% at 1, 3, 5 and 10 years respectively with 100% patient survival during the whole follow up period. Four grafts were lost during the follow up period due to chronic rejection. Biopsy proven acute rejection represented 5% (2 episodes) during the 1st year after transplantation with complete response to pulse steroid. There were in total, 3 (7.5%) cases of post-transplant GN, 2 being recurrent diseases (lupus nephritis and IgA nephropathy) and the third, a case of de-novo membranous GN. Post-transplant diabetes and hypertension were reported in 6 and 2 patients respectively. There were no cases of post-transplant malignancy.

**Conclusions:**

Favorable patient and graft outcome was observed in zero-mismatched renal transplant recipients possibly related to less post-transplant co morbidities.

*Key Words: HLA; renal transplant; outcome ;*



**Medicine**

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## **Essential oils from *Origanum majorana* against foodborne pathogens in chicken and meat products**

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DDI

**Introduction:**

Herbs are beneficial food preservatives without organoleptic adverse changes and loss of nutrients. We aimed to evaluate the use of *Origanum majorana* hydrosol, oil and leaves as an organic preservative for chicken and meat products for different periods of storage.

**Methods:**

In this prospective controlled study, chicken and meat products were divided into 10 parts; first 3 were mixed with 3 levels of *Origanum* oil, second were mixed with 3 levels of hydrosol and third were mixed with 3 levels of ground leaves and the tenth serve as control and all were stored frozen. *Origanum* oil and hydrosol were prepared by hydrodistillation. Food products were assessed monthly for organoleptic properties, pH and microbial profile for 6 months. Dishes with microbial colonies between 5-50 were counted through special equation. K- Wallis test was used for comparing the mean microbial counts.

**Results:**

Both medium and high concentrations of all *Origanum* forms were successful in suppressing aerobic mesophiles in beef burger and chicken samples -but not in minced meat- especially at the last storage period when the count reached below the limit of detection. However, mesophilic counts in all treated samples were significantly lower than that at zero time values and in parallel control ( $p < 0.05$ ). We observed significant continuous reduction in yeast and mold counts in minced meat compared to zero time values; and after one month of storage compared to the control ( $P < 0.05$ ) till it reached below the limit of detection in oil and hydrosol treated samples at the 6th month especially with high oil concentration. We could not detect any mold or yeast at 6th month of storage in all treated chicken and beef burger samples; and the higher the *Origanum* concentration the earlier the disappearance of mold and yeast.

**Conclusions:**

*Majorana* oil was more effective- microbiologically- and more accepted organoleptically –in medium concentration- bio preservative for chicken and meat products.

*Key Words: Origanum; food borne disease; meat and chicken products;*



**Medicine**

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## **Peripheral Arterial Stiffness and Residual Renal Function in Chronic Hemodialysis Patient**

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### **Introduction:**

Patients with chronic kidney disease (CKD) are at increased risk for cardiovascular diseases (CVD) including coronary artery disease (CAD), congestive heart failure, other causes of cardiovascular mortality, & peripheral arterial disease (PAD) that can be used as indicator for CVD. The beneficial effects of residual renal function (RRF) in chronic hemodialysis patients (C-HD) may be due to enhanced toxic middle molecule clearance, improved nutritional parameters, reduced erythropoietin resistance, & reduced ultrafiltration requirement. We aimed to study the effect of RRF in C-HD on the occurrence of PAD.

### **Methods:**

Fifty C-HD were included along with 10 healthy controls. All patients were subjected to history taking, clinical examination, & routine laboratory tests including parathyroid hormone (PTH). Assessment of RRF was done by KRU equation that was corrected using body surface area (KRUBSA). C-HD were sub-classified according to KRUBSA into group 1 (significant RRF) with KRUBSA  $\geq 1$  ml/min, & group 2 (non-significant RRF) with KRUBSA  $< 1$  ml/min. Estimation of the Ankle brachial index (ABI) as an indicator of PAD was done from the contralateral side of the vascular access. Subjects were categorized according to ABI (PAD: 0.41-0.9, Normal: 0.91-1.30, non-compressible or severely calcified vessels:  $>1.30$ ).

### **Results:**

50 C-HD were studied with age  $47.76 \pm 13.65$  years, KRU  $3.92 \pm 2.79$  ml/min, & KRUBSA  $2.09 \pm 1.46$  ml/min. 14% had history of CAD; Aortic calcification (AC) was found in 20% using lateral abdominal X-ray; 67.3% showed normal ABI, 26.5% had PAD, & 6.1% showed non-compressible vessels. There was significant difference between group 1 & group 2 regarding distribution of IHD, AC, & ABI. Additionally, there was significant difference regarding age, dialysis duration, CaXPO4 product, hemoglobin, serum creatinine, between different ABI categories.

### **Conclusions:**

Preserved RRF in C-HD is associated with less prevalence PAD as a parameter of CVD.

*Key Words: Residual Renal Function; Anke Brachial Index; Hemodialysis;*



**Medicine**

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## **Role of Power Doppler Ultrasonography in Detection of Subclinical Hyperuricemia in Patients with Non-Hodgkin's Lymphoma**

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### **Introduction:**

Objective: This study aimed to detect incidence of subclinical arthritis in patients with Non-Hodgkin lymphoma (NHL) and the diagnostic ability of Power Doppler Ultrasonography (PDUS) in detecting subclinical hyperuricemia.

### **Methods:**

We studied 100 NHL patients (divided into 2 groups depending on the presence of the double contour (DC) sign detected by PDUS) and 100 controls in a cross sectional study. Demographic, clinical and serological data were evaluated. PDUS was done to all patients and controls.

### **Results:**

There was a statistically significant difference between the two groups regarding the presence of subclinical hyperuricemia in group 1 ( $p=0.008$ ) who had higher serum creatinine and gouty nephropathy ( $p=0.002$  and  $p=0.001$  respectively).

### **Conclusions:**

PDUS can detect subclinical hyperuricemia and subsequent inflammatory arthritis in NHL patients; also it serves as a non-invasive, bedside tool.

*Key Words: Hyperuricemia;; gouty nephropathy; NHL and PDUS;*



**Medicine**

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## **Analysis of four single nucleotide polymorphisms in the NOD2/Card15 gene in Arab patients with Crohn's disease**

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### **Introduction:**

Single nucleotide polymorphisms (SNPs) in NOD2/Card15 gene have been linked to an increased risk of Crohn's disease (CD). This study aimed to determine the frequency of the SNPs in Arab patients suffering from CD in Kuwait.

### **Methods:**

Blood samples were obtained from Arab patients with CD (n=103) and Arab control subjects (n=100). The isolated genomic DNA from the blood samples were used in PCR for amplification of regions responsible for four SNPs in NOD2/CARD15 gene using four sets of primers specific for each SNP, i.e. SNP5, (Exon 802C>T), SNP8 (Exon4 2104C>T), SNP12, (Exon 8 2722G>C) and SNP13 (Exon11 3020insC). The amplified products were analyzed by gel electrophoresis and sequenced by cycle sequencing method. The sequences were analyzed for the SNPs using a sequence analysis software.

### **Results:**

The SNP5 (Exon4 802C>T) was detected in the NOD2/Card15 gene of 17 (16.5%) Arab patients with CD compared to 32 (32.0%) controls (p<0.05). This difference was statistically significant if the mutation was heterozygous (p<0.05) but not in homozygous (P>0.05). The SNP12 (Exon 8 2722G>C) was found in 24 (23.3%) patients and 10 (10.0%) controls (p<0.05). This difference was statistically significant if the mutation was homozygous (p<0.05) but not in heterozygous (P>0.05). The SNP8 (Exon4 2104C>T) was detected only in one patient but in none of the controls, whereas SNP13 (Exon11 3020insC) was absent in all the CD patients and controls.

### **Conclusions:**

This study, conducted for the first time in Kuwait, suggests variable effects of SNP5 and SNP12 of NOD2/Card15 gene on Arab patients with CD. The former being protective and the latter being pathogenic for CD in Arab patients. The other two SNPs don't seem to play any role in CD in this group of Arab patients.

Supported by Kuwait University Research Sector grants MM01/15 and SRUL02/13.

*Key Words: Crohn's disease; NOD2/Card15; Arab;*



**Medicine**

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## **Annual Data for Kidney Transplant Services in Kuwait in 2016**

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### **Introduction:**

Objectives: Renal transplant services in Kuwait are only provided by the Hamed Al-Essa Organ Transplant Center in Ibn Sina Hospital since. We aimed to annually monitor and record the activity and outcome of annual renal transplants in Kuwait.

### **Methods:**

Data on transplant patients were collected from hospital records from January 1, 2016, through December 25, 2016, at Ibn Sina Hospital.

### **Results:**

Seventy-four patients underwent a renal transplant in Kuwait in 2016; 51 (69%) patients were male and 23 (31%) were female. Of these 74 patients, 30 (40.5%) received a kidney from a deceased donor, 19 (25.7%) received a kidney from a living-unrelated donor, and 25 (33.8%) received a kidney from a living-related donor. Twenty-six (35.1%) patients who were highly sensitized immunologically underwent successful desensitization before transplant according the local protocol; 14 (53.8%) of these patients were male and 12 (46.2%) were female. Five patients (6.75%) experienced biopsy proven acute rejection within the first month after transplant, 2 of them had acute rejection within one week post-transplant that led to loss of the graft in only one patient. One diabetic male patient underwent a pancreas after kidney transplant but it was unsuccessful. Ninety-eight patients who underwent a transplant outside of Kuwait in 2016 were added to the follow-up list; 65 (66.3%) of these patients were male and 33 (33.7%) were female. Of these 98 patients, 37 patients (37.8%) received a kidney from a living-related donor, 57 (58.2%) received a kidney from a living-unrelated donor, and 4 (4%) received a kidney from a deceased donor.

### **Conclusions:**

A total of 74 patients underwent a renal transplant in Kuwait in 2016, only 2 (2.7%) of whom experienced biopsy proven acute rejection in the first week after transplant.

*Key Words: Kidney Transplantation; Acute rejection; Desensitization ;*



**Microbiology and Immunology**

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**Emergence of multidrug-resistant *Candida auris* in Kuwait**

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**Introduction:**

*Candida auris*, first isolated from ear swab in 2009, has now emerged as an important nosocomial pathogen causing invasive infections in many countries. Inadequacies of currently available commercial systems for accurate identification of rare yeast species and multidrug-resistant nature of *C. auris* pose diagnostic and therapeutic challenges. Here, we present data on occurrence of *C. auris* in clinical specimens in Kuwait and its susceptibility to antifungal agents.

**Methods:**

A total of 112 *Candida* species received in Mycology Reference Laboratory during 2014-2016 and forming pink-colored colonies on CHROMagar *Candida* were subjected to further characterization. Phenotypic identification methods included wet mount examination of culture for microscopic morphology, identification by Vitek2 system and susceptibility testing by Etest. Minimum inhibitory concentrations (MICs) were read after 24 h at 35°C. Molecular identification was performed by sequencing of internal transcribed spacer (ITS) and D1/D2 domains of ribosomal DNA (rDNA).

**Results:**

All 112 *Candida* species isolates forming pink colonies on CHROMagar *Candida* were identified as *Candida haemulonii* by Vitek2 yeast identification system. Wet mount examination of cultures for microscopic morphology was not helpful in further identification of *C. haemulonii* complex species. Sequencing of ITS and D1/D2 domains of rDNA identified 110 (98.2%) isolates as *C. auris* and two (1.8%) isolates as *C. duobushaemulonii*. Nine (8.2%) *C. auris* isolates originated from blood samples while 101 isolates were obtained from other specimens. All *C. auris* isolates showed reduced susceptibility to fluconazole (MIC > 8 µg/ml) and 84.5% to amphotericin B (MIC > 1 µg/ml).

**Conclusions:**

*C. auris* is an emerging nosocomial pathogen in Kuwait. *C. auris* is misidentified by routine phenotypic methods hence; molecular methods are needed for accurate identification. Susceptibility testing is also warranted for proper patient management. The study was supported by Kuwait University Research Sector Grant No. MI01/15

*Key Words: Candida auris; Multidrug-resistance; Emergence in Kuwait;*



## **Surveillance of faecal carriage of nosocomially acquired metallo-beta-lactamase-producing carbapenem-resistant Enterobacteriaceae among intensive care unit (ICU) patients.**

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### **Introduction:**

Carbapenem-resistant Enterobacteriaceae (CRE) are a major global medical issue. The digestive tract is the main reservoir for these isolates, therefore, rectal swab surveillance is highly recommended. The purpose of this study was to investigate the rates of faecal carriage and transmission of CRE among patients admitted to the intensive care units (ICUs) in Kuwait as well as to characterise carbapenem-hydrolyzing enzyme production in these isolates.

### **Methods:**

From July to September 2016, 298 non-duplicate rectal swab specimens, obtained from all patients at ICU admission and 64 environmental samples, were screened by KPC agar. Bacterial identification and antibiotic susceptibility tests were done using VITEK-2 system. CRE was defined as isolates showing decreased susceptibility to ertapenem, imipenem, and/or meropenem. PCR method and Xpert® Carba-R were used to detect carbapenemase type and subtypes. Clonal relatedness was assessed by pulsed-field gel electrophoresis (PFGE). Plasmid DNA analysis was performed according to published protocols.

### **Results:**

Out of 298 patients, 13 (4.4%) were found to be carriers of CRE. Of these, the most common species were *Klebsiella pneumoniae* (38.5%), *Escherichia coli* (38.5%) *Enterobacter aerogenes* (15.4%) and *Serratia marcescens* (7.7%). They were highly resistant to meropenem, Ertapenem, imipenem and amikacin. OXA-48 was the commonest CRE type seen in 30.7%, followed by NDM-1 (15.4%) while KPC was seen in only one (7.7%) isolate. One *K. pneumoniae* isolate was OXA negative by PCR and positive by Carba-R. The plasmid profiling showed that all, except one, isolates contained at least two plasmids. Two

of the NDM-1 positive *K. pneumoniae* were clonally identical on PFGE but the rest were heterogeneous. All the environmental surveillance cultures were so far negative.

### **Conclusions:**

This study highlights a relatively high prevalence of nosocomial faecal acquisition of CRE producing OXA-48, NDM-1 and KPC enzymes within ICU.

Funding: Faculty of Graduate Studies, Kuwait University

*Key Words: CRE; surveillance; ICU patients;*



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## **Molecular typing of *Acinetobacter baumannii* colonizing the rectum of intensive care unit (ICU) patients**

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### **Introduction:**

*Acinetobacter baumannii* is a nosocomial pathogen that causes serious disease in debilitated patients in ICU. The normal colonization sites of *A. baumannii* are respiratory tract and skin surface. Gastrointestinal tract including the rectum is also be colonized. The objective of the study was to determine the genetic relatedness of sequential isolates colonizing the rectum of ICU patients.

### **Methods:**

Patients admitted at the ICU of Mubarak Al-Kabeer Hospital, Kuwait were studied for one year from March 2014. Rectal swabs were taken from each patient on first day of admission and then twice weekly until discharge or death. Isolates from patients were included provided they yielded isolates at least on five sampling times. A total of 261 isolates from 32 patients were available for the study. Of these, all 80 isolates from 11 patients were typed by DiversiLab (bioMerieux), and pulsed field-gel electrophoresis (PFGE) (after digestion of the chromosome with *ApaI*). The relatedness in PFGE was calculated by BioNumerics. The concordance between the typing methods was calculated by a two-by-two table of pairwise compared strains either as identical or different.

### **Results:**

The two typing methods showed a concordance of 85% (range, 75% - 100%). There were different patterns of sequential colonization of patients. The patterns were either single type, multiple types, or replacement of an original type with a new type or another earlier type. Sequential isolates from the same patients exhibited identity, relatedness or total unrelatedness.

### **Conclusions:**

Our study showed rectal colonization of ICU patients with a mixture of genetic types of *A. baumannii*. The two typing methods showed discrimination of strains with a high degree of concordance between them. Further studies with whole-genome sequencing are required to understand the origin of diversity in the colonizing strains.

Funding: KUWAIT UNIVERSITY

*Key Words:* *A. baumannii*; PFGE; DiversiLab;



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## **Clinical and microbiological characteristics of invasive *Streptococcus pyogenes* infection**

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### **Introduction:**

*Streptococcus pyogenes* (GAS) were the predominant cause of maternal and neonatal sepsis in 1930's. Since then several reports published describe cases of necrotizing fasciitis, toxic shock-like syndromes associated with high mortality and regional outbreaks of rheumatic fever. We describe the clinical and microbiological characteristics of six cases of GAS sepsis identified in our laboratory in the past seven months.

### **Methods:**

We sought to examine the incidence of invasive GAS (iGAS) infection among all cases of sepsis diagnosed from January to November 2016 in our laboratory. Clinical data, such as, age, gender, clinical presentation, risk factors (if any), treatment received and outcome of the patients, with blood cultures positive for GAS, were recorded from individual files. Blood culture isolates of GAS were identified by Phoenix/Vitek and grouping with specific antisera (StrepPRO Grouping, Hardy diagnostics). Antimicrobial susceptibility was performed by disk diffusion (Kirby-Bauer) method and E test (Biomerieux, France). Three of the isolates were subjected to PFGE. Other laboratory data that were recorded included CBC, CRP and PCT.

### **Results:**

A total of 20,859 blood culture bottles, from adults and children, were processed. Among the 658 clinically significant bacterial isolates there were six strains of GAS. Diabetes mellitus with bullous skin lesions was the common risk factor found in the adult patients whereas among children, mother's vaginal carriage of GAS, tonsillar abscess and exacerbation of bronchial asthma were recorded. All the patients received appropriate antibiotics and improved except one. Biochemical reactions, AS and PFGE results showed no similarities between the GAS isolates tested.

### **Conclusions:**

Our observation suggests that our patients were sporadic, community acquired cases of iGAS with no similarities among the isolates. Rapid diagnosis and right empirical therapy can mitigate the burden of mortality in such cases.

*Key Words: Streptococcus pyogenes; Group A streptococcus; Invasive streptococcal*



**Microbiology and Immunology**

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**A study of the microbial flora of chronic periodontitis in Kuwait**

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**Introduction:**

Periodontal diseases are a group of chronic infections that destroys tissues surrounding and supporting the teeth. There is hardly any data on the aetiology of this disease in the Middle East. This study was undertaken to investigate the anaerobic aetiological agents involved in periodontal diseases in Kuwait

**Methods:**

Patient with chronic periodontitis seen at the Kuwait University Dental Clinics were recruited during a period of 6 months. Samples were collected using Gutta Percha Points directly from inside the gingival pockets and placed in sterile Ringer's solution and thioglycolate broth in duplicates. One set was cultured on appropriate media and the other

**Results:**

Twenty patients, stratified into mild (one patient), moderate (10), and severe (9) and 11 healthy controls were studied. Patients' ages ranged from 20-69 years with most of them (40%) in the 50-59 age group. Male:female ratio was 1.5:1; non-Kuwaitis to Kuwaitis 1.9:1. All patients and controls harbored Prevotella spp. and Fusobacterium spp. Porphyromonas gingivalis were found in 40% and 33.3% of the moderate and severe cases, respectively and none of the controls. Tannerella forsythia was detected in 70% and 88.9% of the moderate and severe cases, respectively compared to 54.6% of the controls ( $P<0.05$ ). Parvimonas micra and Treponema denticola were detected in 90% and 88.9%, and 40% and 77.8% of moderate and severe cases, respectively compared to 63.6% and 27.3% of controls, respectively ( $P<0.0028$  and  $P<0.0001$ , respectively). Aggregatibacter actinomycetemcomitans were present in low numbers in both cases and controls. Culture results are not included in this analysis because of low yield.

**Conclusions:**

Compared with the control, P. gingivalis was associated with the more destructive forms of the disease than the other oral anaerobes. T. forsythia, P. micra and T. denticola were, to a large extent, important causative agents of moderate and severe cases of periodontitis. Funding: College of Graduate Studies, Kuwait University, Kuwait, Research Grant no YM 01/16

*Key Words: Chronic periodontitis; Anaerobic etiology; PCR study;*



## **Lack of immunogenicity of the major outer membrane protein of *Campylobacter jejuni* used as a vaccine in an adult mouse intestinal colonization model**

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### **Introduction:**

*Campylobacter jejuni* is a diarrheal pathogen. Attempts are being made to develop a vaccine against it. The 45-kDa major outer membrane protein (MOMP) of *C. jejuni* encoded by *porA* has serotype-specific epitopes and common epitopes with other serotypes. We reported that MOMP from *C. jejuni* strain C31 (O:6,7) expressed as fusion protein with glutathione S-transferase (GST) was immunogenic and provided broad protection in an adult mouse intestinal colonization model. Since it is not desirable to have GST in a human vaccine (as its safety is not known), we tested a PQE-30 vector- expressed MOMP from *C. jejuni* strain 111 (O:1,44) devoid of a carrier, for immunogenicity in the mouse colonization model.

### **Methods:**

Each of 12 adult female, 6-8 weeks old, BALB/c mice were orally vaccinated once a week for three weeks with a 300 µl solution containing 300 µg MOMP in 4M urea and 25 µg double-mutant (R192G/L211A) heat-labile enterotoxin of *Escherichia coli* as an adjuvant. Twelve control mice received phosphate-buffered saline. Samples for antibody measurement were collected before vaccination and a week after third vaccine dose. Serum IgA and IgG and fecal IgA antibody responses to MOMP were measured by ELISA using a 1:100 diluted serum and 1:20 diluted, total IgA adjusted feces. Optical density (OD) reading was measured at 405 nm. Differences in OD readings were tested by student t test or Wilcoxon rank sum test.

### **Results:**

The mean serum IgG antibody and IgA antibody and fecal IgA antibody OD readings ± standard deviations in test versus control mice were: 0.131±0.061 vs 0.1650±0.085, 0.100±0.032 vs 0.082±0.0, and 0.083±0.008 vs 0.083±0.009, respectively with no significant differences (P<0.05, in all comparisons).

### **Conclusions:**

MOMP may have been degraded in the gastrointestinal tract resulting in no immune response. It has to be stabilized by fusion with a carrier protein safe for human use or delivered in liposomes for immunogenicity.

Funding: Kuwait University Research Sector Grant (MI03/13)

*Key Words: Campylobacter jejuni; Major outer membrane protein; Vaccine;*



## **Detection of multi-drug resistant gram negative organisms in the surveillance samples**

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### **Introduction:**

Reliable detection of multi-drug resistant Gram negative organisms (MDRR) is critical for effective infection control. Routine susceptibility tests can detect phenotypic resistance, but cannot confirm carbapenamase production or distinguish non-susceptible isolates due to other mechanisms such as porin mutants and efflux pumps. Therefore, we evaluated a low cost phenotypic method to isolate potential MDRR and confirmed it by a commercial PCR method.

### **Methods:**

Patients were tested for MDRR colonization with 2 swabs taken each from upper respiratory tract (throat/endotracheal secretion) and the rectum. Each swab was inoculated on to in-house prepared McConkey with 10 mg/L meropenem and regular McConkey agar. After 24 h of incubation identification and antimicrobial susceptibility tests were performed on growing colonies. MDRR were further tested for carbapenamase production by Easyplex SuperBug (Amplex).

### **Results:**

During a period of 6 weeks 599 surveillance samples from 2 sites (upper respiratory and rectum) were processed in our laboratory. Of these, 258 were throat and 341 were rectal swabs. The rate of isolation of MDRR was 55/599 (9.2%), of which 18/465 (3.8%) isolates were from ICU patients and 37/134 (27.6%) were from other inpatients. The proportion of isolated MDRR was *Acinetobacter* spp. (26/55, 47.3%), *Pseudomonas* spp. (19/55, 34.5%), *Klebsiella pneumoniae* (9/55, 16.4%) and *E. coli* (1/55, 1.8%). Among the isolates positive for carbapenamase resistance the common resistance markers present were found to be NDM (28%), CTX-M-1 (20%), OXA-48 (4%), VIM (16%), CTX-M-9 (4%), and none were OXA-181 or KPC.

### **Conclusions:**

Screening for intestinal carriage of MDRR is of significant importance for the development of infection control strategies. Although culture based screening has an advantage of low cost, the turnaround time and sensitivity is suboptimal. Molecular technologies should replace culture methods in screening of MDRR.

*Key Words: Multi-drug resistant gram negtaive; surveillance samples; carbapenamase;*



*Microbiology and Immunology*

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## **A Study of the Rate of Contamination of Blood Cultures in Mubarak AlKabeer Microbiology Laboratory**

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### **Introduction:**

**Background:** False positive blood culture resulting from contamination either from skin normal flora or colonization of indwelling vascular lines are troublesome in the laboratory. The contaminating organisms include coagulase-negative staphylococci, *Corynebacterium* species, *Bacillus* species other than *Bacillus anthracis*, *Propionibacterium acnes*, and *Micrococcus* species. Differentiating between true and false positive blood culture is critical to determine the need to prescribe the appropriate antibiotic therapy or release as contamination. This audit was designed to calculate the rate of blood culture contamination in Mubarak Al-Kabeer hospital. The specific objectives of study are to: 1) calculate the rate of blood culture contamination in Mubarak Al-Kabeer hospital and 2) suggest measures of health care quality by monitoring and lowering the rate of blood culture contamination to keep it within the international standard rate (not exceeding 2-3%).

### **Methods:**

**Methodology:** A retrospective data collection was carried out in the Microbiology laboratory Mubarak Al-Kabeer Hospital database system over a 3-year period (2013-2015) and analyzed to measure the rate of blood culture contamination.

### **Results:**

The rate of contamination was found to be 3.7% in 2013, 3.0% in 2014 and 3.9% in 2015. Coagulase-negative staphylococci was the predominant contaminant.

### **Conclusions:**

The rate of blood culture contamination observed in this study was almost within the internationally accepted standard rate of 2 – 3% for 1 year, and above for 2 years of the study.

*Key Words: Contamination rate; Blood culture; Mubarak Al Kabeer Hospital;*



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**Blood filling volumes in blood culture bottles: A horizontal quality**

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**Introduction:**

Blood filling volumes of blood cultures are critical. As part of our internal quality assurance programme, we conducted a two-months horizontal quality audit about the blood culture bottle filling volumes at Al-Sabah hospital in Kuwait to assess compliance with the standard filling volumes for adults and pediatrics.

**Methods:**

Aerobic, anaerobic, and pediatric blood culture bottles were weighed and marked with their weights before circulating them to all wards. The bottles were re-weighed after inoculation. Volume of blood inoculated was calculated by subtracting pre from post inoculation weight. Bottles from neonates were excluded.

**Results:**

1253 bottles received from adult and pediatric patients. Overall, 22.1% 277/1235(sup)2(endsup) of bottles contained recommended filling volumes. For adults, only 11.5% 105/907(sup)2(endsup) of bottles contained recommended volume of 8-10 mL. For Pediatrics, 49.1% 170/346(sup)2(endsup) of bottles contained recommended volume of 1-3 mL. Compliance rates with the standard filling volumes were highest in pediatric ICU 67% 18/27(sup)2(endsup), pediatric casualty 49% 59/114(sup)2(endsup), adult surgical ICU 46% 50/109(sup)2(endsup), and pediatric hematology center 44% 46/105(sup)2(endsup). Compliance rates of general surgical and medical wards were 3.8% and 1.7% respectively.

**Conclusions:**

Majority of blood culture bottles did not contain the recommended filling volumes, and pediatric wards were more compliant in following the standards blood filling volumes than adult wards. A trend towards better compliance was noticed when blood cultures were collected from arterial and central venous lines compared to peripheral blood cultures.

*Key Words: Blood culture; Blood volume; Audit;*



## **Molecular epidemiology of MRSA isolated in Maternity Hospital a 5-year trend: Is it the right time to introduce antenatal screening program for our population?**

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### **Introduction:**

The emergence and persistence of community –associated MRSA (CA-MRSA) in general population is considered a serious threat that requires continuing public health monitoring. Pregnant women are more susceptible and have risk factors that predispose them to developing infections and transmitting the organism vertically to their neonates. The purpose of this study was to assess MRSA prevalence over 5 years, and to determine phenotypic and molecular characterization of MRSA isolated from women attending

### **Methods:**

Between 2011 and 2015 1,421 *S. aureus* were isolated from HVS and wound/pus samples. Antimicrobial resistance profile, molecular characterization of MRSA strains, SCCmec typing, *mecA* and PVL gene detection were carried.

### **Results:**

The annual proportion of *S. aureus* that were MRSA increased significantly from 26.4% in 2011 to 44.9% in 2015. All MRSA strains were *mecA* positive. Of the 430 MRSA genotyped isolates 75.3% were CA-MRSA, 9.1% were EMRSA-15 and 15.6% were non-typable. However, SCCmec typing showed that type IV was the most frequent (241; 62%), while types V, III and II were detected in (79; 20.3% - 56; 14.4%- 4; 1%) of isolates respectively. PVL was detected in 123/389 of MRSA. The isolates were resistant to ciprofloxacin (15.8%), clindamycin (14%), erythromycin (16.1%), trimethoprim (30.1%) and tetracycline (34.4%). All MRSA isolates were susceptible to linezolid. While all the isolates are considered to be sensitive to vancomycin, an alarming high MIC levels were detected in 32.3% (139/430) and 3.3% (14/430) of CA-MRSA strains with vancomycin MIC of 2 and 3 µg/ml, respectively.

### **Conclusions:**

This study highlights the importance of introducing an effective preventive measure to our population during pregnancy, and we recommend the introduction of low-vaginal MRSA antenatal screening. Our findings also raise concern that more active surveillance may be needed and reinforce the importance of infection prevention strategies

*Key Words: MRSA ; Maternity population; Kuwait community;*



## **Multilocus sequence typing indicates diverse origins of clinical *Candida tropicalis* isolates in a major tertiary care hospital in Kuwait**

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### **Introduction:**

*Candida tropicalis* is a frequently isolated yeast species causing bloodstream, urinary tract and other infections particularly in patients admitted to intensive care units (ICUs) and those requiring prolonged urinary catheterization (UC) or receiving broad-spectrum antibiotics (BSA). Only few studies have explored genotypic heterogeneity among clinical *C. tropicalis* isolates. This study investigated clinical characteristics and genetic relatedness among *C. tropicalis* isolates cultured at Al-Amiri Hospital in Kuwait.

### **Methods:**

Clinical *C. tropicalis* strains (n=48) isolated from blood, genito-urinary, respiratory (RT) and digestive (GIT) tract and wound sites from 41 patients were used. All isolates were phenotypically identified and tested against 6 antifungal drugs by using Vitek 2 system. Molecular identification was done by PCR. Fingerprinting was achieved by multilocus sequence typing (MLST) and data were analyzed by BioNumerics software for phylogenetic relationships.

### **Results:**

Patients mean age was >65 years and >20% patients were from ICUs. Major risk factors included UC, BSA, diabetes and RT/GIT abnormalities. Most candiduria cases had UC, ureteric stent or suprapubic catheters. All isolates were identified as *C. tropicalis* by Vitek 2 and by species-specific PCR and 47 isolates were susceptible to all antifungals. MLST identified 44 diploid sequence types (DSTs) including 39 newly-identified DSTs. *C. tropicalis* isolates from multiple sites of same patient usually belonged to different DSTs. Six isolates from 6 patients belonged to 3 DSTs (clusters), however, *C. tropicalis* in each cluster were isolated >3 months apart.

### **Conclusions:**

Our data show diverse origins of *C. tropicalis* infections in Kuwait as most isolates were unique strains. There was no obvious correlation between 3 clonal clusters with time of isolation and/or hospital ward of their origin. This study presents the first MLST analysis of *C. tropicalis* isolates from the Middle East. The study was supported by Kuwait University Research Sector Grant No. MI02/15

*Key Words: Candida tropicalis; Clinical isolates; Fingerprinting by MLST;*



## **PCR array profiling of antiviral genes in human embryonic kidney cells expressing human coronavirus OC43 membrane protein**

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### **Introduction:**

Human coronavirus OC43 (HCoV-OC43) causes common cold, and is associated with severe respiratory symptoms in infants, elderly and immunocompromised patients. HCoV-OC43 is a member of Betacoronavirus genus that includes also the Severe Acute Respiratory Syndrome (SARS) and the Middle East Respiratory Syndrome (MERS) coronaviruses. Both SARS-CoV and MERS-CoV were shown to express proteins with the potential to evade early innate immune responses. However, the ability of HCoV-OC43 to antagonise the intracellular antiviral defences has not yet been investigated. The objective of this study was to investigate the role of HCoV-OC43 structural membrane (M) protein in the modulation of antiviral gene expression profile in human embryonic kidney 293 (HEK-293) cells using PCR array analysis.

### **Methods:**

HCoV-OC43 M mRNA was amplified and cloned into the pAcGFP1-N expression vector, followed by transfection in HEK-293 cells. Expression of M protein was confirmed by indirect immunofluorescence test. Three days post-transfection, the cells were challenged by Sendai virus. The Human Antiviral Response PCR array system was used to profile the antiviral gene expression in HEK-293 cells, using the fold regulation comparison and the manual normalisation methods.

### **Results:**

A total of 47 genes were downregulated by M protein, the most prominent genes being those critical for the activation of transcription factors involved in the antiviral response like nuclear factor kappa B, interferon regulatory factors and activator protein 1. Among the most important downregulated genes were those coding for MAP kinases, pro-apoptotic and pyroptotic proteins, pro-inflammatory cytokines, pattern recognition receptors and their signaling transduction proteins.

### **Conclusions:**

This study shows for the first time that similarly to SARS-CoV and MERS-CoV, HCoV-OC43 has the ability to downregulate the transcription of genes critical for the activation of different antiviral signaling pathways.

College of Graduate Studies, Research Administration Grant number YM04/15

*Key Words: Coronavirus; Antiviral gene expression; PCR array;*



## **Emergence of Novel Methicillin-resistant *Staphylococcus aureus* (MRSA) in Kuwait hospitals: A National Surveillance, February - July, 2016.**

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### **Introduction:**

The epidemiology of Methicillin-resistant *Staphylococcus aureus* (MRSA) is constantly changing in healthcare facilities worldwide driven by international travels. Regular surveillance is essential to monitor changes in the composition of MRSA strains in healthcare facilities. This study was conducted to characterize MRSA isolates obtained during a surveillance exercise to provide information on the types of MRSA strains

### **Methods:**

A survey of MRSA was conducted from February to July, 2016. One thousand and fifty-eight MRSA were isolated from clinical samples in Kuwait hospitals and typed using antibiogram, SCCmec typing, spa typing, and DNA microarray.

### **Results:**

A total of 167 different spa types were obtained. The majority belonged to spa types t688 (111; 10.4%), t304 (90; 8.5%), t860- (85; 8.0%), t044 (69; 6.5%), t127 (65; 6.1%), t002 (61; 5.7%); and t223 (54; 5.1%). One hundred and sixty-seven isolates were selected for DNA microarray analysis. Twenty-one clonal complexes (CCs) consisting of CC1, CC5, CC6, CC8, CC15, CC22, CC30, CC45, CC59, CC72, CC80, CC88, CC96, CC97, CC121, CC152, CC361, CC398, CC913, CC1153, CC2250/2277 were obtained with the majority belonging to CC5 (94; 56.2%) and CC22 (73; 43.7%). Some strains including CC15-MRSA-V+SCCfus; ST59-MRSA-IV WA MRSA-118; ST59/952-MRSA-VT [PVL+] Taiwan clone; CC96-MRSA-IV [PVL+] Central Asian CA-MRSA; CC152-MRSA-V [PVL+]; CC398-MRSA-IV; CC2250/2277-MRSA-V WA MRSA-114 were identified for the first time in Kuwait hospitals.

### **Conclusions:**

The results demonstrated the diversity of MRSA strains circulating in Kuwait hospitals. The study also revealed the emergence of new MRSA strains including Livestock-associated MRSA (CC398). The emergence of new MRSA strains can impose different challenges for the physicians and infection control teams for treatment and control of MRSA infections in Kuwait hospitals.

*Key Words: MRSA; genotyping; spa typing ;*



## **Caspofungin-induced in-vitro post-antifungal effect and its impact on hemolysin production and adhesion related traits of oral *Candida dubliniensis* isolates**

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### **Introduction:**

Hemolysin production, and adhesion traits such as adhesion to buccal epithelial cells (BEC) and denture acrylic surfaces (DAS), germ tube (GT) formation and cell surface hydrophobicity (CSH) are all virulent attributes associated in pathogenicity of *Candida*. Post-antifungal effect (PAFE) also have an impact on pathogenicity and virulence of *Candida*. *Candida dubliniensis* is associated with both oral and systemic candidosis, which can be managed with caspofungin. There is no information on caspofungin-induced PAFE and its impact on hemolysin production and adhesion traits of *C. dubliniensis* isolates. Therefore, the reason of this study was to determine the in vitro PAFE on 20 *C. dubliniensis* isolates following brief exposure to caspofungin. Furthermore the impact of caspofungin-induced PAFE on hemolysin production and adhesion to BEC and DAS, GT formation and CSH of these isolates were also determined.

### **Methods:**

After establishing the minimum inhibitory concentration (MIC) of caspofungin, *C. dubliniensis* isolates were exposed to sub-lethal concentrations ( $\times 3$  MIC) of caspofungin for 1 hour. Thereafter the drug was removed by dilution and the PAFE, hemolysin production, adhesion to BEC and DAS, GT formation and CSH was determined by previously described in-vitro assays.

### **Results:**

MIC ( $\mu\text{g/ml}$ ) of *C. dubliniensis* isolates to caspofungin ranged from 0.004 to 0.19. Caspofungin-induced mean PAFE (hours) on *C. dubliniensis* isolates was 2.17. Brief exposure to caspofungin suppressed the ability of *C. dubliniensis* isolates to produce hemolysin, adhere to BEC, DAS, GT formation and CSH by a percentage reduction of 17.09%, 69.97%, 71.95%, 90.06% and 32.29% ( $p < 0.001$  for all), respectively.

### **Conclusions:**

Therefore, brief exposure of *C. dubliniensis* isolates to caspofungin would produce an antifungal effect not only by suppressing its growth but also by altering the hemolysin production and adhesion traits of this fungal pathogen. Work was supported by Kuwait University Research Grant Numbers: DB 01/14.

*Key Words: Candida dubliniensis; Caspofungin; Post-antifungal effect;*



## **Molecular Epidemiology and Characterization of Multiple-Drug Resistant (MDR) Clinical Isolates of *Acinetobacter baumannii***

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### **Introduction:**

*Acinetobacter baumannii* has emerged as a predominant cause of healthcare-associated infections world-wide. Risk factors for *A. baumannii* infections, especially in elderly individuals, include: patients having underlying diseases, immune suppression, burns, trauma, invasive medical procedures, mechanical ventilation, catheters, previous antibiotic treatments and extended hospital stay. Of great concern is the recent rise in the frequency of multiple drug resistant (MDR) and extremely drug resistant (XDR)- *A. baumannii* infections. We aimed to identify the genetic relatedness of multiple-drug resistance (MDR) in *Acinetobacter baumannii* clinical isolates recovered from a hospital in Los Angeles.

### **Methods:**

Twenty one MDR *A. baumannii* isolates were collected and their antibiotic susceptibility were determined according to the CLSI guidelines. Genes coding for antibiotic resistance were identified by PCR and their identities were confirmed by DNA sequencing. Clonal relationships were studied by pulsed-field gel electrophoresis (PFGE) and multi-locus sequence typing (MLST).

### **Results:**

MDR consistently correlated with the presence of oxacillinases, mostly in the form of plasmid-mediated OXA-23 enzyme which were detected in 12 (57.1%) isolates. GES-type carbapenemases were found in 20 (95.2%) strains, AAC in all 21 (100%) strains, PER in 7 (33.3%) strains and ISAbal1 has been detected in 16 (76.2%) isolates. The association between ISAbal1 and resistant genes confirms insertion elements as a source of  $\beta$ -lactamase production. Of the 21 clinical isolates, 5 were found to be related to sequence type-1 (ST1) and 16 to ST2 as analyzed by MLST. PFGE demonstrated that the majority of clinical isolates are highly related (>85%).

### **Conclusions:**

This study supports a more complete understanding of genotyping of antibiotic resistance for better assessment of MDR strains transmission.

Funding: KU and UCLA

*Key Words: Acinetobacter baumannii; MLST; MDR;*



## **Humoral immune responses in mice immunized with RD DNA vaccine constructs of pUMVC6 and pUMVC7**

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### **Introduction:**

The aim of this work was to study the antigen-specific antibody responses in mice immunized with recombinant DNA vaccine constructs of pUMVC6 and pUMVC7, containing RD1 and RD9 genes of *Mycobacterium tuberculosis*.

### **Methods:**

Mice were immunized with the parent and recombinant plasmids and sera were tested for antibodies against pure recombinant proteins of RD1 (PE35, PPE68, EsxA, EsxB) and RD9 (EsxV), peptide mixtures of each protein and their individual peptides using enzyme-linked immunosorbent assays. The optical density (OD) values were measured at 405 nm. E/C (OD in antigen-coated wells/OD in antigen uncoated wells) were calculated, and the values of E/C > 2 were considered positive.

### **Results:**

RD1 and RD9 antigen-specific antibodies were detected in sera of mice immunized with the recombinant DNA vaccine constructs (E/C > 2.0). With respect to peptide mixtures and single peptides, only PE35mix and P6 of PE35; PPE68mix and P19, P24 of PPE68 showed antibody reactivity with sera of mice immunized with the corresponding recombinant pUMVC6 and/or pUMVC7 DNA vaccine constructs.

### **Conclusions:**

The results confirm *in vivo* expression and immunogenicity of all the five RD1 and RD9 genes cloned in both of the DNA vaccine vectors.

Funding: Kuwait University Research Sector grants YM 01/03 and SRUL02/13

*Key Words:* *Mycobacterium tuberculosis*; Recombinant vaccine vectors; ELISA, Antigens,



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## **Prevalence of *Aspergillus* section *Nigri* species in Kuwait: molecular characterization and susceptibility to antifungal agents**

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### **Introduction:**

In Kuwait, little is known about the spectrum of species comprising *Aspergillus* section *Nigri* in clinical and environmental (Env) samples. This study reports relative prevalence of different *Aspergillus* section *Nigri* complex species and their susceptibility to antifungal

### **Methods:**

Fifty strains of black *Aspergilli* isolated from clinical (n=43) and Env (n=7) sources over a 28-month period were studied. They originated from sputum (n=12), ear swabs (n=11), nasal/sinus curettage (n=7), endotracheal secretions (n=6), bronchoalveolar lavage (n=4), other (n=3) and Env samples (n=7). The Env strains were obtained by exposing Sabouraud dextrose agar plates in indoor and outdoor air in different places. Based on morphological characteristics, the isolates were provisionally identified as members of *Aspergillus* section *Nigri* complex. Molecular identification was carried out by PCR sequencing of  $\beta$ -tubulin and calmodulin gene fragments and sequence comparisons with NCBI database. Antifungal susceptibility was determined against amphotericin B, voriconazole, posaconazole, caspofungin and micafungin by Etest.

### **Results:**

Based on  $\beta$ -tubulin and calmodulin gene sequences, 43 clinical *Aspergillus* section *Nigri* isolates were identified as *A. awamori* (n=17), *A. tubingensis* (n=16), *A. niger sensu stricto* (n=11), *A. welwitschiae* (n=5) and *A. acidus* (n=1). A noteworthy finding of the study was the isolation of *A. welwitschiae* and *A. acidus* from nasal specimens suggesting their possible role in sinus infections. Of 7 Env *Aspergillus* section *Nigri* isolates, *A. tubingensis* was predominant species (57%). All isolates appeared susceptible to antifungal agents tested.

### **Conclusions:**

This preliminary study reveals that phenotypically identified clinical *A. niger* isolates represent a complex of at least five species in Kuwait. A larger study is required to understand the clinical significance of these species as agents of disease in healthy and immunocompromised individuals.

*Key Words: Aspergillus section Nigri complex; Molecular characterization; Antifungal*



## **Epidemiology of Carbapenem-resistant Enterobacteriaceae among healthy adults in Kuwait.**

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### **Introduction:**

Carbapenem-resistant Enterobacteriaceae (CRE) is a serious threat that requires continuing public health monitoring. Unrecognized personnel colonized with CRE serve as a reservoir for transmission. The prevalence of CRE among food handlers (FH) in commercial eateries in community (CFH) and healthcare settings (HFH) has not been well researched. The objective of this study was to compare the prevalence of CRE carriage among CFH and HFH.

### **Methods:**

Active, laboratory- and population-based surveillance was conducted in 6 Governorate areas of Kuwait. CRE implied Enterobacteriaceae non-susceptible to  $\geq 1$ mg/L of carbapenem. Antimicrobial susceptibility testing was performed using E test.

### **Results:**

A total of 205 CFH and 200 HFH were investigated; they were mainly Indians (46.3%) and Filipinos (20.2%). Non-repetitive species of Enterobacteriaceae comprising 423 (62.3%) *E. coli*, 125 (18.4%) *K. pneumoniae*, 53 (7.8%) *E. cloacae* and 80 (11.8%) others were studied. CRE were detected among 3 (21.4%) *E. coli* isolates from CFH versus 11 (78.5%) from HFH; 1 (12.5%) *K. pneumoniae* from CFH versus 7 (87.5%) HFH and all *E. cloacae* from CFH. Multidrug-resistant (MDR) isolates were detected in 47 (37.7%) *E. coli* from CFH versus 79 (62.7%) from HFH; 3 (13.6%) *K. pneumoniae* CFH versus 19 (86.3%) HFH and 29 (54.7%) of *E. cloacae* (11 (37.9%) CFH versus 18 (62%) HFH). Overall, carriage of MDR and CRE were 42.2% and 8.9% of all isolates from CFH and HFH, respectively and 7.1% were simultaneously colonized by both CRE and MDR. About 70% of CRE colonizers were HFH and of these, 35% were in Hawali Governorate. Approximately 54% FH had history of travel abroad; 7.7% had history of previous antibiotic intake.

### **Conclusions:**

This study highlights a high prevalence of CRE and MDR organisms among the FHs in Kuwait. It is conceivable that these personnel may, in part, play an important role in the acquisition and spread of resistant strains in community and healthcare settings. Supported by Collage of Graduate Studies and Research Administration, Grant No. YM07/15, Kuwait University.

*Key Words: Food-handlers; CRE; faecal carriage;*



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## **Emergence of *Mycobacterium abscessus* as a major non-tuberculous mycobacterial pathogen in Kuwait**

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### **Introduction:**

Mycobacterial infections in Kuwait are mostly (>95%) caused by *M. tuberculosis* (MTB) presenting as pulmonary and extra-pulmonary manifestations of tuberculosis disease. However, many non-tuberculous mycobacteria (NTM) also cause pulmonary and other infections that mimic tuberculosis. Specific identification of NTM is of clinical relevance since treatment varies according to the species. This study was performed to determine species spectrum of NTM causing pulmonary and extra-pulmonary infections in Kuwait.

### **Methods:**

A total of 2166 mycobacterial isolates grown from pulmonary and extra-pulmonary specimens during January 1, 2014 to 30 September 2016 were tested. Isolates were subjected to smear microscopy for acid-fast bacilli (AFB) and identification by AccuProbe DNA probe assay and/or multiplex PCR assay targeting *oxyR-ahpC* intergenic region and *rpoB* gene. Species-specific identification of NTM was performed by INNO-LiPA Mycobacteria v2 assay and/or PCR sequencing of 16S-23S internal transcribed spacer (ITS) region by using pan-mycobacterial primers.

### **Results:**

Of 2166 AFB-positive cultures, 2096 isolates were identified as MTB while 70 isolates were identified as NTM by AccuProbe DNA probe and multiplex PCR assays. NTM isolates were grown from pulmonary (n=55) and extra-pulmonary (n=15) clinical specimens. Ten different NTM species were identified and included *M. abscessus* (n=34), *M. fortuitum* (n=13), *M. avium-intracellulare* complex (n=11), *M. lentiflavum* (n=3), *M. gordonae* (n=3), *M. kansasii* (n=2), *M. chelonae* (n=2), *Mycobacterium* species (n=2) and *M. kumamotoense* (n=1). One NTM isolate contained a mixed culture, *M. abscessus* and *M. fortuitum*. Interestingly, 31 of 34 *M. abscessus* isolates were grown from pulmonary specimens.

### **Conclusions:**

Several NTM species cause infections that mimic TB. Nearly 50% of all NTM infections in Kuwait since 2014 were caused by *M. abscessus*. *M. abscessus* infections have been steadily increasing over the years.

*Key Words: Non-tuberculous mycobacteria; Mycobacterium abscessus; AccuProbe*



## **The Value of a new molecular technique in early diagnosis of *Pneumocystis jirovecii* pneumonia in Kidney Transplant Patients in Kuwait.**

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### **Introduction:**

*Pneumocystis jirovecii* pneumonia (PJP) is a serious and common complication among kidney transplant patients. The delay in diagnosis and treatment is associated with high mortality. This prospective study was conducted to determine the value of a new molecular technique (Unyvero P55 Pneumonia, Curetis, Germany) in the early diagnosis of PJP in kidney transplant patients in Kuwait.

### **Methods:**

All kidney transplant patients diagnosed as community- or hospital-acquired pneumonia and admitted to the Kidney Transplant Center from January to September 2016 were included in the study. Respiratory samples ( Sputum, induced sputum endotracheal secretions and bronchialveolar lavage) were processed by Unyvero in the laboratory Department of Ibn Sina Hospital as per the instruction of the manufacturer. The samples were sent to the reference lab in the Faculty of Medicine for immunofluorescent (IF) technique).

### **Results:**

Out of 132 patients with pneumonia, 15 had positive PJ by Unyvero. Of those, only 3 patients had positive IF. Out of the 15 PJP patients, 5 expired. Of those 5, 2 had positive IF while the rest were positive only by Unyvero. Patients who survived despite positive PJ by Unyvero received full course of treatment for 21 days with double strength co-trimoxazole and discharged on the same drug for 3 months. There was no correlation between the number of copies of PJ by Unyvero and mortality. Following the cluster of cases of PJP in the Kidney Transplant Center, the nephrologists followed a new practice of prolongation of PJ prophylaxis to six months instead of 3 months. For known transplant patients above 6 months, co-trimoxazole is started immediately if rejection is expected with increase in immunosuppressive agents. After this new practice and since September, no new case of PJP was seen.

### **Conclusions:**

The introduction of Unyvero had helped in the early diagnosis, treatment and prevention of PJP in kidney transplant patients in Kuwait.

*Key Words: Pneumocystis jirovecii; kidney transplant patients; Unyvero P55*



## **Audit of Turnaround Time of Positive Blood Cultures in Mubarak AL-Kabeer Hospital**

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### **Introduction:**

It is prudent that Health Care Facilities should deliver the most effective services at the fastest time in order to reduce morbidity and mortality among those seeking treatment in health care settings. The best way of achieving this is by the cooperation of all involved parties in any hospital, including the laboratory department. Turnaround time (TAT) of specimens, from collection to results, is one of the key indicators of laboratory performance and should be audited from time to time. Early diagnosis and detection of bacteremia are of paramount importance in the subsequent treatment and prognosis of this life-threatening infection. Therefore, the objectives of this study are to: 1) assess TAT for positive blood cultures in Mubarak AL-Kabeer hospital and 2) suggest measures to improve TAT of positive blood culture results.

### **Methods:**

Prospective data collection of 100 positive blood culture samples was collated for a period of one month, June to July 2016. TAT of positive blood culture samples, which is the time required from the blood specimen collection to releasing the final report of identification and sensitivity, was determined.

### **Results:**

In the pre-analytical stage, 96% of the samples met the timing in the standards, which is  $\leq 4$  hours. A large percentage (72%) of samples took less than 3 days in the analytical stage. In the post-analytical stage, 73% of cases were reported initially after the Gram stain results within 2 hours of time as in the standards. In 97% of cases, the final report was released within five days as in the standards. Only 3% of reports exceeded the time period because of extended incubation required.

### **Conclusions:**

TAT of positive blood culture reports met the standards of  $\leq 5$  days in majority of cases. Some ways, such as rapid collection, improved internal and external transport arrangements and reporting preliminary positive results through the hospital information system (HIS) are suggested to improve TAT.

*Key Words: Turn-around-time; Blood culture; Mubarak Hospital;*



## **Evaluation of ERIC-PCR, 16S rDNA sequencing and whole genome sequencing for identification and/or typing of *Acinetobacter baumannii* strains isolated in Al-Sabah hospital, Kuwait**

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### **Introduction:**

Introduction: *Acinetobacter baumannii* is an opportunistic multi-drug-resistant bacterial pathogen, and a leading cause of nosocomial infections all over the world. The phenotypic methods for identification and typing of *A. baumannii* are non-specific and non-discriminatory. In the past, various molecular methods have been proposed to identify and/or type the strains of *A. baumannii*. The aim of this study was to test three molecular methods, i.e. the enterobacterial repetitive intergenic consensus (ERIC)-PCR, 16S rDNA sequencing and whole genome sequencing, for identification and/or typing of *A. baumannii* strains isolated in Al-Sabah hospital, Kuwait.

### **Methods:**

Twenty four phenotypically identified clinical strains of *A. baumannii*, isolated at Al-Sabah Hospital in Kuwait, were used in this study. The genomic DNA were isolated from the bacterial cultures using Qiagen kits. The isolated DNA were quantified by Qubit fluorometry. The DNA samples were used for (ERIC)-PCR, 16S rDNA sequencing, and whole genome sequencing using standard methods. The band profiles (in case of ERIC-PCR) and the DNA sequence data (in case of 16S rDNA and whole genome sequencing) were analysed by BioNumerics software for species identification and genotyping analysis.

### **Results:**

All of the 24 isolates were identified as *A. baumannii* by 16S rDNA and whole genome sequencing. The ERIC-PCR divided the 24 *A. baumannii* isolates into six groups with 1 to 7 isolates in each group. The 16S rDNA sequencing divided the isolates into two groups with 10 and 14 isolates in each group. The whole genome sequence single nucleotide polymorphism (SNP) analysis divided the isolates into three groups with 3, 5 and 16 isolates in each group.

### **Conclusions:**

The molecular methods used in this study confirm the identity of the isolates as *A. baumannii* and suggest genetic heterogeneity among them, with the ERIC-PCR showing maximum groups/genotypes.

Funding: The College of Graduate Studies and Research Sector grant SRUL02

*Key Words: Acinetobacter baumannii; Molecular methods; Typing;*



## **Molecular screening is superior to phenotypic drug susceptibility testing of multidrug-resistant *Mycobacterium tuberculosis* isolates to ethambutol**

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### **Introduction:**

With increasing incidence of multidrug-resistant tuberculosis (MDR-TB), accurate drug susceptibility testing (DST) of *Mycobacterium tuberculosis* (MTB) to other first-line drugs is crucial for proper patient management. Radiometric BACTEC 460TB (460TB) for DST of *M. tuberculosis* was replaced by automated *Mycobacterium* Growth Indicator Tube 960 system (MGIT) in 2011 in Kuwait. Performance of 460TB and MGIT for DST of MDR-TB isolates was compared with sequencing of *embB*, *rpsL* and *rrs* genes for detecting resistance to ethambutol (EMB) and streptomycin (STR).

### **Methods:**

MDR-TB strains collected during 2006-2010 (n=39) and 2011-2015 (n=41) and 50 pan-susceptible MTB isolates were used. All isolates were identified as MTB by AccuProbe DNA probe and multiplex PCR assays. Phenotypic DST was performed by 460TB or by MGIT by using SIRE drug kit. Most common EMB and STR resistance-conferring mutations in *embB* and *rpsL* + *rrs* genes, respectively, were detected by PCR sequencing.

### **Results:**

Among 39 MDR-TB strains by 460TB, 22 of 25 EMB-resistant but also 6 of 14 EMB-susceptible strains contained a mutated *embB* gene ( $\kappa=0.47$ , moderate agreement) while 17 of 23 STR-resistant but 0 of 16 STR-susceptible strains contained a mutated *rpsL* and/or *rrs* gene ( $\kappa=0.7$ , good agreement). Among 41 MDR-TB strains by MGIT, 10 of 11 EMB-resistant but also 25 of 30 EMB-susceptible strains contained a mutated *embB* gene ( $\kappa=0.1$ , poor agreement) while 22 of 29 STR-resistant but 0 of 12 STR-susceptible strains contained a mutated *rpsL* and/or *rrs* gene ( $\kappa=0.65$ , good agreement). No mutations were detected in pan-susceptible isolates.

### **Conclusions:**

While MGIT is an acceptable alternative for 460TB for STR, it performed poorly for EMB as many MTB strains with *embB* mutations, which confer low but clinically significant resistance to EMB, were detected as EMB-susceptible. Our data show that molecular screening is superior to MGIT when accurate ethambutol susceptibility results are needed.  
Funding: research sector YM08/14

*Key Words: Mycobacterium tuberculosis; Drug susceptibility testing; Molecular testing;*



## **Invasive group B Streptococcus in Kuwait 2004-2014: serotype distribution and antimicrobial susceptibility profile**

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### **Introduction:**

Group B streptococcus (GBS) is a known etiology of neonatal and postpartum infection. Recently is considered to be an emerging pathogen in adult patients causes severe invasive infections. This study determined the serotype distribution and antimicrobial susceptibility of Invasive GBS isolated over 11 years from neonates and adult patients in Kuwait.

### **Methods:**

From 2004-to-2014,111 isolates studied. The identification was confirmed by streptococcal serogrouping kit. Phenotypic typing and susceptibility tests were done.

### **Results:**

Among 111 isolate,103 were from blood ( 79 neonates & 24 adults) and 8 were CSF. Six serotypes were identified, III 32 (28.8%) was the most prevalent, followed by V 23 (20.7%), Ia & II 17 each (15.3%), Ib 9 (8.1%), IV 8 (7.2%) and VII 1 (0.9%). The serotypes dominance were variable in 2011-2014 serotype Ib was the dominant 18.4% followed by Ia, II, III and V each 15.8%. All isolates were sensitive to penicillin, while 94.6% and 95.5% were resistant to gentamicin and tetracycline respectively. The overall resistance rate to erythromycin was 31.5%, however, it was 13.2% in 2004-2006, 25.7% in 2007-2010, and 55.3% in 2011-2014. Clindamycin resistance rates were 5.3% in 2004-2006, 5.7% in 2011-2014 and 23.7% in 2011-2014 with 11.7% overall rate. A high level erythromycin and clindamycin- resistant strains with MIC > 256 µg/ml were (0% & 50%) in 2004-2006, (11.1% & 50%) in 2007-2010 and (28.6% & 66.7%) in 2010-2014 respectively. Resistance to either erythromycin and/or clindamycin was (50%) among serotype IV, (43.8%, 33.3%, 30%,23.5% & 17%) among serotype III, Ib, V, II & Ia respectively.

### **Conclusions:**

This study in Kuwait, identified the change in the dominance of serotypes associated with invasive infections over the with notable decrease in serotype III & V and increase in Ib. There were significant increase in resistance to erythromycin and clindamycin. Resistant serotypes were different than what was reported.

*Key Words: Group B Streptococcus; Invasive infections; Kuwait;*



*Microbiology and Immunology*

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## **Nucleotide sequence comparison of repA gene of *Helicobacter pylori* cryptic plasmid pHPM179**

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### **Introduction:**

In this study we aimed at comparing a DNA sequence for a cryptic plasmid pHPM179 RepA gene encoding plasmid replication protein.

### **Methods:**

The sequence was retrieved from submitted sequences to Gen bank and was analyzed using DNAsis and DNA inspector Ii computer programs, as well as BLASTP and BLSTN programs provided by NIH. A minimum-length similarity tree was constructed on the basis of the Rep gene variable positions by using algorithm by PhyloBlast.

### **Results:**

The screening of data bases revealed the presence of proteins with homology to RepA in other species of bacteria. In pHPM179 the sequence showed strong amino-acid sequence identity to a putative ORF1 protein of a cryptic pHP180 plasmid, and significant homologies to putative Rep proteins found in twenty one other plasmids isolated from various organisms, including of *Helicobacter pylori*, *Campylobacter*, *Pediococcus*, *Pseudomonas*, *Lactococcus*, *Neisseria* and *Kelbsiella*. Upstream of RepA, a 22-bp sequence was recognized which was tandemly repeated four times, a feature typical for many replication origins (ori) and commonly termed a DNA iteron. Comparison of iterons from five different plasmids of five different strains of *Helicobacter pylori* (pHPM179, pHPM8, pHeL1, pHPM180 and pHPS1) revealed conserved region between all the five plasmids iterons compared. The plasmid repA DNA sequences from various bacterial species were aligned using PhyloBlast and a dendrogram was generated. Alignment of the Rep genes of the twenty three Rep genes revealed 83-91% identity. The main differences in these sequences were clustered into four closely related clusters.

### **Conclusions:**

Organisms that are phylogenetically close have a higher degree of DNA sequence similarity than organisms that are phylogenetically distant. Our comparative sequence analyses for *H. pylori* RepA gene sequence using available databases revealed a high degree of identity suggesting a possibility for a common origin.

*Key Words: Helicobacter; Plasmid; RepA;*



## **Multiple epitopes are recognized by antigen-specific antibodies raised in rabbits against synthetic peptides of Mycobacterium tuberculosis complex specific proteins Rv2346 and Rv3619**

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### **Introduction:**

Antibodies are required to characterize proteins and determine the specificity viz-a-viz cross-reactivity of the epitopes and antigens recognized. The antibodies are normally raised in animals using full-length proteins that are purified using biochemical or recombinant DNA techniques. However, these technologies are quite costly and cumbersome. An alternative approach could be the use of synthetic peptides that are relatively inexpensive and easy to produce. In this study, synthetic peptides corresponding to the sequences of two Mycobacterium tuberculosis complex-specific proteins were used to generate antigen-specific polyclonal antibodies in rabbits.

### **Methods:**

Peptides (30-mer, 50-mer and 100-mer), corresponding to the sequences of M. tuberculosis complex-specific proteins Rv2346 and Rv3619, were synthesized using SymphonyX Peptide Synthesizer. All experiments with animals were performed in accordance with the institutional guidelines. For generation of antibodies, specific pathogen-free New Zealand white rabbits were immunized intramuscularly with the mixture of peptides (1 mg/ml) emulsified with an equal volume of incomplete Freund's adjuvant. The rabbits were boosted twice at two weeks intervals with the same concentration of peptides. The animals were bled from the ear vein before each immunization and two weeks after the last immunization. The antibody titers were determined by ELISA using standard procedures.

### **Results:**

Sera from pre-immunized rabbits did not have antibodies reactive to the peptides of Rv2346 and Rv3619; whereas sera from immunized rabbits had antibodies reactive with the peptide mixtures and the full-length recombinant proteins. Testing of sera with individual peptides showed that multiple epitopes of both the proteins were recognized by antibodies.

### **Conclusions:**

The synthetic peptides of Rv2346 and Rv3619 are immunogenic in rabbits. Furthermore, these proteins have multiple epitopes recognized by antibodies. Kuwait University grant SRUL02/13.

*Key Words: M. tuberculosis; Rv2346, Rv3619, Synthetic peptides; Anti-peptide*



## **Expansion of Methicillin-Resistant *Staphylococcus aureus* belonging to Clonal Complex 5 in Kuwait hospitals**

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### **Introduction:**

Methicillin-resistant *Staphylococcus aureus* (MRSA) belonging to clonal complex 5 (CC5) are widespread globally. The prevalence of CC5-MRSA obtained in Kuwait hospitals increased from 6.5% in 2010 to 8.8% in 2016. This study characterized CC5-MRSA obtained in Kuwait hospitals for their clonal distribution and antibiotic resistance.

### **Methods:**

MRSA strains obtained from different clinical samples from February to July, 2016 were investigated using antibiogram, SCCmec typing, spa typing, and DNA microarray.

### **Results:**

Of 1060 MRSA isolates, 94 (8.8%) belonged to CC5. The isolates carried SCCmec types V (40.4%), IV (36.1%), VI (22.3%) and II (1.0%) and were classified into 10 clones consisting of CC5-MRSA-V-SCCfus (27.6%), CC5-MRSA-VI-SCCfus (23.4%), CC5-MRSA-IV-[PVL+] (18.0%), CC5-MRSA-V-[sed/j/r+] (8.5%), CC5-MRSA-IV-[PVL+/EdinA+] (6.3%), CC5-MRSA-IV-[Paediatric clone] (6.3%), CC5-MRSA-IV-SCCfus-[Maltese clone] (4.2%), CC5-MRSA-V (3.2%), CC5-MRSA-V-[sec/d/j/l/r+] (1.0%) and ST5/ST225-MRSA-II-[Rhine-Hesse EMRSA] (1.0%) with CC5-MRSA-IV-[PVL+], CC5-MRSA-VI-SCCfus, CC5-MRSA-V-SCCfus and CC5-MRSA-V-[sed/j/r+] isolated for the first time in Kuwait. The isolates were susceptible to vancomycin (MIC: 0.5- 2 µg/ml), linezolid, rifampicin, but were resistant to trimethoprim (58.5%), fusidic acid (57.4%), erythromycin and clindamycin (47.9%), ciprofloxacin (34.0%), chloramphenicol (29.8%), tetracycline (28.7%), gentamicin (7.4%), kanamycin (7.4%) and high-level mupirocin (2.1%). Strains belonging to CC5-MRSA-V-SCCfus, and CC5-MRSA-VI-SCCfus expressed multi-antibiotic resistance.

### **Conclusions:**

The results demonstrated the expansion and diversity of CC5-MRSA strains in Kuwait hospitals. While most strains were susceptible to majority of the antibiotics, some strains expressed multi resistance supporting the need for regular surveillance to detect changes in the composition and resistance patterns of MRSA strains.

*Key Words: MRSA; Molecular typing; Antibiotic resistance;*



**Neurology**

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## **Prevalence of Primary Headache Disorders in Kuwait- Hospital based study.**

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### **Introduction:**

Data on the prevalence of primary headaches in Kuwait is scarce. Aim: To determine the prevalence of primary headaches at a tertiary center in Kuwait.

### **Methods:**

A cross-sectional hospital-based study was conducted between 1st. January 2015 up to 31st. December 2015 to assess patients aged 12-65 years who were referred to neurology tertiary hospital. The International Classification of Headache Disorders, 3rd edition-beta, was used to determine the types of headache. Patients with secondary headache were

### **Results:**

A total of 27825 patients were referred to the tertiary hospital; in 2015; of whom 3215 were diagnosed as primary headache disorder. Primary headache prevalence was 11.55% with female predominance 71.7%. Prevalence of primary headache in males was 7.38% versus 14.88% in females ( $P < 0.0001$ ). Mean age was  $39.28 \pm 11.54$  years. Most of them 37.7% in the age group 31-40 years. Episodic migraine was the most prevalent at 46.6% followed by tension-type headache (24.7%), chronic migraine (14.5%), cluster headache (7.4%), medication overuse headache (6.1%) and paroxysmal hemicranias (0.7%). Mean time for referral was  $4.25 \pm 2.85$  years from headache onset, which was significantly longer among patients diagnosed with medication overuse headache ( $9.37 \pm 9.77$ ) and chronic migraine ( $8.45 \pm 2.10$ ) versus episodic migraine ( $3.41 \pm 1.75$ ); ( $P < 0.0001$ ). Most patients were managed by either general practitioners (52.2%) or ENT specialists (30.5%) prior to their referral.

### **Conclusions:**

Primary headache prevalence in Kuwait is comparable to international figures. Improving the awareness of the general practitioners and other specialists may reduce the chronicity of headache.

*Key Words: Primary Headache; Prevalence; Hospital-based ;*



**Neurology**

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## **Characters of Migraine and its treatment options in Kuwait- Hospital based study**

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### **Introduction:**

**Background:** Epidemiological studies of migraine in Kuwait are scarce. Aim: To assess the clinical characteristics and management of migraine in Kuwait.

### **Methods:**

A cross-sectional hospital-based study was conducted between 1st. January 2015 up to 31st. December 2015 to assess patients aged 12-65 years who were referred to the neurology tertiary hospital. The International Classification of Headache Disorders, 3rd edition-beta, was used to diagnose headaches.

### **Results:**

A total of 3215 patients were diagnosed as primary headache while 2063 (64.17%) patients were diagnosed as migraine. Mean age of migraine patients was  $41.32 \pm 11.92$  years with female predominance (75.9%). Migraine without aura represented 60.4%, followed with chronic migraine 22.5%, migraine with aura 12.2% and medication over use headache 4.7%. Topiramate was the most common used drug for episodic migraine (54.2%) while boutilinium toxin A was commonly used for medication overuse headaches (53.6%) and chronic migraine (28.7%). With respect to abortive medication, triptans were the most regularly prescribed medications (50.7%). The longer the time to seek neurologist opinion, the more liable the patient was to have transformed into chronic migraine and medication overuse headache (chronic migraine  $8.46 \pm 2.10$ ; medication over used headache  $9.37 \pm 0.77$  versus  $3.41 \pm 1.75$  in episodic migraine,  $p < 0.0001$ )

### **Conclusions:**

Migraine is the most frequent primary headache disorder in our cohort. Topiramate and Boutilinium toxin A were the most common used prophylactic drugs while triptans were commonly used as abortive medications. Delay in referring patients to neurology services results in transformation into chronic migraine and medication overuse headache.

*Key Words: Migraine,; Epidemiology; Treatment;*



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**Prevalence of primary headache disorders in Kuwait: A national study.**

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**Introduction:**

**Background:** The data on the prevalence of primary headache disorders in the Middle East is scarce.

Objectives: To determine the prevalence of primary headaches in Kuwait.

**Methods:**

A cross-sectional community based study was conducted from 1st January up to 30th April 2016 which included adults aged 18-65 years. Using systematic random sampling, data was collected by the Headache-Attributed Restriction, Disability, Social Handicap and Impaired Participation (HARDSHIP) questionnaire. Responses to the diagnostic questions are transformed into diagnoses algorithmically by the investigators to confirm the diagnosis of primary headache and to rule out secondary headache disorders according to ICHD-III- beta criteria. A comparison of variables between subgroups was performed using the chi-square ( $\chi^2$ ) test for non-numeric variables. A  $P < 0.05$  will be regarded as significant.

**Results:**

A total of 15523 patients were identified; of whom 9527 (61%) were diagnosed as primary headache disorder with female predominance (62.2%). Mean age of the cohort was  $34.86 \pm 10.23$  years. The majority (73.6%) was younger than 40 years compared to 26.4% in older 40 years ( $p < 0.006$ ). Tension-type headache was the most prevalent (29.8%) followed by episodic migraine (23.2%), chronic migraine (5.4%), and medication overuse headache (2.4%) in the studied cohort.

**Conclusions:**

The prevalence of primary headache in Kuwait is comparable to international figures. It is more frequent in females and young adults.

Funding: Research sector, Postgraduate, Faculty of medicine- Kuwait University; Grant number:MM02/15

*Key Words: Primary headache; Prevalence; Kuwait;*



Neurology

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## Assessment of Lymphopenia in Patients with Multiple Sclerosis Treated with Dimethyl Fumarate in a real clinical setting

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### Introduction:

Dimethyl fumarate (DMF), a disease-modifying therapy for multiple sclerosis (MS), causes lymphopenia in a fraction of patients. The clinical significance of this is unknown. Since lymphocytes contribute to MS pathology, lymphopenia may be a biomarker for response to the drug or serious adverse events.

**OBJECTIVE:** To evaluate absolute lymphocyte counts (ALCs) in MS patients treated with DMF in a real clinical setting.

### Methods:

Using the national MS registry, a retrospective study was conducted to identify MS patients who received DMF. Patients included in the analyses received at least 3 months prescription and had ALC values available at baseline (within 6 months prior to DMF initiation) and at one or more times during DMF treatment 3 months post-initiation. Grades of lymphopenia were assigned according to the common terminology criteria for adverse events: grade 1=ALC of 800 to the lower limit of normal, grade 2 = ALC 500–799, and 3=ALC <500.

### Results:

A total of 54 patients met the inclusion criteria; of whom 66.7% were female. Mean age and mean disease duration were 32.3±11.4 and 6.9±6.8 years respectively. Most patients (n=40; 74.1%) received prior DMTs. The mean ALCs decreased from 2190 to 1510 cells/uL (31% decrease) over a mean duration 11.7±5.86 months. Among patients who had at least 2 follow-up ALCs, lymphopenia was seen in 12 (22%) patients; of whom 2 (3.7%) patients had grade 3 lymphopenia necessitating interruption or discontinuation of DMF.

### Conclusions:

ALC profiles in DMF-treated patients were generally stable throughout the observational period. The proportion of patients, who developed severe lymphopenia, was similar to figures in clinical trials. Further studies are needed to assess the time of ALC recovery in severely lymphopenic patients.

*Key Words: Multiple sclerosis; Dimethyl Fumarate; Lymphopenia;*



**Neurology**

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**Effectiveness and Safety of dimethyl fumarate treatment in Multiple Sclerosis Patients in clinical practice.**

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**Introduction:**

Dimethyl Fumarate has been recently approved as a disease modifying therapy for the treatment of Multiple Sclerosis. Objectives: to evaluate effectiveness and safety of Dimethyl Fumarate in a cohort of relapsing Multiple Sclerosis patients in a real clinical practice

**Methods:**

Using the national Multiple Sclerosis registry, we retrospectively identified patients who had been prescribed Dimethyl Fumarate. Data of relapsing Multiple Sclerosis patients with EDSS less or equal 6 and at least 6 months follow up were analyzed. Patients with progressive Multiple Sclerosis were excluded. Primary outcome measure was the proportion of relapse free patients at last follow up. Secondary endpoints included mean change in EDSS at last follow up and proportion of MRI activity at 6 months.

**Results:**

109 patients were eligible and included in the analysis. Women represented 59.7% of the studied cohort. Mean age and mean disease duration were 33.5 years and 8.3 years respectively. 75.6% of the patients received prior disease modifying therapies. Mean duration of Dimethyl Fumarate exposure was 12.4 months. The proportion of relapse free patients increased significantly from 51% to 92% ( $P < 0.0001$ ) while the mean EDSS score decreased from 2.8 at baseline to 2.1 at last follow up visit. Among the 90 patients who had MRI follow-up after 6 months 14% of patients were free of MRI activity compared to 61% at baseline ( $p < 0.0001$ ). Although no serious adverse events were reported 13% of patients discontinued Dimethyl Fumarate. The most common adverse events leading to discontinuation were gastrointestinal upset, lymphopenia and convenience.

**Conclusions:**

In clinical practice Dimethyl Fumarate appeared to effective in reducing disease activity and progression of disability over the observational period. Dimethyl Fumarate was well tolerated with no serious adverse events. Our results are in parallel with what was seen in pivotal clinical trials.

*Key Words: Multiple Sclerosis; Dimethyl fumarate; Efficacy;*



## Role of dBcAMP in survival of neurons in brain injury models- possible mechanism

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### Introduction:

Astrocytes proliferate and accumulate at the margin of the brain injury forming glial scar or astrogliosis. It has been suggested that the glial scar can be beneficial in isolating the damaged region and limiting tissue degeneration. The synthesis of growth factors, cytokines by reactive astrocytes suggest that the astrocytic reaction may play an important role in neuronal regeneration. Dibutyl cyclic adenosine monophosphate (dBcAMP), a cell-permeable synthetic analog of cAMP is known to induce astrogliosis in astroglial culture. However, the exact mechanism underlying how dBcAMP exerts its function in situ is not clear. Objectives: To examine the effects of astrogliosis, induced by dBcAMP, on the survival of cortical and hippocampal neurons in two models of brain injuries (stab wound and kainic acid models).

### Methods:

Stab wound was done on the cerebral cortex of BALB/c mice. Animals were divided into Group A: was treated with dBcAMP for 3,5 and 7 days. Group B was treated with PBS. In kainic acid experiment animals were divided into 1) Sham control (SC), injected with PBS, 2) SC, injected with dBcAMP 3) lesion with kainic acid (KA) injected with PBS 4) Lesion with KA injected with dBcAMP for 3,5 and 7 days. The brains were processed for cresyl violet and Flurojade-B staining to assess the degenerating neurons, GFAP immunostaining to assess the astrogliosis and Iba-1 to assess the microglial response.

### Results:

There was a gradual increase in the number of both astrocytes and microglia in both types of injury with a significant increase in dBcAMP-treated groups. The number of degenerating neurons significantly decreased in dBcAMP-treated groups. In addition, it was found that dBcAMP stimulated the expression of GFAP and brain derived neurotrophic factor (BDNF).

### Conclusions:

dBcAMP induces astrogliosis and protects the neurons in both types of injury by increasing the expression of BDNF. Hence dBcAMP may be used as therapeutic agent in cases of brain injuries.

Funding: Kuwait University grant # MA01/14 and OMICS # SRUL02/13

*Key Words: Astrocytes; Microglia, neurons; dBcAMP, kainic acid ;*



## **Septal/Lateral Wall Ratios in <sup>99m</sup>Tc-Myoview Myocardial Perfusion Scintigraphy: Can It Differentiate Between Hypertensive and Normotensive Patients?**

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### **Introduction:**

The high septal /lateral wall ratio in hypertensive patients referred for myocardial perfusion imaging (MPI) has been previously reported with thallium scintigraphy. Preliminary data assessing this phenomenon with <sup>99m</sup>Tc-Myoview was published. We aimed to assess the value of septal/lateral wall ratios in <sup>99m</sup>Tc-Myoview MPI in differentiating hypertensive from normotensive patients referred for MPI.

### **Methods:**

The study included 102 patients referred for MPI with typical or atypical ischemic heart disease. They were 65 hypertensive patients and 37 normotensive patients. All patients underwent two-day <sup>99m</sup>Tc-Myoview SPECT MPI protocol according department protocol.

The S/L ratio was visually and quantitatively assessed both in rest and stress. Then the results were compared to the patients' clinical data.

### **Results:**

S/L ratio for hypertensive patients during stress was  $1.03 \pm 0.11$ , while it was  $0.98 \pm 0.88$  for normotensives. These ratios were  $1.00 \pm 0.11$  and  $0.97 \pm 0.07$  in rest, respectively. A statistically significant difference was found between stress S/L ratio in all patients group (P value of 0.01). For females there was a significant difference between their stress S/L ratio with P value of 0.02.

For male there was no significant difference between their stress S/L ratio (P value of 0.25). No significant difference was noted in the rest S/L ratio in all patients, females only and males only groups with P value of 0.06, 0.32 and 0.09; respectively. Visual scores were not statistically significantly different between hypertensives and normotensives.

### **Conclusions:**

Stress S/L ratio can differentiate hypertensive from normotensive patients undergoing myocardial perfusion scintigraphy using <sup>99m</sup>Tc-Myoview. However, our study is limited by small number of patients and further studies on a large number of patients is recommended.

*Key Words: Ischemia; Hypertension; Scintigraphy;*



## **Scintigraphic patterns in patients with urinary stones using Tc-99m MAG3 dynamic renal imaging and specialized computer**

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### **Introduction:**

Urinary stones are common in Kuwait and Arabian Gulf region with associated complications of loss of renal function and urinary obstruction. Tc-99m MAG-3 dynamic renal studies (DRS) have been used for evaluation of renal function and to assess urinary drainage and outflow obstruction by diuretic intervention. The objective was to use Tc-99m MAG-3 DRS in patients with urinary stones and to apply specialized software for processing, namely Normalized Residual activity (NORA) and Outflow Efficiency (OE), to provide quantitation of renal output.

### **Methods:**

Archived Tc-99m MAG-3 DRS for 50 patients with stones were retrieved and reprocessed. Findings on renal perfusion, function and drainage both without and with Lasix were recorded and cross-tabulated with presence of ipsilateral stones. Also, the data from the NORA and OE software were recorded and compared to more conventionally derived parameters: visual diuretic effect and half-time after Lasix.

### **Results:**

Stones were significantly associated with reduced perfusion in 38% of kidneys and function in up to 60%. Also, association with dilated pelvicalyceal systems (PCS) (66%) and abnormal spontaneous drainage in 43% was found. The diuretic response was abnormal in 40% and half-time after Lasix in 36%. The 20-min and Lasix end NORA were 29 & 50% abnormal, respectively. While OE at 20 min and Lasix end were abnormal in 8% & 2% respectively.

### **Conclusions:**

the findings of Tc-99m MAG-3 DRS provided a multifaceted evaluation of the renal physiology that was most relevant to presence of urinary stones and their complications. The application of the specialized software held some promise for improving the overall performance of the procedure in this condition. Funding: College of Graduate Studies-Kuwait University

*Key Words: urinary stones; Tc-99m MAG3 dynamic renal studies; urinary obstruction;*



## **Differential regional myocardial perfusion calculation (DRMP) for enhanced ischemia detection in Tc-99m tetrofosmin cardiac SPECT**

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### **Introduction:**

DRMP, defined as the ratio of difference of uptake (counts) of Tc-99m tetrofosmin in adjacent pre-specified pairs of coronary artery territories in myocardial SPECT polar plot to total uptake in that region pair. It is tested for its ability to improve detection of ischemia, assuming blood flow diversion from stenosed to normal branches or sub-branches of the coronary arteries. The higher the ratio, the more likely the presence of ischemia.

### **Methods:**

50 Tc-99m tetrofosmin Stress-Rest myocardial perfusion studies had polar plots with 3 segments for left anterior descending (LAD), circumflex (LCx) and right coronary artery (RCA) territories and 6 subsegments for antero-septal (AS) and anterior (Ant) branches of the LAD and anterolateral (AL) and inferolateral (IL) branches of the LCx and inferior (I) and inferoseptal (IS) branches of the RCA. The DRMP was calculated for adjacent region pairs (total of 4: LAD-LCx, Ant-AS, AL-IL, I-IS). DRMP values were graded as 0 for less than 25% percentile, 1 for 25-50% percentile, 2 for 50-75% percentile and 3 for more than 75% percentile and were cross-tabulated with visual interpretation (Normal, Ischemia or Scar)

### **Results:**

The M:F ratio was 64%:32%, and average age was 57.3 yr. There were 26 (52%) normal, 21 (42%) ischemia, and 3 (6%) scar/fixed defect by visual interpretation. DRMP values (0-3 scores) for the Rest in the 4 region pairs had nearly equal distribution between Normal and Ischemia cases (p: 0.605, 0.480, 0.278, 0.263). For the Stress, however, DRMP values tended to be toward 3 score in Ischemia cases and 0 score in Normal (p: 0.203, 0.366, 0.538, 0.027). DRMP for Stress-Rest difference showed a similar pattern to the Stress DRMP but there were more high scores 2&3 in Ischemia and low scores 0&1 in Normal (p: 0.430, 0.123, 0.144, 0.273).

### **Conclusions:**

DRMP is a semi-quantitative method that could show ischemia tendency in myocardial perfusion studies and could serve as an adjunct for its diagnosis. Funding: College of Graduate Studies-Kuwait University

*Key Words: myocardial perfusion imaging; ischemia; coronary artery disease;*



## **Effectiveness of CT-based morphometric study of cervical spine in the Arab population as prerequisite to transpedicular screw**

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### **Introduction:**

Transpedicular screw fixation of the cervical spine is a recognized method of obtaining biomechanical stability. The screw fixation is based on the principle that allows at least 0.5 mm bony bridge on either sides of the screw nail in order to avoid pedicle violation which can result in neurovascular complications. The standard 3.5-mm screw in the pedicle therefore requires a minimum pedicle diameter of 4.5 mm. We aim to obtain CT based morphometric measurements of the cervical spine to evaluate the feasibility of this technique in Arab people since no data are available about this population.

### **Methods:**

This cross-sectional study involved a retrospective review of computed tomography scans of normal cervical spines of 99 Arab adults. Ten morphometric measurements were obtained. Data were analyzed using a p value of  $\leq 0.05$  as the cut-off level of statistical significance.

### **Results:**

Our sample included 63 (63.6 %) males and 36 (36.4 %) females, with a mean age of  $35.5 \pm 16.5$  years. The morphometric parameters of C3–C7 spine pedicles were larger in males than in females. The outer pedicle width (OPW) was  $< 4.5$  mm in  $> 25$  % of all subjects at C3–C6 vertebrae. Statistically significant differences in the OPW between males and females were noted at C3 ( $p = 0.032$ ) and C6 ( $p = 0.004$ ).

### **Conclusions:**

Inserting pedicle screws in the subaxial cervical spine is feasible among the majority of Arab people  
Funding: Kuwait university grant no MX 01/14

*Key Words: CT; Transpedicular fixation; cervical spine;*



## **Are High Body Mass Index and Smoking Risk Factors for H. Pylori Infection?**

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### **Introduction:**

Helicobacter pylori (HP) known to be a highly prevalent disorder in the world, specifically in the developing countries. A gap in identifying the source and the risk factors for HP infection disease is existing. Accordingly, identifying those who are at high risk of having HP infection is a critical step for fighting the wide spreading of HP and its complications.

### **Methods:**

We applied 14 C-urea breath test to correlate the positive infections of HP with smoking and body mass index (BMI). A total of 211 patients participated in this cohort study in Al Ahmadi city; 52 males and 102 females, aged from 18 to 65 years and 21 males and 36 females, from 7 to 17 years. WHO criteria is used to classify BMI in adults. Statistical analysis involved descriptive statistics and chi-square test.

### **Results:**

The prevalence of those subjects of positive HP was 101/ 154 (65.6 %) in adults and 36/ 57 (63.1%) in an age  $\leq 18$ . The correlation of adults positive infection with high BMI  $\geq 25$ kg/m<sup>2</sup> was found in 79/101 (78.2%) and with normal BMI  $\leq 25$ kg/m<sup>2</sup> found in 22/101 (21.7%). The correlation of smoking with the positive infection was found 34.8 % in the smoker, 24.6 % negative smoker and 40.5% non-smoker. A negative infection correlation in smoker is 23.6 %, negative-smoker 26.3% and non-smoker 50%.

### **Conclusions:**

The preliminary conclusion discerns from this ongoing project across Al Ahmadi city found high prevalence of positive infection, a strong association of positive infection with high BMI and insignificant association with smoking. The study proposes that high BMI could be a risk factor contributing to the infection of HP. A larger sample size is needed to estimate the effect of HP in relation to obesity. If the future studies confirm this association, it may be beneficial for individuals with high BMI to be tested for the presence of H. pylori.

*Key Words: Helicobacter pylori (HP).; Smoking.; Body Mass Index (BMI)*

## Diastolic versus systolic ankle-brachial pressure index using ultrasound imaging & automated oscillometric measurement in diabetic patients with calcified and non-calcified lower limb arteries

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### Introduction:

Ankle-brachial pressure index-systolic (ABI-s) can be falsely elevated in the presence of calcified lower limb arteries in some diabetic patients, and therefore loses its value in this cohort of patients. We aim at investigating the feasibility of using the diastolic (ABI-d) instead of ABI-s to calculate the ABI in diabetic patients with calcified limb arteries.

### Methods:

A total of 51 patients were chosen from the diabetic foot clinic. 26 of these patients had calcified leg arteries by Duplex scan (Group A) and 25 patients did not have calcifications in their leg arteries (Group B). 25 healthy volunteers were enrolled in the study as Group C. Participants from Group C were matched with other participants from group B and A by age and sex. ABI measurement was performed using "boso ABI-system 100 machine". Systolic ABI (ABI-s) and diastolic ABI (ABI-d) were calculated based on bilateral brachial and ankle oscillometric pressures. ABI is considered normal when it is  $\geq 0.9$ . Repeated measurements of ANOVA test was used to compare mean scores for ABI-s and ABI-d across the three groups. Statistical significance is considered when  $P < 0.05$ .

### Results:

The mean age of all participants ( $\pm$  SD) was  $64.30 \pm 7.1$  years (range, 50 - 82 years). ABI-s mean  $\pm$  SD was  $1.3 \pm 0.10$  (range, 1.18 - 1.58) in group A,  $1.07 \pm 0.05$  (range, 1 - 1.16) in group B, and  $1.06 \pm 0.05$  (range, 1 - 1.16) in group C. While ABI-d mean  $\pm$  SD was  $1.07 \pm 0.05$  (range, 1.1 - 1.17) in group A,  $1.06 \pm 0.05$  (1 - 1.14) in group B, and  $1.05 \pm 0.04$  (range, 1.01 - 1.14) in group C. In group A, repeated measurements of ANOVA test showed statistical significant difference between ABI-s and ABI-d ( $P < 0.001$ ) whereas in group B & C was not ( $P > 0.05$ ).

### Conclusions:

ABI-d may be helpful as a complementary measure instead of ABI-s in falsely elevated ABI caused by partial incompressible vessel.

*Key Words: ankle brachial pressure index; peripheral arterial disease; diabetic foot;*



## **Bone Mineral Density Evaluation in Patients with Thalassemia**

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### **Introduction:**

Thalassemia is an inherited disorder of globin chain (mainly alpha or beta) synthesis leading to ineffective erythropoiesis requiring chronic transfusion and iron chelation therapy in its most severe form. While the management of patients with thalassemia has improved markedly in the past few decades, osteopenia and osteoporosis are still important causes of morbidity. Hence, this study was carried out to evaluate bone mineral density (BMD) in patients with thalassemia in comparison to healthy controls.

### **Methods:**

Bone mineral densitometry was performed on 28 patients with beta-thalassemia major in Mubarak Al Kabir hospital and were age-matched with 28 normal controls by dual-energy X-ray densitometry (DXA). Age, height, weight and BMC were recorded. Groups were compared using t-test and Chi square or Fisher's Exact test.

### **Results:**

There were 7 males and 21 females among the control group versus 9 males and 19 females in the study group. The mean age of  $19.8 \pm 4.2$  years among the control group which was similar to that of the study group ( $17.0 \pm 10.1$  years) (p-value  $> 0.05$ ). Osteopenia and osteoporosis were more common among the patients than in the controls 6 (21.4%) and 15 (53.6%) compared to 4 (14.3%) (p-value  $< 0.05$ ) and 2 (7.1%) (p-value  $< 0.001$ ) respectively. BMD z score was significantly lower among the thalassemia patients compared to the controls  $0.674 \pm 0.187$  g/cm<sup>2</sup> vs.  $1.067 \pm 0.189$  g/cm<sup>2</sup> (p-value  $< 0.001$ ).

### **Conclusions:**

Approximately three quarters of the thalassemia patients had a low BMD. We recommend early monitoring of it to avoid morbidity due to osteoporosis and fractures with appropriate therapeutic interventions.

*Key Words: BMD; Thalassemia; Osteoporosis;*



## **Sulesomab in pediatric musculoskeletal infection**

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### **Introduction:**

Bone and joint infections are one of the major causes of morbidity in infants and children. Early diagnosis with prompt treatment, are key to prevent the complications and morbidity. The objective of this study is to evaluate the diagnostic accuracy of <sup>99m</sup>Tc labeled anti-granulocyte monoclonal antibody fragment Fab (Sulesomab, Leukoscan®) for the detection of musculoskeletal infection in pediatric population.

### **Methods:**

This is a prospective study of 55 pediatric patients (30 males and 25 females) with a mean age of 6 years and 9 months (range 1 month to 15 years and 8 months). These patients were referred from out-patient clinic or admitted cases in Pediatrics and Medical wards to the Nuclear Medicine Department. The monoclonal antibody scan and the three phase bone scan were carried out with a maximum interval of 7 days. The patients were injected with age adjusted dose according to Webster's rule taking 20 mCi (750 MBq) as adult dose. The minimum injected dose was 3.5 mCi (130 MBq). Imaging was performed after one and four-hour after injection and in eight cases at 24-hours. Bone scan was acquired according to standard protocols. The sulesomab scan results were compared with final diagnosis, provided by the primary physician on 2-months clinical follow-up along with biochemical tests.

### **Results:**

The accuracy of the Sulesomab scan was 92.7% for the diagnosis of acute musculoskeletal infection. The calculated sensitivity, specificity, negative & positive predicted values were 95.8%, 90.3%, 96.5% and 88.4% respectively. No patient had adverse events.

### **Conclusions:**

Sulesomab was well tolerated with no apparent side effects. It was found highly accurate, had high sensitivity and negative predicted values. Therefore, <sup>99m</sup>Tc-labeled Leukoscan can be used with confidence to rule out acute musculoskeletal infection in pediatric age group.

*Key Words: Sulesomab; Leukoscan; Infection;*



## **Efficacy of Yttrium-90 Time-of-Flight PET/CT in Post Radioembolization Imaging of Microsphere Biodistribution in Radiosynovectomy**

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### **Introduction:**

<sup>90</sup>Y bremsstrahlung scintigraphy suffers from a low spatial resolution (11-15mm) due to indirect imaging of a continuous scatter radiation spectrum without a pronounced photo peak resulting in a coarse representation of the microsphere biodistribution. The authors are investigating the feasibility of <sup>90</sup>Y PET/CT TOF imaging as a technique to improve detection accuracy of <sup>90</sup>Y distribution and leakage post radiation synovectomy in relation to conclusive information of activity presence within the target area.

### **Methods:**

A knee phantom containing saline solution and Dipotassium Hydrogen Phosphate that mimicked the bone and soft tissue scattering/attenuation was developed. A LYSO PET with a 64 slice CT, as well as a 16 slice SPECT/CT camera were used. PET scans were acquired using positron fraction 3.186 × 10<sup>-5</sup>, half-life 64.1 h, 15 min per bed position and 15.7cm AFOV. For bremsstrahlung SPECT imaging the energy windows were set to 55-285 keV.

### **Results:**

An algorithm which incorporates TOF+PSF, non-TOF and 3D-OSEM were used for PET and SPECT image acquisition and reconstruction. The images were assessed for spatial resolution, technical success and detection of non-target activity. The PET images appeared to be suffered from low true coincident rate, but high singles rate. Qualitative evaluation showed superior spatial resolution of PET/CT over bremsstrahlung SPECT with clear edge definition of the phantom. We are aiming to apply the procedure on patient imaging, and it appears the <sup>90</sup>Y PET scan of patients for microsphere bio-distribution in radiosynovectomy is the first time to be done in Kuwait.

### **Conclusions:**

The preliminary study suggests although <sup>90</sup>Y PET imaging is suffering from low true counts, but it has qualitative superiority and results are indicating that it can serve in two primary clinical roles in radiosynovectomy : (1) evaluating technical success (2) predicting treatment efficacy. Funding: KFAS: P115-93MN-02

*Key Words: PET/CT, Molecular & Multimodality Imaging, Radiosy; PET/CT, Molecular*



## **Bremsstrahlung SPECT-CT for localization of inadvertent extra articular injection**

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### **Introduction:**

Bremsstrahlung or braking radiation are secondary radioactive emissions from pure beta-emitting radionuclides emitted when the particles decelerate in matter. This can be used for imaging following radionuclide therapy with these agents as in radiosynovectomy (RSO).

We report on the use of medium-energy collimator versus low-energy collimators for Bremsstrahlung imaging with Yttrium-90 for improved imaging yield.

### **Methods:**

Bremsstrahlung planar imaging is routinely performed using low-energy general-purpose collimators, but we report the use of medium-energy collimator with significant improvement in images. Bremsstrahlung SPECT-CT imaging was performed with the gamma camera set to auto-detect the highest fundamental frequency, which corresponded to xenon-133 window of 81-keV. Bremsstrahlung SPECT-CT images were then obtained using Siemens Symbia TruePoint SPECT-CT camera fitted with LEGP and MEGP collimators.

### **Results:**

The Bremsstrahlung imaging shows that the images obtained with the medium-energy collimator are technically Bremsstrahlung imaging.

### **Conclusions:**

Bremsstrahlung SPECT-CT using medium-energy collimators is recommended for accurate quantification, distribution and localization of beta-emitting therapeutic radiopharmaceuticals following radiosynovectomy. This is the first reported study of its type demonstrating the superiority of medium-energy collimator over low-energy collimator for Bremsstrahlung imaging.

*Key Words: Bremsstrahlung; Radiosynovectomy; Yttrium-90;*



## **Imaging in Acute Bronchiolitis: Evaluation of Utilization and Impact on Patients` Outcome in a Kuwaiti Governmental Hospital**

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### **Introduction:**

Evidence-based guidelines for acute viral bronchiolitis recommend primarily supportive care, but unnecessary treatment measures remains well documented. This study was designed to assess Al-Adan Hospital pediatricians` attitude towards imaging of cases of acute bronchiolitis.

### **Methods:**

The files of 262 cases of bronchiolitis admitted in Al-Adan Hospital were reviewed; number of X rays done and reasons stated in the files were recorded. Bronchiolitis severity was estimated and relevant history and examination items were collected.

### **Results:**

In more than half of the studied bronchiolitis cases the reason for X ray is a clinical severity item, aspiration in 13.4% and the rest is unaccounted for. Significantly more patients who had three or more X rays gave history of gastroesophageal reflux (GERD), were prescribed antibiotics and suffered statistically longer hospital stay in the ward. Significant predictors for the need to PICU admission among bronchiolitis patients were respiratory distress, PH, oxygen saturation and development of apnea. The factors determining the length of hospital stay (LOS) were the number of X rays and history of GERD.

### **Conclusions:**

In more than half of the studied bronchiolitis cases the reason for X ray is a clinical severity item whose importance isn` t agreed upon whether in prediction or prognosis and in one third of cases the reason is actually unaccounted for. The bronchiolitis guideline implementation is thus highly recommended in Al-Adan hospital to decrease the X ray utilization and subsequent unnecessary antibiotic use aiming at decreasing the costs of hospitalization.

*Key Words: Kuwait; Bronchiolitis; Imaging.;*



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## Rate of relapse occurrence in pregnancy and post-partum period

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### Introduction:

**Background:** Although multiple sclerosis (MS) relapse rates are often reduced during pregnancy, disease reactivation may be of a concern after withdrawals of disease modifying therapies (DMTs) prior or at the time of pregnancy confirmation.

**Objective:** To assess the risk of relapse during pregnancy and post-partum period in women with MS.

### Methods:

We conducted a retrospective cross-sectional study using the national Kuwait MS registry to identify pregnant women between 1st October 2011 and 30th September 2016. Data on demographics and clinical characteristics including relapses, prior use of DMTs, and pregnancy outcome were extracted. The primary outcome measure was to assess the rate of relapse occurrence during pregnancy and post-partum period. Additionally we investigated the relationship between the use of different DMTs and their washout periods and relapse occurrence.

### Results:

A total of 73 pregnancies (68 patients) were recorded. Mean age and mean disease duration at the time of pregnancy confirmation were 28.2±4.2 and 4.11±3.9 years respectively. Most patients (88.2%; n=60) were on DMTs in the year prior to pregnancy. Beta-Interferons were the most prescribed medications (42.6%) followed by natalizumab (25%) and fingolimod (19.1%). Thirteen relapses occurred in 16.2% of patients during pregnancy; 7 relapses in the first trimester, one relapse in the second trimester and 5 relapses in third trimester. Natalizumab and fingolimod were associated with relapses in the first trimester. Additional 10 relapses were recorded during post-partum period within 6.2 ± 5.6 weeks of delivery. Four miscarriages/ spontaneous abortions were recorded.

### Conclusions:

The rate of relapse occurrence during pregnancy is higher than expected. Most relapses clustered in the first trimester suggesting that disease reactivation was associated with withdrawal of high-efficacy DMTs and closely related to the washout period prior to pregnancy. Future studies are needed to address the adequate washout period prior to conception and best time to reinstitute DMTs in highly active patients.

*Key Words: Kuwait; Multiple Sclerosis; Pregnancy;*



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## **The Impact of Subchorionic Haematoma on Outcome of Pregnancy**

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### **Introduction:**

Subchorionic haematoma has been associated with adverse pregnancy outcome including miscarriages, abruptio placentae, stillbirths, preterm labour and fetal growth restriction in some reports, although, others have observed no adverse outcome. The aim of our study was to establish the impact of subchorionic haematoma on pregnancy outcome.

### **Methods:**

Patients admitted to Maternity Hospital, Kuwait, January 1st to June 30th, 2016, with a diagnosis of subchorionic haematoma before 20weeks gestation, were identified from our records and formed the study population, group A. Patients admitted with minor disorders of pregnancy such as backache and vomiting and no subchorionic haematoma, in the same gestational age during the same period and matched for age and parity, group B, were compared with group A. The past obstetric/medical/surgical and social bio-data of these patients, the progress and management of the index pregnancy and the outcome of the pregnancies were extracted from the records and the data subjected to statistical analysis.

### **Results:**

Thirty [30] patients were identified for the study group, group A and 44 for group B and there was no statistical difference between the mean age and parity of both groups,  $29.60 \pm 5.41$  and  $29.21 \pm 6.266$ ,  $p=0.78$  and  $1.89 \pm 1.783$  and  $1.40 \pm 1.740$ ,  $p=0.24$ , respectively. Although more patients in group A presented with vaginal bleeding, 86.7% vs 72.3%,  $p=0.24$ , the incidence of first trimester miscarriages in both groups were comparable, 26.7% vs 27.3%,  $p=1.0$ . The complications recorded in group A were rather few and included premature delivery, abruptio placentae, placenta praevia and stillbirth; in group B, one preterm fresh still birth was recorded and no cases of abruptio placentae and placenta praevia. No case of fetal growth restriction was recorded in the study.

### **Conclusions:**

Subchorionic haematoma was not significantly associated with adverse pregnancy outcome in the current study.

*Key Words: Subchorionic; Haematoma; Outcome;*



## **Transport kinetics of de-oxy glucose in gestational diabetic pregnancies: in-vitro study**

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### **Introduction:**

To explore whether transport kinetics of a model hexose, deoxy glucose was altered in gestational diabetic women (GDM) in in-vitro.

### **Methods:**

Placentae from control pregnancies & from GDM women, diagnosed by standard clinical criteria, were collected post-partum & perfused within 45 minutes with NCTC Culture medium buffered with Earls Salt solution. After wash-out period of about ten minutes, 14-C labelled deoxy glucose (specific activity: 45 mCi/mmol, Amersham, UK) along with tritiated water (specific activity 5 mCi/mmol, Amersham, UK) as reference marker were injected as a single bolus (100ul) into maternal arterial circulation of perfused placental lobules & samples collected from maternal & fetal circulations over a period of 5 minutes. In the case of gestational diabetic women (n=5), perfusions were done as mentioned earlier & samples collected from both maternal & fetal circulations as well. Concentrations of deoxy glucose & tritiated water in perfusate samples in control perfusions & in perfusions from diabetic women were assessed by scintillation spectrometry (LKB Wallac Scintillation Spectrometer, Denmark) using double-window counting.

### **Results:**

Differential transport rates of deoxy glucose & tritiated water from maternal to fetal circulation differed significantly (Student's t-test;  $p < 0.05$ ) for all transport fractions in control perfusions (n=6) & in perfusions from diabetic (n=5) women. Transport Fraction index of deoxy glucose compared to reference marker averaged 36.9% in control perfusions (n=6) & 39.90 % in diabetic perfusions (n=5) respectively. Difference observed in TF index of deoxy glucose compared to tritiated water in control & diabetic groups was not statistically significant (Student's t-test,  $p > 0.05$ ).

### **Conclusions:**

Our studies show for first time that transport behavior of a model hexose, deoxy glucose is not significantly different or compromised to alert the clinicians of appropriate measures.

Funding: Kuwait University Research Grant #MO032

*Key Words: deoxy glucose; gestational diabetes; perfusion;*



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## **Autoimmunity in Gestational Diabetes Mellitus: Prevalence of Islet – cell auto-antibodies.**

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### **Introduction:**

Gestational Diabetes mellitus (GDM) results from development of glucose intolerance during pregnancy. It is associated with both maternal and perinatal complications. Objective of the study: To evaluate the prevalence of Islet –cell autoantibodies in women with GDM.

### **Methods:**

Glutamic decarboxylase antibodies (anti-GAD65), protein tyrosine phosphatase ICA 512 (IA2) antibodies (anti-IA2), and Islet Cell Autantibodie(IAA) were assayed in 112 patients with gestational diabetes. A venous blood sample was taken from all women between 12 and 39 weeks of gestational age, and none of them was taking insulin when the autoantibodies are determined. Serum was separated by centrifugation, and kept at -20°C. Anti- GAD65, anti-IA2 and IAA, were determined by Radioligand Assay.

### **Results:**

Of the 112 women with GDM, 8 tested positive for Islet Cell Antibody (ICA) (7.2%) and 4 revealed the presence of CAD -65 antibody (3.6 %). On the whole 12 (10.8%) patients tested positive for Islet cell autoantibodies, and all of were on insulin therapy during pregnancy with 9 (75 %) of them before 24 weeks of gestation.

### **Conclusions:**

Autoimmunity contributes above 10 percent to our patients with GDM. The disease is the result of the autoimmune destruction of the insulin producing beta-cells of the pancreatic islets. More research is needed to unravel the mechanism and signpost research for development for new therapeutic agents.

*Key Words: islet –cell cytoplasmic antibodies, ,; Glutamic decarboxylase antibodies;*



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## **Introduction of Mini-Cex and Evaluation of Medical Students in Obstetrics and Gynaecology Posting.**

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### **Introduction:**

The Mini-CEX is a 20 minute direct observation assessment or “snapshot” of a student-patient interaction by an academic staff for 10 minutes. Objective of study: to evaluate students’ onintroduction of mini-cex into the obstetrics and Gynaecology clinical teaching program.

### **Methods:**

In the mini-CEX, Students are rated observed in seven competencies interviewing, physical examination, professionalism, clinical judgment, counseling, organization, and overall clinical competence using a three-point scale (1. needs significant improvement, 2 Competent with room for improvement and 3. Competent with strength ) and then receive immediate feedback. Each student has two mini-cex sessions during 3rd and 10th weeks of the 11 weeks clinical posting, always by different academic staff or clinical tutors. The results of the two mini-cex sessions are compared (A) needs significant improvement and (B)

### **Results:**

Medical interviewing: A 28 versus 9 and B 12 vs 38 (P<0.0001), Physical Examination A29 vs 9 and B 8 vs 28 (P<0.001), Counselling/communication with patient; A 30 vs 4 and B 14 vs 14 vs 25(P<0.04), Professionalism A 14 vs 1 and B 25 vs 43 (P<0.05), Clinical Judgement A 27 vs 11 and B 3 vs 21 (P<0.001), Organization/Efficiency A 38 vs 16 and 9 vs 27 (P<0.004), Overall clinical Competence A 22 vs 6 and B 5 vs 25 (P<0.002), Student’s view of mini-cex as a method of clinical assessment ( scale of 1 to 9)  $7.6 \pm 1.5$  vs  $8.1 \pm 2.3$  (P<0.008). with positive suggestions of more sessions

### **Conclusions:**

Mini-cex is associated with significant improvement in all domains of the clinical posting. To be most useful, staff should provide timely and specific and comprehensive feedback to the student after each assessment. This is a one to one encounter between staff and student and it be an essential component of the bedside teaching

*Key Words: Mini-cex, Medical Students,; Academic staff, Improvement; Clinical*



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## Effect of Gestational Diabetes Mellitus on Cytokine Network

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### Introduction:

The Cytokine network has an important role in the development of the fetus and the maintenance of pregnancy

Objective of the study: To evaluate the effect of GDM on the cytokine network

### Methods:

In 31 women with GDM and 25 with normal pregnancy, the relationship between cytokines in the maternal serum and fetal serum were evaluated using ELISA for estimation.

### Results:

Serum cytokine levels were compared between GDM and controls. There was downregulation of pro-inflammatory cytokines (pg/ml) by GDM: TNF- $\alpha$ ; 46.9 $\pm$ 21.6 vs 108.7 $\pm$ 84.2 (P<0.03), IL-1 $\alpha$ ; 35.8 $\pm$ 11.0 vs 67.1 $\pm$ 23.1 (P<0.05), IL-6; 6.8 $\pm$ 2.8 vs 11.8 $\pm$ 3.3 (P<0.05), IL-8; 86.7 $\pm$ 23.5 vs 146.4 $\pm$ 52.9 (P<0.05), IL-12; 121.3 $\pm$ 19.0 vs 173.7 $\pm$ 121.3 (P<0.05) but upregulation of anti-inflammatory cytokines (pg/ml): IL-4; 8.4 $\pm$ 6.2 vs 5.8 $\pm$ 5.8 $\pm$ 4.6 (P<0.002), T helper 3 IL-17; 49.8 $\pm$ 14.8 vs 56.8 $\pm$ 21.8 (P<0.062). Conversely, the cord serum revealed upregulation of pro-inflammatory cytokines: TNF- $\alpha$ , IL-6, IL-8 and IL-12 while anti-inflammatory cytokines IL4 and IL-13 were downregulated. Placental histopathology revealed increased intervillous space, wider blood vessels and decreased syncytial knots with GDM.

### Conclusions:

The cytokine network is altered in GDM with downregulation of the proinflammatory cytokines and upregulation of the anti-inflammatory cytokine. These findings may contribute to the maternal and perinatal complication associated with GDM

*Key Words: Gestational diabetes; altered cytokine network; proinflammatory, anti- inflammatory cytokines*



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## **Teenagers' Awareness of Peers Substance & Drug Use in Kuwait**

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### **Introduction:**

Teenage substance use is a global challenge and youths residing in Kuwait are not immune from it. Tobacco products are licit; however, alcohol and other mood altering illicit substance are prohibited with severe penalties. Aims: To determine licit and illicit substance use by teenagers residing in Kuwait and explore their awareness of substance use among their peers.

### **Methods:**

Study Design: A cross sectional survey using snowball sampling technique was used to recruit 190 teenagers aged 15 to 18 years residing in Kuwait. Research tool was 130- item questionnaire adapted from 1998, New Jersey Triennial Public High School Survey of Drug and Alcohol use questionnaire. Data collection was from September 2012 to June 2013. Data analysis: SPSS for windows version 22 was used. Pearson's Chi-square, Kruskal-Wallis and Mann-Whitney U tests were used to test the hypotheses.

### **Results:**

Tobacco was the most commonly used substance by these teenagers, 8.4% are current smokers and 50% have experimented. The age of initiation of 21% of them was before 14 years. Hashish (Marijuana) was the most commonly used illicit drug used, with 3.7% current users and 5.3% claiming to have ever used it. Chi-square result was ( $\chi^2 = 27.428$ ,  $df = 5$ ,  $p = 0.000$ ) with more males than females in grade nine using tobacco products.

### **Conclusions:**

The use and abuse of mood / mind altering licit and illicit substances appear to be on the increase among older teenagers. Intensifying campaigns about the hazards of substance use and drug testing should start from primary school level.

*Key Words: Teenagers' awareness, drug use; drug addiction; substance use & abuse;*



**Oncology**

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## **Enhancement of the Anticancer Activities of Paclitaxel by COL-3 in Human Breast Cancer Cell Lines**

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**Introduction:**

**Background:** Recently, chemically modified tetracycline-3 (COL-3) was reported to protect against neuropathic pain induced by the anticancer drug paclitaxel in a mouse model. The aim of this study was to evaluate the effect of COL-3 on the anticancer activity of paclitaxel on breast cancer cell lines: the estrogen receptor positive (ER +ve) MCF-7 and the ER -ve endocrine resistant pII and MDA-MB-231 cells.

**Methods:**

The effects of paclitaxel, COL-3 or their combination on cell proliferation and apoptosis were examined using the MTT and PE Annexin V/7AAD assays. Cell cycle arrest was measured using the propidium iodide DNA staining assay. The degree of cell invasion was determined using the Cultrex® BME cell invasion assay. The expression levels of several groups of proteins involved in cell proliferation, apoptosis, and invasion were determined using proteome profiler array kits.

**Results:**

Treatment with paclitaxel or COL-3 alone inhibited cell proliferation in a concentration-dependent manner in all cell lines. The anti-proliferative effects of paclitaxel and COL-3 combination regimens varied from synergism against ER -ve cells to nearly additive and slight antagonism against ER +ve cells. In the highly proliferative and invasive pII cells, the observed synergistic anti-proliferative effect was shown to be mediated in part through modulating cell apoptosis, but not cell cycle arrest. COL-3 inhibited invasion of pII cells. The combination regimen significantly inhibited the expression of only two proteases; ADAMTS1 and proteinase 3.

**Conclusions:**

COL-3 potentiates the anti-cancer activity of paclitaxel by enhancing its anti-proliferative effects on breast cancer cells mediated in part via the induction of cell apoptosis and the modulation of specific downstream molecules. This suggests that COL-3 could be a useful adjunct to paclitaxel-based anticancer regimens to improve both therapeutic outcomes and reduce the dose-limiting neuropathic pain adverse effect of paclitaxel. College of Graduate Studies YP01/14, Research unit for genomics, proteomics and Cellomics studies (OMICS) SRUL02/13

*Key Words: Paclitaxel; COL-3, PINP; Breast cancer ;*



**Oncology**

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**Natural phenolic compounds enhance the lethality of the multi-kinase inhibitor Sorafenib in human hepatocellular cancer cells.**

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**Introduction:**

Drug resistance & the unenviable side-effects are major obstacles to successful chemotherapeutic treatment. Sorafenib (Sora), FDA approved multi-kinase inhibitor, with potent antiangiogenic & antitumor activities. Effective strategies to reduce the side-effects & enhance the activity of Sora are much required. In this study, we endeavored to investigate the effects of combination treatment with Sora & natural phenolic compounds (NPC), on human hepatocellular carcinoma (HCC) cell growth, & intracellular transduction pathways involved in cell cycle & apoptosis.

**Methods:**

MTT assay was used to monitor the cytotoxicity of 14 NPCs on fibroblast cells CRL1554 & to measure the lethality of Sora, NPC & their combinations on HCC cells; Hep3b & HepG2 using three different approaches; sequential, reverse sequential & simultaneous. Cell cycle was analyzed by flowcytometry. Apoptosis was assessed by; DNA fragmentation, Annexin V/PI double staining assay & mitochondrial membrane potential assay (MMP). Finally, gene expression of apoptosis & cell cycle proteins was evaluated by western blot analysis.

**Results:**

Four NPCs; curcumin (Cur), quercetin (Que), kaempferol (Kmf) & resveratrol (Rsv) were selected, for their %Cytotoxicity ( $0 \leq 20\%$ ) on CRL1554 cells. Combination treatments of Sora & the selected NPC against HCC cells proved to be cytotoxic in a dose & schedule dependent manner where; Cur ( $p < 0.0001$  &  $p < 0.002$ ) and Kmf ( $p < 0.024$ ). Cell cycle analysis showed that HCC cells growth arrest at the S & G2/M phases. DNA fragmentation depended on the dose & type of treatment. Annexin V assay, demonstrated a high percentages of cell displayed early & late apoptotic phenotypes. Furthermore, assessment of MMP revealed extensive membrane damage. Finally, western blot analysis showed that protein expression is altered in a dose-dependent manner.

**Conclusions:**

Results showed a marked enhancement of Sora efficacy on HCC cells. In vivo & clinical studies of the combination treatments are needed. College of Graduate Studies and Research Sector, Project No. YS01/15, Kuwait University.

*Key Words: Hepatocellular carcinoma; Sorafenib; Natural phenolic compounds;*



**Oncology**

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**RAS gene mutations in follicular variant of papillary thyroid cancer in Kuwait**

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**Introduction:**

Papillary thyroid cancer (PTC) accounts for 85% of thyroid cancers and is ranked within the five most common cancers in Kuwait. Different histological variants exist and are found to be associated with different genetic mutations. The rat sarcoma viral oncogenes homolog (RAS) gene is a proto-oncogene that activates diverse signaling pathways and ultimately regulates cell proliferation and differentiation. The RAS gain of function mutations specifically at codons 12, 13, and 61 of the three RAS isoforms (HRAS, KRAS and NRAS) have been described in many types of cancers including the follicular variant of PTC (FVPTC). The objective of this study is to investigate the prevalence and type of RAS mutations in PTC in Kuwait, starting with the HRAS isoform.

**Methods:**

DNA was extracted from 67 PTC (including 50 FVPTC and 12 other PTC types) and 5 multinodular goiter tissue samples that were collected after thyroidectomy. HRAS exons 1 and 2 housing the mutational hot spot regions were amplified by PCR and sequenced by dideoxy cycle sequencing. Sequences were analyzed by manual readout of electropherograms and the NCBI's online BLAST database.

**Results:**

No mutations in HRAS exons 1 and 2 were detected. However, HRAS polymorphisms were identified in codons 14 (8%), 18 (21%), 19 (4%), 27 (21%) and 42 (6%) of the FVPTC samples. Comparison of these alterations with the patients' clinicopathological data did not reveal any significant associations.

**Conclusions:**

HRAS does not appear to be the oncogene associated with FVPTC in Kuwait. Other RAS isoforms are being studied.

Kuwait University research sector, project # MG 02/13

*Key Words: Papillary thyroid cancer; RAS oncogene; HRAS mutations;*



**Pathology**

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## **Extragonadal Germ Cell Tumors: The experience of Kuwait Cancer Control Center**

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### **Introduction:**

Extragonadal germ cell tumors (EGGCT) are rare heterogeneous neoplasms of germ-cell lineage arising outside the gonads, most commonly in midline mediastinum, retroperitoneum, pineal gland & sacrococcyx. They can arise primarily from embryologically maldescended germ cells or may represent a metastasis from an occult or burnt out gonadal tumor. Histologically, EGGCTs share similar features to their gonadal counterparts. Herein we present the clinicopathologic features of a series of EGGCTs obtained from the pathology archives of Kuwait Cancer Control Center (KCCC) over a period of 10 years.

### **Methods:**

We searched the KCCC pathology archives for all EGGCTs diagnosed between 2005 and 2015. The glass slides were retrieved and reviewed by 2 pathologists. Clinical features & follow-up data were retrieved from the patients' files.

### **Results:**

A total of 13 EGGCTs were identified but 5 were excluded for lack of sufficient clinical data. The remaining 8 EGGCTs were found in male patients ranging in age from 19-52 years (mean 35 years). Five tumors occurred in the mediastinum and 3 in the retroperitoneum. Tumor markers (AFP,  $\beta$ hCG, LDH) were normal or slightly elevated at presentation. Histologically, 6/8 (75%) were seminomas, 1/8 mature teratoma, and 1/8 embryonal carcinoma. On ultrasound, 1/5 mediastinal and 3/3 retroperitoneal cases (3 seminomas & 1 embryonal carcinoma) were found to be associated a testicular mass. All tumors, except mature teratoma, were treated by surgical excision plus adjuvant chemotherapy. Clinical follow-up ranged from 1-7 years: 7/8 cases had no residual disease while 1/8 (mediastinal seminoma) showed persistent LDH elevation & was found to have a testicular mass 3 years post chemotherapy.

### **Conclusions:**

Primary EGGCTs are very rare and diagnosis requires a thorough clinico-radiological screening to exclude an underlying testicular primary. Seminomatous tumors carry a favorable outcome regardless of location.

*Key Words: Extragonadal; Germ cells; Tumors;*



**Pathology**

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**Ultrasonographic features of well differentiated thyroid carcinoma (WDTC): A study of 46 cases from Al-Farwaniya hospital in**

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**Introduction:**

Thyroid cancer is the most prevalent endocrine malignancy, comprising 5.6% of all malignancies in Kuwait. The incidence is rising in all areas including our region, demanding efficient diagnostic tools. Ultrasound (US) imaging is a cost-effective test for evaluating the thyroid gland. With the use of US, thyroid nodules can be detected in up to 25% of adults; however, only 5% of all nodules are malignant. These figures necessitate precision in US reporting as an initial step of management. The commentary on US features curated by the American Thyroid Association (ATA) fairly correlates with malignancy. Thus, avoiding unnecessary fine-needle aspirations, surgical consultations and anxiety for the patients. This study was conducted to assess completeness of US reports and US features associated with WDTC.

**Methods:**

The archives of the Department of Pathology in Farwaniya Hospital were searched for WDTC in 2006–2013. All tumors  $\geq 1$  cm with available pre-operative US reports were included. The reports were assessed for 9 radiological features recommended by ATA: echogenicity, solid composition, cystic change, calcification, increased vascularity, halo sign, border irregularity, tall more than wide, and enlarged lymph nodes.

**Results:**

46 cases were included of which 33 are females and the age range is 23-65 years. Only 1 US report commented on all features recommended by ATA, and 10 reports mentioned  $\geq 6$  features. All reports commented on lymph nodes; however, out of 7 cases with enlarged lymph nodes on US, only 2 were positive for metastasis. The features most commonly associated with WDTC are calcifications (54.5%) and increased intra-nodular vascularity

**Conclusions:**

The Majority of the US reports are incomplete in our series. The most commonly reported features associated with WDTC are in harmony with findings from other studies. This study was conducted to increase the awareness of the importance of US reporting in the management of WDTC.

*Key Words: Thyroid; pathology; Ultrasound;*



**Pathology**

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**Correlation of bronchoalveolar lavage and brushings with bronchial biopsy in the diagnosis of lung malignancies – MAKH**

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**Introduction:**

Bronchogenic carcinoma is the leading cause of all cancer associated deaths in the world. In Kuwait lung carcinoma is the sixth common cancer with a distribution of 73% and 37% in Kuwaiti males and females. The objectives of this study was to compare bronchial biopsy with bronchoalveolar lavage (BAL) and brush cytology in the diagnosis of lung

**Methods:**

Over a period of 5 years (2010-2015) BAL and bronchial brushings (BB) with simultaneous bronchial biopsy received in the cytology and histopathology laboratories of Mubarak Al Kabeer Hospital were reviewed.

**Results:**

A total of 225 cases with BB and/or BAL with a bronchial biopsy were received. Age ranged from 12 – 83 years with 81 (36%) females and 144 (64%) males. In 73 cases a diagnosis of bronchogenic carcinoma namely 9 small cell carcinoma, 17 adenocarcinoma, 9 non-small cell carcinoma, 24 squamous cell carcinoma, 3 adenosquamous carcinoma, 5 lymphoreticular malignancy and 6 miscellaneous tumors was rendered. BAL alone was positive in 11 of 27 cases, BB alone was positive for tumor in 4 of 7 cases. Both BAL and BB were available in 39 carcinoma cases and tumor was seen in both BAL and BB in 20 cases while tumor was seen in BAL and negative in BB in 3 cases and seen in BB and negative in BAL in 7 cases. Both BAL and BB were negative for tumor in 5 cases. The sensitivity, specificity, NPV and PPV of BAL and BB were 56.5%, 98.3%, 81.1%, 94.6% and 72.7%, 72.7%, 57.1%, 84.2% respectively. A significant difference between the BB and BAL was observed.

**Conclusions:**

Combination of BB and BAL complement each other and enhance the diagnostic efficacy of lung tumors in conjunction with bronchial biopsy. Thus, all these techniques should be used concurrently to diagnose lung carcinomas.

*Key Words: Bronchial brushing; bronchoalveolar lavage; bronchial biopsy;*



**Pathology**

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## **Gender Dimorphism Is a Significant Determinant of the Associations of Vitamin D Deficiency in First-Degree Relatives (FDR) of Patients with Type 2 Diabetes (T2DM)**

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### **Introduction:**

Studies have shown that vitamin D plays a role in glucose metabolism via effects on insulin secretion and insulin sensitivity. First-degree relatives (FDR) of patients with Type 2 diabetes (T2DM) have increased risk of developing the disease. We hypothesized that apparently healthy FDR with Vitamin D deficiency would have abnormal glucose tolerance that would further increase T2DM risk.

### **Methods:**

Fasting 25(OH) Vitamin D (25(OH)D), adiponectin, insulin, glucose, and full lipid profile were determined in 391 (173M, 218F) FDR of T2DM subjects. Insulin resistance was assessed with the homeostasis model (HOMA-IR). None of the subjects were on Vitamin D supplements. Subjects were classified by glycemic status (HbA1C), HOMA-IR and 25(OH)D status.

### **Results:**

205 were 25(OH)D deficient (< 50nmol/L). There was gender dimorphism with female subjects having significantly higher mean (SD) 25(OH)D 45.1 (34) Vs 32.1 (21.7) in males. 35 of the FDR were diabetic; 12 of these had 25(OH)D deficiency. Gender dimorphism was observed in the associations of 25(OH)D with HbA1c, insulin sensitivity (%S) and steady state beta cell function (%B). 25(OH)D showed stepwise decrease across categories of glucose tolerance in males but not in females; mean HOMA-IR was lower in females with 25(OH)D deficiency compared to females with normal 25(OH)D (1.3 vs 2.3) but the opposite effect was observed in males (2.0 vs 0.9). Similar opposite trends were observed with regard to %S and %B. Mean adiponectin was higher in females with 25(OH)D deficiency compared with females with normal 25(OH)D (6.8 vs 4.2 ug/mL) but in males, the opposite effect was observed (4.5 vs 6.9 ug/mL).

### **Conclusions:**

Associations of 25(OH)D deficiency are gender dependent. It is critical that studies that explore 25(OH)D supplementation as a preventive measure and/or evaluate the effects of 25(OH)D deficiency on metabolic processes consider gender dimorphism as a significant confounding effect. Grant Support: KFAS-2011-1302-01.

*Key Words: Vitamin D; Type 2 Diabetes mellitus; gender;*



**Pathology**

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## **Seventeen cases of noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP): A pilot study from Kuwait Cancer Control Center**

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### **Introduction:**

Encapsulated follicular variant of papillary thyroid carcinoma (EFVPTC) is a highly indolent tumor type that is currently treated similar to classic papillary thyroid carcinoma (PTC). An international consensus group recently refined the diagnostic criteria and proposed the term “noninvasive follicular thyroid neoplasm with papillary-like nuclear features” (NIFTP) to avoid overtreatment. Our aim is to evaluate the consensus group diagnostic algorithm on a cohort of follicular variant PTCs from Kuwait Cancer Control

### **Methods:**

We searched all thyroid pathology records of 2015 for follicular variant PTCs, encapsulated & non-encapsulated. Four pathologists evaluated the H&E glass slides. Demographic & gross pathology data were obtained from the pathology reports.

### **Results:**

Of 264 thyroid nodules diagnosed in 2015, 166 (62.9%) were follicular variant PTC. After slide review, 17 (10.2%) nodules were re-classified into NIFTP, in 12 women and 5 men (F:M=2.4:1) aged 19-66 years (mean 40.4 years). Size ranged from 1.6 to 7 cm (mean 3.7 cm). Histologically, all nodules demonstrated a well-formed capsule &/or clear demarcation, and no capsular or lymphovascular invasion. All had a follicular architecture, no true papillae or solid pattern. None had mitosis >3/10HPF, necrosis or extrathyroidal extension. PTC nuclear features were widespread in 15/17 cases and patchy in 2/17 cases. Lymph nodes were available for evaluation in 3/17 cases, all were negative for metastases. Initial surgical treatment was lobectomy (7/17), followed by completion thyroidectomy in 3/7 cases, or total thyroidectomy (10/17).

### **Conclusions:**

The newly proposed morphological algorithm seems to discriminate a subset of indolent follicular neoplasms from true PTC. The use of the NIFTP terminology is expected to prevent overtreatment and ease the psychological impact on patients by eliminating the “cancer” label. A larger retrospective study with molecular correlation is our next goal.

*Key Words: Thyroid; Papillary carcinoma; NIFTP;*



**Pathology**

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### **Pediatric Renal Tumors in Kuwait**

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**Introduction:**

Renal tumors are relatively uncommon and represent the 6th most common pediatric solid tumors. Most occur in the 1st decade of life and they can be sporadic or associated with congenital disorders. Spectrum of renal tumors occurs in infants and children ranging from benign mesoblastic nephroma to most aggressive rhabdoid tumor. However, the most common renal tumor is Wilm's tumor. Herein, we evaluate the clinicopathological features and disease outcomes in pediatric renal tumors in Kuwait during a 5 year period.

**Methods:**

Patient < than 13 years old with a renal tumor reviewed at Kuwait Cancer Control Center pathology lab between 2010 and 2015 were identified. Clinical features and follow-up data were obtained from patients' records and the treating oncologist.

**Results:**

Sixteen patients were identified with 0.8:1.0 male to female ratio. Mean age was 28 months, ranged from 3 months to 8 years. The most common diagnosis was Wilm's tumor (n=13, 81%). Other histological types Cystic partially differentiated nephroblastoma (n=1), Clear cell sarcoma (n=1) and Rhabdoid tumor (n=1). Surgery performed in 15/16 of cases. Thirteen out 16 received pre and postoperative chemotherapy and 3/16 received additional radiotherapy. The tumors were staged based on SIOP as stage I (7/16), stage II (6/16), stage III (2/16) and 1/16 stage IV. Twelve out of 16 were disease free with no recurrence on a follow up period of 12 to 52 months. Two out of 16 were lost to follow up and 2/16 with high grade pathology developed metastasis and died of the disease.

**Conclusions:**

The incidence of pediatric renal tumors in Kuwait is 1.6/100000 and the majority of cases have excellent survival. The findings are comparable to published data. Patient treatment is based on histological findings and tumor stage.

*Key Words: Pediatric; renal tumor; wilms;*



**Pediatrics**

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## **Normal reference ranges for cardiac valve cross sectional areas in preterm infants.**

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**Introduction:**

Objective: To establish normal reference ranges for cardiac valve cross sectional areas in preterm infants and their correlation with gestational age, body weight and chronological age.

**Methods:**

In a prospective study, 268 pre-term babies, who fulfilled the criteria for inclusion were examined. Echocardiograms were performed to measure aortic, pulmonary, mitral and tricuspid valve cross sectional areas on 0-6 day(s) of life and at weekly intervals until they reached 36 weeks. The gestational age was grouped into three: (24-27), (28-31) and (32-35) weeks, and body weight into five:  $\leq 999$ , 1000-1499, 1500-1999, 2000-2499 and  $\geq 2500$  grams. The overall group differences were compared for each period of life: (0-6) days, 1-2, 3-4 and  $\geq 5$  weeks.

**Results:**

The mean gestational age was 29.8 ( $\pm 2.38$  SD) weeks, ranging between 24 and 35, and the mean body weight 1,479 ( $\pm 413$  SD) grams, ranging between 588 and 3380. All the cardiac valve cross sectional areas correlated well with body weight. A significant gradual increase was noticed in all valve cross sectional areas with body weight during each period of life. Overall, a progressive and significant increase for all valve cross sectional areas was observed during the first nine weeks of life.

**Conclusions:**

The cardiac valve cross sectional areas were found to have significant correlation with body weight. The study also provides reference data, which can be used as normal reference tool for valve cross sectional areas for preterm infants against the gestational age, body weight and chronological age.

*Key Words: valve cross sectional area; reference ranges; preterm infants;*



*Pediatrics*

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## Forced Expiratory Volume in 1 sec (FEV1) in Children with Sickle Cell Disease

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### Introduction:

Abnormalities of pulmonary function (PFT) are common in sickle cell disease (SCD) and a decline in predicted forced expiratory volume in 1 sec (FEV1) is an independent predictor of earlier death in adult patients. The current study was carried out to compare PFT in pediatric Kuwaiti SCD patients in comparison to age-matched controls. The association with past history of acute chest syndrome (ACS) and the use of hydroxyurea were investigated in the patients. The correlation with markers of hemolysis (total bilirubin, reticulocyte count and lactate dehydrogenase, LDH) was also examined.

### Methods:

Methods: The patients were being followed in the pediatric hematology clinic and were in steady state, i.e. no acute illness in the preceding 6 weeks and free of any other chronic disease. The controls were healthy, non-sickle siblings of the patients and children of some hospital staff. The predicted values of FEV1, FVC, TLC and DLCO were obtained using constant volume-variable pressure body plethysmograph. Hematological and other laboratory parameters were determined with standard methods.

### Results:

Results: There were 37 SCD patients and 37 controls with comparable mean ages of  $11.0 \pm 4.2$  and  $10.9 \pm 3.5$  years respectively. The predicted FEV1 value of  $83.1 \pm 14.1\%$ , among the patients, was significantly lower than the  $92.4 \pm 12.0\%$  in the controls ( $P = 0.003$ ). The predicted FVC was also significantly lower ( $P = 0.022$ ) in the former, although the values were generally in the normal range. There was no association of FEV1 with pain episodes, ACS or blood transfusion history. Neither was there significant correlation with reticulocytes, bilirubin or LDH.

### Conclusions:

Conclusions: Changes in PFT, especially FEV1, develop early in SCD patients. There is no demonstrable association of FEV1 with frequent VOC, ACS and other variables. However, there is a need to follow up the patients with serial PFTs to identify which patients are vulnerable and may need intervention to prevent early mortality.

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*Key Words: Sickle cell disease; Kuwait; Pulmonary function;*



*Pediatrics*

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## **IgA enhances IGF-1 mitogenic activity via receptor modulation in glomerular mesangial cells: Implications for IgA-induced**

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### **Introduction:**

Aim: Glomerulonephritis due to mesangial proliferation is responsible for renal dysfunction in IgA nephropathy (IgAN), however molecular mechanisms of pathogenesis are not well known. We examined the effect of IgA on Insulin-like Growth Factor-1 (IGF-1) activity, a potent mitogen with vital role in growth and development of children, in cultures of glomerular mesangial cells (GMC).

### **Methods:**

GMC were isolated from rat kidneys using sieving and enzymatic digestion of tissue homogenates, and cultured in RPMI 1640 medium. GMC cultures were treated with IgA (0-10 µg/ml) in the presence or absence of IGF-1, platelet-derived growth factor (PDGF) and fetal bovine serum, and (5-Bromo-2-deoxyUridine) BrdU incorporation was measured. IGF-1 levels were assayed along with real-time PCR quantification of IGF-1R mRNA.

### **Results:**

Treatment of GMC with IgA (5 -10 µg/ml) significantly ( $p < 0.01$ ) increased the BrdU incorporation in the presence or absence of FBS, IGF-1 or PDGF, however the IgA-mediated effects were more pronounced in IGF-1 treated cells. IgA significantly increased the levels of IGF-1 in culture supernatants and GMC homogenates. IGF-1R mRNA was significantly ( $p < 0.01$ ) more in IgA treated cells whereas PDGF mRNA content remained unaltered.

### **Conclusions:**

These findings show that IgA enhances the IGF-1 activity in GMC via stimulation of IGF-1R gene transcription and suggest a role for IGF-1 in pathogenesis of IgAN. Supported by research project MK01/14 funded by Research Sector, Kuwait University.

*Key Words: IgA; IGF-1; Nephropathy;*



*Pediatrics*

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## **Awareness of Food Allergies: A Survey of Pediatricians in Kuwait**

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### **Introduction:**

Early diagnosis of food allergies (FA) is important for a favorable prognosis. This study aimed to determine the level of awareness of FA among pediatricians in Kuwait.

### **Methods:**

A 43-item self-administered questionnaire was designed and distributed to pediatricians working at 4 government hospitals in Kuwait.

### **Results:**

A total of 140 pediatricians completed the questionnaire, with a participation rate of 51.1% (81 males and 59 females). The mean age of participants was 40.81 years, and the mean number of years working in pediatrics was 13.94 years. The mean overall knowledge score was 22.2. The pediatricians' overall knowledge scores were found to be significantly associated with their age (older pediatricians had higher overall scores) and years of experience as a pediatrician but were independent from hospital site, gender, or rank. A multiple linear regression revealed pediatrician age and gender were the only variables that were significantly associated with the overall knowledge score. Only 16.4% of the participants answered at least 2/3 of the survey questions correctly. The questions that were correctly answered by  $\leq 2/3$  of the participants constituted 80% of clinical presentation questions, 66.6% of diagnostics questions, 77.7% of treatment questions, and 42.8% of prevention questions. Interestingly, among 68 pediatricians (48.5%) who determined that they felt comfortable evaluating and treating patients with FA, only 12 (17.6%) passed the questionnaire.

### **Conclusions:**

This survey demonstrates that there is a noteworthy deficiency of pediatricians' awareness about FA. The implementation of strategies to improve pediatricians' awareness is critical to diagnose food allergy patients early and improve their health and outcomes.

*Key Words: Food allergy; Survey; Pediatrics;*



**Pediatrics**

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## **Pediatric liver transplantation for metabolic liver disease in Kuwait**

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### **Introduction:**

The liver is a highly metabolic organ where many pathways of intermediary metabolism are located. Dysfunction in any of those pathways may lead to deleterious manifestations known as metabolic liver disease (MLD). MLD is currently considered an indication for pediatric liver transplantation (LT). Our aim is to study our pediatric MLD patients who were managed with LT.

### **Methods:**

The records of LT patients followed up in the pediatric gastroenterology unit from January 2000 to May 2016 were retrospectively reviewed.

### **Results:**

Among the 62 pediatric LT cases followed, MLD was the indication in 52%, biliary atresia in 24% and other disorders 24%. Progressive familial intrahepatic cholestasis and Crigler Najjar syndrome were the main categories among MLD cases. Kuwaiti nationals were 81% and 56% were females. The median age at transplant was 5 years (Range: 0.4-13.5). Extrahepatic manifestations were the main problem in 50% of MLD cases before LT. The majority (72%) received a cadaveric transplant with a whole liver graft in 74%. Combined liver and kidney transplant was performed in 13% of cases. All patients were maintained on tacrolimus. Post LT complications included hepatic artery thrombosis, biliary strictures and post-transplant lymphoproliferative disease were encountered in 6, 8 and 2 patients respectively. A re-transplantation was required in 3 patients due to acute graft dysfunction. Patient survival rates at 1 and 5 years were 97 and 94% respectively, however, graft survival rates were 90 and 88% at 1 and 5 years respectively. On follow up, 31% of the patients manifested neurodevelopmental delay.

### **Conclusions:**

MLD constitutes the main indication of pediatric LT in Kuwait. Considering our high consanguinity rate, more MLD cases are pooled thus increasing the demand on LT.

*Key Words: Pediatric; Liver transplantation; Metabolic liver disease;*



## **Ex Vivo Incubation with H<sub>2</sub>S Donor Attenuates Diabetes-Induced Impaired Reactivity in Isolated Carotid Artery and Corpus Cavernosum of SD Rats**

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### **Introduction:**

GY4137 is a novel hydrogen sulfide (H<sub>2</sub>S) releasing molecule. Increasing evidence has proven that H<sub>2</sub>S has a positive role in regulating diabetic vascular injury. The objective of this study was to determine if ex-vivo incubation with GYY4137 protects the isolated carotid artery (CA) or corpus cavernosum (CC) tissues against high glucose-induced abnormal function.

### **Methods:**

Male SD rats weighing 250 g were used according to the National Institutes of Health Guide for the Care and Use of Laboratory Animals. Type-1 diabetes was induced by ip injection (55 mg/kg) of streptozotocin (STZ). After 4 weeks of diabetes induction, rats were sacrificed. Strips of CC and segments of CA from control and diabetic rats were suspended in organ-baths. Reactivity of the tissues to GYY4137 (10<sup>-9</sup> to 10<sup>-4</sup> M) was determined by measurement of changes in isometric tension. Concentration response curves were established for carbachol or PE using CC and CA tissues from control and diabetic animals. The relaxant responses to carbachol or GYY4137 were expressed as percentage reduction of tension induced by pre-contraction with phenylephrine (PE) (10<sup>-7</sup> M), while contractile responses to PE were calculated as gm/gm tension. Effect of ex vivo incubation with GYY4137 (10<sup>-5</sup>M) for 30 min on the responses of CC and CA from diabetic animals to carbachol or PE was investigated. Data are presented as mean ± S.E.M. of number of experiments (n=6).

### **Results:**

GY4137 induced relaxant responses in both tissues isolated from control and diabetic rats. Relaxant responses to GYY4137 were significantly attenuated in tissues from diabetic rats (p<0.05). Ex vivo incubation of CC or CA from diabetic rats with GYY4137 resulted in a significant improvement in the vascular responses to the agonists (p<0.05).

### **Conclusions:**

GY4137 is a relaxant agonist in the CC and CA of SD rats and may provide a novel therapeutic approach to minimize diabetes-induced vascular or penile dysfunction.

*Key Words: GYY4137; Carbachol; Relaxation;*



## **Camel Urine Sensitizes MDA-MB-231 Breast Cancer Cells to Doxorubicin by Preventing Epithelial-Mesenchymal Transition**

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### **Introduction:**

Emerging evidence suggests that EMT is associated with the increased enrichment of cancer stem-like cells (CSCs) and these CSCs display mesenchymal characteristics that are resistant to chemotherapy and target therapy. Camel urine (CU) is widely used in the Arab world as a remedy for a number of diseases including cancer. However, the exact mechanism for its action is still not yet clear. Objectives: To investigate the therapeutic potential of CU in effectively reversing EMT induced by doxorubicin and subsequently inhibiting CSCs in MDA-MB-231 breast cancer cells.

### **Methods:**

MDA-MB-231 cell line was treated with CU alone or co-treated with doxorubicin for indicated time and utilized for western blot, Flow cytometry and immunostaining. The anti-metastatic feature of CU was examined by scratch assay, migration and invasion assay.

### **Results:**

Treatment with CU and Doxorubicin enhances Doxorubicin cytotoxicity and induce apoptosis. This was concomitant with activation of apoptotic proteins and a reduction in anti-apoptotic protein levels. Interestingly, CU prevented MDA-MB-231 cells undergoing epithelial-mesenchymal transition in response to doxorubicin. The presence of CU significantly reduce doxorubicin-induced mesenchymal markers N-Cadherin and Vimentin proteins and enhances epithelial markers E-cadherin proteins. Also, a significant reduction in inflammation cytokine proteins (IL-6 and IL-8), closely associated with the development of CSCs, induced by doxorubicin was recorded in the presence of CU. Subsequently, STAT3 activation was reduced significantly and as a result STAT3-mediated stem cell marker ALDH protein expression was effectively suppressed.

### **Conclusions:**

Collectively, our result showed that CU leads to the mesenchymal–epithelial transition (MET) process and might have potential effect on CSC enrichment induced by chemotherapeutic drugs.

*Key Words: Camel Urine; Breast cancer; cancer stem cells;*



## **The role of the endocannabinoid system in a mouse model of antiretroviral-induced neuropathic pain**

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### **Introduction:**

Development of sensory neuropathy sometimes limits the use of nucleoside reverse transcriptase inhibitors (NRTIs) in HIV/AIDS management. Cannabis has shown efficacy in relieving HIV-associated sensory neuropathy. In this study we evaluated whether the endocannabinoid system plays a role in NRTI-induced neuropathy.

### **Methods:**

Female BALB/c mice (n=150) were treated with 25 mg/kg of 2',3'-dideoxycytidine (ddC). The expression of the endocannabinoid system molecules was evaluated by real-time PCR in the brain, spinal cord and paw skin post ddC administration. The effects of 2-arachidonoyl glycerol (2-AG) and anandamide, cannabinoid receptor antagonists, AM251 and AM630, and G protein-coupled receptor 55 antagonist ML193 on ddC-induced thermal hyperalgesia were evaluated using the hot-plate test.

### **Results:**

Mice treated with ddC developed mechanical and cold allodynia, and thermal hyperalgesia compared to baseline and vehicle-treated mice ( $p<0.05$ ). Treatment with ddC increased transcripts of phospholipase C-1beta only in the paw skin compared to vehicle-treatment ( $p<0.05$ ). The transcripts of fatty acid amide hydrolase and monoacyl glycerol were downregulated only in the brain and paw skin of ddC-treated mice compared to vehicle-treated mice ( $p<0.05$ ). 2-AG and anandamide had antihyperalgesic effects against ddC-induced thermal hyperalgesia compared to vehicle-treated mice ( $p<0.001$ ), but had no effect in naïve mice. The antihyperalgesic activity of 2-AG was antagonized by AM251 and ML193 ( $p<0.001$ ), but not by AM630 compared to mice treated with 2-AG alone, whereas the activity of anandamide was antagonized by AM251 and AM630 compared to mice treated with anandamide alone ( $p<0.001$ ).

### **Conclusions:**

Our results show that ddC induces painful neuropathy, which is associated with dysregulation of the endocannabinoid system. Agonists of cannabinoid receptors could be useful therapeutic agents for the management of NRTI-induced painful sensory neuropathy.  
Funding agent: KU Graduate Studies Grant YM 02/15

*Key Words: ddC; neuropathic pain; endocannabinoid system;*



## **Role of Nitric Oxide and ATP-Sensitive K<sup>+</sup> Channels in Mediating Pharmacological Actions of GYY4137 in Isolated Carotid Artery and Corpus Cavernosum of SD Rats**

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### **Introduction:**

Hydrogen sulfide (H<sub>2</sub>S) has been shown to exert various physiological effects in the body. H<sub>2</sub>S plays a role in the regulation of vascular homeostasis. A role of H<sub>2</sub>S in the physiology of penile erection has been recently suggested. GYY4137 is a slow-releasing H<sub>2</sub>S donor. The objectives of this study were to: (1) investigate the effect of GYY4137 on the reactivity of isolated tissues, namely carotid artery (CA) and corpus cavernosum (CC) from normal SD rats, and (2) examine the role of nitric oxide and ATP-sensitive K<sup>+</sup> (KATP) channels in mediating the vascular responses to GYY4137.

### **Methods:**

GYY4137 was synthesized using literature procedure. Male SD rats weighing 250 g were used according to the National Institutes of Health Guide for the Care and Use of Laboratory Animals. Relaxant responses to GYY4137 (10<sup>-9</sup> to 10<sup>-4</sup> M) and carbachol (10<sup>-9</sup> to 10<sup>-4</sup> M) were investigated in CC strips and CA segments after pre-contracting the tissues with phenylephrine (PE 10<sup>-7</sup> M). The relaxant responses were expressed as percentage reduction of tension induced by pre-contraction with PE. Effect of acute incubation with inhibitors of nitric oxide synthase, L-NAME (10<sup>-4</sup>), or KATP channels, glibenclamide (10<sup>-5</sup>), for 30 min on the responses of CC or CA to GYY4137 was tested. From the dose-response curves, pD<sub>2</sub> (the negative logarithm of the molar concentration of a drug producing 50% of the maximal effect) and E<sub>max</sub> (the maximal effect produced by the agonist) were calculated. Data are presented as mean ± S.E.M. of n number of experiments (n=6).

### **Results:**

GYY4137 and carbachol produced dose-dependent relaxation in the CC and CA segments. GYY4137-induced relaxation was significantly reduced (p<0.05) in CC and completely abolished in CA after incubation with L-NAME or glibenclamide.

### **Conclusions:**

These results show that GYY4137 can produce nitric oxide-dependent relaxation in the CC and CA of SD rats, partly through activation of KATP channels. Kuwait University, Research Sector, General Facilities Grants GS01/03 & GS01/05

*Key Words: Hydrogen sulfide; Relaxation; Glibenclamide, L-NAME;*

## **Epidermal growth factor (EGF) receptor and Src kinase activation are essential for the development of allergic airway responses**

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### **Introduction:**

Asthma is characterized by airway inflammatory responses associated with epithelial damage and repair. This can account for an altered epithelial phenotype with enhanced expression and activation of the epidermal growth factor (EGF) receptor. Objectives: In this study, we sought to determine the broncho-protective effects of the EGFR inhibitor, AG-1478, and the Src kinase inhibitor, SU6656, on the development of allergic airway responses *in vivo* in mice.

### **Methods:**

The effects of AG-1478 (a selective EGFR inhibitor) and SU6656 (a selective Src kinase inhibitor) were evaluated using an ovalbumin (OVA) challenged murine model of allergic asthma and administered following OVA sensitization but before aero-challenge, over four days. On day five, airway responsiveness to inhaled methacholine was assessed, bronchoalveolar lavage fluid (BALF) was performed and lungs were histologically assessed. BALF was also assessed for its ability to modulate neutrophil chemotaxis.

### **Results:**

Treatment with either AG-1478 (n=10-12) and SU6656 (n=10-12) significantly blocked total cell influx ( $29.5 \pm 4.4$  versus  $90.9 \pm 15.5 \times 10^4$  cells/ml and  $39.3 \pm 5.2 \times 10^4$  versus  $77.0 \pm 11.5 \times 10^4$  cells/ml, respectively), airway eosinophils ( $6.3 \pm 2.7$  versus  $43.3 \pm 8.6 \times 10^4$  eosinophils/ml and  $7.9 \pm 2.1$  versus  $34.5 \pm 5.1 \times 10^4$  eosinophils/ml, respectively) and T lymphocyte recruitment ( $1.1 \pm 0.4$  versus  $8.0 \pm 1.7 \times 10^4$  lymphocytes/ml and  $1.5 \pm 0.4$  versus  $3.0 \pm 0.6 \times 10^4$  lymphocytes/ml, respectively) in BALF. AG-1478 and SU6656 also decreased the ovalbumin-induced perivascular and peribronchial inflammation, fibrosis and goblet cell hyper/metaplasia. AG-1478 significantly inhibited the development of airway hyperresponsiveness (AHR) to inhaled methacholine ( $5.01 \pm 0.6$  versus  $8.1 \pm 1.6$  cm H<sub>2</sub>O/ml/sec). In addition, BALF from OVA challenged mice significantly enhanced neutrophil chemotaxis compared to PBS challenged mice, *ex vivo*, and this was abolished by BALF from AG-1478 treated mice.

### **Conclusions:**

These results demonstrate that blockade of EGFR or Src kinase signaling prevents allergen-induced airway inflammatory responses and AHR in mice with an allergic asthma phenotype. Funding: KURS (PT01/12)

*Key Words:* EGFR; Inflammation; Signaling;



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## **Evaluation of inhalation techniques among asthma patients in Kuwait**

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### **Introduction:**

Several studies show that correct inhalation techniques are essential in the management of asthma as incorrect inhalation technique lead to insufficient drug delivery and insufficient drug deposition in the lungs. In April 2016, a campaign organized by pharmacists targeted asthma patients aimed to promote safe and effective use of inhalers as well as to evaluate the inhalation techniques among patients in public as there is a lack of studies investigating the use of inhalers in Kuwait.

### **Objective:**

To assess the appropriateness of inhaling techniques of different inhalers in asthma and COPD patients in Kuwait

### **Methods:**

A cross sectional observational study conducted in 243 patients using at least one inhaling device. The study targeted patients in a public shopping mall in part of a national asthma campaign on (8th and 9th of April 2016). The data was collected by a team of pharmacists that had been trained over a period of four weeks in preparation for the campaign. The data was collected using a questionnaire and inhalation techniques were assessed using a validated checklist.

### **Results:**

The study consisted of 243 patients using at least one inhaler device. 128 (52.7%) were females and 115(47.3%) were males. The number of overall demonstrations evaluated was 219. Of those, 65(29.5%) demonstrations were described to be poor, 87(40%) were acceptable, and 67(30.5%) were good. The number of demonstration done using MDI, turbohaler, and discus inhalers were 127(58%), 17(8%), and 75(34%) respectively. MDI had the highest percentage of poor inhaling techniques with 31.5%. People using turbahalers had the lowest percentage of poor inhaling techniques with a percentage of 12%. Almost 30% of the total population using discus had poor inhaling techniques.

### **Conclusions:**

The prevalence of inappropriate inhaling techniques is high in Kuwait and further studies and appropriate plans are needed to promote the effective use of inhalers.

*Key Words: Asthma; inhalation techniques; Kuwait;*



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## **The Influence of Reduced Paracetamol Doses on the Co-prescribing of Other Analgesics in Elderly.**

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### **Introduction:**

There is an increase in reporting of unintentional paracetamol overdose resulting in acute liver failure. Consideration should be given to reducing the paracetamol dose in patients who are under 50kg in weight. However, it is unknown if reducing the paracetamol dose drives prescribing of other analgesics to control pain. This study compares post-operative analgesics between low-body weight and normal/over-body weight elderly patients.

### **Methods:**

In a comparative study, 70 postoperative patients aged 65 years and over were recruited to different types of orthopaedic surgeries, and divided into two groups ( $\leq 50$ kg or  $>50$ kg). The number of patients  $\leq 50$  kg who had their paracetamol dose modified was recorded. Their subsequent pain scores, additional analgesic co-prescribed other and their side effects profiles to treatment were documented and compared to patients  $>50$ kg who received four gram of daily paracetamol.

### **Results:**

Morphine equivalent doses were significantly higher in patients  $>50$ kg primarily because they had different type of orthopaedic surgeries that resulted in a higher severity rating of pain ( $p$ -value $<0.05$ ). Adding an NSAID to post-operative orthopaedic analgesia did not reduce the need of prescribing opioids ( $p$ -value is  $>0.05$ ) in patients  $>50$  kg. Despite the difference in opioid doses between the two groups; results did not show any statistical differences in the prevalence of opioid-related side effects such as constipation and itching between the two groups.

### **Conclusions:**

Post-operative orthopaedic patients usually experience a moderate-severe pain during the first two days, which cannot be relieved by paracetamol alone since all patients needed at least one dose of opioid to be co-prescribed. Pain perception rapidly de-escalated and a reduced paracetamol dose (2 g/day) provided optimal pain control. The need for the co-prescribing of other analgesics is not significantly related to the paracetamol dose.

Funding: Civil Commission (Kuwait)

*Key Words: Paracetamol; elderly; post-operative pain;*



## **Knowledge, Attitude and Practice toward Pharmacovigilance and Adverse Drug Reactions Reporting among Private Hospital Physicians in Kuwait.**

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### **Introduction:**

Adverse drug reactions (ADRs) may not be detected until a very large number of patients have received the drug over long time periods. From this comes the importance of the science of pharmacovigilance (PV) which involves the detection, assessment, understanding and prevention of (ADRs) or other drug related problems. This study aims to explore Knowledge attitude and practice (KAP) of physicians, who work in the private hospitals in Kuwait, with regard to PV and ADRs reporting. Knowledge means the theoretical or practical interpretation of a specific issue, attitude is responding positively or negatively towards a specific situation, whereas practice is the application of knowledge or practical approach to specific matter.

### **Methods:**

A descriptive cross-sectional study was conducted using a questionnaire; 33 questions comprising closed- and open-ended questions. Physicians who work in private hospitals in Kuwait were invited to take part. The data were analyzed using the statistical package for social science (SPSS), version 23.

### **Results:**

A total of 302 physicians (out of 364) agreed to take part, giving a response rate of 80.7%. The median age was 46 years (min 28, max 73). Although the majority identified the purpose of PV (75.2%) and the correct definition of ADRs (76%), less than half of physicians (48.7%) gave the correct response regarding the PV definition. The majority of physicians had good attitude regarding reporting ADRs, reflected by their agreement that that ADR reporting is necessary and it is a professional obligation and. Although the majority of physicians have identified at least one ADR incident during their practice, only minority (42.2%) did have reported it.

### **Conclusions:**

Physicians had mixed results regarding knowledge of PV and ADRs, however, they showed good attitude toward reporting ADRs. Underreporting of ADRs and poor knowledge about the existence of any reporting system in Kuwait and the lack of knowledge on where and how to reports ADRs.

*Key Words:* KAP; PV; ADRs;



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## **Knowledge and awareness of pharmacovigilance and adverse drug reactions (ADRs) among physicians in Kuwait**

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### **Introduction:**

Adverse drug reactions (ADRs) have been associated with major threats towards patients' safety. Therefore, there is a need for a system to assess, detect and prevent these ADRs which is called "pharmacovigilance". Due to the lack of data about the practice of ADRs reporting, this study was among physicians working in Governmental Hospitals in Kuwait.

### **Methods:**

A descriptive, cross-sectional study was conducted using a questionnaire. A total of 653 questionnaires were distributed to physicians working in 7 Governmental Hospitals in Kuwait. Descriptive statistics were carried out for data analysis.

### **Results:**

The response rate was 84.2%. Physicians' awareness of pharmacovigilance was inadequate, however, they correctly identified the purpose of pharmacovigilance and the definition of ADRs. Most of the participants (n= 423, 76.9%) recognized the types of ADRs that should be reported and similarly the majority (n= 489, 88.9%) agreed that physicians are the most qualified healthcare professionals to report ADRs. However, the majority of physicians (71.4%) were unsure whether there is a center or system in Kuwait to report ADRs or not. The overall willingness of the physicians towards pharmacovigilance and reporting ADRs was good. The most reported factors for underreporting among physicians were lack of the effective communication between all healthcare professionals, lack of awareness of pharmacovigilance and the importance of ADRs reporting, lack of standard forms for ADRs reporting and poor managements.

### **Conclusions:**

Results from the current study emphasized on the need for a standard ADRs reporting process, an effective educational intervention and the necessity to establish an independent center for ADRs reporting and monitoring in Kuwait.

*Key Words: ADR, adverse drug reactions, attitude, awareness; doctors, drug surveillance*



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## **Evaluation of Tacrolimus Dosage Guideline and Monitoring in Kidney Transplant Recipients**

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### **Introduction:**

Tacrolimus is immunosuppressant agent used in solid organ transplantation to prevent rejection. Tacrolimus has a high inter and intra-patient variability in absorption and clearance necessitates the need to monitor its level in the blood. Since no study was found in the literature to evaluate tacrolimus dosage regimen and monitoring after transplantation in Kuwait. This study was conducted to assess the adherence to hospital immunosuppressant protocol regarding dosing and monitoring of tacrolimus in kidney transplant recipients and evaluate the achievement of target tacrolimus trough

### **Methods:**

An estimated sample size of 212 randomly selected patients were approached. Patients on tacrolimus and aged >18 years old, with immediate and slow graft function, and first, second or multiple transplants were included.

### **Results:**

Out of 212 patients, only 147 (69.3%) patients were included in the study. Patients included were 55% males and 45% females. For the initial tacrolimus dosing, 38% patients' dose were in agreement with the local hospital protocol. Nearly 19.2% of tacrolimus trough levels were obtained as per the institution's protocol. In addition, the number of tacrolimus trough levels within the target during week 1 to 4 was increasing from 20.0% to 31.4%. In terms of toxicity, 65.4% new patients had used anti-hypertensive medications by week 4. Also, 38.7% patients had new onset diabetes after transplantation by week 4. Moreover, 39.1% patients have been using anti-lipid medications by week 4.

### **Conclusions:**

Physicians' adherence to local hospital guideline to initiate and monitor tacrolimus level is low following kidney transplant in Kuwait. The consistent high tacrolimus trough level by week 4 is an alarming observation and requires intervention. A high proportion of patients had their tacrolimus level out of the range and may increase the risk of toxicity and rejection.

*Key Words: Tacrolimus; Monitoring; Transplant;*



## **Inhibition of polysialylation of Neural Cell Adhesion Molecule in the Kelly Neuroblastoma Cell Line by Hexane Extract of the Roots of *Withania somnifera***

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### **Introduction:**

Polysialic acid (PSA) is a developmentally regulated cell-membrane glycan. In mammals, PSA consists of alpha-2,8-linked monomers of N-acetylneuraminic acid, a derivative of sialic acid family. It is mainly expressed on neural cell adhesion molecule (NCAM), where polysialylated NCAM is abundant in embryonic tissues, and restricted to areas of neural plasticity in adult brain. PSA is re-expressed in a number of highly metastatic cancers where it appears to be associated with tumour progression. The aim of this study was to investigate the potential of the non-cytotoxic inhibition of PSA expression in human neuroblastoma cell line (Kelly) by natural compounds present in roots of an Ayurvedic plant, *Withania somnifera* (*W. somnifera*) or ashwagandha, commonly used for enhancing memory and rejuvenation.

### **Methods:**

Constituents of powders of *W. somnifera* roots were extracted with Water (W), Ethanol (E), DMSO (D), Chloroform (C) or Hexane (H), and extracts were evaporated. Cells were seeded in 96-well flat bottom plates to be treated with DMSO or plant dried extracts re-constituted in DMSO. Treated cells were analysed in parallel with ELISA and MTT assays.

### **Results:**

DMSO exerted a proliferative effect at 0.5 % and no effect on cell viability at 2.5 %; both correlated with increased PSA level. For *W. somnifera*, treatment with the W extract exhibited a reduction in cell viability with a concomitant decrease in the PSA level. Similar results were obtained for the D extract at 0.5 mg/ml, however the extract was cytotoxic and drastically reduced PSA at 2.5 mg/ml. The E and C extracts exerted cytotoxicity associated with a drastic decrease in PSA. On the other hand, the H extract promoted slight proliferation, however with 20 and 30 % reduced levels of PSA at 0.5 and 2.5 mg/ml respectively.

### **Conclusions:**

The hexane extract of *W. somnifera* roots has the potential to inhibit PSA expression in Kelly cell line without exerting cytotoxicity.

Funding: Kuwait University (Research Project PC02/08)

*Key Words: Polysialic acid; Withania somnifera; Kelly cell line, neuroblastoma;*



## Antibacterial and antiproliferative activity of novel triazolyl oxazolidinones

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### Introduction:

Oxazolidinones exhibit biological actions such as antibacterial, anticancer, and MAO inhibition. The presence of H-bond donor or acceptor group at C4 position of the phenyloxazolidinone pharmacophore gave derivatives with potent antibacterial activity due to enhanced binding to 50S ribosomal subunit. Some 5-triazolylmethyl-oxazolidinone derivatives have been shown to exhibit antiproliferative effect against cancer cell lines. We now investigate antibacterial and anticancer activity of some novel oxazolidinones.

### Methods:

Selected oxazolidinone derivatives were synthesized and analyzed by spectroscopic and other analytical methods. Antibacterial activity was tested against standard reference Gram-positive and -negative bacterial strains. Minimum inhibitory concentrations (MIC's, ug/ml) were determined by agar dilution method on Mueller Hinton agar. Cell viability was determined cancer lines using MTT assay. UV-Vis and CD spectra of the substances in the presence of increased concentrations of ctDNA were measured. Inhibition of topoisomerase I and II were investigated.

### Results:

PH-145, -181, -189 and -193 exerted superior activity against selected Gram-positive bacteria compared with linezolid. In the 1,4-dihydro-1,8-naphthyridine derivatives, the glycyl containing compound SA-20-15 showed superior antibacterial activity compared with SA-12-15 and linezolid against *S. epidermidis* and *E. faecalis*. The 5-nitrofuoyl derivatives exhibited cytotoxicity against sensitive and cisplatin-resistant ovarian cancer cells. These results showed that PH-145 and -189 may act on tumor cells selectively. Moreover, CD spectra of ctDNA with increased concentrations of the compounds did not show any remarkable change with the exception of compound SA-20-15. Electrophoretic separation proved that none of these compounds inhibits topoisomerases.

### Conclusions:

Compounds showed strong antibacterial and some anticancer activities. Anticancer activity was not due to interaction with DNA. Kuwait University, Research Sector, General Facilities Grants GS01/03 & GS01/05 and VEGA Grant Agency of the Ministry of Education of the Slovak Republic No. 1/0790/14 & 1/0007/17.

*Key Words: antibacterial; antiproliferative; triazolyl-oxazolidinones;*



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## **Knowledge, Attitudes and Practices on Pharmacovigilance and Adverse Drug Reaction Reporting among Primary Care**

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### **Introduction:**

Adverse drug reactions (ADRs) are a significant cause of morbidity and mortality worldwide. Despite these observations, ADR are consistently underreported by healthcare professionals. Pharmacovigilance (PV) is pivotal to ensure collection, detection, assessment, monitoring and prevention of ADRs and ultimately to promote rational and safe use of medicines.

Objective: The objective of the study is to assess the knowledge, attitude and practices of pharmacists in primary health care towards ADRs and PV.

### **Methods:**

This is a cross-sectional study using a self-administered questionnaire distributed to pharmacists in 38 primary care polyclinics across the five health regions in Kuwait. The statistical analysis was done using the Statistical Package for Social Science (SPSS) Software for Windows, version 23. Descriptive statistics were used to analyze the data [frequency and percentages; mean  $\pm$  standard deviation (SD)].

### **Results:**

A total of 167 pharmacists completed the questionnaire, which provided a response rate of 85%. Results show that 62.9% and 77.7% of participants could correctly define PV and ADR, respectively, while about three quarters (74.1%) knew the purpose of PV. However, the majority of participants (85.7%) were not aware of an ADR reporting center in Kuwait. Pharmacists in the study showed a positive attitude towards PV and ADRs; all believed it is necessary to report ADR and most (88%) believe that ADR reporting is a professional obligation. Although 81% of participants reported being willing to implement ADR reporting in their practice, 70% had ever identified ADRs and only 22% have ever reported any ADRs. The major barrier reported by 65% of participants for underreporting is not knowing how to report ADRs.

### **Conclusions:**

Overall, participants in our study have an adequate knowledge regarding PV and ADRs and positive attitudes towards reporting but this is not reflected in their practice. Based on the barriers identified in the study, ADR reporting could be improved by implementing targeted training sessions that are supported by a formal national PV center in Kuwait.

*Key Words: Pharmacovigilance; Adverse drug reaction; Pharmacist knowledge,*



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## **Economic Burden of Multiple sclerosis on Kuwait Health care system**

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### **Introduction:**

This study aims to measure the cost of health resources utilization by multiple sclerosis (MS) patients and to examine the difference in utilization and its attributed costs among patients with different types of MS and expanded disability status scale (EDSS) scores.

### **BACKGROUND**

Multiple sclerosis is a chronic neurological disease with heavy economic and social burdens resulting in significant disability and social dependence. The prevalence of MS is in an upward trend in Kuwait reaching 85.05 per 100,000 in 2011.

### **Methods:**

A cross-sectional study using Kuwait National MS registry was conducted to estimate the costs of utilization of resources. Data of patient demographics, clinical features, and diagnostic / therapeutic utilizations between 2011 and 2015 were extracted. Kruskal-Wallis was used to examine the difference in costs between types of MS and EDSS scores.

### **Results:**

By end of 2015, 1344 MS patients were included in the registry; of whom 75.9% were of relapsing remitting (RR) form, and 83.3% had EDSS scores  $\leq 3$ . The average annual cost per MS patient has increased from 4,532 KD in 2011 to 6,753 KD in 2015. Utilization of disease modifying therapies (DMTs) was the main driver of costs reaching 89.9% in 2015. The number of treated patients increased by 12.7% due to the availability of oral DMTs. Throughout the five-year period, relapse severity decreased as the proportion of relapses treated in ambulatory settings increased by 5.8% while hospitalizations decreased by 2.6%. There was a significant difference between the average cost per patient in different type of MS and different EDSS categories ( $p < 0.0001$ ), with patients with RR course and moderate EDSS score (3.5-6) having the highest average 7,144 KD and 10,544 KD respectively.

### **Conclusions:**

Multiple sclerosis has a significant economic burden on the Kuwait healthcare system. Disease modifying therapies seem to be the main driver of cost.

*Key Words: Multiple Sclerosis; Economic burden; Kuwait;*



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## **Beliefs about medications: A Kuwait Perspective**

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### **Introduction:**

According to WHO, the average adherence to long term regimens is about 50% among patients. Lack of adherence to medication regimens is associated with disease complexity and presence of multiple comorbidities, resulting in increased morbidity, mortality and healthcare costs.

Objectives: To investigate beliefs about medications and self-reported adherence among chronically ill patients in Kuwait and to assess the association between beliefs and adherence.

### **Methods:**

This is a cross sectional study conducted in 23 polyclinics across the five major health regions in Kuwait. Data were collected using the Beliefs about Medication Questionnaire (BMQ) that measured the patient's perceptions about overuse, harm and benefit of medications. Self-reported adherence was measured by the Medication Adherence Report Scale (MARS-5).

### **Results:**

A total of 541 patients completed the questionnaire yielding an 86% response rate. Results show that over 50% of participants did not report intentional non-adherence to their medications but rather, over 80% reported unintentional lack of adherence by forgetting to take their medication. More than half of the study population believed that physicians overuse medications. About 40% to 50% of participants did not believe medications are harmful and in fact, most participants believed that medications are beneficial for their health. Correlation analysis showed that there is an association between general beliefs and adherence among patients.

### **Conclusions:**

Healthcare providers must acknowledge that patient's beliefs about medications influence their adherence to their therapy and as such, patients should be given the opportunity to express their beliefs. Further investigations must be done in the future for a better understanding of the strategies that should be developed and implemented to improve adherence to medications for patients in Kuwait.

*Key Words: Chronic disease; Beliefs; Medication adherence;*



## Formulation and Evaluation of Directly Compressible Medicated Chewing Gum for Dental Pain Relief

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### Introduction:

Medicated chewing gum (MCG) is a novel drug delivery system containing masticatory gum base with pharmacologically active ingredient(s) intended for either local or systemic treatment. The objective of this study was to design MCG formulation containing a combination of two local anesthetics; viz. Lidocaine HCl (LID) and Prilocaine HCl (PRIL) for relief of dental pain by causing temporary numbness.

### Methods:

MCG formulations (F1 – F8) were prepared by direct compression using different concentrations of synthetic gum base, flow enhancers, sweeteners and flavoring agents. Different formulations were evaluated for their organoleptic and micromeritic properties. FTIR and DSC studies were performed to ensure absence of drug-excipient interactions. The optimized blend was into tablets, and further evaluated for various physico-chemical properties. A suitable validated UFLC method was developed to study the MCG drug content.

### Results:

The MCG-F8 exhibited excellent flow properties; viz. angle of repose ( $26.01^\circ \pm 0.097$ ), % compressibility ( $5.36\% \pm 0.097$ ) and Hausner's ratio ( $1.04 \pm 0.015$ ). It was feasible to directly compress the granules without any stickiness due to an appropriate combination. Addition of mannitol may also improve the pain numbing effect of the anesthetic drug(s). FTIR and DSC studies showed good compatibility between the drugs and excipients. The developed UFLC method was rapid, precise with a regression value of 0.9999 and showed good resolution between the two drugs (PRIL:  $R_t = 5.106\text{min.}$  and LID:  $R_t = 7.357\text{min.}$ ). The MCGs complied for all physico-chemical tests; viz. weight variation ( $499.65\text{mg} \pm 0.381$ ), diameter ( $10.02\text{mm} \pm 0.040$ ), thickness ( $6.56\text{mm} \pm 0.119$ ), hardness ( $4.03\text{ kg/cm}^2 \pm 0.253$ ), friability ( $0.034\% \pm 0.062$ ) and assay ( $99.16\% \pm 0.587$ ).

### Conclusions:

MCGs prepared by direct compression method can be used as a suitable drug delivery system for oral health care and other medical conditions.

*Key Words: Medicated chewing gum; direct compression; dental pain relief;*



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## **Knowledge, Attitudes and Practices on Pharmacovigilance and Adverse Drug Reactions of Primary Care physicians in Kuwait**

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### **Introduction:**

Adverse drug reactions (ADRs) are a significant cause of morbidity, mortality and economic burden. Appropriate ADR reporting is essential for the development of a reliable pharmacovigilance (PV) program.

### **Objective**

This study aims to determine the current status of knowledge, attitude and practices (KAP) towards ADR reporting and PV among primary healthcare physicians in Kuwait.

### **Methods:**

A descriptive, cross sectional study was carried out among primary healthcare physicians. A validated self-administered questionnaire consisting of 33 questions was distributed randomly to 386 physicians working in 34 primary care clinics across the five health regions of Kuwait. The statistical analysis was done using the Statistical Package for Social Science (SPSS) Software for Windows, version 23. Descriptive statistics were used to analyze the data [frequency and percentages; mean  $\pm$  standard deviation (SD)].

### **Results:**

Out of 386 physicians, 318 completed the questionnaire giving a response rate of 82.4%. A total of 47.5% and 55.7% of physicians were knowledgeable about PV and its purpose, respectively. Almost two thirds (66.7%) knew the definition of ADRs. The majority (96.5%) thought it was necessary to report ADRs; however, only 78% felt that ADR reporting was a professional obligation. When evaluating practice, a total of 80.8% reported having previously identified ADRs but only 30.8% had reported them. Two major factors were cited as discouraging factors to reporting ADRs, which included not knowing how to report (75.2%) and what information to report (43.7%).

### **Conclusions:**

Despite the good attitudes and perception, the findings of this study indicated inadequate knowledge and practice among primary care physicians with regards to ADR reporting and PV. Based on this, it is imperative to not only offer physicians targeted training on ADR reporting but also to collaborate with regulatory bodies and administrators to facilitate a better ADR reporting culture and practices in government hospitals in Kuwait.

*Key Words: Knowledge, attitudes and practices; Adverse drug reactions;*



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## In Vitro and in-vivo Evaluation of Tablets Containing Meloxicam-PEG 6000 Ball-Milled Co-Ground Mixture

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### Introduction:

Meloxicam (MLX) is one of the Cox II inhibitors and considered safer than other NSAIDs. However, the major problem with the drug is its very low solubility in biological fluids. This study aimed at a) preparing MLX tablets containing ball milled co-ground mixture with PEG 6000 (1:4); b) evaluating the relevant in vitro quality parameters and stability, and c) comparing the bioavailability of the developed tablets with that of a reference meloxicam tablets (Mbc□) in 6 human subjects.

### Methods:

The physicochemical properties of the developed tablets were evaluated in vitro. The bioavailability of the formulated tablets was conducted in vivo in human subjects vs. a marketed tablet brand as a reference in a cross-over design.

### Results:

Dissolution rate of the prepared tablets was higher than that containing ball-milled or unmilled drug alone, as well as being higher than four marketed meloxicam tablets. Upon storage for 12 months at 25±1°C / 60% RH, no remarkable changes in physical appearance of the prepared tablets, %- drug content, thickness, disintegration time and in dissolution rate were observed. The prepared meloxicam tablets showed higher bioavailability, which was indicated by significant higher AUC and significant shorter Tmax. The bioavailability of the developed test tablets was 126.45%, relative to the marketed brand product (Mbc tablets).

### Conclusions:

Grinding of MXL with PEG 6000 resulted in a fast MLX release, which may provide rapid onset of action and allow also a reduction of required dose necessary to obtain the therapeutic effect. This, in turn, may further reduce the most common side effects observed with non-steroidal anti-inflammatory drugs (NSAIDs).

*Key Words: Meloxicam tablets; MLX-PEG co-grinding; In vitro & in vivo;*



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## **Evaluation of medication use in elderly patients**

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### **Introduction:**

The aim of this study was to determine the prevalence of potentially inappropriate medications (PIM) use, potentially prescribing omissions (PPO), and medication adherence among the elderly population.

### **Methods:**

A descriptive, cross-sectional study was conducted by interviewing and accessing the medical files of 233 Kuwaiti elderly patients attending nine polyclinics that provide geriatric care. Data analysis were performed using SPSS version 23.

### **Results:**

Two hundred and fifty five were approached, 233 agreed to participate, response rate 91.4%. Forty three patients (18.5%; 95% CI: 13.8-24.2) and 52 (22.3%; 95% CI: 17.3-28.3) were prescribed at least one PIM according to Beers' and STOPP criteria, respectively. The most commonly used PIMs were orphenadrine and glibenclamide. One hundred and fifty six patients (67.0%; 95% CI: 60.5-72.9) were prescribed one or more medications inappropriately. Based on START criteria, 39.1% had at least one PPO. Low dose aspirin, statins, and metformin were the most common PPOs. Polypharmacy was found to be a significant predictor for PIMs and PPOs ( $p < 0.05$ ). Optimal adherence was defined as having a score of greater than 6 on the 8-item Morisky medication adherence scale (MMAS-8). Using this cut-point, 61.3% ( $n = 138$ ; 95% CI: 54.6-67.7) of respondents had optimal adherence and 38.7% ( $n = 87$ ; 95% CI: 32.3-45.9) had poor adherence. Respondents with high education, those taking  $\geq 5$  medications, and those had  $\geq 3$  diseases were found to be significantly more non-adherent than those with low-intermediate education, those taking 1-4 medications or had 1-2 diseases high ( $p < 0.05$ ). The most common reasons for non-adherence were forgetfulness, lack of pharmacists' communication, polypharmacy and worries about long-term adverse effects.

### **Conclusions:**

These findings should be recognized by healthcare professionals and be used in designing multifaceted interventions to improve the quality of prescribing and adherence among the elderly.

*Key Words: Elderly; Medication use; Adherence;*



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## **Development and Validation of Bio - Analytical Method for the Estimation of Lacidipine in Human Plasma by Using LC-MS/MS**

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**Introduction:**

Pancreas-kidney transplantation is the best therapeutic option for diabetic patients with end-stage renal failure.

Aim of the work:

We aimed to describe early Kuwait experience regarding simultaneous Pancreas-kidney transplantation.

**Methods:**

Data of patients who underwent simultaneous kidney pancreas transplantation were collected including their demographic and clinico-laboratory parameters. All patients were suffering type 1 diabetes. We have paid attention to patient and graft outcome, rejection episodes and associated complication. Rejection of the pancreas was diagnosed by combined clinical and laboratory parameters while kidney rejection was confirmed.

**Results:**

From January 2012 to December 2014, 9 SKP transplants (3 women and 6 men) have been performed at Hamed Al-Essa Organ transplant center of Kuwait. The median age of recipients was 28 years, with a range of 25 to 36 years. One-year patient survival rate was 100% while the graft survival was 95% for the pancreas graft and 90% for the kidney graft. One pancreas was lost in the first two weeks due to a graft artery thrombosis. All patients showed normalization of their blood sugar within one week after transplantation and remain so even at the time of rejection (2 cases). The mean creatinine was 82  $\mu\text{mol/L}$  at 1 year and 126  $\mu\text{mol/L}$  at two years follow up. We reported biopsy proven rejection in 2 patients which were treated successfully according to our antirejection protocols (pulse steroid for T-cell mediated rejection; and plasma exchanges, IVIG and rituximab for antibody mediated rejection).

**Conclusions:**

A successful pancreas transplant program can be established in a single small-volume institute. A meticulous surgical technique and early anticoagulation therapy are required for further improvement in the outcomes.

*Key Words: Lacidipine, Amlodipine (ISTD).; The column employed in this*



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## In Vitro anti-mycobacterial activity of novel D/L alaninyl 5-(1H-1,2,3-triazolyl) methyl oxazolidinones

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### Introduction:

Tuberculosis (TB) caused by *Mycobacterium tuberculosis* (M.tb) accounted for 10.4m cases in 2015 with an estimated 480000 new cases of multidrug-resistant TB(MDR-TB). Drug resistance continues to be a growing health issue hence the urgent need for development of new anti-TB agents. Oxazolidinones are active against both Gram-positive bacteria and M. tb.

### Methods:

D/L alaninyl 5-triazolylmethyl oxazolidinones were synthesized according to reported synthetic methods. The synthesized oxazolidinones were evaluated against M.tb H37Rv in BACTEC 12B medium-Microplate Alamar Blue Assay. Cytotoxicity was determined by measuring THP-1 human monocytic cell line viability after 3 days in the presence of test compounds using the cell titer-Glo luminescent cell viability assay (Promega) which uses ATP as an indicator of cell viability. Initially, 15 compounds were screened by measurement of growth in liquid medium of a fluorescent reporter strain of H37Rv, using a Biotek Synergy 4 plate reader. Rifampicin and metronidazole were used as controls for aerobic and anaerobic killing of M.tb, respectively. The 7 most active compounds were subjected to further in vitro antimycobacterial activity characterization. Time-kill assay was used to measure the bactericidal activity of each compound. MIC and MBC were measured under both aerobic conditions and under low O<sub>2</sub> activity and against 5 resistant strains of M. tb.

### Results:

D/L alaninyl triazolyl oxazolidinones showed MIC values in the range of 0.39- 4.9  $\mu$ M and 0.14- 33  $\mu$ M against M. tb H37Rv and resistant strains, respectively. The 7 compounds were all bactericidal (MBC range: 0.17 till 24.50  $\mu$ M) and had good activity against resistant strains. Two compounds, PH224(D) and PH232(L), were shown to be cytotoxic.

### Conclusions:

Novel D/L-alaninyl 5-(1H-1,2,3-triazolyl) methyl oxazolidinones showed potent activity against M.tb H37Rv in vitro. Compounds with high bactericidal activity and no cytotoxicity will be considered for in vivo testing. Kuwait University, Research Sector General Facilities Grants GS01/03, and GS01/05

*Key Words: oxazolidinones; Mycobacterium tuberculosis; Minimum inhibitory*



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## Prevalence and treatment options for diabetic neuropathic pain in Kuwait.

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### Introduction:

Epidemiological data on Painful diabetic peripheral neuropathy (PDPN) is scarce in Kuwait. Purpose: To study the prevalence of PDPN among diabetic patients and to assess its treatment modalities in Kuwait.

### Methods:

This cross-sectional study collected data from 5 clinics in the primary, secondary and tertiary centres. Diabetic patients aged >18 years were included. PDPN was diagnosed based on combination of history of typical pain in extremities and objective neurological examination. Socio-demographic data and treatment modalities were extracted from the medical records. Questionnaires of patients` and practitioners` perceptions were collected from patients` and care health providers respectively. Descriptive and chi-square analyses were used to measure the statistical significance.

### Results:

A total of 202 diabetic participants; 109 were diagnosed as PDPN, representing a prevalence of 53.9% [95% confidence interval (CI), 50.7% – 58.5%] of the studied sample. The PDPN cohort had a mean age of 52.77±12.2 years. Patients with PDPN were older (39.6% versus 21.3%; p <0.005), taller (37.1% versus 23.8%; P <0.013), had longer disease duration (35.1% versus 21.8%; P <0.011), had body mass index > 30 (42.6% versus 26.2%; P <0.001) and higher fasting blood glucose (29.7% versus 18.8%; P <0.044) compared with patients without PDPN. The most commonly prescribed pain treatments were Non-steroidal anti-inflammatory drugs (25.68%) and anticonvulsants (22.93%).

### Conclusions:

Disease duration, poor glycemic control and high BMI were associated with increased risk of PDPN. Patient education and management of neuropathic pain control need to be optimized.

*Key Words: Peripheral Neuropathy; Diabetes; Treatment;*



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## **Cytotoxic Activity of (itl) *Launaea nudicaulis* (itl) Alcoholic Extract**

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### **Introduction:**

(itl) *Launaea nudicaulis* (itl) (Asteraceae) is a perennial herb widely distributed in North Africa including Egypt. Several species of (itl) *Launaea* (itl) are used in folk medicine as bitter stomachic and for various skin diseases. (itl) *Launaea nudicaulis* (itl) was reported to have insecticidal, antibacterial, antifungal, antioxidant and cytotoxic activities. However, the bioactive compounds have not been identified. This study aimed at investigating the cytotoxic activity of (itl) *Launaea nudicaulis* (itl) extract against eleven carcinoma cell lines which might culminate in isolation of the active compounds.

### **Methods:**

The shade-dried aerial parts of (itl) *Launaea nudicaulis* (itl) were coarsely powdered and extracted with ethanol (96%). The previously reported Skehan method [Skehan et al., 1990] was used to evaluate the cytotoxic activity of the dried alcoholic extract against prostate PC3, intestine CACO, colon HCT116, liver HEPG2, larynx HEP2, cervix HELA, lung H1299 and A549, and breast MCF7, T47D and MDA-MB-231 carcinoma cell lines. Normal fibroblasts BHK and melanocytes HFB4 cell lines were used for comparison. IC<sub>50</sub> (microgram/mL) of the extract was determined using doxorubicin as a standard cytotoxic agent.

### **Results:**

The alcoholic extract of (itl) *Launaea nudicaulis* (itl) aerial parts exhibited potent cytotoxic activities against PC3, HCT116, MCF7, T47D, HEPG2, MDA-MB-231, and HELA carcinoma cell lines. IC<sub>50</sub> values were 35.0 ± 0.04, 45.0 ± 0.04, 35.5 ± 0.02, 41.5 ± 0.03, 49.0 ± 0.04, 36.5 ± 0.03 and 36.5 ± 0.06, respectively.

### **Conclusions:**

This study showed that (itl) *Launaea nudicaulis* (itl) extract has potential cytotoxic effects against prostate, breast, and cervix carcinoma cell lines. However, the least potent effects were shown to be against liver and colon carcinoma cell lines. These results support the need to proceed with bioactivity-guided fractionation to identify the potential cytotoxic compounds.

*Key Words: (itl) Launaea nudicaulis (itl); Cytotoxic activity; Bioactivity-guided*



## **In search of cure: Experience with stem cell transplantation in spinal cord injury patients in Kuwait**

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### **Introduction:**

At present there is no effective cure available for neurological deficits caused by spinal cord injury (SCI). Stem cell therapy (SCT) offers hope to patients but is still in the experimental stages and functional recovery in humans is questionable. Our objective was to analyze recovery in patients with SCI who underwent stem cell transplantation therapies outside Kuwait and to note patients own perception of recovery.

### **Methods:**

8 patients with SCI who were under follow up in Physical Medicine and Rehabilitation Hospital and had undergone SCT were identified. Their pre-transplantation data was collected from hospital records and post transplantation status was assessed using standard neurological evaluation, American Spinal Injury Association Impairment Scale (ASIA), change in disability status, and patient's perception of improvement after SCT.

### **Results:**

There were 7 males and 1 female: 3 tetraplegics and 5 paraplegics, 6 were included in ASIA scale A and 2 were grade C. The mean age was 22.5 years. The SCT was done  $60.3 \pm 43.8$  months post SCI. 3 patients (37.5%) received autologous bone marrow transplantation and 4 of them underwent multiple procedures (50%). 7 patients (87.5%) reported perceived improvement as follows: increased deep tissue sensation below the injury (100%) and increase in bladder sensation (14.3%). Objective examination post SCT using ASIA at  $67.5 \pm 36.8$  months revealed that none of the patients demonstrated improvement in motor score or their level of disability. Only one individual showed recovery in two sensory levels.

### **Conclusions:**

No objective clinically useful improvement was documented in motor, autonomic or functional status in Kuwaiti SCI individuals after stem cell transplantation therapy. This is the first report from Kuwait on patients who underwent SCT.

*Key Words: Spinal cord injury; stem cell therapy; Kuwait;*



*Physical Medicine and Rehabilitation*

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## **Awareness about stem cell therapy among spinal cord injury patients in Kuwait – a survey**

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### **Introduction:**

Stem cell therapy (SCT) inspires hope of cure in persons who have incurable, severely disabling conditions like spinal cord injury (SCI). Clinical trials in humans have not reported any significant benefits in SCI. Stem cell tourism is a subject of concern as patients are exploited by unscrupulous commercial stem cell centers abroad claiming major recovery. The objective of this study is to assess the knowledge about stem cell therapy and its outcome among SCI patients in Kuwait.

### **Methods:**

25 SCI patients who were attending the Physical Medicine and Rehabilitation Hospital outpatient department between October to December 2016 were surveyed using a questionnaire.

### **Results:**

There were 25 patients in the study, 19 males and 6 females, of which 17 (68%) were paraplegic and 8 (32%) tetraplegic. The mean age was 38.7 years. 12 patients (48%) had University level education and 7 (28%) had completed high school. 22 (88%) of them were aware about SCT. The source of information for the patients was from internet 9 (36%) and from friends in 7 (28%). 10 patients (40%) knew that SCT was for regeneration of the nerves. Only 3 (12%) thought it was a successful treatment with good recovery while 5 (20%) thought that the improvements were small. 11 (44%) knew persons who had undergone SCT with only 1 (4%) having good outcome and 2 (8%) fair to poor outcome. 15 (60%) were willing to undergo SCT. 14 (56%) knew about countries offering SCT and the approximate cost 11 (42%). 22 patients (88%) would like SCT to be available in Ministry of Health, Kuwait.

### **Conclusions:**

Even though the number of patients in the study were small, majority of our patients had heard about SCT especially from the internet, the social media and friends but not from the doctors. Although only few thought it was a successful treatment, more than half of the patients were willing to undergo SCT. Education of the patient is important to protect them from exploitation.

*Key Words: Spinal cord injury; Stem cell therapy; Kuwait;*



## **Prevalence of depression among patients with spinal cord injury in Kuwait – a pilot study**

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### **Introduction:**

Depression is a common consequence of spinal cord injury (SCI) and is known to be greater in persons with SCI than in the general population. Hence it is important that the clinician is able to detect it early and treat appropriately. Our objective was to screen SCI patients in Kuwait for depression and to evaluate its prevalence and associated factors.

### **Methods:**

Patients with SCI who attended Physical Medicine and Rehabilitation Hospital outpatient department between October to December 2016 and were more than 1 year post injury, were screened for depression using the Patient Health Questionnaire (PHQ-9). The socio-demographic characteristics of the patients were noted during the interview.

### **Results:**

There were 25 patients in this study, 18 males and 7 females; mean age was 41.4 years, 13 (52%) had university degree and those currently unemployed were 10 (40%). Majority of them were traumatic 22 (88%), paraplegic 17 (68%), and wheelchair dependent 20 (80%). The PHQ 9 screening test showed that 10 patients (40%) were not depressed, 5 (20%) had mild depression, 10 (40%) had moderate to severe depression. The data showed no difference in prevalence of depression according to age or years post trauma. However, prevalence of depression was more in those who were graduates (66.7%), divorced (100%), unemployed or retired due to medical condition (60%), wheelchair dependence (45%), incontinence (45.5%), dependence in daily activities of living (47.1%) and less involved in social activities outside home (50%). Due to small sample size the differences were not statistically significant.

### **Conclusions:**

Our results show that 40% of our patients had clinically significant depression. This preliminary study shows the importance of continued research on measuring depression in persons with SCI and on treatment for depression after SCI. Self-report measures of depression should be viewed as screening tools to alert the clinician to arrange a more thorough evaluation.

*Key Words: Spinal cord injury; Depression; PHQ9;*



## Gender-dependent effect of prenatal immune challenge on adult hippocampal neurogenesis.

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### Introduction:

Early life psychological stress alters neurogenesis during adulthood in male progeny. The impact of early life challenges on female had received less attention. In the current study, we explored the long lasting impact of an immune challenge during pregnancy on hippocampal neurogenesis in male and female adult progeny. Since serotonin has been shown to promote neurogenesis, we also explored the impact of prenatal immune stress on hippocampal serotonin (5HT) and its transporter.

### Methods:

Pregnant Sprague Dawley rats were given either lipopolysaccharide (LPS, 100 µg/kg i.p.) or saline on gestation days 15, 17 & 19. Hippocampal neurogenesis was monitored male and female offspring using immunofluorescent detection of doublecortin (DCX), a marker of newly born neurons. Expression levels of 5HT (raphé nucleus) and 5HT-transporter (hippocampus) were assessed using immunofluorescence and western blot respectively.

### Results:

We observed no significant effect of prenatal LPS on hippocampal neurogenesis in one-month-old male and female rats. However, the expression of 5HT transporter was higher in male offspring when compared to that seen in female offspring regardless of early life challenge. There was no apparent effect of prenatal exposure to LPS on serotonin in the raphé nucleus. Interestingly, prenatal exposure to LPS significantly reduced hippocampal neurogenesis in the two-month-old female offspring. Such effect was not observed in the male offspring. Moreover, prenatal immune challenge significantly increased the expression levels of 5HT transporter within the hippocampus of both male and female rat offspring.

### Conclusions:

Collectively, these data suggest that prenatal immune challenge selectively alters hippocampal neurogenesis in female offspring, an effect that was accompanied by an increase in the levels of 5HT transporter in the hippocampus. Future studies will explore this gender biased effect of early life immune stress.

*Key Words: Fetal programming; Serotonin; Neurogenesis;*



## Contractility and motility of rat brain pericytes under normal conditions and during anoxia in vitro

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### Introduction:

Contradicting evidence exists on whether or not a prolonged contraction of brain pericytes after stroke contributes to the impaired blood flow following re-perfusion. A prolonged contraction inevitably reduces ability of pericytes in culture to move and length of their cellular processes. Thus, we explored effects of oxygen glucose deprivation (OGD) on motility and length of processes of rat brain pericytes.

### Methods:

Brain pericytes from Sprague-Dawley rats were cultured under standard conditions and were imaged in a cell observer every 5min over 15h twice, before and after 20min-3h (OGD) protocols. OGD was achieved by exposing the cultures to <0.3% oxygen, 5% CO<sub>2</sub>, 5% hydrogen in nitrogen in glucose free cell culture medium. Stacks of images of 11-22 cells from 3 different flasks for every experiment were analyzed using a self-written image analysis software to assess differences before and after OGD protocols in the single cell membrane mobility (SCMM) and in the two parameters of cell processes' length: the area/perimeter ratio (APR) and fractal dimension (FD). The paired and unpaired t-tests were used to analyze significance of differences in SCMM and parameters of contractility, respectively.

### Results:

Twenty minutes and 1h OGD protocols caused a significant reduction in SCMM ( $p < 0.05$  and  $p < 0.01$ , respectively). There was no significant difference in SCMM values before and after 3h OGD protocol ( $p > 0.05$ ). There was a significant increase in APR after 20min OGD protocol ( $p < 0.01$ ), while a significantly decreased APR ( $p < 0.05$ ) and a significantly increased FD ( $p < 0.01$ ) were revealed after 3h OGD protocol.

### Conclusions:

This study suggested that pericytes contracted after 20min OGD protocol and then possibly remained contracted after 1h OGD protocol. After 3h OGD protocol pericytes were not contracted more than before the protocol. Thus, we could not find evidence that pericytes remained contracted for a long period of time after OGD.  
Kuwait University Research Sector YM 04/16

*Key Words: Pericytes; Oxygen glucose deprivation; Stroke;*



**Physiology**

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## **Muscarinic receptor agonist prolongs survival in the hot**

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Department of Physiology, Faculty of Medicine Kuwait University

### **Introduction:**

During heat stress, initially high parasympathetic activity is reduced virtually to zero before the heatstroke appears. We tested the hypothesis that stimulation of peripheral muscarinic receptors with betanechol may delay heatstroke development in the hot

### **Methods:**

Male Wistar-Kyoto rats were implanted with telemetric transmitters to monitor ECG, aortic pressure and body temperature. Rats were randomly divided into 2 groups (n = 7) and examined in a climatic chamber with air temperature of 44.4 °C. Time-frequency analysis was employed to estimate the high-frequency power of RR-interval variability (HFRRI). Numerical data represent the mean and (standard deviation) compared with t-test.

### **Results:**

Placing animals into the hot environment initiated continuous increase in core body temperature (T<sub>c</sub>) with an average speed of 0.079 (0.008) °C/min. Heat stroke developed after 64.9 (5.4) min at T<sub>c</sub> of 42.9 (0.2) °C and was characterized by the rapid (11.9 (2.7) mmHg/min) decline in mean arterial pressure. Cardiac parasympathetic activity based on HFRRI, which was 3.2 (0.4) ms<sup>2</sup> outside the climatic chamber, increased to 25 (6) ms<sup>2</sup> upon heat stress and declined to 0.4 (0.01) ms<sup>2</sup> after T<sub>c</sub> of 41.5 (0.4) °C was reached. Ten minutes after the betanechol i.p. injection (0.01 mmol/kg) T<sub>c</sub> reduced from 37.6 (0.4) °C to 36.6 (0.4) °C, (P < 0.001), however the speed of T<sub>c</sub> rise as well as T<sub>c</sub> at which the heatstroke developed did not change. Betanechol augmented HFRRI response to heat stress (52 (14) ms<sup>2</sup>) but it was abolished at lower T<sub>c</sub> (40.9 (0.6) °C). Time to heat stroke development increased to 77.1 (9.1) min, P < 0.01.

### **Conclusions:**

Stimulation of peripheral muscarinic receptors prolonged survival in the hot environment by 20%. The hypothermic effect of betanechol seems to be the most probable mechanism of delayed heat stroke appearance.

Kuwait University Research Grant No. MY02/11

*Key Words: Thermoregulation; Heatstroke; Parasympathetic;*



**Physiology**

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**Rat brain astrocytes: secretome profiles of cytokines during anoxia.**

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Department of Physiology, Faculty of Medicine, Kuwait University.

**Introduction:**

Cerebral ischemia triggers pathophysiological pathways in the brain; one of the least clarified pathway is the development of inflammation. A comprehensive profile of cytokines' release from astrocytes during ischemia have not been established yet, so this study was aimed to explore that profile using primary culture of rat astrocytes.

**Methods:**

Primary cultures were exposed either to control conditions (5% CO<sub>2</sub> in air) or to anoxia (<0.3% O<sub>2</sub>, 5% CO<sub>2</sub>, 5% H<sub>2</sub> in N<sub>2</sub>) for 2-24h and profiling of 29 cytokines in the cell culture medium was done using the rat cytokine array panel (R&D Systems, USA). The data were analyzed using Kruskal-Wallis test. Core Analysis tool of Ingenuity Pathways Analysis (IPA) software (Qiagen, USA) was used to relate change in secretion of cytokines to a particular molecular

**Results:**

After 2h anoxia there was an increase in 9 cytokines, including interferon gamma, macrophage inflammatory proteins (MIPs), tissue inhibitors of metalloproteinase (TIMPs) and vascular endothelial growth factor (VEGF). This was followed by a significant increase in all 29 cytokines after 6h anoxia, including 10 interleukins and tumor necrosis factor alpha. Concentrations of 22 cytokines remained increased after 24h anoxia, while concentrations of MIPs, TIMPs and VEGF were not significantly different from the corresponding controls. The IPA revealed that these cytokines are involved in pathways triggered by hypoxia inducible factor (HIF) 1, interleukin 1 beta, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit gamma and cathepsin S.

**Conclusions:**

Three pathways that were triggered by anoxia were included, at least partially, in the immune response, while the HIF-1 mediated pathway was aimed to provide adaptation to hypoxia. Overall, it appears that astrocytes play an important role in triggering inflammation in the brain following cerebral ischemia.

Kuwait University Research Sector YM 03/16

*Key Words: astrocytes; anoxia; cytokines;*



**Psychiatry**

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## **Mental and physical comorbidity in an Arab national primary health care setting**

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### **Introduction:**

**Objectives:** To estimate the prevalence of the comorbidity between common mental disorders (anxiety/ depression / somatization) and common chronic physical illnesses among primary health care attendees, and explore the relationship of comorbidity with type of illness and socio-demographic characteristics.

### **Methods:**

The Physical Health Questionnaires (PHQ-SADs) were administered to a randomly selected sample of 1046 primary clinic attendees in all the five governorates of the country over a 5-month period. Physical diagnoses were ascertained by the attending physicians based on ICD-10 coding.

### **Results:**

Of 1046 respondents, 442 (42.25%) had at least one mental disorder, while 670 (64.1%) had a physical illness diagnosis, viz: diabetes mellitus (37.01%), hypertension (34.18%), heart diseases (7.2%) and non-chronic physical illnesses (9.4%). Physical comorbidity was significantly associated with older age, divorce, illiteracy, and poorer living conditions. Of the 670 with physical illness diagnoses, 53.7% had physical-mental comorbidity; and of 376 without physical illness, 82 (21.8%) had at least one mental disorder (OR = 4.1, P < 0.001. The commonest comorbid mental disorders were somatization and the simultaneous presence of all 3 mental disorders. There was an increase in the prevalence of mental disorders with increase in the number of physical illnesses, and increase in psychopathology scores with number of physical comorbidity. Subjects with heart diseases and asthma consistently had higher psychopathology scores.

### **Conclusions:**

The findings call for the primary care physicians to be sensitive to the psychosocial context of patients who present primarily with physical conditions; more so for patients with multiple medical illnesses and social disadvantage.

*Key Words: Mental and physical comorbidity; Arab; Primary health;*



*Psychology*

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## **Factor Structure of Trauma Distress: Posttraumatic Stress Disorder**

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### **Introduction:**

A trauma is defined as an event involving actual or threatened loss of life or personal integrity such that one experiences extreme helplessness, depression, anxiety, and posttraumatic stress disorder. The current study used explanatory & confirmatory factor analysis to examine the latent structures of Distress Following Trauma which associated symptoms of posttraumatic stress disorder (PTSD), depression, anxiety and hopelessness.

### **Methods:**

Participants were (370) Kuwait University students (242 males & 128 females) motor-vehicle, motorcycle, and motor scooter accident survivors, with a mean age of (20.79 ±1.25). The PTSD Checklist for DSM-5 (PCL-5), The Beck Depression Inventory (BDI-II), the Beck Anxiety Inventory (BAI) and Beck Hopelessness Scale (BHS) were administered to participants to assess Psychological Distress, including demographics.

### **Results:**

The explanatory factor analysis (EFA) extracted one unipolar factor with the following loading: (.82) for depression (BDI-II), (.80) for PTSD (PCL-5), (.69) for anxiety (BAI) and (.56) for Hopelessness (BHS) which explains 52.14% of the total variance. The Confirmatory factor analysis (CFA) extracted one unipolar factor with the following loading: (.74) for depression (BDI-II), (.71) for PTSD (PCL-5), (.55) for anxiety (BAI) and (.42) for hopelessness (BHS) which explains 38.05% of the total variance and was labeled trauma

### **Conclusions:**

The construct level analyses suggested that depression, PTSD, anxiety, and hopelessness are distinguishable but highly correlated variables following a traumatic event. Kuwait University Research Sector, Project Number: OP04/15

*Key Words: posttraumatic stress disorder; depression; anxiety;*



## The Structure of Mental Health: Explanatory & Confirmatory Factor Structure of Psychological Distress and Psychological Well-Being Measures

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### Introduction:

Psychological distress (PD) is usually based on the level of anxiety and depressive symptoms while psychological well-being (PW) is usually conceptualized as some combination of positive affective states such as happiness, optimism, satisfaction with life, and hope. The question of whether psychological distress and psychological well-being are the opposite poles of the same axis of mental health or independent constructs will be addressed in this study.

### Methods:

The sample consisted of (510) Kuwait University students, (240) males and (270) females, with a mean age of  $(22.81 \pm 4.13)$ , students were required to return the signed consent form to their teacher by the date of the study. The Beck Depression Inventory (BDI-II) and the Beck Anxiety Inventory (BAI) were administered to participants to assess Psychological Distress. In addition, the Oxford Happiness Questionnaire (OHQ), the Revised Life Orientation Test (LOT-R), the Satisfaction with Life Scale (SWLS), and the Adult Hope Scale (AHS) were administered to assess Psychological well-being. Participants completed the Arabic versions of OHI, LOT-R, SWLS, AHS, and BDI-II & BAI including demographics.

### Results:

The explanatory factor analysis (EFA) extracted one bipolar factor with the following loading: (.88) for OHQ, (.84) for LOT-R, (.81) for SWLS, (.74) for AHS, (-.70) for BDI-II, and (-.53) for BAI which explains 56.16% of the total variance. The Confirmatory factor analysis (CFA) extracted one bipolar factor with the following loading: (.70) for OHQ, (.81) for LOT-R, (.77) for SWLS, (.69) for AHS, (-.72) for BDI-II, and (-.44) for BAI which explains 48.88% of the total variance and was labeled psychological well-being vs. psychological distress.

### Conclusions:

Psychological distress is the opposite end of the continuum to psychological well-being of the same axis of mental health. However, these findings must be viewed within the limitations imposed by the age of the sample.

Kuwait University, Research Sector Project NO:OP03/16

*Key Words: Psychological Distress; Psychological Well-Being; Factor Structure ;*



## **Baby walkers; mothers' knowledge, prevalence of use and associated injuries in Kuwait.**

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### **Introduction:**

Most parents hold the impression that baby walkers (BWs) are useful to accelerate gait acquisition and to keep children safely entertained. However, studies suggest that these notions are incorrect; and that BWs increase the risk of injury. The objectives of this study were to: 1) explore the mothers' knowledge about BWs in Kuwait, 2) estimate the prevalence of BW use, and 3) estimate the prevalence of injuries related to BWs among

### **Methods:**

A cross-sectional study was conducted on 785 mothers attending vaccination centers in all governorates of Kuwait. Data were collected through face-to-face interview using a structured questionnaire. Logistic regression was used to investigate the association between BW use and related factors.

### **Results:**

Of 839 mothers invited to participate, 785 (93.5%) responded. The prevalence of BW use (ever use) was 700 (89.2%; 95% CI: 86.8-91.2%). Of the study group, 290 (36.9%) thought BWs have benefits but no harms; while 444 (56.6%) thought BWs make children walk earlier. Of the total users, 463 (66.1%) reported using BWs to strengthen the legs of their children; and 8 (1.1%) reported an injury that required hospital admission while 35 (5.0%) reported injuries that required medical treatment without hospital admission. Factors that were significantly associated with BW use included mother's education, having a domestic helper (maid), age of the youngest child, and factors related to knowledge on BWs.

### **Conclusions:**

Several misconceptions about the benefits of BWs prevail among mothers in Kuwait. The use of BWs is extremely common with substantial number of users had BW related injuries. Our findings support the calls for banning BWs which several professional organizations have already issued.

*Key Words: baby walker; knowledge; injuries ;*



*Surgery*

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## **Evaluation of Modified Alvarado Scoring System and RIPASA Scoring System as Diagnostic Tools of Acute Appendicitis**

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### **Introduction:**

Acute appendicitis is the most common surgical condition presented in emergency departments worldwide. Clinical scoring systems such as Alvarado and the modified Alvarado score were developed with the aim of reducing the negative appendectomy rate to 5-10%. The Raja Isteri Pengiran Anak Saleha Appendicitis (RIPASA) scoring system was established in 2008 especially for the Asian and Oriental population.

### **Methods:**

This is a retrospective diagnostic study to evaluate the modified Alvarado score and RIPASA score based on sensitivity, specificity, positive predictive value, negative predictive value, diagnostic accuracy, and receiver operative curve. The study included 136 patients who underwent appendectomies and were documented as "acute appendicitis" or "Abdominal pain" in the operative theater log book unit B from November 2014 to March 2016.

### **Results:**

In our study, the cut-off threshold point of the modified Alvarado score was set at 7.0. This yielded sensitivity of 82.8% and specificity of 56%. The positive predictive value was 89.3% and the negative predictive value 42.4%. The cut off threshold point of the RIPASA score was set at 7.5. This yielded 94.5% sensitivity and 88% specificity. The positive predictive value was 97.2% and the negative predictive value was 78.5%.

### **Conclusions:**

The RIPASA score is a simple scoring system that has better sensitivity and specificity than the Alvarado score in the Asian and Oriental population. It consists of 14 clinical parameters which can be obtained from good history, clinical examination and laboratory

*Key Words: acute appendicitis; modified Alvarado score; RIPASA score.;*



**Surgery**

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### **Revisional Metabolic Surgery After Failed Primary Restrictive**

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Surgical Department, MKH; Surgical department, Kuwait University

**Introduction:**

There is no doubt that bariatric surgery accepted to be one of the most successful therapies to treat morbid obesity and to control the associated complications of it. Even though there are a high number of patients who required revision of bariatric surgery because of undesirable outcomes of primary procedure or failure to maintain weight loss.

**Methods:**

A retrospective study of (100) patients carried to review the indications of revision and outcomes post revision. The study carried for those patients who underwent revision at different centers during the period Jan. 2009 – Jan 2015 for a primary restrictive procedure. Data are presented as mean +/- standard deviation for continuous variables. Characteristic were analyzed using (Mann-Whitney test) for continuous variables and chi-square test for categorical variables.

**Results:**

Total of (132) patients were carried to the study where (32) patients excluded because of missing of clinical data or had lost follow-up. The final total number (N=100), majority were females (N= 63), and (N=37) males. Mean age of participants = 37 years old. Where the mean period for follow-up post revision is 14 months. We encountered one case of leak post revision procedure of LAGB to LSG. Patients divided based on their primary procedure. Different primary restrictive procedures showed different results regarding weight loss and control of undesired symptoms according to the choice of revision procedure type. For that we classified the revision procedures as restrictive revision and malabsorptive revision. Restrictive revision procedure included Lap Sleeve gastrectomy (LSG), Lap Re-Sleeve. Where malabsorptive revision included Minigastric bypass (MGB) and Roux en y gastric bypass (RYGB).

**Conclusions:**

Revision of bariatric surgery is feasible & safe and showed effective weight loss results and resolution of undesirable symptoms.

*Key Words: Restrictive; Malabsorptive; Bariatric ;*



**Surgery**

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## **Clinical Outcomes of Surgery For Perforated Duodenal Ulcer**

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### **Introduction:**

Despite improvements in medical therapy, perforated duodenal ulcer (PDU) still occurs at a rate of 4 – 14 per 100,000 yearly<sup>1</sup>. Laparoscopic repair of PDU has been shown to confers superior short-term benefits in terms of postoperative pain and wound morbidity.<sup>2</sup>

### **Objectives**

To report the outcomes of laparoscopic repair of PDU compared with open repair.

### **Methods:**

Patient's selection:

A retrospective review of all consecutive adult (>17 years) patients who underwent emergency repair of PDU. The study was conducted at two major hospitals in Kuwait between January 2009 – January 2015.

Statistical methods:

### **Results:**

During the study period, 108 patients underwent emergency surgery for PDU. (N=8) were excluded due to missing clinical information. Patients divided into two groups, Open repair (N=22) and laparoscopic (N=78) repair. The mean age for both groups (45.4 +/- 15.4). The sample showed higher male predominance of (68 %). 60 % of the patients were Arabs Vs. non-Arabs. Patients were classified according to their level of education, socio-economic class & level of expertise. The highest proportion were those of the middle-lower socioeconomic class. Most patients [resented with abdominal pain (78%), Nausea& vomiting (74%), shock (10%) & (80%) had guarding on examination. More than (85%) of the patients were ASA score 1 & 2 on presentation. And (93%) presented with symptoms of less than 24 hours. (82%) were repaired by omental patch repair. Different post-operative outcomes encountered for both groups, where (N=7) patients who underwent lap repair admitted to the ICU in comparison to (N=6) patients in the open repair group. (N=1) patient of the lap repair group had DVT post-op which managed conservatively. (N=1) mortality in the open repair group.

### **Conclusions:**

Laparoscopic repair of PDU is feasible & is associated with improved short term outcomes.

*Key Words: Perforated\_ulcer; Lap\_repair; Open\_repair*



**Urology**

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**Does a standardized algorithm for managing patients post robot assisted radical prostatectomy improve recovery? A prospective non-randomized longitudinal cohort study**

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**Introduction:**

Prostate cancer was the most common cancer in Kuwaiti males in 2011 according to statistics from Kuwait Cancer Control Center. After acquiring the Da Vinci Si robot in 2013, a robot assisted radical prostatectomy (RARP) program was established. We examined the impact of a standardized post-operative algorithm on the first 36 robotic prostatectomies performed at Sabah Al-Ahmad Urology Center in Kuwait.

**Methods:**

We collected data prospectively on all robotic cases performed between Feb 2014 and Nov 2016. We used the Clavien–Dindo system to grade complications. Major complications were defined as Clavien grade  $\geq 3$ . We examined recovery variables on all patients. Since Apr 2015, we adopted a standardized post-operative algorithm called the optimized surgical journey (OSJ) for managing our patients post-operatively.

**Results:**

A total of 95 robotic cases were performed at our center between February 2014 and December 2016 of which 36 were RARPs. Mean age for RARP patients was 62 years. Mean prostate volume was 48.81g. Average estimated blood loss was 109.67ml. 3 patients had positive surgical margins. Mean Foley catheter removal was at 11.3 days (SD: 2.5). First 12 RARPs were managed with non-standardized post-operative orders. Mean hospital stay for this group was 4.83 days. Since Apr 2015, 24 patients had the OSJ protocol implemented. Length of hospital stay was reduced by 2.33 days ( $p < 0.001$ ). Adjusting for age did not affect our results. We report no episodes of ileus before or after OSJ implementation. Four patients in total had complications, all were minor and not significantly associated with the OSJ.

**Conclusions:**

Following a standardized post-operative pathway improves recovery of patients undergoing major surgical procedures like RARP. The OSJ protocol decreased length of hospital stay for our patients without compromising surgical or oncologic outcomes. We realize limitations of our study with small number of patients and lack of randomization.

*Key Words: Prostatic Cancer; Prostatectomy; Length of Stay;*



**Urology**

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**Robotic assisted partial nephrectomy: Initial experience from a single center**

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**Introduction:**

Advances in urology have focused on minimizing the invasiveness of surgical procedures without compromising oncologic outcomes. We present Kuwait's initial experience and outcomes of robot assisted partial nephrectomy (RAPN) using the da Vinci Si robot

**Methods:**

After IRB approval data was recorded for all patients who underwent robotic surgery at Sabah Alahmad Urology Center in Kuwait. Complications were graded using the Clavien-Dindo classification. Major complications were defined as  $\geq$  Clavien grade III.

**Results:**

From February 2014 to December 2016 a total of 95 cases were done robotically in our center. Of these, 13 were RAPN. Mean age for patients who underwent RAPN was 50.1 years. Mean size of renal masses was 3.29 cm (IQR= 2.6 – 3.75 cm, SD = 1.15cm). Mean RENAL Nephrometry score was 7.46 (IQR= 9 – 7, SD = 2), with our most complex tumor having a score of 9 a+h. Eight of 13 tumors were posteriorly located. Transperitoneal approach was utilized in all cases. Two patients required blood transfusion given post-operatively but were hemodynamically stable throughout their hospital stay. All patients were subjected to either warm or zero ischemia partial nephrectomy. There was one major and five minor complications. Median hospital stay was three days. Mean estimated blood loss was 287.5 ml (IQR: 100 - 425ml). Pathology included 12 malignant renal cell carcinomas with negative surgical margins and one benign tumor. There was no tumor recurrence over a mean follow up of 15 months.

**Conclusions:**

Our center's initial experience with RAPN performed by a single surgeon shows good patient and operative outcomes. However, a larger number of cases is required to draw a definite conclusion. The first Robotic unit in Kuwait was recently established. establishing such a unit requires proper selection of patients with continuous training of all members of the unit to ensure quality of care.

*Key Words: Renal Cancer; Nephrectomy; Robotic;*



## **Characterization of Cellular Immune Subsets Associated with Persistent Hepatitis C Virus Infection.**

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### **Introduction:**

Between 130 and 170 million people are chronically infected with hepatitis C virus (HCV). The interplay between the virus and host innate and adaptive immune responses determines the outcome of infection. The present study aims to determine the level of cellular immune subsets in HCV-infected patients and to compare it to healthy controls.

### **Methods:**

This will be carried out by investigating the immunophenotype of immune cells in the peripheral blood of patients and healthy controls before treatments. The immunophenotyping of mononuclear cells in the peripheral blood will be assessed by flow cytometry using antibodies specific to CD3+ (mature T cells), CD4+ (T helper cells), CD8+ (T cytotoxic cells), CD26+ (activated T cells), CD3-CD56+CD16+ (NK cells), CD3+CD56+CD16+ (NKT cells), CD19+ (pan B cells), and CD4+CD25+ (regulatory T cells).

### **Results:**

There were significantly lower mean values for absolute counts of T lymphocytes (CD3+,  $P < 0.007$ ), T cell subsets (CD3+CD8+,  $P < 0.005$ ), NK cells (CD3-CD56+CD16+,  $P < 0.05$ ), NKT cells (CD3+CD56+CD16+,  $P < 0.005$ ), regulatory T cells (CD4+CD25+,  $P < 0.005$ ) and activated T cells (CD8+CD26+,  $P < 0.05$ ) between HCV-infected patients and healthy donors.

### **Conclusions:**

This study identified significantly lower mean values in absolute count of cellular immune subsets (peripheral T lymphocytes, T cell subsets, NK cells, NKT cells, regulatory T cells and activated T cells) in HCV-infected patients compared to healthy donors in Kuwait. This data may be useful for further understanding of the underlying immune responses in persistently HCV-infected patients.

Funding: Research Sector MIO2/13

*Key Words: Hepatitis C virus; Immunophenotyping; Cellular immune subsets;*



## Case Reports

### Allied Health

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#### A case report Neurofibromatosis: insights for rehabilitation intervention with Motor control approach

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#### CASE REPORT

**Background:** Neurofibromatosis (NF) is a disorder that develops tumors anywhere along the nervous systems. It is genetic and diagnosed in childhood. It is classified into three types; neurofibromatosis I, neurofibromatosis II, and Schwannomatosis. Mostly patients who have NF experience problems related to balance and muscle wasting; the reason for referrals to a physical therapist (PT) for evaluation and treatment. Our role as PT is to provide a wide perspective for the treatment to better the patients' functional outcome and their quality of life. Motor Control is known as the ability to regulate the mechanisms essential to movement. It explores how the central nervous system organize functional movements and how the sensory information of the body and the environment integrated to help the patient. Also, how the movement behavior is changed by the perception of the task instructed to do and the environment in which the task is performed in. Therefore, the Purpose of this report is to focus on the importance and benefits of applying motor control intervention Strategies during physical therapy practice.

**Case summary:** A known case of a child (XY, related parents) 3yrs old was diagnosed with neurofibromatosis I. He was born at 30 week of gestation due to rapture of membranes with a 4 week NICU stay. History of mild retinopathy of prematurity treated by laser at 4 days old. Also, adenoidectomy and bilateral myringotomies were done on 8/2015 due to difficulty in breathing through the nose and chronic middle ear effusions. He had a C1/C2 Schwannoma extended into ventral spinal canal subcutaneous occiput and left neck. Cervical laminectomy was performed on 6/2016. After PT examination, his problems were mainly in standing and walking. The plan of treatment was designed to include strengthening and balance exercises.

**Conclusion:** In such cases, physical therapy rehabilitation is crucial to let the child reach his/her developmentally and age appropriate milestones.

**Key Words:** neurofibromatosis; Motor control; Balance



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**Case Report: Neurologic Amytropy**

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**CASE REPORT**

**Background**

Neurologic amytropy(NA) is an uncommon disorder of the peripheral nerves system that affects neurons of the brachial plexus characterizing by sudden onset of neck and shoulder pain followed by flaccid paralysis. NA can be idiopathic or heredity through a mutation in the SEPT9 gene. 1-2 cases per 100,000 person-years has been reported in US. Diagnosis of NA is based on clinical features and exclusion of other diseases. No specific treatment has been proven to be efficient in treating NA. However, physiotherapy is essential to gain muscles strength and improve motor control. Therefore, the aim of this paper is to report a case of two and half years old girl patient known of G6PD deficiency. The patient was a full term with normal delivery and had a normal milestone. December 2015, patient had a history of upper respiratory tract infection with productive cough and high grade fever. Three days later, she developed left facial asymmetry. The day after, patient had flaccid paralysis. CT and MRI for brain and spine were normal. Blood virology showed Cytomegalovirus DNA by Polymerase chain reaction Cytomegalovirus IgG positive. EMG showed severe drop of median compound muscle action potential and moderate drop of ulnar compound muscle action potential. Also, EMG revealed severe denervation activity with no motor unit potentials for left biceps, triceps and deltoid. The patient was diagnosed with NA on December 2015. Physical therapy program mainly focused on improving motor control and muscle strength. After 3 months of physical therapy, patient was able to control elbow extension and improved hand function and muscle tone.

Conclusion: neurologic amytropy is a very rare disorder that cause nerve damage and muscle atrophy. Intensive medical treatment and physical therapy intervention are essential to have better prognosis. However, more research is needed to understand the cause of NA and to have better outcomes.

**Key Words:** Neurologic Amytropy; Motor control; G6PD deficiency



**Anatomy**

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**A rare case of anomalous precentral cerebellar vein causing hydrocephalus**

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**CASE REPORT**

**Background**

Developmental venous anomalies (DVAs), previously known as venous angiomas, are rare benign entities often incidentally discovered at MRI examinations. They represent variants of typical transmedullary veins that provide normal drainage of brain parenchyma. They are characterized by a network of thin-walled, dilated transmedullary veins draining into a large collector vein, which lacks a smooth muscle layer and elastic lamina. Supratentorially, the deep collectors drain into the vein of Galen via the subependymal veins of the lateral ventricles. Infratentorially, the deep collectors drain directly into the subependymal veins of the fourth ventricles.

**Case summary**

We present a case of 28-year old female who had several attacks of mild headache. She was referred for CT scan of paranasal sinuses which revealed dilated supratentorial ventricular system and further assessment of the brain by MRI was recommended. Post contrast MRI of the brain revealed venous angioma at right cerebellar hemisphere and midbrain with collector vein coursing through the aqueduct of Sylvius with subsequent mild dilatation of both lateral ventricles and the third ventricle.

In this patient, the cerebellar DVAs drained into a subependymal vein in the fourth ventricle. Further drainage was atypical, through a subependymal vein that coursed through the aqueduct of Sylvius to enter the vein of Galen causing obstruction to the cerebrospinal fluid (CSF) flow.

**Conclusions**

Venous angiomas have been very rarely associated with CSF obstruction. DVAs are usually treated by endoscopic third ventriculostomy. However, after considering the complexity of this venous anomaly and the fact that the patient's complaint is mild and is well controlled by medical treatment at the time of diagnosis, there was no reasonable indication for surgical intervention. Instead, the patient received a detailed explanation of her condition and was instructed to do a regular follow up yearly.

**Key Words:** Venous angiomas; Subependymal vein; Aqueduct of Sylvius ;



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**Intrathyroidal Parathyroid carcinoma: Report of a case on fine needle aspiration cytology**

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**CASE REPORT**

**Background:** Parathyroid carcinoma (PC) is an uncommon malignancy and the probability of an intrathyroidal location is low. And to the best of our knowledge, only ten cases of intrathyroidal PC are reported in the literature. Fine needle aspiration cytology (FNAC) attempted on these presumably “thyroid nodules” can lead to misinterpretation because of the similarities in cytological features of parathyroid and thyroid lesions. We report a rare case of intrathyroidal PC with a discussion on the challenges faced in cytological diagnosis.

**Case summary:** A 60-year-old female was admitted in Mubarak Al-Kabeer hospital with one year history of hypercalcemia. Biochemical and radiological evaluation revealed an elevated parathyroid hormone (PTH) and an ultrasound finding of a nodule approximately 3.6×3.3 cm in the right thyroid gland respectively. Imaging-guided FNA smears showed dyscohesive clusters of monomorphic cells with round to oval nuclei having fine chromatin, prominent nucleoli and vacuolated cytoplasm. The **Background** showed numerous bare nuclei, a few follicular cells, lymphocytes and absence of colloid. The possibility of a follicular lesion was considered. In view of the vacuolated cytoplasm of the cells immunocytochemistry was done to confirm a thyroidal lesion. The cells were negative for TTF-1 and Thyroglobulin which raised the suspicion of a parathyroid neoplasm. A histopathological examination confirmed the diagnosis of intrathyroidal PC.

**Conclusion:** US-guided FNAC is an accepted technique in the management of thyroid nodules. Parathyroid lesions presenting as thyroid nodules are rare and pose a diagnostic challenge. PC though rare should be suspected in patients with hypercalcemia and increased parathormone levels. However, histopathological examination is required for a final diagnosis of parathyroid carcinoma.

**Key Words:** Intrathyroidal; Parathyroid Carcinoma; Fine needle aspiration



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**Role of Fine Needle Aspiration Cytology and Immunocytochemistry in the Diagnosis of Malignant Mesothelioma: A Case Report.**

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**CASE REPORT**

**Background:** Diffuse malignant mesothelioma is the most common primary tumor involving the pleura. Unfortunately, it also poses the most difficulty for physicians to diagnose and treat. Pathologic verification remains challenging. The primary distinctions to be made are between reactive and neoplastic mesothelial processes and between malignant mesothelioma and metastatic adenocarcinoma. Without treatment, the median survival time is between 4 and 13 months. Patients in whom the disease is detected early have a survival benefit from a multimodality therapeutic approach. We present one case of intrathoracic malignant mesothelioma diagnosed by imaging guided FNA cytology and immunocytochemistry (ICC).

**Case summary:** Case 1: A 45-year-old man, smoker and known case of Diabetes mellitus (DM) was admitted to Mubarak Al-Kabeer Hospital with CT-scan finding of a large right sided pleural effusion and pleural based mass, suggestive of malignancy, malignant mesothelioma Vs metastatic adenocarcinoma. Imaging-guided FNA smears showed tumor cells arranged in loose cohesive clusters and sheets as well as dispersed singly having round to oval pleomorphic nuclei, binucleation and multinucleation with abundant dense cytoplasm. Many cells showed cytoplasmic vacuolations and intracytoplasmic material. Many clusters of spindle shaped cells were also noted. ICC results showed that the tumor cells were positive for calretinin and epithelial membrane antigen (EMA), and Stain for carcinoembryonic antigen (CEA) was non-contributory. Cytological diagnosis was malignant mesothelioma.

**Conclusion:** Malignant mesothelioma can be difficult to diagnose and is nearly untreatable. Adequate tissue sampling is important to permit accurate diagnosis. Adenocarcinoma poses the most important diagnostic challenge. Immunocytochemical studies may be of help to arrive at a specific diagnosis, if there is any diagnostic dilemma.

**Key Words:** Intrathoracic; Malignant Mesothelioma; Fine needle aspiration



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**A Graftless Approach to Restore a Severely Resorbed Maxilla Complicated with a Failed Subperiosteal Implant using Zygoma and Root-form Implants: A Case Report**

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**CASE REPORT**

**Background:** As a result of severe bone resorption, subperiosteal implants have been used to provide support for prostheses in edentulous patients, however with unpredictable outcomes. The introduction of root form and Zygoma implants to treat edentulous severely resorbed maxillary arches have been reported in the literature with high success rates. This modality has been considered as an alternative option for extensive grafting procedures in the maxilla to compensate for the severe bone resorption negating implant placement. The aim of this report is to present a case of a failed subperiosteal maxillary implant managed with a fixed profile prosthesis supported by zygoma and root form implants using a graftless approach.

**Case summary:** A 51 year old female presented complaining of pain and prosthesis mobility related to her maxilla. Patients received treatment of subperiosteal maxillary implant and PFM prosthesis abroad 5 years ago. Medical history was considered to be non-contributory. Radiographic exam revealed a maxillary subperiosteal implant placed to support the prosthesis associated with severe bone resorption. After meticulous planning, a decision was made to provide the patient with a fixed profile prosthesis replacing the failed prosthesis supported by two Zygoma implants placed on each side and two axial root-form implants placed in the premaxilla using a graftless approach. An immediate load protocol was planned.

**Conclusions:** Authors in this case report present a patient with severe maxillary bone resorption as a result of a failed subperiosteal implant that was managed with a fixed profile prosthesis supported by zygoma and root-form implants, immediately loaded, using a graftless approach.

**Key Words:** Zygoma Implants; Subperiosteal Implants; Fixed prostheses;



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**Diabetes education program can help in diabetes stigma in young Kuwaiti girl with LADA**

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DDI

**CASE REPORT**

**Background:**

Twenty two year-old- single highly educated Kuwaiti girl, who was maintained on L-thyroxin since 2012 because of hypothyroidism. Her body mass index was 36 but no family history of diabetes. She was not adhered to SMBG or exercise. She was anxious to get diabetes so she started reading a lot about diabetes, and she decided to reduce her weight and followed with a dietitian who advised strict low calorie diet for 18 months with a reduction of her weight (BMI of 24). Later on, she was diagnosed as type 2 diabetes (HbA1c 10.3%) and started oral agents for 2 years without improvement. After 6 months Anti-GAD was 98.72 IU/ml supporting diagnosis of LADA, so her management program was shifted to insulin. She has stigma of being diabetic and did not want to inform any member rather than her family. She was trying to maintain her weight by low carbohydrates diet. I discussed with her the high prevalence of diabetes worldwide, and the importance of telling her co-workers of being diabetic as she might need their help if complication happen. Patient was encouraged to start doing enjoyable exercise and was convinced to monitor BG more frequently to control BG. After 3 education sessions, she was monitoring BG before and after meals, able to manage her diabetes with improved glucose readings and able to use correction doses of insulin and to manage diabetes during sick days.

**Conclusion:**

Proper diabetes education program is recommended to can help young diabetic patients with stigma.

**Key Words:** diabetes education; LADA; outcome



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**Role of education program in controlling new onset after transplantation in recent renal transplant body builder**

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DDI, OTC

**CASE REPORT**

**Background:**

New-onset diabetes mellitus is a common complication of solid organ transplantation and is likely to become even more common with the current epidemic of obesity in some countries. Many risk factors were identified as hepatitis c, immunosuppression and genetics. We aimed to present the role of diabetes education in improvement of NODAT in kidney transplant body builder.

**Case Summary**

Thirty six-year-old bodybuilder who was suffering idiopathic end stage kidney disease that was triggered with excessive exercise induced myoglobinuria. He underwent live unrelated renal transplant in Egypt which was complicated with NODAT within 1st 3 months which was partially controlled by oral agents and insulin. His c-peptide was acceptable and anti-GAD antibodies were negative as he was abusing insulin therapy in his exercise as a body builder. In view of his high HBA1C, he was subjected to our intensive education program –regarding diabetic diet, proper exercise, blood sugar monitoring, sick day management and pathophysiological role of his medications- and within 3 months his blood sugar became well controlled and his diabetes medications started to be minimized. Nowadays, he is enjoying stable graft function with HBA1c around 5.6.

**Conclusion:**

Proper diabetes education program is recommended to help renal transplant recipients with early NODAT in controlling their diabetic state. Success requires close evaluation as well as a multidisciplinary approach.

**Key Words:** NODAT; kidney transplant; education;



*Medicine*

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**Resistant acute T cell mediated rejection in pregnant renal transplant recipient:  
outcome of treated with antithymocyte globulin**

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OTC

**CASE REPORT**

**Background:**

To avoid graft rejection during pregnancy, frequent monitoring of serum drug levels is recommended. Pregnancy induces hyper-filtration in transplanted kidneys, as in native kidneys, therefore detection of rejection can be very difficult when monitoring by serum creatinine. If rejection is suspected, ultrasound guided graft biopsy can be done and once proven it can be treated with pulse steroid but data are scarcely regarding other agents. We aimed to present pregnant lady with resistant acute rejection with fruitful pregnancy outcome.

**Case Summary:**

Mrs. X. is a 28-year-old Kuwaiti lady who was suffering end stage kidney disease secondary to lupus nephropathy and underwent live renal transplantation on May 2013 after hemodialysis support for 1 year. She received thymogluobulin as an induction and was maintained on prednisolone, MMF and Tacrolimus. She has normal renal graft function without proteinuria and after counseling, she got pregnant on Feb, 2015. She was presented with acute graft dysfunction on Jun 2015 with S. creatinine 365 umol/L. Her abdominal ultrasound showed mild hydronephrosis and viable fetus. She received empirical pulse steroids with partial response and her graft biopsy showed acute T-cell mediated rejection and negative C4d. Intravenous immunoglobulins and mini pulse steroids were tried without response. After gynecological counseling and informed consent, she received 5 doses of thymoglobulin. She was dialysis dependent till premature vaginal labor was carried on with viable 2-kgm boy.

**Conclusion:**

Fruitful outcome of pregnancy might be expected with close monitoring, daily dialysis in kidney transplant lady with resistant rejection.

**Key Words:** pregnancy; renal transplant; rejection;



*Medicine*

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**Sirolimus induced cast nephropathy in a renal transplant recipient: A case report**

Nair M P, Gheith O, Halim MA, Said T, Tawab KA, Nampoory MRN.

OTC

**CASE REPORT**

**Background:** Rapamycin is an immunosuppressive drug used for maintenance therapy with designs to decrease steroid and/or calcineurin inhibitor exposure. Rapamicin related cast nephropathy has been reported in the setting of delayed graft function in the early postoperative period in renal transplant recipients and in animal models with protein overload nephropathies. We report an unusual case of rapamycin induced cast nephropathy in a patient, 45 months post renal transplant.

**Case summary:**

A 13 year old Kuwaiti girl with infantile polycystic kidney disease and stage V chronic kidney disease underwent a preemptive live renal transplant in October 2006. Her immunosuppression included induction with two doses of Basiliximab and maintenance with steroids, cyclosporine and rapamycin. She had good initial graft function and continued to have stable renal function with creatinine around 120umol/L and no proteinuria. In July 2010 she presented with graft dysfunction with a rise in serum creatinine to 200umol/L. After routine investigations a renal biopsy was performed which revealed cast nephropathy with extensive intratubular casts which were negative for light chain staining. Evaluation for myeloma including serum and urine electrophoresis, urine light chains and skeletal survey failed to demonstrate any abnormalities. Rapamycin induced cast nephropathy was considered as the cause of cast nephropathy and the drug was discontinued. Her renal function steadily improved over the next few weeks and a repeat renal biopsy performed six weeks after discontinuing rapamicin revealed a much improved cast nephropathy. Her serum creatinine reached baseline value of 115 umol/L and she continues to have excellent renal function till date.

**Conclusion:**

Rapamycin can induce tubular toxicity with a unique form of cast nephropathy and withdrawal of the offending drug leads to clinical and histological resolution.

**Key Words:** sirolimus; renal transplant; outcome;



*Medicine*

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**Unusual cause of proximal myopathy**

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**CASE REPORT**

**Background:** Muscle pain and joint pain can be related to rheumatologic, endocrine, metabolic or inflammatory conditions. Weakness is the most common and most reliable clinical indicator of myopathy.

**Case summary:** 16-year old male, admitted with pain in both knee joints which subsided, then the patient started to feel pain in both thigh muscles and hip joints more on the right side of 3 weeks duration to the extent he cannot walk in the last week and cannot stand from a sitting position. No morning stiffness and no oral ulcer. H/O upper respiratory tract infection and fever since one month and cured. O/E no cervical lymphadenopathy, normal throat, no skin rash. Chest, heart and abdominal examination are unremarkable. Neurological examination showed waddling gait, normal tone, normal deep tendon reflexes, bilateral plantar responses. There was tenderness on the right and left quadriceps muscles more on the right. The knee and ankle joints were not swollen with normal range of movement.

Laboratory investigations: the liver, renal and thyroid functions were normal. Anti-streptolysin O titre was negative. Procalcitonin = < 0.05 ng/ml, CBC: WBC = 10, Hb = 105 hypochromic microcytic, Plt = 366 ESR = 41 CRP = 4.4 mg/dl (normal 0 – 0.8), CPK = 461 IU/L (normal 38-255), vitamin D = 18.75 nmol/l (normal 51.5 – 117.5). Serum Iron = 6 umol/l (normal 11-32), ferritin = 105.1 ng/ml (normal 7-142), urine routine: no leucocytes, no erythrocytes or protein. Hepatitis B and C viruses were negative, brucella agglutination test: negative. The patient received vitamin D injection 600 000 units and the following day he started to walk normally with the disappearance of the muscle pain and the joint pain.

**Conclusion:** Vitamin D deficiency is a preventable disease which can be presented with or without symptoms. Screening of those individuals who are at risk for vitamin D deficiency, including osteoporosis, malabsorption syndrome, obese persons, other medical conditions.

**Key Words:** arthralgia; myopathy; vitamin D;



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**Infective endocarditis complicated by right ventricular thrombus caused methicillin resistant *Staphylococcus aureus***

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**CASE REPORT**

**Background:** Infective endocarditis (IE), an infection of the endocardial surface of the heart, is a significant cause of morbidity and mortality. IE is rare, accounting for 3-7 cases per 100 000, with *Staphylococcus aureus* as the leading pathogen. We present a case of Methicillin Resistant *S. aureus* (MRSA) IE in a neonate successfully treated with a combination of linezolid and rifampicin.

**Case summary**

An 18- day - old Kuwaiti girl, product of full term pregnancy with an unremarkable prenatal history, presented with fever, decreased activity and macular erythematous skin rash. She was irritable, hemodynamically unstable and had low urine output. Shortly after, she developed severe respiratory distress and was intubated, kept on mechanical ventilator and shifted to the intensive care unit. Full septic workup performed, and patient started on intravenous ceftriaxone and vancomycin. ECHO showed a right ventricular thrombus (6X6mm). CAT scan of abdomen revealed a second thrombus in the right and left portal vein branches. She was started on thrombolytic therapy. Blood cultures from central and peripheral lines and endotracheal secretion yielded MRSA. A diagnosis of septic shock secondary to MRSA IE was made. Antibiotic susceptibility test using Etest revealed MIC values of vancomycin (5 µg/mL), teicoplanin (1 µg/mL), linezolid (2µg/mL) and rifampicin (0.006 µg/mL). Her renal function deteriorated following vancomycin therapy, and repeated blood cultures over 10 days still grew MRSA. Treatment was switched to linezolid and rifampicin. Blood cultures became sterile eight days into new treatment. The patient recovered after five weeks of combination therapy, was extubated and discharged without surgical intervention. Patient was well on 4 month follow up and repeat ECHO showed complete resolution of the thrombus.

**Conclusion:** IE in a neonate caused by MRSA successfully treated with a combination of linezolid and rifampicin as an alternative salvage therapy.

**Key Words:** *Staphylococcus aureus*; MRSA ; Infective endocarditis ;



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**Anti-GBM disease - a rare cause of renal failure in children: Case report**

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**CASE REPORT**

Anti-GBM disease is a rare cause of acute renal failure and known to have bad prognosis regarding renal functions recovery and patient survival especially with delayed diagnosis and presentation with severe renal failure that require dialysis. We report a case of eleven years old child with acute renal failure secondary to anti-GBM disease and associated with ANCA positive vasculitis. He was presented with persistent vomiting and gross hematuria and hypertension. He was diagnosed based upon renal biopsy results along with serum anti-GBM Antibody level. He was treated with multiple plasmapheresis sessions, steroids and cyclophosphamide with good recovery of his kidney functions. In conclusion Anti GBM disease is extremely rare in children, however, it should be considered in the differential diagnosis of rapidly progressive glomerulonephritis, even in the absence of pulmonary involvement. p-ANCA-p may be a good prognostic marker and early treatment will favor satisfactory outcome.

**Key Words:** Good Pasture syndrome; systemic vasculitis; acute renal failure;



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**Fatal Rhino-Orbito-Cerebral Mucromycosis in child with renal transplant: case report**

Makkeyah YM\*<sup>1</sup>, Gheith O<sup>1</sup>, Al-Otaibi T<sup>1</sup>, Nampoory MRN<sup>1</sup>, Nair P<sup>1</sup>, Said T<sup>1</sup>, Hassan R<sup>1</sup>, Halim M<sup>1</sup>, Balaha M<sup>1</sup>, Abdeltawab K<sup>1</sup>, Abouatteya H<sup>1</sup>, Zakareya Z<sup>1</sup>, Yagan J<sup>1</sup>, Shetty S<sup>2</sup>, Abdullah A<sup>2</sup>, Abdullah B<sup>3</sup>, Al-Sheikh T<sup>4</sup>, Bastaki J<sup>5</sup>

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**CASE REPORT**

Invasive fungal infection in immunocompromised patient is a potential fatal complication for over immunosuppression. We present a case of a 12-year-old child who underwent cadaveric kidney transplant 5 years ago. He was maintained on steroid, mycophenolate and sirolimus after CMV infection 2 years post-transplant. He was presented with polyphagia, lethargy & elevated hepatic transaminases. CT brain revealed hypothalamic lesions favoring craniopharyngioma and MRI brain revealed deep thalamic space occupying lesion. The patient's father refused to proceed for any invasive measures. The patient was kept on intravenous steroid as a brain dehydrating measures. After few days, the patient developed left eye ptosis and left upper limb weakness, hydrocephalus was diagnosed by CT scan and VP shunt was inserted. Later on, the patient developed left cheek swelling and discoloration, for which functional endoscopic sinus surgery (FESS) was performed, and found to have extensive blackish debris in the sinuses which was surgically removed, and the diagnosis of rhino-orbito-cerebral mucromycosis (ROCM) was confirmed histopathologically. Despite, intensive use of liposomal amphotericin B in addition to posaconazole and frequent debridement the patient's condition deteriorated and the fungus continued to invade his skull, and the patient died after 2 weeks.

**Key Words:** Mucromycosis; Renal transplant; immunosuppression;



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**Cryptococcal meningitis in renal transplant recipient following use of T-cell depleting antibodies: case report**

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**CASE REPORT**

Fungal infection among renal transplant patients following the use of T-cell depleting antibodies is not uncommon complication. We are presenting a case of Mr. A., he underwent renal transplant in Egypt on December 2015 without induction. After few days post-transplant he was given 2 subsequent doses of anti-thymocyte globulin (ATG) for graft dysfunction. He traveled to Kuwait 2 weeks post-transplant and started follow up at our center and was discovered to have graft dysfunction. Allograft biopsy was performed and showed acute cellular rejection (ACR2b) that was managed by pulse steroid and ATG (additional 3 doses). His graft function gradually improved with optimization of his immunosuppressives. His target tacrolimus trough level was difficult to be achieved and required higher doses of tacrolimus than usual. Eight weeks later, he started to complain of severe headache and photophobia. Diagnosis of cryptococcal meningitis was established after detecting cryptococcal isolates in the cerebrospinal fluid (CSF). He was managed by liposomal amphotericin B and Fluconazole for 2 weeks as induction phase (due to the unavailability of flucytosine), followed by fluconazole daily as consolidation for 8 weeks, then to continued fluconazole as maintenance for 6-12 months. Initially, he had improvement of his symptoms and disappearance of the isolates from CSF with persistence of detection of antigen. However, the treatment was complicated by elevated CSF pressure (reaching 46 cmH<sub>2</sub>O), which required multiple CSF drainage procedures and acetazolamide administration. In conclusion, in the current era of organ trafficking and the use of T-cell depleting antibodies in kidney transplantation fungal infection should be always suspected, and timed initiation of antifungal therapy can prevent undesired outcomes.

**Key Words:** Renal Transplant; Cryptococcal meningitis; Thymoglobulin;



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**Solitary sternal metastasis from cancer bladder diagnosed by bone scan and SPECT/CT**

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**CASE REPORT**

**Background**

The axial skeleton is a common site of metastases, the sternum is rarely affected, especially by an isolated metastasis. 3 Two thirds of sternal masses are metastatic as they often come from breast, lung, kidney, thyroid gland cancer, while direct invasion of the sternum occurs mostly by lymphoma, bronchogenic carcinoma, breast cancer as well as pleural & mediastinal malignancies. 5

Case summary: A 65-years old male patient, presented with right sided neck swelling as he sought for medical advice. He has done neck ultrasound that revealed right sided sizable cervical & supra-clavicular lymphadenopathies. FNAC was done from those nodes as they appeared to be metastatic from a high grade bladder cancer. Bone scan was requested as part of metastatic work up which showed an isolated very high tracer uptake exclusively in the body of sternum with no other skeletal hot lesions. SPECT/CT was done for more evaluation as it showed predominantly sclerotic lesion in the entire body of sternum with few focal areas of destruction at its inner surface cortex.

**Key Words:** Sternal metastasis; Cancer bladder; bone scan;



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**Spinal cord compression due to brown tumor in spine**

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**CASE REPORT**

**Background:**

Spinal cord compression due to the brown tumor (BT) is extremely rare. In Literature, 42 cases of vertebral BT (27 cases in secondary and 15 cases in primary hyperparathyroidism) have been reported. Primary hyperparathyroidism was responsible for BT mostly in the past. Due to advances in treatment of the patients with end-stage renal disease receiving hemodialysis, secondary hyperparathyroidism is on the rise. MRI and CT features of BT in the suitable clinical situation mostly lead to the correct diagnosis. We present an unusual case of thoracic spine BT in patient with secondary hyperthyroidism presenting with acute backache and neurological involvement due to cord compression.

**Case summary:**

A 37 year-old ESRD female patient on regular hemodialysis presented to causality with intolerable back pain and walking difficulty. Neurological examination revealed loss of reflexes in the lower limbs and extensor planter reflex. Biochemical parameters suggested secondary hyperparathyroidism. MRI of the dorsal spine revealed cord compression by posterior extradural mass causing significant localized cord compression at T10 level. Complementary CT scan demonstrated the expansile lytic lesion with remodeling and thinning out of the related posterior arch. All features were suggestive of brown tumor. Surgical decompression of the tumor resulted in relief of cord compression and neurological symptoms. Histopathology proved the diagnosis of brown tumor.

**Conclusions:**

BT should be considered in differential diagnosis in a patient of secondary hyperparathyroidism in ESRD patients presenting with cord compression. Emergency MRI to detect the level of cord compression followed by prompt decompression surgery will improve the neurological deficits in such patients.

**Key Words:** Brown tumor; Cord compression; Computed tomography and MRI;



**Oncology**

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**Left Atrial Metastasis by Large-Cell Neuroendocrine Carcinoma of the Lung**

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**CASE REPORT**

**Background:** Cardiac metastasis is found in up to 14% of malignancies with distant metastasis. However, left atrial involvement is a very uncommon finding and has many complications, including showering of tumourous emboli, cardiac outflow obstruction, and mitral valve dysfunction.

**Case summary:** A 45-year-old, previously healthy, male presented to the emergency department with confusion, dizziness, and headache of 2 hours duration. He had dysarthria, pinpoint reactive pupils, right-sided weakness, and upward plantar response. Brain computed tomography (CT) scan showed no acute insult after which thrombolytic therapy was given. His Glasgow coma scale score was 8/15, so he was intubated and put on mechanical ventilation. He developed inferior myocardial infarction on the same day. Moreover, he developed acute kidney injury the day after. Follow-up head CT scan showed bilateral multiple ischaemic infarcts. Trans-oesophageal echocardiography demonstrated a left atrial mass with multiple thrombi attached to it. He developed hemoptysis after 17 days in the intensive care unit. Bronchoscopy revealed a white mass in the left upper lobe. Chest CT scan showed a left upper lobar neoplastic mass that was invading directly into the left atrium. Large-cell neuroendocrine carcinoma of the lung was evident on biopsy of the left upper lobar tumour.

**Conclusions:** Patients who are known to have a malignancy and present with cardiac or thromboembolic complications should be evaluated for cardiac metastasis; however, this could be their first presentation. Metastasis to the left atrium is very uncommon, and patients can present with thromboembolism to the systemic circulation as in atrial myxoma.

**Key Words:** cardiac metastasis; lung cancer; oncology;



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**Extra Skeletal Ewings Sarcoma in the abdominal wall: A Case report.**

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**CASE REPORT**

**Background:** Extraskeletal Ewing's Sarcoma (EES) is a rare soft tissue tumour that is morphologically indistinguishable from the more common Ewing's sarcoma of bone. The most frequent sites of occurrence are paravertebral spaces, lower extremities, head and neck, and pelvis. Other rare reported locations of EES include skin, chest wall and abdominal wall.

**Case summary:** A 14 year old male patient presented with a painless mass in the anterior abdominal wall. Ultrasonography and computed tomography showed a well defined rounded soft tissue lesion with lobulated margins in the subcutaneous tissue, fixed to the skin and indenting the upper part of right rectus abdominus muscle. An ultrasound guided fine needle aspiration cytology (FNAC) was performed which showed cellular smears comprising of predominantly dispersed round cells. These cells had scant to moderate vacuolated cytoplasm, coarse chromatin and conspicuous nucleoli. Occasional rosette formation was seen. On immunocytochemistry these cells stained positive for CD99 and negative for LCA, S-100, Desmin, CD56 and chromogranin. Based on cytomorphology and immunocytochemistry the diagnosis of round cell tumour favoring Ewing's sarcoma was given. A wide local excision of the anterior abdominal wall mass was done. Microscopic examination combined with immunostains showed a tumour consistent with extraskeletal Ewing sarcoma. Fluorescence in situ hybridization was positive for EWSR1 rearrangement, confirming the diagnosis of Ewings sarcoma.

**Conclusion:** EES has a low incidence rate and accounts for 1.1% of malignant soft tissue tumours. We report this case as only very few cases of EES of the abdominal wall have been reported in the literature. With the recent advances in the therapeutic protocols for EES, cytology has gained importance for an early and accurate diagnosis, thereby avoiding a more invasive open surgical biopsy.

**Key Words:** Extraskeletal; Ewings Sarcoma; Abdominal wall;



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**Bronchogenic adenocarcinoma versus squamous cell carcinoma: diagnostic delimitations in a case with multiple cytologic and biopsy specimen for histopathology**

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**CASE REPORT**

**Background:** There are examples of composite tumors consisting of sarcoma and carcinoma or different types of carcinomas and sarcomas, in which the biopsy may not always be representative of the entire lesion, thus leading to diagnostic difficulties. We report a case of a mass in the lung which was signed out as adenocarcinoma on 3 different cytologic specimens; however, it was signed out as a well differentiated squamous cell carcinoma on histopathology.

**Case summary:** A 55 year old male patient presented with a hilar mass in the lung along with pleural effusion. Cytological examination of the pleural fluid was reported as ‘positive for malignancy, the features favouring an adenocarcinoma’. A week later, a transbronchial biopsy was performed on the hilar mass along with bronchial brushings and bronchoalveolar lavage and both the cytology specimens were reported as ‘positive for malignancy, cytomorphology being consistent with adenocarcinoma’. However the biopsy was reported as ‘well differentiated squamous cell carcinoma of the lung’; with a comment that the possibility of adenosquamous carcinoma cannot be ruled out. The biopsy lesion also showed precursor lesions with atypical squamous and glandular epithelium. Whereas limited immunocytochemical studies favoured an adenocarcinoma in cytologic specimens, the immunohistochemical studies were in favour of a squamous cell carcinoma.

**Conclusion:** Differentiation of squamous cell carcinoma from adenocarcinoma of lung has currently assumed great importance due to availability of targeted therapy and its associated complications with specific subtypes of lung carcinoma. The above case illustrates that even with multiple specimens and ancillary studies the diagnostic delimitations cannot be always sorted out.

**Key Words:** bronchogenic; adenocarcinoma; cytology;



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**Discrepancy in lymphoglandular bodies content between histopathology and fine needle aspiration (FNA) smears: report of two non-Hodgkin lymphoma cases with immunocyto/histochemical studies.**

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**CASE REPORT**

**Background:** Lymphoglandular bodies (LGBs) are cytoplasmic fragments, which favors a diagnosis of malignant lymphoma rather than non-lymphomatous malignancies in fine needle aspiration (FNA) smears and H&E stained histologic specimens. In the present report, we illustrate 2 cases of diffuse large B-cell lymphomas in which there was marked variation in LGB content between FNA smears and paraffin sections of excised lymph node mass; we also suggest the possible reason behind this discrepancy.

**Case summary:** Case 1 was a 60-year-old man with generalized lymphadenopathy of 2 months duration. FNA smears from right axillary lymph node containing numerous CD20+ LGB in the **Background** was diagnosed as T-cell-rich B-cell lymphoma (TCRBCL). The histopathological diagnosis was a diffuse large B-cell lymphoma (DLBCL) with following immunohistochemical results: CD20+, CD79a+, BCl2+, BCl6+ and CyclinD1+. There were very few LGB in H&E stained sections, which were mostly CD20+, and to some extent CD79a+ and Bcl2+. Case2 was a 26-year-old man who presented with right cervical lymphadenopathy of one month duration. The FNA cytodiagnosis of cervical lymph node was a gray zone lymphoma with features intermediate between Burkitt lymphoma and large B-cell lymphoma. There were a few LGBs in smears. The histopathological diagnosis was DLBCL; the lymphoma cells were CD20+, CD79a+, BCl2 + and EBV+. There were numerous LGBs which were CD20+; however, CD79a+ and BCl2+ LGBs were relatively few. Conclusion: LGBs are present in both FNA smears and histopathological paraffin sections of B-cell NHL; the variation in their number between cytologic and histopathological samples may represent different states of formation and release. As per review of literature, cytoplasmic fragments resembling LGB are formed by action of anti-CD20 and other antibodies, and thus, their formation and release may have therapeutic implication.

**Key Words:** Non-Hodgkin lymphoma; lymphoglandular bodies; fine-needle aspiration cytology;



*Pediatrics*

**201**

**Re-challenging a child with Hemophilia B Who Developed Inhibitors to Prophylactic Therapy**

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**CASE REPORT**

**Background:** Inhibitors can develop in children with severe hemophilia B on prophylactic therapy and management can be challenging.

**Case summary:** We report a 3 year old boy who was diagnosed at 7 months with severe hemophilia B, and was started with twice weekly prophylactic factor IX replacement therapy, with minimal minor bleeds later on. After 32 treatment exposures, treatment was interrupted for 8 weeks as the family went for holiday, and then was resumed. Afterwards he developed multiple bleeding episodes and investigations revealed prolongation of coagulation profile as well as inhibitor level of 10.4 B.U. Prophylactic treatment with factor IX was held and was treated with recombinant factor VII, and later continued as prophylaxis. Inhibitors disappeared after a month of the start of treatment. The child developed multiple manageable bleeding episodes while on prophylaxis which lasted for nine months before factor IX was successfully and slowly reintroduced under cover of steroids and recombinant factor VII was withdrawn. Currently on prophylactic treatment with factor IX and doing well for more than one year.

**Conclusion:** Inhibitors management in children with severe hemophilia B is successful when at low levels.

**Key Words:** Haemophilia B; Haemophilia B, Deficiency; Factor IX;



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### **Abdominal Tuberculosis in a 5 Years Old Child**

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#### **CASE REPORT**

**Background:** Abdominal tuberculosis (TB) is a rare manifestation of TB in children. It is characterized by long standing abdominal symptoms that are usually confused with many conditions, including inflammatory bowel disease, malignancy, and other infectious diseases. It is thought to develop by hematogenous spread from a distant primary focus (usually the lung), or via lymphatic spread from tuberculous lymph nodes or solid organs. The diagnosis of abdominal TB is usually delayed due to lack of specific symptoms and pathognomonic findings.

#### **Case summary:**

A five years old child was admitted to Adan hospital pediatric department suffering from abdominal distention for a month and fever for two weeks. He had anorexia, weight loss and drowsiness. He did not receive BCG vaccine and there was a history of contact with his aunt with TB on treatment. On examination he was lethargic with digital clubbing, diminished air entry on his right chest plus hepatosplenomegaly and moderate ascites. Blood chemistry and urinary analyses were normal. The erythrocyte sedimentation rate was 112 mm/hr and C-reactive protein 62. Blood film showed thrombocytosis with no blast cells. Peritoneal fluid was negative for Culture and acid fast bacilli. Tuberculin skin test was done using the purified protein derivative (PPD) and was 18 mm (significantly positive) and interferon-gamma release assay was also positive. Chest X-ray showed right lower lobar consolidation with enlarged mediastinal lymph nodes. Computed tomography (CT) of the chest and abdomen showed mediastinal caseating lymph nodes, Right sided pleural effusion with severe ascites, hepatosplenomegaly and highly suspected peritonitis. Our patient was started on anti tuberculous treatment showing a good response on follow up.

#### **Conclusion:**

Abdominal TB should be suspected in any child presented with fever, weight loss, abdominal pain, and abnormal chest radiography. History of exposure to TB plus CT findings of abdominal TB support the diagnosis.

**Key Words:** tuberculosis; abdominal; children;



*Surgery*

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**Complete large bowel obstruction by a rare pelvic mass**

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**CASE REPORT**

**Background:** Retroperitoneal fibromatosis are extremely rare. We present a case of a big mass in the true pelvis causing complete large bowel obstruction in a 59 years male.

**Case summary:** A 59 years old male patient presented with 4 days history of colicky abdominal pain and distension, nausea, vomiting with absolute constipation. Plain abdominal X-ray showed greatly distended colon with air-fluid levels. Abdominal CT-scan revealed complete large bowel obstruction due to external compression and complete occlusion of the rectum by a big well circumscribed mass in the presacral region, occupying the whole true pelvis. The patient underwent emergency laparotomy and a left loop colostomy to relieve the obstruction. Subsequent MRI study revealed a well encapsulated deep supralelevator pelvic mass filling the presacral concavity of 13 x10 x 8 cm, causing complete collapse and obstruction of the rectum. The radiologic features suggested a GIST or mesenchymal tumour. During laparotomy, the mass was snugly filling the true pelvis and was not possible to deliver either from the perineum or the abdominal. After several attempts, it was delivered intact trans-abdominally by a using baby “delivery forceps”. The patient had an uneventful recovery and his colostomy was later closed. Histopathology showed benign retroperitoneal fibromatosis.

**Conclusion:** In the presence of complete bowel obstruction, the priority in management is first to vent the bowel and relieve the obstruction. Following that, the obstructed mass should be investigated and later excised. Many pathologies can present as solid presacral masses like lipoma/liposarcoma, leiomyoma/leiomyosarcoma, fibroma/fibrosarcoma, Desmoid tumors, ganglioneuromas, paragangliomas, and lymphoma. Preoperative diagnosis may be possible by fine needle aspiration cytology or core biopsy.

**Key Words:** Retroperitoneal fibromatosis; Abdominal CT-scan; mesenchymal



*Surgery*

**204**

**Migration of an Intra-gastric Balloon: a case report**

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**CASE REPORT**

**Background:** Intra-gastric balloons are a non-surgical treatment option for obesity.

**Case summary:** We report a case of a 28-year old Kuwaiti woman, with a history of BioEnterics intra-gastric balloon insertion two years ago, presented with vomiting and epigastric pain of one day duration. After thorough history taking and investigation she was diagnosed with bowel obstruction secondary to a BioEnterics intra-gastric balloon migration.

**Conclusions:** Most intra-gastric balloons, should be removed in 6 months, to reduce complications. In our case, lack of followup and removal of the intra-gastric balloon lead to the deflation and migration of it. This migration lead to the bowel obstruction. In conclusion, we report a rare complication of the BioEnterics intra-gastric balloon. We strongly advise the adherence to manufacturers' and doctors recommendations to avoid serious complications.

**Key Words:** BioEnterics; Intra-gastric balloon; bariatric;



*Surgery*

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**Acute appendicitis as rare cause of mechanical small bowel obstruction and managed with laparoscopic appendectomy: Case report**

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**CASE REPORT**

**Background:** Acute appendicitis is the most common surgical condition in emergency departments worldwide. It is also a rare cause of intestinal obstruction. The clinical feature of small bowel obstruction could obscure the clinical picture of appendicitis.

**Case report:**

A fifty-three-years-old male patient presented to our emergency department with generalized lower abdominal pain associated with nausea and vomiting 2 days of duration and constipation with duration of 4 days. There was no history of previous abdominal surgery. The physical examination showed minimal generalized tenderness in the lower abdomen more right side than left side with no rebound tenderness or guarding. There were exaggerated bowel sounds. The laboratory investigations were unremarkable. The erect abdominal X-ray showed multiple air-fluid levels in the small bowel with no free air under the diaphragm. Initially, the patient was admitted to the surgical care ward with the diagnosis of intestinal obstruction. CT of the abdomen was requested to confirm the diagnosis. The findings were dilated small bowel with an inflamed appendix. The patient underwent diagnostic laparoscopy. Intra-operative findings were thickened edematous appendix with the tip adherent to the terminal ileum. The appendix was removed via laparoscopy. The histopathology report confirmed suppurative acute appendicitis. The patient was discharged on second day postoperatively with no complications.

**Conclusion:**

Acute appendicitis is a rare cause of mechanical intestinal obstruction. The underlying pathology of intestinal obstruction caused by acute appendicitis is categorized by mechanical obstruction or adynamic (paralytic ileus). Acute appendicitis causing intestinal obstruction can be managed with explorative laparotomy or diagnostic laparoscopy where other etiologies could be excluded.

**Key Words:** Acute Appendicitis; intestinal obstruction; mechanical intestinal obstruction;



*Surgery*

**206**

**Three cases of Ruptured Hepatocellular Carcinoma (HCC) during 16 years period in the Liver Unit, Mubarak Al-Kabeer Hospital**

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**CASE REPORT**

**Background:** Spontaneous bleeding from HCC is rare. It presents as an acute intraperitoneal bleeding and shock. Delay in treatment leads to death.

**Case summary:** Between the years 2000-2016, the liver unit at Mubarak Al-Kabeer Hospital treated 3 cases of spontaneous rupture of a liver mass. They presented with shock and signs and symptoms of intraperitoneal bleeding. The first case was a 66 years old Kuwait patient with a tumour in segment VI and VII presented in April; 2004. Emergency resection was performed with an uneventful outcome. He remained under follow up, after 5 years he developed new HCC foci in the left liver lobe but no local recurrence at site of resection. He received chemotherapy and now after 12 years remains alive. The other two cases presented 2016 (Jan. and Nov.). They were 59 and 57 year old Egyptian gentlemen. Both had signs and symptoms of intraperitoneal bleeding confirmed by Emergency CT-Scan which showed tumour in segment VI of the liver (both patients) with active arterial bleeding. Emergency resection of the tumours with safety margin was performed. Both had uneventful postoperative recovery except for postoperative ascites which was initially managed by percutaneous drainage and later Aldactone and Lasix tablets. Both proved to be HepC-positive and were discharged from the hospital. They are alive at the time of writing this report under care of the hepatologist and the liver surgeon.

**Conclusion:** Ruptured HCC is rare, it presents with signs and symptoms of intraperitoneal bleeding. Emergency surgical resection is the treatment of choice. Arterial embolization is another choice in the absence of an experienced liver surgeon or in the presence of severe co-morbidities precluding emergency surgery.

**Key Words:** Hepatocellular carcinoma; Intraperitoneal Bleeding; Ruptured HCC;



*Surgery*

207

**Schistosomiasis as a cause of Acute Appendicitis in non-endemic areas**

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**CASE REPORT**

**Background:** Schistosomiasis also known as bilharzia, bilharziosis and snail fever, is a waterborne trematode, and is one of the most widespread parasitic diseases in the world. It occurs in well-defined endemic areas. There are about 200 million people infected worldwide, 85% of whom are concentrated in Africa, south of the Sahara. The most common organisms are *Schistosoma haematobium* and *S. mansoni*. Schistosomiasis causing and presenting as acute appendicitis are reported up to 6.3%, representing 28.6% of chronic appendicitis in endemic areas.

**Case summary:** A 29 years' old Egyptian Gentleman presented to our Emergency Department with diffused lower abdominal pain, nausea and vomiting of five days of duration. On examination, the patient was afebrile, conscious and oriented. There was rebound tenderness and guarding in the lower abdomen, more in the right iliac fossa area. Laboratory investigation showed an elevated white blood cells count. The patient was admitted to the surgical ward as a case of acute appendicitis. He underwent open appendectomy. The post-operative period was unremarkable. He was discharged from the hospital on the third post-operative day. Microscopic examination of paraffin embedded 4 µm-thick section of the appendix stained with hematoxylin and eosin (H &E) revealed transmural suppurative and granulomatous inflammatory infiltration consisting mainly of neutrophils, eosinophils, lymphocytes and plasma cells. Non-necrotizing granulomas with histiocytes, eosinophils are multinucleated langerhans giant cells were seen surrounding bilharziasis ova.

**Conclusion:**

Schistosomiasis could present and cause acute appendicitis in non-endemic areas. The incidence of appendicular schistosomiasis in non-endemic areas is because of traveling and labor migration. The diagnosis of appendicular schistosomiasis is purely histological. Treatment with appendectomy and anti-helminthic therapy are adequate to limit further extensive disease or chronic complications.

**Key Words:** Appendicular Schistosomiasis; acute appendicitis; , Schistosomiasis;



**208**

**Atraumatic splenic Rupture in adult patient with chickenpox**

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**CASE REPORT**

**Background:** Chickenpox is a commonly encountered infection in children. It is usually a self-limiting infection. However, in adult population, chickenpox is much less common and may lead to serious complications and death. Serious complications include severe skin infections, pneumonia, septicaemi and meningitis. In extremely rare occasions spontaneous splenic rupture may occur.

**Case summary:**

Thirty-seven years old healthy female came to Jahra hospital casualty with one-day history of sudden onset left sided abdominal pain and vomiting. Four days ago, she noticed eruption of similar rash as her five years daughter had two weeks ago. No history of trauma. On examination, the patient was alert with pale skin and lips. Vitals were Pulse 88, Bp 85/40 and temp 37.9 C. There was generalized papulovesicular rash over the body. There was left sided abdominal tenderness but no ecchymosis, rigidity or guarding. Investigations revealed Hb (10.3 gm/dL), WBC 8 (\*10<sup>9</sup>/L) and platelets 127 (\*10<sup>9</sup>/L). Fast scan found intraperitoneal fluid with no solid organ damage. The patient was resuscitated with crystalloid fluids and started on vasopressor (norepinephrine). After initial resuscitation and stabilization, CT scan abdomen with contrast done and showed anterior splenic wall rupture with hemoperitoneum. No Active contrast leakage detected. Afterward, the patient was shifted to the ICU for close observation and conservative management. However, on the third day, she had worsening abdominal pain, vital signs were unstable and hemoglobin dropping. Thus, she had urgent blood transfusions and shifted to the theatre. Intra-operatively, active bleeding was seen near the hilum of the spleen with splenectomy successfully followed.

**Conclusion:**

Adult chickenpox may impose life-threatening surgical emergency to patients' life. Splenic rupture after chickenpox infection is extremely rare. This complication may initially be missed. Thus, immediate attention, suspicion and, if necessary, surgical intervention is required.

**Key Words:** Splenic; rupture; chickenpox;



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## Introduction and Background

Kuwait Foundation for the Advancement of Sciences (KFAS) has a 40 year history of supporting the advancement of science and technology in Kuwait. In 1976, a visionary call by the late Amir of Kuwait, Sheikh Jaber Al- Ahmad Al-Jaber Al-Sabah, then Crown Prince and Prime Minister of Kuwait, was favourably embraced by the Chamber of Commerce and leaders of the economic sector in the country. It resulted in the establishment of the Kuwait Foundation for the Advancement of Sciences by an Amiri Decree on 12<sup>th</sup> December 1976; stating its mandate as a private non-profit organization devoted to supporting scientific research today. The Foundation's work is overseen by a Board of Directors, chaired by H.H. the Amir, Sheikh Sabah Al-Ahmad Al-Jaber Al-Sabah. It is financially supported by Kuwaiti private sector companies who have made generous contributions throughout the years, the contribution is currently set at 1% of their net annual profit.

One of the foremost goals of KFAS is to promote scientific development in the State of Kuwait by supporting scientific projects, the scientific community, and the country's scientific infrastructure.

While much has been accomplished by KFAS and related scientific institutions in Kuwait, there is much still to be sought after. The State of Kuwait has grown rapidly in terms of population and economy, the latter as a result of steadily increasing oil revenues. Today, the public sector accounts for more than 70% of the GDP and employs more than 85% of the national workforce. The consensus among the majority of stakeholders is that this growth is not structurally sustainable in the long run and that alternative national development strategies, based on building a complimentary, efficient and competitive private sector economy, are urgently needed.

Recognizing this need, H.H. the Amir of Kuwait, Sheikh Sabah Al-Ahmad Al Jaber Al-Sabah, commissioned in 2007 a "blue-ribbon panel"; the Kuwait Research Review Panel (KRRP), which was tasked to review the organization and the performance of Research and Development and make recommendations for restructuring and advancing Science, Technology and Innovation (STI) in Kuwait.

The panel presented a number of recommendations aimed at strengthening the overall STI system and culture throughout Kuwait, i.e. improving the capabilities and in some cases redirecting the activities of several STI institutions including KFAS, Kuwait University (KU), Kuwait Institute for Scientific Research (KISR), Public Authority for Applied Education and



Training (PAAET), National Technology Enterprises Company (NTEC), and the Kuwait Science Club (KSC).

Recognizing its unique role within the national STI system in Kuwait and responding to the recommendations in the panel's report, KFAS conducted an extensive assessment of its historical performance by benchmarking itself against similar institutions in the region and on a global level. KFAS consulted with representatives from its key stakeholders and worked closely with recognized leading international and domestic experts in Research and Development (R&D), policy, and STI evaluation to support this assessment. Based on the KRRP's recommendations and external assessment and findings in 2009, KFAS management embarked on developing a new strategic plan that would help meet the future needs of Kuwait's STI system. The preparatory steps were carefully designed.

The first step was the evaluation of current situation (status quo), followed by numerous steps like the determination of the basic requisites, identification of the targeted sectors, revision of vision and mission, defining the primary goals of the strategy and the expected results. An examination of the on-going and proposed programs and activities were then made.

Problem and solution trees for each program were carefully prepared and analysed, and the institutional requirements and arrangements to achieve the goals of the strategic plan were identified. The last step was to come up with a set of key performance indicators to measure the degree of success over the years at all levels.

## **KFAS Strategy (2012 – 2016)**

The strategy is a result of intensive consultation through numerous meetings lead by the management team at KFAS and its centers. It reflects the latest thinking on the STI needs of Kuwait, the proper role of KFAS and its centers in meeting part of those needs, and a more systematic approach to formulating and selecting programs for KFAS funding.

KFAS programs in the strategy are directed towards contributing tangibly to the development of an effective STI system and culture in Kuwait.

In addition to supporting R&D capacity and activities in priority fields, such as water, energy, the environment, and the development and the dissemination of STI culture, the plan puts further emphasis on STI capacity building of the private sector and strengthening of innovation system.

### **Vision:**



**“An Effective Science, Technology and Innovation System and Culture, to which KFAS has contributed, that underpins the sustainable development of the State of Kuwait”**

This vision statement reflects several important concepts based on the Foundation’s past experience and current philosophy. It is nationally-focused and draws on valuable resources to successfully position Kuwait to compete in a knowledge-based economy in the future.

**Mission:**

**Stimulate, support, and invest in initiatives and human resources that contribute to the building of a strong STI system and culture and fostering an enabling environment. The initiatives include improving public understanding of science; strengthening innovation and research capacity and enhancing the enabling cultural environment; supporting the gifted and talented; translating knowledge into innovation; and encouraging private technology capabilities.**

This mission statement defines KFAS’ role and ambitions driving the strategy outlined below. It primarily redefines KFAS as a funding institution. Given its modest annual resources, when compared to the overall STI funding by public institutions at the national level; KFAS will need to effectively leverage its targeted investments and efficiently execute its role as a catalyst to achieve its goals.

**Strategic Thrust Areas**

In developing the strategy, four thrust areas were identified. They address the development and human resource needs of the Science, Technology and Innovation System by leveraging the resources of KFAS and other stakeholders. Distribution of KFAS’ available resources was given great consideration to ensure maximum impact.

**Strategic Thrust 1 – Advocacy of Scientific Culture:**

**Contribute to the development of a strong advocacy for science including science education, support the gifted and talented, and to help advance scientific culture and the enabling environment in Kuwait**

**Strategic Thrust 2 – Scientific Research:**

**Enhance and integrate Research and Development capacity in and among Kuwaiti Scientific Institutions to address national development priorities**

**Strategic Thrust 3 – Innovation in Science and Technology:**



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**Support innovation and assist in developing the required links to commercialization within a framework of an integrated Science, Technology and Innovation (STI) system**

**Strategic Thrust 4 – Innovation and Enterprise:**

**Supporting the development of the Private Sector's scientific and technological capacities and participate in building a knowledge economy**



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